Blue Nevus of the Colorectal Mucosa
(POSTER No. 1)

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The blue nevus is a benign melanocytic proliferation that generally occurs on the skin. Infrequently, blue nevi are found on mucosal surfaces. The most common location for mucosal blue nevi is the oral mucosa, with reported cases in the sinonasal mucosa, genital tract, and other locations. To our knowledge, blue nevi of the anorectal mucosa have not been reported. We report the case of an asymptomatic 60-year-old woman who presented for a high-risk screening colonoscopy after being diagnosed with 2 tubular adenomas during the previous year. The study revealed a pigmented lesion in the colorectal region, adjacent to the anal transition zone. Histologic sections revealed otherwise unremarkable colonic and transitional mucosa with pigmented cells in the lamina propria. The pigmented cells consisted predominantly of long dendritic melanocytes with scant cytoplasm and abundant fine melanin granules. The nuclei were round to ovoid with a uniform chromatin pattern and inconspicuous nucleoli. No cytocytic atypia or mitotic figures were identified. Scattered melanophages were also present. All of the previously mentioned features are consistent with the diagnosis of blue nevus (Figure 1). As with any pigmented lesion, the possibility of melanoma should be considered. Although mucosal melanomas are rare, 24% arise in the anorectal region. These patients commonly present with pain, rectal bleeding, and a polypoid mass. There are also rare reports of malignant transformation of cutaneous blue nevi. Pigmented lesions, including blue nevi, of the anorectal region are rare and sampling is indicated to rule out malignancy.

Evaluation of Mast Cells and Their Association to Eosinophils in the Gastrointestinal Tract of the Pediatric Population
(POSTER No. 2)

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Context: Intestinal mast cells have been known to be related to food allergy and immediate hypersensitivity and are implicated as a th2-mediated regulator in eosinophilic gastritis. In this study, numbers of mast cells and eosinophils were investigated in biopsies from the upper gastrointestinal tract of children (n = 30; mean age, 14 years) with histopathologically confirmed eosinophilic enteropathy (n = 7), inflammatory bowel disease (n = 10), nonspecific chronic inflammation (n = 6), and no pathologic changes (n = 7).

Design: Paraffin sections of formalin-fixed samples from stomach and duodenum were stained using toluidine blue to highlight the mast cells. Quantitative evaluation of mast cells and eosinophils was performed counting their number per 10 high-power fields.

Results: Within the histopathologically defined groups, clear correlation between mast cell and eosinophil numbers was detected in patients with eosinophilic enteropathy (stomach, P = .02; duodenum, P = .03) and inflammatory bowel disease (stomach, P = .004; duodenum, P = .02). Overall, the mean number of mast cells was higher in stomach than in duodenum in all groups aside from their pathologic diagnosis (11.6 ± 1.3 stomach vs 8.1 ± 1.9 duodenum, mean ± standard error of the mean, P = .004).

Conclusions: Our results demonstrate the participation of mucosal mast cells in stomach and duodenum in disease process with more eosinophils and in inflammatory bowel disease. In these cases, increased numbers of mucosal mast cells along with eosinophils may indicate a role of mast cells as a regulatory mediator of visceral hypersensitivity due to either dietary antigens or inflammatory stimulator. Further studies will help in understanding the role and distribution of mast cells particularly in the gastrointestinal tract of children.

A Case of Systemic Mastocytosis and Ana Squamous Carcinoma
(POSTER No. 3)

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Accepted for publication June 11, 2009.
Reprints not available.
Acinar Cell Carcinoma With a Prominent Intraductal Growth Pattern
(Poster No. 4)

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Acinar cell carcinoma of the pancreas is rare, accounting for less than 1% of pancreatic cancer. Patients are typically between the fifth and seventh decade of life and show a 2:1 male predominance. Symptoms tend to be nonspecific, and approximately 50% of patients have metastasis at time of presentation. There have been recent case reports of acinar cell carcinoma showing both intraductal and/or papillary patterns of growth that could potentially be mistaken for intraductal neoplasia. The cases reported to date have presented as solitary nodules. We describe the first case of acinar cell carcinoma with intraductal and tubuloglandular growth diffusely involving the pancreas. The patient is a 31-year-old woman who had suffered from multiple attacks of pancreatitis beginning in March 2007 requiring several hospitalizations. Imaging studies showed chronic obstructive pancreatitis and diffuse duct dilatation. The patient underwent distal pancreatectomy and splenectomy. Macroscopic examination revealed acinar cell carcinoma with an intraductal growth pattern diffusely involving the pancreas (Figure 2) and extending to the proximal margin. Histologic findings in the completion pancreatectomy specimen revealed multiple foci of tumor with similar histologic findings to those seen in the distal pancreatectomy. Despite chemotherapy, the patient developed liver metastasis 6 months following her second surgery. We present a case of acinar cell carcinoma with a rare, diagnostically challenging histologic appearance. It is important to correlate clinical, histologic, and immunohistochemical findings to differentiate this lesion from a more benign intraductal neoplasm, notably intraductal papillary mucinous neoplasm.

Acute Fulminant Hepatic Necrosis in First 12 Hours of Amiodarone Administration
(Poster No. 5)

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Amiodarone is a commonly used antiarrhythmic with well-known common side effects with prolonged therapy. We present a case of fulminant hepatic necrosis proven by liver biopsy following intravenous administration of amiodarone within the first 12 hours of infusion. A 60-year-old man with a history of congestive heart failure, chronic renal insufficiency, and positive serology for hepatitis C antibody was admitted to the hospital with complaints of gradually increasing shortness of breath and dyspnea on exertion. The results of initial liver function tests showed values within the reference range. An electrocardiogram on admission revealed atrial flutter with a variable rate and the patient was administered intravenous amiodarone. Within the first 12 hours of infusion repeat liver function testing showed extremely high hepatic parameters: aspartate aminotransferase 3491 U/L, alanine aminotransferase 2029 U/L, and bilirubin 3.77 mg/dL. Infusion of amiodarone was stopped. The patient developed symptoms of acute abdomen and an exploratory laparotomy was performed with a concern of ischemic bowel. However, other than an acutely edematous liver, there was no evidence of acute pathology, and wedge liver biopsy was taken. Microscopic examination of the liver sample revealed acute hepatic necrosis with minimal steatosis and mild chronic inflammation. The findings were consistent with acute fulminant hepatic necrosis secondary to intravenous amiodarone administration. Electron microscopy showed hepatocytes with phospholipid inclusions with occasional foci suggestive of amiodarone-type inclusions, with areas of cholestasis and steatosis. Although acute amiodarone hepatic toxicity is rare, pathologists should be aware of this possibility and associated histologic findings.

Assessment for Residual Intestinal Metaplasia and Dysplasia in Postablative Barrett Esophagus Using Deeper Jumbo Biopsies
(Poster No. 6)

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Context: Recent therapeutic trends for Barrett esophagus (BE) with high-grade dysplasia (HGD) are evolving toward local ablative therapies. Such therapy resolves both the dysplastic area and metaplastic bed. However, this poses new challenges in follow-up as residual and recurrent metaplastic or dysplastic foci become endoscopically invisible, buried under regenerated neosquamous lining. This study documents our surveillance of postablative BE with deeper jumbo biopsies, ensuring recovery of buried glands.

Design: Review of our records from 2004 to 2008 identified 8 patients with BE who underwent ablation and follow-up surveillance with jumbo biopsies. The following characteristics were reviewed: indication, follow-up duration, presence of residual or recurrent metaplasia, dysplasia, and/or carcinoma.

Results: All 8 patients (6 men, 2 women; 62–83 years; mean age, 69 years) underwent ablation and HGD surveillance with jumbo biopsies. The following characteristics were reviewed: indication, follow-up duration, presence of residual or recurrent metaplasia, dysplasia, and/or carcinoma.

Morphoproteomics Defines the Cell Cycle Biology of Fibrolamellar Hepatocellular Carcinoma
(Poster No. 7)

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Medical School, Houston; and 4Department of Pathology, MD Anderson Cancer Center, Houston, Texas.

Context: Fibrolamellar hepatocellular carcinoma (FLHCC) has a better prognosis than conventional hepatocellular carcinoma. Nevertheless, it has a propensity to recur and has limited responsiveness to chemotherapy, and its biology has not been defined. This study sought to provide insight into the biology of FLHCC and, specifically, its cell cycle biology as it relates to its relatively indolent nature and chemoresponsiveness.

Design: Morphometric and protein analyses indicating cell cycle progression and inhibition were assessed in 7 cases of FLHCC. These included Ki-67 (G1, S, G2, and M phases), S-phase kinase-associated protein (Skp) 2, and mitotic index. Inhibitors of G1 to S phase included p27Kip1 and p16INK4a. The percentage of Ki-67–positive nuclei was determined by an automated cellular imaging system. Immunoreactivity of other markers was assessed for subcellular localization by bright-field microscopy.

Results: The mean percentage of Ki-67 nuclear positivity in neoplastic hepatocytes ranged from 1.0% to 29.7% in the 7 cases. Nuclear Skp2 immunoreactivity was negative and the mitotic index was very low (0–1 per 10 high-power fields). Correspondingly, all showed p16INK4a nuclear positivity. The adjacent nonneoplastic hepatocytes were negative for p16INK4a expression. Immunoreactivity for p27Kip1 was negative in 6 of 7 cases.

Conclusions: Morphoproteomic analysis reveals cell cycle arrest in the G1/S, phase in FLHCC, associated with overexpression of the cell cycle inhibitor p16INK4a in the nuclei of tumoral cells vis-à-vis the nonneoplastic hepatocytes. In conjunction with our previous demonstration of a constitutively activated NF-κB pathway in FLHCC, cell cycle arrest helps explain the biology of its indolent nature and also its relative chemoresistance.

A Rare Finding in a Patient With Crohn Disease

(Poster No. 8)

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Crohn disease can occur anywhere in the gastrointestinal tract, with ileum and colon being the most affected parts. Rarely, it can occur in other places like the upper digestive tract, peritoneum, or tonsils. We report a case of involvement of the palate tonsils, manifested as chronic tonsillitis. A 23-year-old African American woman with a history of Crohn disease that was managed with immunosuppressive therapy presented with an episode of tonsillitis. A year prior she had experienced a sore throat and a peritonsillar abscess, which was treated with incision, drainage, and antibiotics. Considering the recurrent nature of the tonsillitis, it was decided to proceed with a tonsillectomy. Microscopic examination of the tonsils revealed noncaseating epithelioid granulomas, along with reactive follicular hyperplasia, but no active inflammation. Acid-fast, Gomori methenamine silver, and Gram stains were performed to exclude tuberculosis infection, fungi, and bacteria, respectively, and were read as negative. Considering the patient’s history, the findings were consistent with involvement of tonsils by Crohn disease. This is a rare manifestation of Crohn disease. Repeated episodes of tonsillitis in such a clinical setting should always raise the suspicion for granulomatous tonsillitis to proceed with the best management for the patient.

Second Primary Colon Cancers Associated With First Primary Colon Cancers: A Population-Based Study

(Poster No. 9)

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Context: Patients diagnosed with a primary colorectal cancer are at increased risk of developing a second primary colorectal cancer. We studied second primary colon cancers in a population.

Design: Data were obtained from the Surveillance, Epidemiology, and End Results (SEER) registry for 1973 to 2005. Data included the first and second primary invasive colorectal carcinoma. According to SEER, a tumor is considered a second primary if diagnosed more than 2 months after the first primary. The SEER Multipoint Primary-Standardized Incidence Ratio tool was used to calculate the incidence of second primary cancers (observed/expected [O/E]).

Results: Of 574726 cases with a first primary cancer in the colorectum, 7137 developed a second primary in the colorectum (O/E, 1.45). Mean age at first primary was 67.9 years and for the second primary was 73.5 years. When stratified by race, African Americans had higher incidence of second primary tumors than whites (O/E, 1.83 vs 1.43), as well as a higher age-adjusted rate of first primary tumors. First and second primaries occurred at an earlier age in African Americans than in whites. All anatomical divisions of the colon showed a decrease in O/E with age. When analyzed by surface area, the mucosal surface of the colorectum was equally susceptible to second primary cancers in all anatomic divisions.

Conclusions: Persons with a first primary colorectal cancer are more susceptible to second primary cancers, specifically in the colon. First and second primary cancers in the colorectum show racial variations. No anatomic division of the colon appears to be more susceptible than any other to a second primary.

Cystic Lesions of the Pancreas: A Review of Cases in a 4-Year Period

(Poster No. 10)

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Context: Cystic lesions of the pancreas represent a significant proportion of pancreatic tumors. The characterization and classification of these has evolved in recent years and will continue changing according to the increasing number of biopsies and resections performed.

Design: Pancreatectomy specimens collected during a 4-year period that had diagnosis of pancreatic cyst(s) were reviewed. The demographic and pathologic features were recorded.

Results: Of 361 pancreatic lesions, 97 cysts corresponding to 95 patients were studied. Overall, 61% occurred in women and the mean age was 60 years. Among the 97 cysts, 8% were nonneoplastic (pseudocysts, enterogenous, congenital, oncocytic, and squamous cysts) and 92% were neoplastic (58% benign, 10% borderline, 24% malignant) (Table). Intraductal papillary mucinous neoplasm (IPMN) was the most common diagnosis (48%). Benign and borderline neoplasms were mostly seen in the head (42% and 70%, respectively), whereas nonneoplastic and malignant cysts were more common in the tail (37% and 42%, respectively). Excluding patients with solid and cystic pseudopapillary tumor (SCPT) who were significantly younger (23 years; range, 16–38 years; P = .001), patients with borderline and malignant neoplasms were older (mean, 65.6 and 65.1 years, respectively) than patients with nonneoplastic cysts and benign neoplasms (mean, 61.6 and 61.1 years, respectively). Malignant cysts were significantly larger than benign and borderline lesions (mean, 4.7 cm; P = .05).

Conclusions: In our series, most cystic lesions were neoplastic, mostly benign mucinous and malignant tumors. Location is not useful in differentiating malignant from nonneoplastic cysts. Malignancy in cystic neoplasms was associated with older age (when excluding SCPT and larger size).

Distribution of Pancreatic Cystic Lesions

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benign nonneoplastic (n = 8; 8.2%)</td>
<td>3 (3.0)</td>
</tr>
<tr>
<td>Pseudocyst</td>
<td>2 (2.0)</td>
</tr>
<tr>
<td>Enterogenous cyst</td>
<td>1 (1.0)</td>
</tr>
<tr>
<td>Congenital cyst</td>
<td>1 (1.0)</td>
</tr>
<tr>
<td>Oncocytic cyst</td>
<td>1 (1.0)</td>
</tr>
<tr>
<td>Squamous cyst</td>
<td>1 (1.0)</td>
</tr>
<tr>
<td>Benign neoplastic (n = 56; 57.7%)</td>
<td>31 (55.4%)</td>
</tr>
<tr>
<td>Mucinous cystadenoma</td>
<td>11 (19.6%)</td>
</tr>
<tr>
<td>Oligocystic serous cystadenoma</td>
<td>11 (19.6%)</td>
</tr>
<tr>
<td>Microcystic serous cystadenoma</td>
<td>11 (19.6%)</td>
</tr>
<tr>
<td>IPMN benign</td>
<td>22 (22.6%)</td>
</tr>
<tr>
<td>Cystic schwannoma</td>
<td>1 (1.0)</td>
</tr>
<tr>
<td>Borderline neoplasms (n = 10; 10.3%)</td>
<td>1 (1.0)</td>
</tr>
<tr>
<td>Borderline mucinous neoplasm</td>
<td>1 (1.0)</td>
</tr>
<tr>
<td>Borderline IPMN</td>
<td>9 (9.2)</td>
</tr>
<tr>
<td>Malignant neoplasms (n = 23; 23.7%)</td>
<td>1 (4.4)</td>
</tr>
<tr>
<td>IPMN malignant noninvasive</td>
<td>2 (8.7)</td>
</tr>
<tr>
<td>IPMN malignant invasive</td>
<td>1 (4.4)</td>
</tr>
<tr>
<td>Neuroendocrine cystic</td>
<td>1 (4.4)</td>
</tr>
<tr>
<td>SCPT</td>
<td>6 (6.1)</td>
</tr>
</tbody>
</table>
Discriminating Between Benign and Malignant Gastrointestinal Stromal Tumors Using CD10 Immunohistochemistry

(Poster No. 11)

Sharif Ali, MD (sali2@hfhs.org); Hwajeong Lee, MD; Adrian Ormsby, MD. Department of Pathology and Laboratory Medicine, Henry Ford Hospital, Detroit, Michigan.

Context: Prediction of gastrointestinal stromal tumor (GIST) behavior has been studied for many years. The problem is that proposed tumor risk indices do not correlate closely with the malignant potential. Researchers are developing targeted anti-CD10 monoclonal antibody therapy, which may impact the future management of CD10 immunoreactive tumors. Our study aims to assess the utility of CD10 immunostaining in GIST and whether it can be a useful adjuvant to define malignant tumor.

Design: Seventeen cases occurring since 2000 with at least 3 years of clinical follow-up were retrieved. Tumor locations included stomach (10 cases), small intestine (3), and colon (4). Two microarray blocks were created using a 3-mm needle, 2 cores from each case and the 5 metastatic sites.

Results: Cases were divided into benign (10 cases; no metastasis, local invasion, high-risk morphology, or recurrence) and malignant (7 cases; 6 exhibited distant metastases, 1 was locally invading the fallopian tube [Table]). Histologically only the malignant cases exhibited variable cytologic atypia, high mitotic rate (>6–10 per high-power fields), areas of necrosis, and large tumor size. All benign tumors showed no reactivity with CD10 (0 of 6). In contrast, 3 of 6 (50%) malignant metastatic cases were strongly CD10-positive (3+). One case (1 of 6) showed weak (1+) staining in the corresponding metastatic liver tissue. The locally invasive case was negative.

Conclusions: CD10 immunoreactivity may be helpful in identifying cases of GIST with metastatic potential (50% of cases are positive). Also CD10-positive cases may be of clinical interest with the new therapy.

### Summary of Cases

<table>
<thead>
<tr>
<th>Location</th>
<th>Size, cm</th>
<th>Metastatic Sites</th>
<th>c-Kit and CD34 Staining</th>
<th>CD10</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stomach (6 cases)</td>
<td>1.2–7.0</td>
<td>None</td>
<td>Both +</td>
<td>Negative</td>
</tr>
<tr>
<td>Small intestine (2 cases)</td>
<td>7.5 and 18</td>
<td>None</td>
<td>Both +</td>
<td>Negative</td>
</tr>
<tr>
<td>Colon (2 cases)</td>
<td>3.5 and 5</td>
<td>None</td>
<td>Both +</td>
<td>Negative</td>
</tr>
<tr>
<td>Stomach (2 cases)</td>
<td>4 and 12</td>
<td>Splenic, liver, and lymph node</td>
<td>Both +</td>
<td>Negative</td>
</tr>
<tr>
<td>Colon (2 cases)</td>
<td>11 and 27</td>
<td>Mesentery, uterus, small bowel nodules, and local invading fallopian tube</td>
<td>Both +</td>
<td>Negative</td>
</tr>
<tr>
<td>Small intestine</td>
<td>3.5</td>
<td>Omentum</td>
<td>Both +</td>
<td>+ (strong)</td>
</tr>
<tr>
<td>Stomach</td>
<td>15</td>
<td>Anterior abdominal wall</td>
<td>Both +</td>
<td>+ (strong)</td>
</tr>
<tr>
<td>Stomach</td>
<td>8.5</td>
<td>Liver, omentum, peritoneum</td>
<td>Both +</td>
<td>+3 (strong), (weakly staining +1 of metastatic liver site)</td>
</tr>
</tbody>
</table>

Angiosarcoma of the Sigmoid Colon Complicated by Disseminated Intravascular Coagulation: A Case Report and Literature Review

(Poster No. 12)

Christopher N. Thompson, MD (cthompson@swmail.sw.org); Debby Rampisela, MD; Ludvik R. Donner, MD, PhD. Department of Pathology, Scott and White Hospital, Temple, Texas.

We report a case of angiosarcoma of the sigmoid colon in an elderly man. Multiple metastases to the liver were identified during sigmoid colon resection. The tumor cells were strongly and diffusely positive for endothelial markers CD31, CD34, Fli-1, and von Willebrand factor. The patient later developed disseminated intravascular coagulation and expired 4 months after surgery. A review of the literature was performed. Eighteen cases of colonic angiosarcoma, including our case, are known. A slight majority (55%) of the patients were female. The patient ages ranged from 16 to 77 years with a mean age of 55 years. Most patients presented with rectal bleeding. Nine cases involved the sigmoid colon, 4 cases the cecum, 3 cases the rectum, 1 case the descending colon, and 1 case involved the cecum, transverse colon, and rectum. Six of 7 patients with colonic angiosarcoma less than 5 cm were alive at last follow-up (13–48 months postoperatively), whereas only 2 of 8 patients with tumor size greater than 5 cm were alive at last follow-up. Five of 6 patients younger than 50 years were alive at last follow-up, whereas 8 of 12 patients older than 50 years had rapid progression of their disease leading to death. The longest survival without evidence of recurrence was 3 years and occurred in a 16-year-old girl.

Positive Immunoreactivity of Thyroid Transcription Factor 1 in Colorectal Carcinoma: A Tissue Microarray Study of 104 Cases

(Poster No. 13)

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Context: Thyroid transcription factor 1 (TTF-1) is a member of homeo-domain transcription family expressed in epithelial cells of thyroid and lung. Although TTF-1 nuclear expression is generally considered a specific marker for lung and thyroid neoplasms, nuclear immunoreactivity was reported in other types of tumors. Few studies examined TTF-1 expression in colorectal carcinoma (CRC) with inconsistent results. The purpose of this study is to investigate TTF-1 expression in CRC.

Design: During metastatic adenocarcinoma workup for patients who have history of CRC, we identified 4 of 14 cases that had TTF-1 expression using a more specific antibody clone (clone 8G7G3/1). Therefore, we sought to retrospectively investigate the expression of TTF-1 in 90 CRC cases constructed in tissue microarray (TMA) blocks as well as whole tissue sections of the 4 primary tumors corresponding to the 4 positive metastases.

Results: In TMA studies, although all 90 cases had negative nuclear expression of TTF-1, cytoplasmic expression was seen in 1 case (1%). Four of 14 cases of metastatic CRC displayed positive nuclear staining of TTF-1. Three of the 4 corresponding primary carcinomas were also positive for TTF-1 in the whole tissue sections.

Conclusions: Our results suggest that during immunohistochemical workup, especially when the differential diagnosis includes lung and CRC, TTF-1 results should be interpreted with caution as a small subset of CRC expresses this marker. Positive TTF-1 nuclear expression in a metastatic carcinoma cannot rule out colorectal primary. Clinicopathologic correlation combined with a panel of immunohistochemical markers is essential to render correct diagnosis.

Correlation of Histologic and Endoscopic Scores for Evaluation of Crohn Disease Recurrence After Ileal Resection and Infliximab Therapy

(Poster No. 14)

Miguel F. Palma Diaz, MD; Miguel Regueiro, MD; Wolfgang Schraut, MD; Leonard Baidoo, MD; Marilyn Pesci, MD; Janet Harrison, MD; Kevin E. Kip, PhD, FAHA; Scott E. Plevy, MD; Antonia R. Sepulveda, MD PhD (asepu@mail.med.upenn.edu). Department of Pathology & Laboratory Medicine, University of Pennsylvania, Philadelphia; Department of Medicine, University of Pittsburgh, Pittsburgh, Pennsylvania; College of Nursing Research Center, University of South Florida, Tampa; and Department of Medicine, University of North Carolina, Chapel Hill.

Context: Evaluation of Crohn disease recurrence after ileal resection requires assessment of endoscopy with biopsy. Studies evaluating the cor-
relation between histologic and endoscopic grading for follow-up of disease activity and response to infliximab are lacking.

**Design:** Twenty-four adult Crohn disease patients who underwent ileocolonic resection were assigned to receive either intravenous infliximab 5 mg/kg or placebo for 1 year in a randomized 2-armed double-blind placebo-controlled trial. Follow-up endoscopy with neoterminal ileal biopsy at 1 year was performed in all patients. Endoscopic grading ranged from 0 to 4. Biopsy samples stained with hematoxylin-eosin were scored with a modified Crohn disease endoscopy grading system for epithelial damage, crypt architectural changes, mononuclear or neutrophils in the lamina propria or epithelium, erosion or ulcer, and granulomas and pyloric metaplasia.

**Results:** The overall Pearson correlation coefficient between histologic activity score and endoscopy grade was 0.73 (P < .001). Among individual histologic criteria, endoscopy grades correlated with neutrophils (R² = 0.74, P < .001), presence of erosion or ulcer (R² = 0.60, P = .004), epithelial damage (R² = 0.76, P < .001), and crypt architecture changes (R² = 0.61, P = .003). Agreement between endoscopy grades and histologic scores was significant for the presence of neutrophils, erosion or ulcer, and crypt architectural changes with χ₂ values of 0.82, 0.58, and 0.75, respectively.

**Conclusions:** Application of a well-defined histologic scoring system for evaluation of Crohn disease activity in the neoterminal ileum of patients randomized to receive placebo or infliximab therapy correlated well with endoscopic activity grades. The single most significant histopathologic change correlating with endoscopic evaluation of Crohn disease activity was the presence or absence of neutrophils in biopsy specimens.

**Primary Rectal Kaposi Sarcoma: Presentation of a Case in a 23-Year-Old Human Immunodeficiency Virus–Positive Male**

(Renuka Kulkarni, MBBS (rkulkarni@mcc.edu); Ningli Cheng, MD; Scott Drury, MD; Michelle Reid-Nicholson, MBBS. Department of Pathology, Medical College of Georgia, Augusta.

A 23-year-old homosexual male with HIV and full-blown acquired immunodeficiency syndrome presented with rectal bleeding and constipation. He was diagnosed with HIV at 14, used illicit drugs, was noncompliant with antiretroviral treatment, and had steadily decreasing CD4 counts with quadrupling viral titers in the previous months. Rectal examination revealed a mass involving 80% of the rectal circumference. Rectal biopsy revealed CD31- and CD34-positive spindled cells, slitlike vascular channels, extravasated red blood cells, and hyaline globules, consistent with Kaposi sarcoma (KS). Because of the absence of concomitant skin lesions, the tumor was classified as primary rectal KS. Abdominal and chest computerized tomography (CT) scan revealed a mass involving 80% of the rectal circumference. CT also showed a single 5-mm lung nodule and several subcentimeter liver nodules. The patient opted for local radiation. One month later he presented to the emergency room with acute dyspnea and chest pain. CT revealed multiple “too numerous to count” bilateral lung and liver lesions that had not been seen on the earlier CT scan. Chemotherapy was then initiated and the patient remains alive 2 months postdiagnosis. This case is notable because of the unusual primary location of KS in the rectum, the patient’s extremely young age, and his extensive local and metastatic disease. The tumor’s rapid progression was likely the result of the patient’s extremely young age, and his extensive local and metastatic disease.

**Medullary Carcinoma Also Occurs in the Ampulla of Vater: Report of a Case and Its Association With Microsatellite Instability**

(Haitham Nasser, MD (haitham.nasser@stjohn.org); Paul Kowalski, MD; N. Volkan Adsay, MD; 1Department of Pathology, St John Hospital and Medical Center, Detroit, Michigan; and 2Department of Pathology, Emory University Hospital, Atlanta, Georgia.

Medullary carcinoma of the gastrointestinal tract is a distinct tumor type that has been shown to have strong association with microsatellite instability and, in some cases, with hereditary nonpolyposis colorectal carcinoma. We report a 22-year-old woman with family history of colon cancer who presented with a tumor arising in the ampullary region causing obstructive jaundice. Grossly, it appeared solid, homogenous, and tan fleshy. Histologically, it revealed a poorly differentiated carcinoma with out any precursor lesions in the ampulla, duodenum, or pancreas. The tumor showed characteristic “medullary” morphology, displaying syn-
Context: Gastroesophageal reflux disease–associated Barrett esophagus (BE) and Helicobacter pylori–associated carditis with intestinal metaplasia (CIM) differ in their risk of malignancy and implications for patient management but are difficult to distinguish in biopsies of the gastroesophageal junction (GEJ). We used a polymerase chain reaction (PCR) assay for H pylori in a series of GEJ biopsies to establish the prevalence of H pylori in groups diagnosed as BE and CIM on the basis of established histologic criteria.

Design: Ninety patients with reflux-induced esophageal disease who underwent upper endoscopy and had GEJ biopsies were the study subjects. Biopsies with intestinal metaplasia (IM) were divided into BE and CIM using established histologic criteria. Helicobacter pylori status was determined by multiplex PCR performed on concomitant esophageal biopsies.

Results: Twenty-seven (30%) patients demonstrated IM at the GEJ. Of these, 13 of 27 (48%) were classified as BE (4 or more BE histologic features) and 14 of 27 (52%) as CIM (fewer than 4 BE histologic features). The incidence of H pylori infection determined by PCR is shown in the Table. The infection rate at the distal esophagus did not significantly differ among those with IM versus those without, or in relation to the number of BE features among those demonstrating IM.

Conclusions: As determined by PCR, there is a high prevalence of esophageal H pylori infection in patients with reflux-induced esophageal disease, irrespective of their histologic categorization. The role of PCR for H pylori in stratifying the risk of development of neoplasia in gastroesophageal reflux disease requires further study.

<table>
<thead>
<tr>
<th>Incidence of Helicobacter pylori (HP) Infection in Distal Esophagus Biopsies</th>
</tr>
</thead>
<tbody>
<tr>
<td>HP Positive.</td>
</tr>
<tr>
<td>No IM at GEJ</td>
</tr>
<tr>
<td>IM with 4 or more BE features</td>
</tr>
<tr>
<td>IM with fewer than 4 BE features (CIM)</td>
</tr>
</tbody>
</table>

The Role of JAK3/STAT3 Pathway in Colorectal Carcinogenesis and Colorectal Carcinoma Progression in Egyptian Patients: An Immunohistochemical Study

(Mohamed M. Shareef, MD, PhD; Maha M. Shamloul, MD, PhD; Asem A. Elfert, MD, PhD; Mohamed I. El-sawaf, MD, PhD; Hanan H. Soliman, MD, PhD; Departments of Pathology, Tropical Medicine, and Surgery, Faculty of Medicine, Tanta University, Tanta, Egypt.

Context: The JAK3/STAT3 pathway is involved in the genesis of several cancers and proposed as a molecular target in such malignancies as colorectal carcinoma (CRC) in Western patients. The unique clinicopathologic and molecular characteristics of CRC in Egyptian patients has stimulated us to investigate the JAK3/STAT3 pathway in CRC and its precursors in Egyptian patients.

Design: Tissue sections from 10 samples of normal colonic mucosa, 10 colonic adenomas, 15 cases with ulcerative colitis, and 45 cases with primary CRC were evaluated immunohistochemically for JAK3 and STAT3 expression and their phosphorylated forms (p-JAK3 and p-STAT3).

Results: Frequency of p-JAK3 expression was positively correlated with degree of dysplasia in adenomas (P = 0.01). The frequency of p-STAT3 expression increased significantly with the degree of dysplasia in cases with ulcerative colitis (P = 0.003). The frequency of expression of all the JAK3/STAT3 pathway proteins was significantly higher in CRC than in precancerous lesions (P = 0.01, 0.03, 0.04, and 0.02 for JAK3, p-JAK3, STAT3, and p-STAT3, respectively). In CRC cases, p-STAT3 expression showed significant correlation with grading (P = 0.02) and nodal status (P = 0.04). The expression of JAK3, p-JAK3, and STAT3 in CRC showed positive correlation with the pathologic stage (P = 0.046, 0.003, and 0.046, respectively) (Table).

Conclusions: Increased expression of the components of JAK3/STAT3 pathway with increasing grades of dysplasia and malignant transformation points to their potential role in colorectal carcinogenesis. The significant correlation of the JAK3/STAT3 pathway components with anaplasia and invasion suggests a definitive role in progression of CRC, making this pathway a promising target for therapy in Egyptian patients.
We report a unique synchronous presence of an adenocarcinoma, carcinoid tumor, and gastrointestinal stromal tumor in a near-total gastrectomy specimen from a 75-year-old woman with a long-standing history of pernicious anemia (Figure A). A pedunculated polypoid mass (6.2 × 4.1 × 3.0 cm) was identified in the middle third of the gastric body with the stalk base attaching to the lesser curvature. Microscopic examination of the polyp revealed a moderately differentiated adenocarcinoma invading the lamina propria of the stalk. In the polyp stalk, a carcinoid tumor of 0.6 cm in greatest dimension was noted consisting of monotonous cells with granular cytoplasm and centrally located nuclei, which are strongly and diffusely positive for both chromogranin and synaptophysin, confirming their neuroendocrine origin. Approximately 11.2 cm away, in the subserosa of the greater curvature, one 0.8-cm firm nodule with a tan cut surface was incidentally identified consisting of spindle cells with high nuclear to cytoplasmic ratio, displaying a fascicular or storiform growth pattern, and with a diffuse and strong positive immunoreaction for CD117. It was negative for smooth muscle actin and desmin, consistent with gastrointestinal stromal tumor. The adenocarcinoma and carcinoid components in our case were entirely separated into adjacent but distinct areas, with no transition or intermixing between these 2 different tumors, indicating a collision pattern. To the best of our knowledge, this is the first case of such a triple entity occurring simultaneously in the stomach.

\[\text{α-Methylacyl Coenzyme A Racemase Expression in Barrett Esophagus, Low- and High-Grade Dysplasia, and Carcinoma (Poster No. 22)}\]

Anupama Gupta, MD; Woojin Yu, MD; W. Remotti, MD; Helen Remotti, MD. Department of Pathology, Columbia University, New York, New York.

**Context:** Surveillance biopsies in patients with Barrett esophagus (BE) are done for morphologic detection of preneoplastic/neoplastic lesions to determine future therapy. It is often a challenge to histologically distinguish reactive changes from preneoplastic/neoplastic changes in this location. Some authors have proposed the use of α-methylacyl coenzyme A racemase (AMACR) in such situations. This study was performed to evaluate utility of AMACR expression in detecting low-grade dysplasia (LGD), high-grade dysplasia (HGD), and carcinoma (CA) in patients with BE.

**Design:** Twenty-three esophageal resection and 5 endoscopic mucosal resection (EMR) specimens with histologically confirmed dysplasia and/or CA in BE were obtained from the archival files of the Department of Pathology, Columbia University. Immunohistochemical staining for AMACR (Dako, rabbit anti-human P504S, Clone 13H4) was performed on all cases. The percentage of lesional cells staining with AMACR was noted and the intensity of staining was graded from 1+ (faint) to 4+ (strong). Less than 1% of lesional cells staining was considered negative. BE, LGD, HGD, and CA were evaluated and graded separately on each case.

**Results:** AMACR positivity was seen in 0% (0 of 19) of BE, 0% (0 of 6) of LGD, 20% (3 of 15) of HGD, and 32% (7 of 22) of CA. When positive, the percentage of immunoreactive lesional cells ranged from 1% to 40% in HGD and 5% to 80% in CA (Table).

**Conclusions:** AMACR staining when positive is helpful; however, negative staining does not rule out HGD or CA. Low sensitivity and variability in extent of staining limits the diagnostic utility of AMACR immunostaining for detection of preneoplastic/neoplastic lesions in BE, especially in small surveillance biopsies.

<table>
<thead>
<tr>
<th>AMACR Staining</th>
<th>Type of Lesion</th>
</tr>
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<tbody>
<tr>
<td>1+</td>
<td>% of Cells Staining</td>
</tr>
<tr>
<td>2+</td>
<td>Intensity of Staining</td>
</tr>
<tr>
<td>3+</td>
<td></td>
</tr>
<tr>
<td>4+</td>
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</tbody>
</table>

**Serrated Lesions of the Appendix: Morphologic and Immunohistochemical Appraisal (Poster No. 23)**

Jonathan Rock, MD (Jonathan.Rock@osumc.edu); Andrew M. Bellizzi, MD; William L. Marsh, MD; Wendy L. Frankel, MD. Department of Pathology, The Ohio State University Medical Center, Columbus.

**Context:** There is increasing interest in serrated colorectal polyps. Less is known regarding morphologically similar appendiceal lesions. We performed a morphologic and immunohistochemical assessment, appropriating diagnostic terminology and immunohistochemical markers shown useful in differentiating serrated polyps of the colon.

**Design:** Fifty-three noninvasive epithelial appendiceal lesions were classified hyperplastic polypl (HP), sessile serrated adenoma (SSA), mucinous cystadenoma (MCA), MCA with serrated features (MCAS), or conventional adenoma (CAD). Cytokeratin (CK) 20, Ki-67, MUC6, and β-catenin staining was performed. CK20 was normal (Nl, surface staining), expanded (Ex, beyond surface), expanded/irregular (Ex/I, expanded with random expression in deep crypts), diffuse, or no pattern. Ki-67 was Nl (base), Ex (beyond base), Ex/I (expanded with asymmetry), or no pattern. MUC6 was positive or negative. β-Catenin was Nl (membranous) or abnormal (nuclear/decreased membranous).

**Results:** Diagnoses of HP (6), SSA (12), indeterminate (3), MCA (14), MCAS (16), and CAD (2) were rendered. All HPs showed Ex CK20 expression and Ex (3/6) or NI (3/6) Ki-67 expression; MUC6 was positive in 1. Most SSAs and MCASs showed Ex or Ex/I CK20 expression, and Ex, Ex/I, or NI Ki-67 expression. MUC6 was positive in all SSAs and 8 of 16 MCASs. Flat architecture of MCAs made CK20 and Ki-67 difficult to interpret; MUC6 was negative. CAD expressed CK20 and Ki-67 Ex/I and MUC6 negative; abnormal β-catenin was noted in one.

**Conclusions:** Serrated appendiceal lesions can be categorized using terminology from the colon. MUC6 is most associated with SSA morphology. Similar patterns of MUC6, CK20, and Ki-67 reactivity in SSA and MCAS suggest a link between these lesions.

**A Rare Case of Gastric Leiomyosarcoma in a Young Hispanic Man (Poster No. 24)**

Nisrin Motiwala, MD (nmotiwala@mccg.edu); Jeffrey Lee, MD; Nidia Messias, MD; Suash Sharma, MD; Asha Nayak-Kapoor, MD. Departments of Pathology and Hematology, Medical College of Georgia, Augusta; and Department of Pathology, Charlie Norwood Veterans Affairs Medical Center, Medical College of Georgia, Augusta.

Leiomyosarcomas of the stomach are vanishingly rare neoplasms. In fact according to the World Health Organization, classification of tumors as true gastric leiomyomas and leiomyosarcomas are so infrequent that there are no significant data on demographic, clinical, or gross features. In the few cases found in literature, patients presented at older age (median age, 60 years). Most of the tumors historically designated as leiomyosarcomas are now classified as gastrointestinal stromal tumor (GIST), hence the older literature on gastric leiomyosarcomas largely pertain to malignant GISTs. This is a case of a 26-year-old Hispanic man who initially presented with gastrointestinal bleeding. Gross examination revealed a circumscribed, exophytic proximal gastric mass measuring 7.0 cm in maximum dimension, located within the submucosa, and arising from the muscularis mucosa. Microscopic findings were that of a highly cellular pleomorphic tumor with eosinophilic cytoplasm and abundant...
Mitoses (>20 per 10 high-power fields) with atypical mitotic figures. Immunohistochemistry was diffusely positive for desmin and smooth muscle actin and negative for CD117 and CD34. Molecular studies were negative for C-KIT and PDGFR-α mutations, thus confirming the diagnosis of leiomyosarcoma and not GIST, which is one of the most important differential diagnoses. GIST accounts for 2.2% of malignant gastric tumors in the SEER data. It is extremely important to differentiate leiomyosarcoma from GIST, as they require radically different courses of treatment. Most GISTs (80%) are responsive to the tyrosine kinase inhibitor imatinib, whereas leiomyosarcomas are treated with chemotherapy.

**Clostridium difficile Colitis Presenting as Collagenous Colitis on Biopsy**: Case Report and Review of Literature (Poster No. 25)

Saryn V. Stramecki Doucette, MD1; Alan Epstein, MD2. Departments of 1Pathology and 2Gastroenterology, Roger Williams Medical Center, Providence, Rhode Island.

Rare reports describe the development of collagenous colitis after prolonged Clostridium difficile infection. We describe C. difficile colitis presenting as collagenous colitis on initial biopsies. A 49-year-old man with a history of bipolar disorder and polysubstance abuse in remission presented with a 1-month history of acute-onset watery diarrhea. His medications included celecoxib, methadone, and quetiapine fumarate. Colonoscopy was suggestive of ulcerative colitis and showed pancolitis, scattered ulcerations, and a normal terminal ileum and rectum. Multiple biopsies throughout the colon and rectum showed increased subepithelial collagen deposition (trichrome verified), increased lamina propria chronic inflammation, and minimal neutrophilic infiltrates without crypt architectural abnormalities (Figure 5). Biopsy of the terminal ileum showed normal villous architecture and increased intraepithelial lymphocytes. Results of stool cultures, C. difficile assay, and celiac serologies were negative. Treatment with metronidazole and 5-aminosalicylic acid mildly improved the diarrhea. However, because of continuing diarrhea 4 weeks later, colonoscopy was repeated and showed pancolitis with rectal involvement and ulcerations. Subsequent biopsies showed less collagen deposition and more active inflammation. A repeated C. difficile toxin assay was positive and vancomycin was given with prompt resolution of diarrhea. Our case is an unusual histologic presentation of C. difficile colitis. We wish to emphasize that a histologic diagnosis of collagenous colitis with endoscopically evident colitis should prompt rigorous workup for a cause. Expansion of the subepithelial collagen layer may be a protective/reactive response to enterotoxins produced by C. difficile. Although the exact etiology of idiopathic collagenous colitis is unknown, luminal antigens/toxins are believed to be triggers.

**Granulomatous Inflammation Presenting as an Ileocecal Mass With Involvement of the Bladder and Abdominal Wall**: Case Report and Review of Literature (Poster No. 26)

Yuanming Zhang, MD1; Roberto Bergamaschi, MD, PhD2; Philip Kane, MD3; Meenakshi Singh, MD1. Departments of 1Pathology and 2Division of Colorectal Surgery, State University of New York at Stony Brook University Medical Center, Stony Brook.

A 34-year-old man presented with signs and symptoms of subacute intestinal obstruction. Radiology revealed a mass involving the ileocecum, bladder, and abdominal wall. There were no prior biopsies. The ileocecal resection specimen consisted of distorted adherent bowel with a 5.5 cm firm, tan-brown mass that extended transmurally. Frozen and permanent sections revealed transmural granulomatous inflammation and marked fibrinopurulent infiltrate extending to margins. The bladder “mass” and pelvic/abdominal wall “mass” also showed granulomatous inflammation. No neoplasm or features of Crohn disease were identified. Special stains did not show acid-fast bacilli. The granulomatous inflammation had abundant foreign body-type giant cells, some of which contained polarizable foreign material, including vegetable matter. This is consistent with a phlegmon, secondary to long-standing bowel perforation. This case emphasizes that the history may not be particularly helpful in arriving at an accurate diagnosis and the etiology may not be evident at frozen section analysis. Cultures should be submitted to rule out an infectious agent. Crohn disease and tuberculosis are certainly more common causes of granulomatous inflammation of the bowel and tuberculosis may produce a mass effect. Gross and histologic examination with adequate sampling, negative cultures, and special stains for organisms can help exclude this diagnosis. A careful look at the giant cells and a polarized light examination can help identify the foreign body nature of the granulomatous inflammation. Food material in the wall of the bowel serves as “foreign matter.” An exuberant response to it can lead to a mass effect and may mimic a neoplasm.

**Adenomyoma of the Jejunum: Report of an Unusual Case** (Poster No. 27)

Xin Qing, MD, PhD (dqingx@yahoo.com); Samuel French, MD. Department of Pathology, Harbor-UCLA Medical Center, Torrance, California.

Adenomyoma of the small intestine is an extremely rare benign nonneoplastic lesion. The rarity of this entity may be attributed to underreporting or nonrecognition by both surgeons and pathologists. Although it has been theorized that this lesion may represent incomplete heterotopic pancreas, its pathogenesis is not clearly understood. We describe an unusual case of adenomyoma in the jejunum with new pathologic and immunohistochemical features. The patient was a 61-year-old woman with cancer of the sigmoid colon and multiple liver cysts who underwent exploratory laparotomy and sigmoidectomy for cancer. At surgery, a polypoid lesion was incidentally found in the lower jejunum, which was resected. On histologic examination, the lesion was located in the submucosa and composed of an admixture of different types of glandular structures and surrounding smooth muscle. The large glands were lined by columnar/cuboidal epithelium with occasional goblet cells. The surrounding small glands were morphologically similar to, but immunohistochemically different from, Brunner glands. There were foci of connections between the epithelial component of the lesion and the overlying small intestine mucosal epithelium. No pancreatic or enteric epithelium was identified. The immunohistochemical features are summarized in the Table. In conclusion, these novel findings suggest that adenomyoma of the small intestine is a form of intestinal epithelial hamartoma with altered differentiation, instead of incomplete heterotopic pancreas. Increased vigilance in watching for this entity and a better pathologic knowledge of it may result in an increase in its diagnosis and spare the patient unnecessary surgery.

<table>
<thead>
<tr>
<th>Immunohistochemistry of Epithelial Cells in Adenomyoma, Small Intestine, and Brunner Gland</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adenomyoma (Large Gland)</td>
</tr>
<tr>
<td>CK7</td>
</tr>
<tr>
<td>CK20</td>
</tr>
<tr>
<td>CA 19-9</td>
</tr>
<tr>
<td>CDX-2</td>
</tr>
<tr>
<td>HMW</td>
</tr>
<tr>
<td>(34BE12)</td>
</tr>
<tr>
<td>AE1/AE3</td>
</tr>
</tbody>
</table>

**Mesenteric Fibromatosis Mimicking a Gastrointestinal Stromal Tumor: Case Report and Review of Literature** (Poster No. 28)

Kilik Kesha, MD (kilak.kesha@danhosp.org); Ramapriya Vidhun, MD. Department of Pathology, Danbury Hospital, Danbury, Connecticut.
The differentiation of mesenteric fibromatosis (MF) from a gastrointestinal stromal tumor (GIST) involves careful analysis of specific pathologic features. We report a case of MF initially diagnosed as a GIST. A 33-year-old man presented to the emergency department with a history of nausea and vomiting. Computed tomography (CT) scan showed a partial small bowel obstruction. On resection, a diagnosis of GIST was made. Two years later the patient was diagnosed by CT scan with a mass in the mesentery. The patient underwent a second resection for a well-circumscribed, tan white, firm nodule measuring 2.5 cm in greatest dimension. Histologic sections showed fascicles of monotonous spindle and stellate cells. These cells had abundant eosinophilic cytoplasm and bland basophilic nuclear features. The cells were strongly positive for c-Kit and were negative for CD34, actin, desmin, and S100. These morphologic and immunohistochemical features are consistent with a MF. On retrospective review of the slides from the prior resection 2 years prior, it was noted that the morphologic and immunohistochemical features are similar and consistent with a fibromatosis. Historically, even though there is an overlap in their immunohistochemical profiles, these entities can be distinguished primarily by their light microscopic and ultrastructural features. Recent studies have shown that β-catenin can be used to distinguish between these entities (90% positive staining in fibromatoses; 0% in GIST) (Table). We recommend that multiple diagnostic features including CD34 and β-catenin expression be used in conjunction with c-Kit to accurately differentiate GIST from MF.

### Key Features Between Mesenteric Fibromatosis and Gastrointestinal Stromal Tumor

<table>
<thead>
<tr>
<th>Feature</th>
<th>Mesenteric Fibromatosis</th>
<th>GIST</th>
</tr>
</thead>
<tbody>
<tr>
<td>Location</td>
<td>Mesentery or retroperitoneum</td>
<td>60%–70% stomach</td>
</tr>
<tr>
<td></td>
<td>May extend into small bowel</td>
<td>20%–30% small bowel</td>
</tr>
<tr>
<td>Immunohistologic staining</td>
<td>Positive C-kit/CD117 (0%–75%)</td>
<td>Positive C-kit/CD117 (95%)</td>
</tr>
<tr>
<td></td>
<td>Negative CD34</td>
<td>Positive CD34 (60%–70%)</td>
</tr>
<tr>
<td></td>
<td>Positive β-catenin (&gt;90%)</td>
<td>Negative β-catenin</td>
</tr>
<tr>
<td>Morphology</td>
<td>Uniform spindle cells</td>
<td>Spindle-shaped fascicles</td>
</tr>
<tr>
<td></td>
<td>Microscopic infiltrative borders</td>
<td>High mitotic count/atypia</td>
</tr>
<tr>
<td></td>
<td>Keloidlike collagen</td>
<td>Foci of necrosis</td>
</tr>
<tr>
<td></td>
<td>Small arteries/dilated vein</td>
<td>Hyalinized vessel walls</td>
</tr>
<tr>
<td>Clinical features</td>
<td>Associated with FAP, Gardner syndrome, and surgical trauma</td>
<td>Prognosis related to size and mitotic index</td>
</tr>
<tr>
<td></td>
<td>No metastatic potential</td>
<td>Low metastatic potential</td>
</tr>
<tr>
<td>Treatment</td>
<td>Resection</td>
<td>Resection with or without imatinib mesylate</td>
</tr>
</tbody>
</table>

Abbreviation: FAP, familial adenomatous polyposis.

### Russell Body Gastritis: A Unique Association With Gastric MALToma and Gastric Ulcer

*(Poster No. 29)*

Sreelakshmi Ravula, MD (sree.lrus@yahoo.com); Jacek Polski, MD. Department of Pathology, University of South Alabama Medical Center, Mobile.

Russell body gastritis is a recently recognized lesion of the gastric mucosa associated with inflammatory conditions like Helicobacter pylori, human immunodeficiency virus, and fungal infections. We report a case of Russell body gastritis in an elderly patient. A 90-year-old male patient was admitted to our emergency department with bleeding gastric ulcer. Partial gastrectomy was performed. There was thickening of the stomach wall and a transmural gastric ulcer with granular border and slight palisading of the rugae at the edge. Microscopic analysis revealed gastric ulcer, extranodal marginal zone lymphoma (MALToma) with perigastric lymph node involvement, and chronic active and Russell body gastritis (Figure 6). No H pylori microorganisms were identified on Wright stain.

Fungal yeast forms colonizing some glandular crypts were identified. Flow cytometry confirmed B-cell lymphoma, consistent with marginal zone lymphoma. The Russell bodies stained mostly for c light chains. Our case represents a unique combination of gastric ulcer, gastric MALToma, and Russell body gastritis in the same patient not associated with H pylori infection. Only about less than 10 cases of Russell body gastritis were reported in the literature so far, none with associated MALToma. To our knowledge, this is the first case of Russell body gastritis associated with gastric MALToma and gastric ulcer.

### Signet Ring Cell Change in Pseudomembranous Colitis: An Underrecognized Gastrointestinal Phenomenon?

*(Poster No. 30)*

Paula A. Navarro, MD (pnavarro@tuftsmedicalcenter.org); Tee U. Lang, MD; Jennifer J. O’Brien, MD, PhD; Joseph Alroy, DVM; Maria L. Garcia-Moliner, MD. Department of Pathology, Tufts Medical Center, Boston, Massachusetts.

**Context:** Signet ring cells are characteristic of high-grade adenocarcinoma, particularly of the gastrointestinal tract. Signet ring cell change (SCC) has also been reported in benign gastrointestinal processes, such as pseudomembranous colitis (PMC), tubular adenomas, and inflammatory bowel disease. The purpose of our study is to determine the incidence of SCC in cases of PMC because this phenomenon can represent a diagnostic challenge to pathologists, especially in small biopsies.

**Design:** Archival hematoxylin-eosin–stained slides from 21 resected colonic specimens with the diagnosis of PMC accessioned at Tufts Medical Center between 1994 and 2008 were reviewed for the presence of SCC and their pattern of distribution in the colon.

**Results:** Of these 21 cases, 18 (86%) demonstrated SCC within the crypts and within overlying exudate. Interestingly, one case showed signet ring–like cells in the lamina propria. The remaining 3 cases show the classic histologic changes of PMC but no SCC.

**Conclusions:** Our study highlights that SCC is a common finding in colon specimens with PMC. These changes may be focal and, hence, go unrecognized. When more extensive or, as in one of our cases, when the crypts are disrupted with spillage of signet ring–like cells into the lamina propria, there may be diagnostic confusion with adenocarcinoma. The mechanism for the production of this change is unclear but may represent a degenerative change. Pathologists must become aware that SCC is a phenomenon present in a variety of nonneoplastic gastrointestinal processes. Overdiagnosis of this pathologic change as signet ring cell adenocarcinoma may have serious consequences.

### Polarity Rather Than Count of Eosinophils Better Discriminates Between Eosinophilic and Reflux Esophagitis

*(Poster No. 31)*

Dawn Brady, MD (dawn.bradly@rush.edu); Ajay Patel, MD; Maria McIntire, MD; Deborah Giusto, MD; Shriram Jakate, MD. Department of Pathology, Rush University Medical Center, Chicago, Illinois.

**Context:** Eosinophilic esophagitis (EE) and gastroesophageal reflux disease (GERD) often have overlapping histologic features, particularly eosinophilia. Previous attempts to differentiate based on the quantity of intraepithelial eosinophils have shown conflicting results. We sought to...
Adipose tissue can be present in the colonic submucosa as nonspecific diffuse lipomatous infiltrate related to obesity, as multiple solitary lipomas, and as lipomatous polyposis. Although the first 2 are common, lipomatous polyposis is a rare condition first described in 1959 with only 3 well-documented cases reported in the English literature. We report a case of a 64-year-old male patient with no familial history of cancer who on endoscopy in 1998 was found to have hundreds of polyps throughout his colon, several of which were biopsied and found to be hyperplastic and adenomatous. The patient was then followed for 10 years during which he was diagnosed with large B-cell lymphoma and prostate cancer. The patient opted to have a subtotal colectomy in 2008 given his previous diagnosis of colonic adenomas. One hundred and twenty centimeters of his colon was removed and found to be diffusely involved by innumerable polyps ranging from 0.2 to 0.5 cm (Figure 8). A total of 50 polyps were microscopically examined, all of which were submucosal lipomas. No additional adenomatous polyps were identified. Our case is unique given the previous diagnoses of hyperplastic and adenomatous polyps.

### Collagenous Sprue: Case Study and Review of Literature

**Collagenous Sprue: Case Study and Review of Literature**  
(Poster No. 32)

Xiangrong Zhao, MD, PhD (xzhao@bhs1.org); Rebecca Johnson, MD. Department of Pathology and Laboratory Medicine, Berkshire Medical Center, Pittsfield, Massachusetts.

Collagenous sprue is a rare, severe malabsorptive disorder. There are only 49 cases reported to date in the English medical literature worldwide, including cases reported under different terms in early records, for example it was first described as idiopathic malabsorption in 1947. We report a case of collagenous sprue in a 69-year-old Caucasian woman who presented with severe watery diarrhea. She was seronegative for classic celiac disease. History, physical examination, and laboratory tests excluded other etiologies for diarrhea. Endoscopy revealed diffuse tiny white mucosal papillae, especially prominent in the distal jejunum. Biopsies showed severe small intestinal villous blunting with crypt atrophy, in contrast to the crypt hyperplasia seen in classic celiac disease. Characteristic for collagenous sprue, there were diffuse subepithelial collagen deposits (thicker than 12 µm) entrapping small capillaries and lamina propria cellular elements, as shown in hematoxylin-eosin (Figure 7) and trichrome (inset A) stains of biopsies from duodenum, jejunum, and ileum. There were aberrant intraepithelial and lamina propria CD3-positive (inset B), CD8-negative (inset C) T lymphocytes. Due to the rarity of collagenous sprue, its exact relationship with classic celiac disease and other refractory sprue-like intestinal disorders remains controversial. Our report represents the 50th collagenous sprue case described to date, with relevant literature reviewed and the histologic phenotype characterized with special and immunohistochemical stains.

### Intestinal Necrosis Following Oral Administration of Sodium Polystyrene Sulfonate (Kayexalate) in Sorbitol: A Report of 5 Cases

**Intestinal Necrosis Following Oral Administration of Sodium Polystyrene Sulfonate (Kayexalate) in Sorbitol: A Report of 5 Cases**  
(Poster No. 34)

Bryan L. Janssen, MD (B.L.Janssen@mhhs.org); Hema Khurana, MD; Ashok Balsaver, MD. Department of Pathology, The Methodist Hospital, Houston, Texas.

Sodium polystyrene sulfonate (Kayexalate) in sorbitol, a cation exchange resin used to treat hyperkalemia in uremic patients, has been well implicated in cases of intestinal necrosis. The incidence of this complication, however, is not known and the literature for many years has represented this as something of a rare entity. We report here a series of 5 patients at our institution in whom, during a 1-year period, Kayexalate crystals were observed on either endoscopic biopsy (n = 1) or surgical resection specimens (n = 4) demonstrating intestinal necrosis. All of the patients had documented oral administration of Kayexalate on admission to the hospital and clinical history of renal insufficiency with 3 of the 5 patients receiving hemodialysis. Currently, the available literature reports only sporadic cases and the largest case study (n = 15) spans a 10-year period. We propose that Kayexalate-induced intestinal damage continues to be an underrecognized and underreported entity. The purpose of this study is to further highlight the clinical and pathologic features of Kayexalate-associated intestinal necrosis.

### The Use of IgG4 to Distinguish Autoimmune Hepatitis From Hepatic Cholangiopathic Diseases

**The Use of IgG4 to Distinguish Autoimmune Hepatitis From Hepatic Cholangiopathic Diseases**  
(Poster No. 35)

Sherry M. Thompson, MD1 (smthompson78@hotmail.com); Pablo A. Bejarano, MD2; Monica T. Garcia, MD2; Chakradhar Reddy, MD. Departments of 1Pathology and 2Gastroenterology, University of Miami Hospital/Jackson Memorial Hospital, Miami, Florida.

Context: Primary biliary cirrhosis (PBC), primary sclerosing cholangitis (PSC), autoimmune hepatitis (AIH), and the so-called overlap syndrome (OS) share clinical and histologic characteristics, making them difficult to distinguish from each other. Immunoglobulin (Ig) G4–positive plasma cells detected by immunohistochemistry have been identified in patients...
with extrahepatic autoimmune disorders. However, the role of IgG4 in distinguishing various liver diseases has not been fully investigated.

**Results:** Portal triads with IgG4-positive plasma cells showed strong cytoplasmic staining. Of the 81 patients, 64 had the following clinical diagnoses: 24 AIH, 14 PBC, 10 OS, 3 PSC, 1 ductopenia of adulthood, 1 Alagille syndrome, and 11 non-AIH, noncholangiopathic (NANC) diagnoses. The mean ratio of IgG4-positive plasma cells to PTs was 1.80 for AIH, 0.22 for PBC, 0.19 for OS, 0.54 for PSC, and 0.39 for NANC. The P value of IgG4 separating AIH from PBC was 0.02, and was 0.02, 0.03, and 0.06 for OS, NANC, and PSC, respectively.

**Conclusions:** IgG4-positive cells are more predominant in AIH compared with other hepatic diseases with cholangiopathic features. Staining portal triads with IgG4 may elucidate disease processes among various hepatic entities. Although the numbers of PSC cases were few, PSC may also be driven by an association with IgG4.

**Histoplasma capsulatum Granulomatous Hepatitis: Clinicopathologic Analysis of 6 Cases** (Poster No. 36)

Kirttee Raparia, MD; Mary R. Schwartz, MD; Alberto G. Ayala, MD; Steven S. Shen, MD; Jae Y. Ro, MD. Department of Pathology, The Methodist Hospital, Houston, Texas.

**Context:** The increased rate of *Histoplasma capsulatum* infection is an emerging issue among immunocompromised individuals. The differential diagnosis of granulomatous inflammation in the liver is important for the accurate identification of the etiology and appropriate treatment.

**Design:** We report 6 cases of *H capsulatum* granulomatous hepatitis seen at our institution from 1999 to 2008, three of them in women.

**Results:** There were 4 women and 2 men ranging from 42 to 73 years. All patients had underlying diseases: 2 patients had rheumatoid arthritis, 1 had systemic lupus erythematosus, 1 patient was infected with human immunodeficiency virus, and 2 patients had received neoadjuvant chemotherapy for colon/rectal carcinoma. Two patients had rheumatoid arthritis that were on Remicade medication. A urine histoplasma antigen test was performed in 3 of the 6 cases and all showed moderate elevation (4.73–5.58 ng/mL). A liver biopsy showed multiple noncaseating granulomata mainly in the lobular parenchyma in 4 of 6 cases. Hyalized and calcified granulomata were present in the remaining 2 cases. The organisms were generally few in number and were both intracellular and extracellular. The organisms were highlighted by the GMS stain but were generally well visualized with periodic acid-Schiff with diastase-PAS.

**Conclusions:** Infection by *H capsulatum* should be considered in the differential diagnosis of granulomatous hepatitis in immunocompromised patients. Urine Histoplasma antigen assay, liver tissue culture, and identification of the fungal organisms by GMS stain can be critical in identifying this infection.

**IMPD, S100P, and XIAP Are Valuable Biomarkers in the Distinction Between Chronic Pancreatitis and Pancreatic Ductal Adenocarcinoma** (Poster No. 37)

Ognjen Kosarac, MD; Qihui Zhai, MD; Hidehiro Takei, MD; Dina R. Mody, MD; Mary R. Schwartz, MD; Philip T. Cagle, MD. Department of Pathology, The Methodist Hospital, Houston, Texas; and Department of Pathology, The Methodist Hospital and Weill Cornell Medical College, Houston, Texas.

**Context:** The differential of pancreatic ductal adenocarcinoma (PDA) versus chronic pancreatitis is a challenge in daily practice with significant therapeutic implications. The aim of our study was to evaluate a panel of biomarkers in this setting.

**Design:** Following a search of our database for PDA from 2003 to 2008, 14 pancreatic resections of PDA were selected with paired chronic pancreatitis from 10 men and 4 women with mean age of 66.2 years (range, 48–82 years). Immunostains for IMP3, S100P, and XIAP were performed on formalin-fixed, paraffin-embedded sections. Staining intensity (0, no staining; 1+, weak; 2+, moderate; 3+, strong) and proportion of positive cells (<10%, negative; 1+; 10%–25%; 2+, 25%–75%; 3+, >75%) were assessed. Positive stains were defined as >10% with at least 1+ intensity.

**Results:** The sensitivity of S100P, IMP3, and XIAP immunoreactivity for a diagnosis of PDA was 100.0%, 85.7%, and 100.0%, respectively. All 3 immunostains were negative in all tested nonneoplastic pancreatic tissue (Table). Eleven OS, or ductopenia PDA had positive staining for all 3 biomarkers. Additionally, S100P (85%) and IMP3 (75%) showed more consistent moderate to strong staining than XIAP in most cases.

**Immunohistochemical Results for S100P, IMP3, and XIAP in Pancreatic Ductal Adenocarcinoma (PDA) and Nonneoplastic Pancreatic Tissue (NPT)**

<table>
<thead>
<tr>
<th>Immunostain</th>
<th>PDA, No. (%)</th>
<th>NPT, No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>S100P</td>
<td>14/14 (100.0)</td>
<td>0/14 (0)</td>
</tr>
<tr>
<td>IMP3</td>
<td>12/14 (85.7)</td>
<td>0/14 (0)</td>
</tr>
<tr>
<td>XIAP</td>
<td>14/14 (100.0)</td>
<td>0/14 (0)</td>
</tr>
</tbody>
</table>

Nonneoplastic pancreatic tissue including chronic pancreatitis.

**Conclusions:** These novel biomarkers have high sensitivity and specificity in the diagnosis of PDA, especially when used as a panel. We recommend using at least 2 of these biomarkers in difficult cases of well-differentiated PDA versus chronic pancreatitis. Studies of additional cases are needed to confirm the sensitivity and specificity of these antibodies for this differential diagnosis.

**Spectrum of Hepatic Dysgenesis and Associated Disorders in Explanted Polycystic Liver Disease** (Poster No. 38)

Marlene Gallegos, MD; Shirram M. Jakate, MD. Department of Pathology, Rush University Medical Center, Chicago, Illinois.

**Context:** Polycystic liver disease (PCLD) belongs to a family of hepatic ductal plate malformations, with variable presence of other components of biliary dysgenesis and cysts in other organs. PCLD may be associated with intracranial aneurysms and inguinal hernias, and its complications include infected liver cysts and cholangiocarcinoma. Our study addresses the spectrum of dysgenesis and associated conditions in 4 PCLD patients.

**Results:** We searched our databases for PCLD and found 3 cases in 1200 OLIs between the years 1996 to 2008 (~0.3%) and 1 autopsy case. The patients' clinical data, imaging studies, and pathology findings were reviewed. A search was performed for cysts in other organs, associated clinical features, spectrum of biliary dysgenesis, and complications of PCLD.

**Results:** All 4 patients were women (34–61 years; mean, 48.5 years) and had hepatic PCLD and renal cysts. One third of the patients with OLT had concomitant renal transplant, while 1 of 4 had inguinal hernia. All 4 patients had enlarged livers (average, 2800 g) with diffuse cysts and admixed von Meyenberg complexes (VMCs). Three cases had infected cysts and the autopsy case had cholangiocarcinoma with VMCs, partial congenital hepatic fibrosis, extensive biliary dysplasia, and widespread metastasis.

**Conclusions:** PCLD is quite rare and is seen predominantly in middle-aged women. There is a strong concomitance of renal cysts, but cysts in other organs and other associated conditions are uncommon. PCLD is always admixed with VMCs and sometimes with congenital hepatic fibrosis. Explanted native livers frequently show infected cysts and when cholangiocarcinoma occurs, it tends to be multifocal with extensive biliary dysplasia and poor prognosis.

**Colorectal Mucinous Adenocarcinoma: A Clinicopathologic Study of 74 Cases** (Poster No. 39)

Xiaoxian Li, MD PhD; Jae Y. Ro, MD PhD; Mary R. Schwartz, MD; Steven S. Shen, MD, PhD. Department of Pathology, The Methodist Hospital, Houston, Texas.

**Context:** Mucinous adenocarcinoma is defined as adenocarcinoma with significant extracellular mucin. Some studies have suggested that colorectal mucinous adenocarcinoma has unique clinical presentations and is associated with more advanced stage and worse prognosis. However, these results have not been corroborated by others. In this study, we present our experience with 74 colorectal mucinous adenocarcinomas.

**Results:** Slides and reports of 521 invasive colorectal adenocarcinomas were reviewed. Only cases of conventional and mucinous adenocarcinomas (~50% extracellular mucin) were included. Carcinomas associated with inflammatory bowel disease or familial polyposis syndromes were...
excluded. Multiple clinicopathologic factors were studied to compare mucinous adenocarcinoma with conventional adenocarcinoma.

**Results:** Seventy-four of the 521 cases were identified as mucinous adenocarcinoma. The average tumor size of mucinous adenocarcinoma was slightly larger than that of conventional adenocarcinoma (4.9 vs 3.8 cm, P < .001). Mucinous adenocarcinoma tended to present at more locally advanced stage (81.1% vs 61.5%, P = .001) and was more likely to be associated with adenomatous change than conventional adenocarcinoma (45.9% vs 22.8%, P < .001). In addition, mucinous adenocarcinoma was more likely to be located in the right colon (48.6% vs 31.8%, P < .001). No significant difference was found in age, total number of lymph nodes recovered, incidence of positive lymph nodes, or grade distribution between mucinous and conventional adenocarcinoma.

**Conclusions:** Compared with conventional adenocarcinoma, mucinous adenocarcinoma tends to be in the right colon, present with larger tumor size and more advanced stage, and is more commonly associated with adenomatous changes. Our results suggest that mucinous adenocarcinoma has distinctive clinicopathologic features and may warrant special attention.

**Duodenal Inflammatory Pseudotumor: An Additional Extrapancreatic Manifestation of Autoimmune Pancreatitis**

*(Poster No. 40)*

Jane I. Bernstein, BA (janise@mail.med.upenn.edu); Rachel H. Gornley, BS; Emma E. Furth, MD. Department of Pathology and Laboratory Medicine, University of Pennsylvania School of Medicine, Philadelphia.

Autoimmune pancreatitis may present as a localized sclerosing process; however, it is now recognized that this inflammatory process is part of a wider, systemic IgG4-associated sclerosing disorder. We report the first case of a duodenal inflammatory pseudotumor with concomitant autoimmune pancreatitis, in which the duodenal polyp exhibits a similar lymphoplasmacytic sclerosing process with infiltration of IgG4-positive plasma cells as seen in the pancreas. A 71-year-old man presented to his clinician with a 30-lb weight loss during the preceding 6 months. A computed tomography scan of the abdomen revealed a 5.7-cm mass in the head of the pancreas. Because of the clinical suspicion of pancreatic carcinoma, the patient underwent a pancreaticoduodenectomy. Intraoperative gross examination revealed a diffusely firm, white pancreas and multiple white nodules studding the liver. Histologic evaluation of the pancreas revealed a dense lymphoplasmacytic infiltrate centered on the ducts and vessels. Biopsy of the hepatic nodules showed a similar process with a sclerosing cholangitic pattern. Examination of the resection specimen revealed a previously unsuspected duodenal polyp located approximately 5 cm distal to the ampulla (Figure 9). Microscopic examination of this lesion revealed a histologic pattern similar to that seen in both the liver and pancreas. Immunohistochemically, IgG4-positive plasma cells were identified infiltrating the duodenal lesion. This case adds to the broadening collection of extrapancreatic lesions associated with autoimmune pancreatitis. It also raises this entity as a potential consideration in the differential diagnosis of a small bowel polyp.

**The Demographics and Clinical Course of Carcinoid Tumors and Small Cell Carcinomas of the Gallbladder and Extrahepatic Bile Ducts**

*(Poster No. 41)*

Jorge Albores-Saavedra, MD (alboresjorge@yahoo.com); Arnold M. Schwartz, MD, PhD; Kristen Batich, BA; Nadera Ahmadzai, MBBS, MPH; Donald E. Henson, MD. 1Department of Pathology, Instituto Nacional de Ciencias Medicas y Nutricion, Mexico City, Mexico; 2Department of Pathology, George Washington University Medical Center, Washington, DC; 3Department of Cancer Prevention and Control, George Washington University Cancer Institute, Washington, DC; and 4Department of Epidemiology and Biostatistics, The George Washington University School of Public Health and Health Services, Washington, DC.

**Context:** Neuroendocrine tumors of the gallbladder (GB) and extrahepatic bile ducts (EHBD) include carcinoid tumors (CTs) and small cell carcinomas (SCCs). They are uncommon and little is known about their demographics and clinical course.

**Design:** Using data from National Cancer Institute’s SEER Program (1973-2005), demographics and 10-year survival rates of patients with CTs and SCCs of the GB and EHBD were analyzed. Logarithmic transformation plots of age-adjusted incidence were analyzed.

**Results:** Among GB cancers, 119 cases (0.85%) were CTs and 54 (0.39%) were SCCs. Within EHBD, 31 cases (0.34%) were CTs and 17 (0.19%) were SCCs. In the female to male ratios of CTs in the GB and EHBD were 2.7 and 1.6, respectively. The ratios for SCC in the GB and EHBD were 2.2 and 1.1, respectively. In the GB the mean age of diagnosis for CT and SCC was 64.5 and 67.5 years, respectively. In the EHBD the mean ages for CT and SCC were 58.2 and 68.4 years, respectively. The 10-year relative survival rate of CTs of the GB and EHBD were respectively 36% and 79%. For SCC, there were no survivors in either site at 10 years. Transformation plots identified CT and SCC as separate carcinogenic pathways.

**Conclusions:** CT and SCC of the extrahepatic biliary tree are more common in women, more frequent in the GB, and show differences in biologic behavior. Therefore, these tumors should be separately classified and not designated with the single generic term “neuroendocrine carcinoma” without further specification. CTs and SCCs, though possibly similar in histogenetic origin, have distinct carcinogenic pathways.

**Persistent Gastrocutaneous Fistulas: A Histopathologic Analysis of Antral and Oxyntic Mucosa Containing Fistulas in the Pediatric Population**

*(Poster No. 42)*

Michael A. Gilger, MD (gilger@bcm.edu); Todd M. Leleux, MD; Edwina J. Popek, DO. 1Department of Pathology, Baylor College of Medicine, Houston, Texas; and 2Department of Pathology, Texas Children’s Hospital, Houston, Texas.

**Context:** Percutaneous endoscopic gastrostomy (PEG) is the preferred method of tube feeding gastrostomy in pediatric patients. PEG placement typically occurs above the incisura angularis, along the greater curvature, corresponding to the region of oxyntic gland mucosa. It has been reported that up to 24% of cases develop a persistent gastrocutaneous fistula (GF) following PEG removal. Previous research links the duration of tube placement, fibrosis of tract, and obesity as significant factors involved in GF formation. Published data are lacking regarding the type of gastric mucosa found in this population.

**Design:** Archived hematoxylin-eosin–stained slides limited to GF cases following PEG placement from the past 5 years at a single large pediatric institution were retrieved for review. Two pathologists, blinded to the mucosa type, reviewed the slides. Mucosa type was placed into one of 3 categories: oxyntic mucosa only, antral mucosa only, or both types.

**Results:** A total of 161 cases were reviewed. Eighty-two cases (51%) showed only antral mucosa, 35 cases (22%) showed only oxyntic mucosa, and 43 cases (27%) showed features of both. Statistical analysis between groups revealed the P value for the source of variation between these groups to be P < .001.

**Conclusions:** A statistically significant difference was detected when comparing GF mucosa types among pediatric patients at our institution. Although the oxyntic mucosa region of the stomach is the typical target for PEG tube insertion, GF with antral gland mucosa was the predominant finding in our study. This finding raises questions regarding the pathophysiology of antral mucosa in GF formation.
Mucosal Hyperplasia of the Appendix: A Retrospective Review of 33 Cases

(Video No. 44)

Robert Willim, BS (robert.willim@hsc.stonybrook.edu); Sui Y. Zee, MD. Department of Pathology, Stony Brook University Hospital, Stony Brook, New York.

Context: The term “mucosal hyperplasia” (MH) of the appendix has been used to describe nondysplastic serrated hyperplastic lesions of the mucosa. Recent attempts were made to reclassify some of these lesions as sessile serrated adenoma (SSA). This entity is similar to its colonic counterpart. An association between MH and colorectal carcinoma has been reported. We evaluated cases with a diagnosis of MH to determine its incidence in our patient population, to see if this association exists in our cohort, and to better classify the epithelial proliferations.

Design: We identified 33 appendices diagnosed with MH. Each epithelial proliferation (EAP) was categorized as reactive hyperplasia (RH), hyperplastic polyp (HP), SSA, serrated adenoma (SA), or mixed lesion (ML).

Results: Of the 33 cases, 16 were reclassified SSA, 10 as HP, 4 as ML, 2 as RH, and 1 as SA. Four patients (3 HP and 1 SSA) had colorectal carcinoma (12%). Fifteen patients (8 SSA, 3 HP, 3 ML, and 1 RH) had gynecologic neoplasms (46%). Eleven patients (5 SSA, 3 HP, 1 RH, 1 ML, and 1 SA) presented with acute appendicitis (33%). Three patients (2 SSA and 1 HP) had other pathologies (9%) (Table).

Conclusions: Many of the AEPs were reclassified as SSAs. In our study, a lower percentage of patients had AEP with concurrent or past history of colorectal carcinoma. In addition, we identified an unexpectedly large number of patients with AEP and concurrent gynecologic neoplasia. Further studies are needed to determine the significance of this finding.

Epithelial Proliferations of the Appendix

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>No. (%)</th>
<th>Type of Mucosal Epithelial Proliferation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Colorectal carcinoma</td>
<td>4 (12)</td>
<td>3 HP, 1 SSA</td>
</tr>
<tr>
<td>Gynecologic neoplasm</td>
<td>15 (46)</td>
<td>1 RH, 3 HP, 8 SSA, 3 ML</td>
</tr>
<tr>
<td>Appendicitis</td>
<td>11 (33)</td>
<td>1 RH, 3 HP, 5 SSA, 1 SA, 1 ML</td>
</tr>
<tr>
<td>Other</td>
<td>3 (9)</td>
<td>1 HP, 2 SSA</td>
</tr>
</tbody>
</table>

Appendiceal Mucinous Neoplasms: The Mayo Clinic Experience

(Video No. 45)

David A. Barrett, MD (barrett.david@mayo.edu); Tsung-Teh Wu, MD, PhD; Thomas Smyrk, MD. Department of Laboratory Medicine and Pathology, Mayo Clinic, Rochester, Minnesota.

Context: There has been a debate in the literature as to the terminology applied to appendiceal neoplasms. This is especially true when peritoneal mucin is discovered. Various terms have been used to describe these neoplasms including low-grade appendiceal mucinous neoplasm (LAMN), mucinous neoplasm of low malignant potential, disseminated peritoneal adenocarcinomatosis, peritoneal mucinous carcinomatosis, and mucinous adenocarcinoma. In this study we looked at 52 patients with mucinous appendiceal neoplasms (not including typical mucinous cystadenomas) to determine the correlation between histologic features and clinical outcomes.

Design: The slides were then reviewed by 2 pathologists and divided into 5 groups: group 1, low-grade morphology with mucin/epithelium confined to periappendiceal tissue; group 2, high-grade morphology with mucin/epithelium confined to periappendiceal tissue; group 3, low-grade morphology with intraabdominal mucin (no epithelium); group 4, low-grade morphology with intraabdominal mucin and mucinous epithelium; and group 5, high-grade morphology with intraabdominal mucin and mucinous epithelium. These patients had a follow-up period ranging from 6 to 151 months (mean, 43.2 months).

Results: The outcomes by group are shown in the Table.

Conclusions: When there is mucin plus epithelium in the abdominal cavity, there is significant potential for recurrence and ultimately fatal course. Intraabdominal mucin without epithelium appears to have an intermediate prognosis. Although the numbers in this study are small, mucin and low-grade epithelium confined to the periappendiceal area had a uniformly benign outcome.

<table>
<thead>
<tr>
<th>Outcomes by Group</th>
<th>Group (n)</th>
<th>Mean Age, y</th>
<th>NEOD, %</th>
<th>AWD, %</th>
<th>DOD, %</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1 (11)</td>
<td>59</td>
<td>100</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>2 (2)</td>
<td>46</td>
<td>50</td>
<td>0</td>
<td>50</td>
</tr>
<tr>
<td></td>
<td>3 (6)</td>
<td>53.8</td>
<td>83.3</td>
<td>0</td>
<td>16.6</td>
</tr>
<tr>
<td></td>
<td>4 (26)</td>
<td>61.5</td>
<td>34.6</td>
<td>34.6</td>
<td>34.6</td>
</tr>
<tr>
<td></td>
<td>5 (7)</td>
<td>58.8</td>
<td>14.2</td>
<td>28.5</td>
<td>57.1</td>
</tr>
</tbody>
</table>

Abbreviations: AWD, alive with disease; DOD, died of disease; NEOD, no evidence of disease.

Cholecystic Cyst With Associated Signet Ring Cell Carcinoma of the Ampulla

(Video No. 46)

Timothy R. Pal, MD (t_pal@notes.cc.sunysb.edu); Kevin Watkins, MD; Sui Y. Zee, MD. Departments of Pathology and Surgery, Stony Brook University Medical Center, Stony Brook, New York.

A cholecystic cyst is a dilatation of the biliary system with a well-established increased risk of carcinoma. Although many of the neoplasms arise within the cyst wall, some have been described in the gallbladder, the pancreas, and nondilated portions of the biliary system. We report the first case of a type 1 cholecystic cyst with a concurrent ampullary signet ring cell carcinoma. A 48-year-old woman presented with right upper quadrant abdominal pain, elevated liver enzymes, and jaundice. Computerized tomography and magnetic resonance imaging revealed a type 1 choledochal cyst. The patient underwent excision of the cholecystic cyst. The gallbladder was received with an attached cystic duct and an 8-cm choledochal cyst. Following the excision of the cyst, palpation of the duodenal bulb revealed a 1.5-cm mass in the ampulla of Vater. The ampullary mass was excised and on frozen section showed signet ring cell carcinoma. A subsequent pancreatoduodenectomy was performed. Histologic examination of the cyst showed mucosal ulceration, marked acute and chronic inflammation, and fibrosis. The ampulla was infiltrated by signet ring cell carcinoma involving the duodenal wall (Figure 10). Lymphovascular invasion was present, but the lymph nodes were uninvolved. To our knowledge, this is the first case of ampullary signet ring cell carcinoma seen in conjunction with a type 1 choledochal cyst.
Signet Ring Cell Change of the Gallbladder: Case Report and Review of the Literature
(Poster No. 47)

Amanda C. Mullins, MD1 (amullins@utmem.edu); Thomas R. Callihan, MD2; Department of Pathology, University of Tennessee-Memphis; and 2Department of Pathology, Trumbull Laboratories, LLC, German-town, Tennessee.

The presence of signet ring cells in gastrointestinal specimens typically indicates malignancy. Rarely, however, they can be found in benign specimens as a degenerative feature. We present the case of a 65-year-old woman who presented with symptoms of cholecystitis. A cholecystectomy was performed and the gallbladder submitted to pathology. Gross examination revealed acute, subacute, and chronic cholecystitis. Microscopic examination of hematoxylin-eosin slides revealed signet ring cells on the mucosal surface and within gland lumens. Mitotic activity was not noted and nuclei were bland. The signet ring cells were positive for mucin, for cytokeratin (CK) 7, for E-cadherin, and variably for CK20. They were predominantly negative for carcinoembryonic antigen and for Ki-67. These features are consistent with benign signet ring cell carcinoma.

Is the Diagnosis of Flat Low-Grade Dysplasia on Surveillance Biopsy for Inflammatory Bowel Disease an Indication for Colectomy?: The Hartford Hospital Experience
(Poster No. 48)

Christopher J. Nero, MD (cjnero@gmail.com); Saverio Ligato, MD. Department of Pathology & Laboratory Medicine, Hartford Hospital, Hartford, Connecticut.

Context: In patients with chronic inflammatory bowel disease (IBD) the presence of flat high-grade dysplasia (fHGD) is a major risk factor for the development of adenocarcinoma and is an indication for colectomy. However, there is controversy regarding the appropriate management of patients with flat low-grade dysplasia (fLGD). The goal of our study is to assess whether the discovery of fLGD during surveillance colonoscopy for IBD may represent an indication for colectomy.

Design: We reviewed 175 colectomies performed for IBD at Hartford Hospital (1998–2009). All patients had at least one surveillance colonoscopy within a year prior to colectomy. All diagnoses of dysplasia were independently reviewed by the authors.

Results: Dysplasia was identified in 8 (6 fLGD and 2 fHGD) of 138 (5.8%) colectomies performed for IBD without a prior diagnosis of dysplasia. fHGD was identified in 2 of 7 (29%) colectomies with a prior diagnosis of flat dysplasia (within 4.5 months after surveillance biopsy) of fLGD. Invasive carcinoma was found in 6 of 13 (46%) colectomies with a prior diagnosis of fHGD.

Conclusions: In our IBD population, the failure rate of surveillance colonoscopy and biopsy to identify dysplasia was 5.8%. We confirmed that fHGD is associated with a high rate (46%) of adenocarcinoma. The finding of fLGD is associated with a significant risk (29%) of concurrent advanced dysplasia and in our opinion justifies serious consideration for a colectomy in these patients.

Preexisting Villous Adenoma in Colorectal Adenocarcinoma Predicts the Status of KRAS Mutation in Targeted Therapy
(Poster No. 49)

Hui Chen, MD, PhD (hui.chen@hitchcock.org); Joel A. Lefferts, PhD; Gregory J. Tsongalis, PhD; Arief A. Suriawinata, MD. Department of Pathology, Dartmouth-Hitchcock Medical Center, Lebanon, New Hampshire.

Context: Cetuximab is an epidermal growth factor receptor inhibitor effective in treating advanced colorectal adenocarcinoma (CA); however, patients with downstream mutations, such as KRAS mutants at codon 12 or 13, respond poorly to cetuximab. Although KRAS mutations had been previously reported to associate with isolated villous adenoma (16%–40%), the correlation of KRAS mutation with a histologic subset of CA is still lacking.

Design: Recent surgical resection specimens of CA (n = 27) were collected. The histopathologic features of these CAs were thoroughly reviewed, including tumor types, differentiation, and the presence of persistent preexisting adenomatous polyposis. DNA was extracted from formalin-fixed paraffin-embedded sections. These DNA samples were amplified by polymerase chain reaction, using a pair of primers flanking the first coding exon of the KRAS, sequenced using the CEQ 8000 platform (Beckman Coulter), and analyzed for mutations in codons 12 and 13.

Results: KRAS mutation was found in 4 cases (15%) and was undetectable in the remaining 23 cases (85%). The mutations (G12D, G12V, G12C, and G13D) were consistent with previously identified mutations that predict poor response to cetuximab treatment. Interestingly, all 4 cases with KRAS mutation had gross and histologic features of CA with a persistent preexisting adenomatous polyposis with villous architecture (4 of 4; 100%). None of the cases without KRAS mutation showed this feature. Furthermore, other histologic features are not associated with KRAS mutation.

Conclusions: KRAS mutations have a strong association with CA with persistent preexisting villous adenoma. Patients with a large villous adenoma that progresses to invasive adenocarcinoma may not respond to cetuximab.

An Unusual Coexistence and Impending Collision of a Malignant Gastrointestinal Stromal Tumor and Ovarian Cystadenocarcinomas
(Poster No. 50)

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Malignant gastrointestinal stromal tumors (GISTs) are infrequent neoplasms that are usually solitary and are rarely associated with other malignant neoplasms. We present a case of coexisting malignant GIST of the colon and bilateral ovarian cystadenocarcinomas. A 59-year-old woman was admitted for deep venous thrombosis, pulmonary embolism, upper gastrointestinal bleed, renal failure, and a large abdominal mass. Exploratory laparotomy revealed a large intraperitoneal mass wrapping around a segment of colon and bilateral ovarian masses. The ovarian tumors were cystadenocarcinomas with serous and endometrioid differentiation. There were multiple invasive metastatic tumor nodules in the pericolic fat that were composed of pure adenocarcinoma. The colon and peritoneum had multiple, necrotic, friable tumor nodules with transmural tumor extension into colonic mucosa. These tumors were composed of spindle cells with varying degree of nuclear pleomorphism, large areas of necrosis, and more than 50 mitoses per 50 high-power fields. Additionally, some of these spindle cell tumors were admixed with areas of metastatic ovarian cystadenocarcinoma. The spindle cell tumors stained positive for c-Kit, smooth muscle actin (SMA), desmin, and myoglobin and were negative for cytokeratin (CK) 20, CD34, S100, estrogen receptor, and progesterone receptor. These findings were consistent with the diagnosis of malignant GIST. Both the ovarian cystadenocarcinomas and the glands admixed with the GIST were positive for pancytokeratin, CK7, CAM 5.2, and progesterone receptor, and negative for desmin, c-Kit, SMA, and CK20. Neither carcinosarcoma nor sarcomatous differentiation was identified in the ovarian tumors. This case represents an unusual coexistence and impending collision of a malignant colonic GIST and ovarian cystadenocarcinomas.

Retropereitoneal Margin Involvement in Whipple Procedure Correlates with Tumor Characteristics
(Poster No. 51)

Hayma Al-Ghawi, MD1; Oluymomi Asojo, MD1 (asojooa@ucmail.uc.edu); Ninad Patil, MD; Laura James, MS2; Seyed Ahmad, MD1. Department of Pathology, University of California—San Francisco, San Francisco, California.

Context: Anatomical resection of the retropertioneal (RP) margin in Whipple procedure (WP) is considered a tracer of tumor characteristics. The aim of this study was to determine the probability of RP involvement in WP in terms of tumor characteristics and their clinical significance.

Design: The RP margin was examined in all resection specimens, and pathological features and clinical data were reviewed. The incidence of RP involvement was evaluated based on demographic data (age, sex, smoking status), clinical characteristics (operative time, complications), and pathological features (yp-stage, tumor characteristics). Statistical analysis included univariate and multivariate regression analysis.

Results: In total, 508 resections were reviewed. The incidence of RP involvement was 31.3%. The incidence of RP involvement was significantly higher in advanced yp-stage tumors (36.5% vs 25.4%, p < 0.05). Other factors, such as tumor characteristics (lymphovascular invasion, perineural invasion, distant metastasis), were not significantly associated with RP involvement.

Conclusions: The incidence of RP involvement in WP is significantly higher in advanced yp-stage tumors. Further studies are needed to determine the clinical significance of RP involvement.

Abstracts 1621
ments of Pathology and Laboratory Medicine, Surgery, and Surgery, Division of Surgical Oncology, University of Cincinnati, Cincinnati, Ohio.

Context: Pancreatic cancer is a malignant tumor with extremely poor prognosis. The status of the retroperitoneal resection margin (RPM) in Whipple procedure is an independent prognostic factor in predicting survival. We attempt to evaluate if certain tumor characteristics are associated with positive RPM.

Design: Seventy cases of Whipple procedure performed to treat pancreatic ductal adenocarcinoma were retrospectively studied to assess the relation between the status of RPM and certain tumor characteristics. These include site, size, histologic grade, lymph nodes metastasis, vascular and perineural microscopic involvement, and extrapancreatic extension.

Results: The pancreatic head was the primary site of tumor in 93% of cases. The RPM was microscopically involved by tumor in 14 cases and the superior mesenteric artery was grossly and microscopically involved in only one case. Positive RPM was significantly associated with tumor size ($t = -2.27, P = .02$). The mean size was 3.67 cm in the positive RPM group and 2.84 cm in the negative group. Microscopic vascular involvement correlated with positive RPM ($\chi^2 = 5.03, P = .02$) with 71.4% in the positive RPM group versus 33.9% in the negative group. Histologic grade, perineural involvement, lymph node metastasis, and extrapancreatic extension did not correlate with positive RPM ($P$ values .19, .47, .66, and .20, respectively).

Conclusions: The retroperitoneal margin in Whipple procedure tends to be involved by tumor in cases of larger tumor size and intratumoral vascular involvement.

Enteritis Cystica Profunda Mimicking Invasive Adenocarcinoma in an Adolescent Patient with Peutz-Jeghers Syndrome (Poster No. 52)

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Enteritis cystica profunda is a rare benign intestinal lesion associated with Peutz-Jeghers syndrome and other conditions, including Crohn disease. It mimics adenocarcinoma radiographically, grossly, and histologically and, thus, may pose a difficult diagnostic challenge. We describe the case of a 16-year-old boy with Peutz-Jeghers syndrome who presented with intussusception. At exploratory laparotomy, there was a hemorrhagic mass emerging from a previous staple line, and a segment of small bowel was resected. Extending through the intestinal wall and onto the serosal surface was a Peutz-Jeghers polyp whose stalk displayed features suggestive of infiltrative adenocarcinoma, including dilated glands, mucin pools, and transmural misplaced epithelium. However, the lack of significant cytologic atypia and desmoplasia, as well as the lamina propria associated with the misplaced epithelium, supported a benign lesion. Immunohistochemical staining for biomarkers that are frequently overexpressed in intestinal type gastric adenocarcinoma were negative for IMP3. AJCC stage grouping 3 and 4 cases showed statistically significant higher IMP3 expression compared with AJCC stage grouping 1 and 2 cases ($P < .05$). Intestinal type GAC showed statistically significant higher IMP3 expression compared with diffuse type GAC ($P < .007$).

Conclusions: IMP3 is overexpressed in a subset of GAC and is usually not overexpressed in NNGM. Higher level of IMP3 overexpression is seen in intestinal type GAC than in diffuse type GAC. Furthermore, higher level of IMP3 expression is associated with higher tumor stage.

Downregulation of Bax-Interacting Factor 1 in Pancreatic Ductal Adenocarcinoma (Poster No. 54)

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Context: Bax-interacting factor 1 (Bif-1) protein is a member of the spindle-associated protein family that plays a critical role in apoptosis, autophagy, and mitochondrial morphology. Loss of Bif-1 suppresses programmed cell death and promotes tumorigenesis. To date, the role of Bif-1 in pancreatic carcinogenesis has not been studied.

Design: To determine Bif-1 expression in human pancreatic ductal adenocarcinoma (PDA), we performed immunohistochemistry (IHC) using pancreatic cancer tissue microarrays containing 82 PDAs and 82 samples of nonneoplastic pancreatic ductal epithelium (NMP). Both PDA and NMP from the same patient were stained in 75 cases. In an additional 7 patients only PDA samples were stained. In an additional 7 patients only NMP samples were stained. Formalin-fixed, paraffin-embedded core sections on the tissue array were immunostained using the avidin–biotin–peroxidase method and the anti–Bif-1 murine monoclonal antibody (dilution 1:2500; Imgenex, San Diego, California). The Bif-1 stain was scored by 2 independent observers.

Results: High Bif-1 expression (IHC score 6–9) was identified in 55% (45 of 82) of PDAs but 73% (63 of 82) of NMPs. This difference was statistically significant ($P = .003$; RR 0.58). Low Bif-1 staining (IHC score 0–4) was present in 45% (37 of 82) of PDAs but in only 23% (19 of 82) of NMPs. This difference was also statistically significant.

Conclusions: We report the downregulation of Bif-1 during the transition from NMP to PDA in a subset of PDAs. This is a novel finding in agreement with the tumor suppressor function of Bif-1.

Activation of Mammalian Target of Rapamycin (mTOR) in Gastrointestinal Stromal Tumors (Poster No. 55)

James W. Horvath, MD* (james.horvath@osumc.edu); Wendy L. Frankel, MD; Andrew M. Bellizzi, MD; Mark Bloomston, MD; Obiajulu H. Iwenofu, MD. Departments of Pathology and Surgery, The Ohio State University Medical Center, Columbus.

Context: Recent data suggest that alteration of PI3K/Akt could be a crucial survival pathway in gastrointestinal stromal tumors (GISTs). Mammalian target of rapamycin (mTOR) is a serine/threonine kinase of the PI3/Akt signaling pathway known to play an important role in tumor growth as well as a therapeutic target in cancer therapy. Phosphorobsonostaining for p-S6rp expression. We examined the reactivity of 61 GISTs for p-S6 expression.

Design: Tissue microarrays were built from 61 cases of GIST. Cases included high-risk (n = 18), intermediate-risk (n = 22), and low-risk (n = 21) tumors. Outcome data on the response to imatinib, stratified into complete response, partial response, stable disease, and progressive disease, were available in 15 of 61 patients. Sections were stained with the
antibody to p-56K (cell signaling) and cytoplasmic staining was scored 0 to 3+.

Results: There is a high frequency of p-56K expression indicating activation of the mTOR pathway in GIST. Overall, 41 of 61 cases were positive (67%) and 20 were negative (33%). Twenty-four were 1+ (39%), 11 were 2+ (18%), and 6 were 3+ (10%). Approximately a third of the cases showed intermediate to high expression. Response to imatinib did not correlate with expression of p-56K.

Conclusions: Our data show a high frequency of activation of mTOR (a third with intermediate to high-level expression), suggesting a possible role for mTOR inhibitor therapy in addition to conventional treatment. Testing a large cohort in a prospective fashion is needed to confirm clinical utility.

Primary Small Bowel Mucosal Melanoma in a Patient With a Previous History of Lentigo Maligna
(Poster No. 56)

Laura L. Nelsen, MD (Laura.nelsen@usd.edu); Ali D. Jassim, MD, PhD. Department of Pathology, Sanford School of Medicine of the University of South Dakota, Sioux Falls.

Although metastatic melanoma can commonly spread to the small bowel, it rarely is the primary presentation and usually involves the serosa; mucosal melanoma is a rare condition. A completely excised lentigo maligna also rarely progresses to metastatic melanoma. Five years after complete excision of a lentigo maligna on his left temple, a 65-year-old man presented to our hospital for gastrointestinal bleeding. The patient had an exploratory laparoscopy with small bowel resection; along with a 20-cm segment of small bowel, an obstructive 4-cm mass was removed. The heavily pigmented tumor grossly appeared to mostly involve the mucosal surface with cut sections showing minimal extension into the muscularis propria of the small bowel. Microscopically, the tumor consisted of diffuse sheets of highly malignant cells with large nuclei, prominent nucleoli, and abundant cytoplasm with occasional pigmentation (Figure 11). Immunohistochemically, these cells were positive for S100, HMB-45, and MART-1 in clear cell sarcoma. Further cutaneous survey and evaluation failed to assess a primary site for the current melanoma. It is exceedingly rare to see metastatic disease with this magnitude from a lentigo maligna. It is also exceedingly rare to see a primary malignant melanoma of the small bowel. In light of the absent source of a distant primary melanoma, we believe this tumor represents a primary small bowel mucosal melanoma. The relationship between the patient's previous lentigo maligna and this lesion is undetermined.

Sclerosing Mesenteritis: Intraoperative Evaluation of a Clinically Nonspecific Mesenteric Lesion
(Poster No. 57)

Daniel S. Atherton, MD (daniel.atherton@bhsala.com). Department of Pathology, Baptist Health System, Birmingham, Alabama.

Sclerosing mesenteritis is a rare disease characterized by an expansive tumorlike process that can affect both the small and large bowel mesenteries. Because it is not a common diagnosis, along with the fact that its presentation can be identical to more common abdominal disorders, sclerosing mesenteritis is often only first suspected and diagnosed intraoperatively. A 48-year-old woman presented to our institution with progressive symptoms of upper abdominal pain along with sporadic episodes of nausea and occasional vomiting. Imaging showed a complex left upper quadrant lesion with both solid and cystic components. Exploratory laparotomy revealed a mesenteric mass with extensive adhesions affecting the small bowel. A portion of small bowel with the associated mesenteric mass was received for frozen section. Microscopically, the mass demonstrated elements of chronic inflammation, fat necrosis, and significant areas of characteristic fibrosis, indicating a diagnosis of sclerosing mesenteritis. The nomenclature attached to this process has been less rigid in the past, with terms such as “mesenteric lipodystrophy,” “mesenteric panniculitis,” and “sclerosing mesenteritis” commonly used in conjunction with the relative proportions of the 3 most common histopathologic findings: fat necrosis, chronic inflammation, and collagen deposition. It has been suggested that the term sclerosing mesenteritis is adequate when there is some degree of characteristic fibrosis. This case underscores the importance of recognizing sclerosing mesenteritis, especially in the absence of clinical suspicion, in the differential of nonspecific mesenteric lesions and supports the contention that sclerosing mesenteritis can be confidently diagnosed intraoperatively.

Improved Identification of Dysplastic Lesions in Barrett Esophagus
(Poster No. 58)

Tanya Varma, MD* (tvarma@lsuhsc.edu); Mary L. Nordberg, PhD; Department of Pathology, Louisiana Health Sciences Center, Shreveport; and Department of Pathology, Feist-Weiller Cancer Center, Shreveport, Louisiana.

Context: Detection of certain biomarkers is useful in identifying cases of Barrett esophagus with dysplasia (high and low grade). The detection of low-grade dysplasia remains the grey zone as many dysplastic lesions are missed using light microscopy alone.

Design: Eleven cases of Barrett esophagus with no dysplasia and low-grade dysplasia on light microscopy were studied. Immunohistochemistry (IHC) for Ki-67 (Ventana), and α-methylacyl coenzyme A racemase (AMACR) (Ventana), and α-methylacyl coenzyme A racemase (AMACR) (Abcam, Cambridge, Massachusetts) was performed. The cases that showed increased expression by IHC were analyzed by fluorescence in situ hybridization (FISH) for loss of heterozygosity (LOH) at 17p13.1 (p53 gene) and abnormal copy numbers of chromosome 17 using centromeric enumeration probe (CEP17).

Results: The IHC results for Ki-67, p53, AMACR, and FISH are shown in the Table.

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Ki-67</th>
<th>p53</th>
<th>AMACR</th>
<th>FISH</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Normal</td>
<td>Normal</td>
<td>Increased</td>
<td>Trisomy (+17), no LOH</td>
</tr>
<tr>
<td>2</td>
<td>Increased</td>
<td>Increased</td>
<td>Normal</td>
<td>Trisomy (+17), no LOH</td>
</tr>
<tr>
<td>3</td>
<td>Normal</td>
<td>Normal</td>
<td>Normal</td>
<td>Trisomy (+17), no LOH</td>
</tr>
<tr>
<td>4</td>
<td>Increased</td>
<td>Borderline</td>
<td>Normal</td>
<td>Trisomy (+17), no LOH</td>
</tr>
<tr>
<td>5</td>
<td>Normal</td>
<td>Normal</td>
<td>Normal</td>
<td>Trisomy (+17), no LOH</td>
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<td>Normal</td>
<td>Normal</td>
<td>Trisomy (+17), no LOH</td>
</tr>
<tr>
<td>11</td>
<td>Increased</td>
<td>Normal</td>
<td>Increased</td>
<td>Trisomy (+17), no LOH</td>
</tr>
</tbody>
</table>

Abbreviation: TBD, to be done.

Conclusions: The p53 stain by IHC was normal in all but 3 cases; therefore, its expression is usually unaltered in low-grade dysplasia. FISH analysis showed trisomy of chromosome 17 but no LOH at 17p13.1(p53). Ki-67 is a proliferation marker; hence its expression would be increased in regeneration or repair. The efficacy of this marker is not reliable in the 3 biopsies with increased expression but with significant inflammation. AMACR proved to be a sensitive marker to detect dysplasia. The cases with increased staining with AMACR also showed trisomy of chromosome. Studies to include more cases of high-grade dysplasia are ongoing.
Assessment and Follow-Up of Explanted Livers in α-1-Antitrypsin Deficiency (Homozygous ZZ Genotype) (Poster No. 59)

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Context: Accumulation of defective α-1-antitrypsin (A1AT) in the liver may lead to hepatocellular injury and cirrhosis. Diastase-resistant periodic acid-Schiff (d-PAS)–positive A1AT globules are currently the only significant pathologic finding. We aim to evaluate pathologic findings in explanted livers, coexistent pulmonary disease, and posttransplantation follow-up.

Design: From January 1993 to May 2008, patients with ZZ genotype (PiZZ) who underwent orthotopic liver transplantation were selected at our institution among 1200 transplants. The explants were reviewed for gross and histologic findings, concomitant liver disease, pulmonary disease, and follow-up hepatic graft biopsies.

Results: A total of 3 patients were identified (0.2% of total transplants). All patients were men (age range, 56–58 years). All showed mixed macro- and micronodular cirrhosis and abundant d-PAS–positive large hepatocytic cytoplasmic globules. One case showed incidental moderately increased iron. Another case showed severe macrovesicular steatosis consistent with incidental coexistent NASH. None had a dysplastic nodule or carcinoma. There was no symptomatic pulmonary dysfunction, but 2 cases exhibited mild emphysematous changes on computed tomography scan and chest x-ray. One case required retransplantation due to bile duct stenosis within 1 year. Follow-up biopsies of the grafts for up to 5 years showed no reaccumulation of d-PAS–positive globules.

Conclusions: A1AT deficiency is an extremely rare indication for hepatic transplantation. Other than d-PAS–positive globules and incidental findings such as NASH and increased iron, there are no distinctive pathologic findings. No A1AT globule reaccumulation is seen in the graft. There is no coexistent pulmonary dysfunction, and only mild pulmonary emphysema is detected radiologically.

Diagnostic Utility of von Hippel-Lindau Gene Product (pVHL) and S100P in Adenocarcinoma and Dysplasia of the Gallbladder (Poster No. 60)

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Context: Our recent study demonstrated the nearly perfect inverse correlation of upregulation of S100P and downregulation of von Hippel-Lindau gene product (pVHL) in pancreatic intraepithelial neoplasias and ductal adenocarcinoma of the pancreas (Lin et al. AJSP. 2008;32:78–91). This study investigates the utility of these 2 markers in the diagnosis of adenocarcinoma and dysplasia of the gallbladder.

Design: Immunohistochemical staining for S100P and pVHL were performed on 65 gallbladder specimens, including adenocarcinoma (n = 25), cases also containing glandular dysplasia, reactive glandular atypia (n = 20), and normal gallbladder (n = 20). The staining intensity was graded as weak or strong. The distribution was recorded as negative, +, ++, +++, and +++.

Results: The results demonstrated a nuclear and cytoplasmic staining pattern of S100P in 19 of 25 (76%) adenocarcinoma cases and 8 of 8 (100%) cases with glandular dysplasia. In contrast, none of the 40 reactive/normal gallbladder cases was positive for S100P. Glandular epithelia in all normal and reactive cases were diffusely (+++) positive for pVHL with membranous/cytoplasmic staining. In contrast, all cases of adenocarcinoma and dysplasia were negative for pVHL, whereas metaplasia showed normal ductal/glandular epithelia were positive for pVHL.

Conclusions: Our data suggest that (1) the findings of upregulation of S100P and downregulation of pVHL in adenocarcinoma and dysplasia are similar to that of pancreatic intraepithelial neoplasia and pancreatic ductal adenocarcinoma, indicating a possible role of these 2 proteins in tumorigenesis and (2) the expression patterns of pVHL and S100P can be used as a pair of diagnostic markers to confirm the diagnosis of adenocarcinoma and dysplasia of the gallbladder.
ative inflammation that was highlighted by nondescript deposits, col-
larized by a thick and dense eosinophilic cell reaction, and occasional gran-
ulomatata (Figure 12), resulting in intestinal loop fibrinoid adhesions and
small intestinal obstruction. Removal of the inflammatory debris and
lysis of intestinal loop adhesions were also well tolerated. Six-month and
1-year follow-up showed no recurrence of the problem. This nonfatal case
is probably the first demonstration of the histopathologic changes asso-
ciated with contaminated heparin used in pelvic and peritoneal washing
to lyse extensive, adherent postoperative blood clots.

Sessile Serrated Adenoma of the Colon:
A Case Report and Review of the Literature
(Poster No. 63)

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ogy, The George Washington University Medical Center, Washington, DC;
2Department of Hepatic and Gastrointestinal Pathology, Armed Forces
Institute of Pathology, Washington, DC; and 3Department of Pathology and
Laboratory Medicine Services, Veterans Affairs Medical Center, Washing-
ton, DC.

Sessile serrated adenomas, a recently described entity of colonic polyps,
display features similar to hyperplastic polyps such as serrated architec-
tural growth and lack of cytologic dysplasia. These lesions commonly
arise in the proximal colon and appendix. Grossly, they appear flat or
slightly raised in relation to the adjacent mucosa (Figure 13, A). Micro-
scopic features include basal dilation and flask-shaped crypts, often ori-
ted parallel to the muscularis mucosae conferring an inverted T- or L-
shaped appearance to the crypts. Cells lining the crypts are cytologically
bland and serration is often present at the surface and bases of the crypts
(Figure 13, B through D). Patients are generally treated and followed the
same as those with traditional adenomatous polyps.

Expression of Claudin-3 and Claudin-4 Proteins in
Gastric Adenocarcinoma
(Poster No. 65)

Reenu Malhotra, MD; Amanda L. Peterson, MD (amanda.l.peterson@uth.tmc.edu); Wei Li, MD. Department of Pathology, University of Texas Health Science Center-Houston.

Context: Claudins comprise a family of integral membrane proteins,
which play a major role in tight junction formation and function. Abber-
ations in expression of claudins have been described in various malig-
nancies and have been suggested as possible biomarkers and targets for
cancer therapy. The aim of this study was to determine the expression
pattern of claudin-3 and claudin-4 in gastric adenocarcinoma and correlate
expression with clinicopathologic variables.

Results: Claudin-3 and claudin-4 are strongly expressed in intesti-
nal and diffuse subtypes of gastric adenocarcinoma. The upregulation
of claudin expression suggests their possible role in gastric carcinogenesis,
their potential utility as diagnostic biomarkers, and possible targets for
innovative therapy.

A Pancreatic Mass in a 56-Year-Old Woman
(Poster No. 66)

Fernando Antelo, MD1 (antelo@ucla.edu); Bruce E. Stabile, MD; Sam-
uel W. French, MD1. Departments of Pathology and Surgery, Harbor-UCLA Medical Center, Torrance, California.

We report a rare case of pancreatic cystic tumor with features of both
serous microcystic adenoma and mucinous cystic adenoma. Our patient
is a 56-year-old woman evaluated for epigastric pain, with identification
of a 9-cm mass in the pancreas on computed tomography (arrow, Figure
14, A). A distal pancreatectomy with splenectomy was performed. On
gross examination, the pancreatic tumor was composed largely of innu-
merable small, thin-walled cysts, ranging in size from less than 0.1 to 0.5
cm (Figure 14, B). Light microscopy revealed that these cysts were lined by
a single layer of clear cuboidal epithelial cells (Figure 14, C); staining

Constitutive Activation of ERK Pathway Is Associated
With Tumoral Angiogenesis and Fibroplasia in
Fibrolamelar Hepatocellular Carcinoma
(Poster No. 64)

Sadhna Dhingra, MD1 (Sadhna.Dhingra@uth.tmc.edu); Wei Li, MD; Dongfeng Tan, MD; Robert E. Brown, MD.1 Department of Pathology and Laboratory Medicine, University of Texas Health Sciences Center—Medical School, Houston; and 2Department of Pathology, MD Anderson Cancer Center, Houston, Texas.

Context: Angiogenesis is the propelling force for tumor growth and
metastasis of hepatocellular carcinoma (HCC). Antiangiogenic agents like
bevacizumab and sorafenib, targeting vascular endothelial growth factor
(VEGF-A) and the VEGF receptor (VEGFR), respectively, have become a
standard of care for conventional HCC. Because VEGF-A and VEGFR
activate the extracellular signal-regulated kinase (ERK) 1/2 pathway, we
analyzed the relative expressions of VEGF-A and activated (phosphory-
lated) ERK 1/2 in this study of fibrolamelar hepatocellular carcinoma
(FLHCC).

Design: Morphometric analysis was performed in 7 cases of
FLHCC using immunostaining for the detection of VEGF-A and a phos-
phospecific probe at the putative sites of activation, threonine 202 tyrosine
204 on ERK 1/2. Subcellular immunolocalization of the chromogenic sig-
nal was determined and signal intensity was graded on a scale of 0 to
3+ by bright-field microscopy.

Results: All 7 of 7 cases showed strong (3+) P ERK 1/2 nuclear ex-
pression in endothelial cells of intratumoral vessels and fibroblasts. This
overexpression was most prominent at the interface of the neoplastic
hepatocytes and fibrosis. VEGF-A expression was observed in the cytoplas-
mic of neoplastic hepatocytes in all 7 cases. The signal intensity was variable
(1–3+). Focal cytoplasmic positivity for VEGF was also seen in fibroblasts.

Conclusions: ERK pathway is constitutively activated and contributes
to angiogenesis and fibroplasia in FLHCC. Targeting this pathway by
therapeutic agents may be beneficial in FLHCC. The molecular mecha-
nism(s) of ERK pathway in FLHCC progression merits further investiga-

Expression of Claudin-3 and Claudin-4 Proteins in
Gastric Adenocarcinoma

Reenu Malhotra, MD; Amanda L. Peterson, MD; Wei Li, MD. Department of Pathology, University of Texas Health Science Center-Houston.

Context: Claudins comprise a family of integral membrane proteins,
which play a major role in tight junction formation and function. Abber-
ations in expression of claudins have been described in various malig-
nancies and have been suggested as possible biomarkers and targets for
cancer therapy. The aim of this study was to determine the expression
pattern of claudin-3 and claudin-4 in gastric adenocarcinoma and correlate
expression with clinicopathologic variables.

Design: Paraffin-embedded tissues from 21 cases of gastric adenocar-
cinoma (11 intestinal, 10 diffuse/mixed subtypes) were analyzed for ex-
pression of claudin-3 and claudin-4 protein by immunohistochemistry.
Additionally, expression of these proteins in 20 gastric biopsies with
chronic active gastritis and intestinal metaplasia were evaluated for com-
parison. The protein expression was categorized into 3 grades: 1+ (weak),
2+ (moderate), or 3+ (strong) based on staining intensity.

Results: Moderate to strong staining of claudin-3 and claudin-4 was
detected in 90.1% and 72.7%, respectively, of the intestinal type and 90%
and 80%, respectively, of the diffuse subtypes of adenocarcinoma. In com-
parison, weak to moderate staining of claudin-3 was observed in chronic
active gastritis and intestinal metaplasia (P = .007). Significant statistical
difference in claudin-4 protein expression was observed between carci-
noma and chronic active gastritis and intestinal metaplasia (P < .001).

Conclusions: Claudin-3 and claudin-4 are strongly expressed in intesti-
nal and diffuse subtypes of gastric adenocarcinoma. The upregulation
of claudin expression suggests their possible role in gastric carcinogenesis,
their potential utility as diagnostic biomarkers, and possible targets for
innovative therapy.
with periodic acid-Schiff for glycogen and anti-inhibin antibodies was consistent with serous microcystic adenoma. The tumor also contained a focus of cystic spaces lined by a single layer of tall columnar cells with apical vacuoles (Figure 14, D); staining of the epithelium with Alcian blue/periodic acid-Schiff for mucin and of the stroma with anti-smooth muscle actin antibody was diagnostic of mucinous cystadenoma. Three cases have been previously described in Japan (Abe et al. Pancreas. 2005; 31:98–100). To our knowledge, this is the first case of mixed serous and mucinous cystic tumor of the pancreas in the United States.

Intraluminal Papillary Mucinous Neoplasm of the Pancreas: Histopathologic Characterization of 46 Consecutive Cases
(Poster No. 68)

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Context: Intraluminal papillary mucinous neoplasms (IPMNs) of the pancreas are intraductal mucin-producing cystic tumors showing variable degree of atypia ranging from adenoma to invasive carcinoma. We investigated the incidence and histopathologic characteristics of IPMNs in a single tertiary center.

Design: We reviewed 350 consecutive pancreatectomies performed during a 4-year period. The IPMNs were assessed for size, location, malignant features, perineural invasion (PNI) or lymphovascular invasion (LVI), and TNM when applicable.

Results: Of 243 pancreatic neoplasms, 18.3% were IPMNs. The mean age of patients was 66.9 years and tumor size was 3.3 cm. Sixty-seven percent of IPMNs were located in the head, 15% in the body, 15% in the tail, and 2% in heterotopic pancreas. Forty-eight percent were adenomas, 15% were borderline, 4.3% showed in situ carcinoma, and 32.6% showed invasive carcinoma. Five cases of IPMNs were associated with ductal carcinoma. Three cases showed IPMN with serous cystadenoma, endocrine microadenoma, and ampullary adenocarcinoma. Most ductal carcinomas with associated IPMN were pT3 (83%) or N1 (80%), whereas 53% of the invasive-IPMN were pT3 and 27% were N1. LVI was observed in 33% of the invasive-IPMN and 67% of ductal carcinomas with associated IPMN-adenoma. PNI was observed in 53% of invasive-IPMN and 100% of ductal carcinomas with associated IPMN-adenoma (Table).

Conclusions: In this series, IPMNs represent 18% of all pancreatic tumors. IPMNs without the presence of invasive carcinoma were more common. Patients with invasive-IPMN showed lower TNM stage and less LVI and PNI compared with patients whose pancreas contained both conventional ductal carcinoma and IPMN-adenoma (P <.001).

<table>
<thead>
<tr>
<th>IPMN</th>
<th>Mean Age, y/ Size, cm</th>
<th>TNM</th>
<th>LVI, %/ PNI, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adenoma</td>
<td>66.1/2.9</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Borderline</td>
<td>67.3/3.1</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>In situ IPMN</td>
<td>59.6/1.8</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Invasive IPMN</td>
<td>66.8/4.4</td>
<td>53% T3/33/53</td>
<td>27% N1</td>
</tr>
<tr>
<td>Adenoma associated with ductal carcinoma</td>
<td>73.1/2.0</td>
<td>83% T3/67/100</td>
<td>67% N1</td>
</tr>
</tbody>
</table>

First Report of a Massive Hepatocellular Carcinoma of the Liver in a Pediatric Patient, as a Sequela of Therapy for a High-Grade Glioma
(Poster No. 69)

Sreelakshmi Ravula, MD1 (sree.rusu@yahoo.com); Jeffrey Soonsowski, MD, PhD2; Elizabeth Manci, MD3; Department of Pathology, University of South Alabama Medical Center, Mobile; and 1Department of Pediatric Pathology, University of South Alabama Children’s and Women’s Hospital, Mobile.

Hepatocellular carcinoma (HCC) of the liver is one of the common malignant tumors in children. We present an unusual case of HCC of the liver in a pediatric patient with high-grade glioma. This is the first re-
ported case of a patient with glioma developing a 12-cm HCC as a sequela of tumor therapy. An 11-year-old white girl with 2- to 3-days’ history of headaches and vomiting was referred to our institution. Brain magnetic resonance imaging study revealed a 3.0-cm right parietal mass and a 0.7-cm satellite lesion in the right globus pallidus. She underwent craniotomy and the tumor was diagnosed as high-grade glioma. Her postoperative course was significant for seizures that were controlled with Keppra. She was treated with radiotherapy. After completion of radiotherapy, her maintenance chemotherapy included temozolomide and leomustine. With-in 1 month of initiation of chemotherapy she developed nausea, vomiting, epigastric pain, dehydration, and loss of weight. She had multiple hospital admissions during the course of 6 weeks. Her laboratory workup revealed elevated liver enzymes. Abdominal computed tomography scan showed a hypodense mass within the left lobe of the liver measuring 12.0 × 7.5 cm. Her liver lesion was resected with a final diagnosis of HCC. We believe this is the first reported case of HCC in a pediatric patient with high-grade glioma. Second, this is the largest reported mass in a case of HCC postchemotherapy in a pediatric patient.

**Direct Immunofluorescence in Esophageal Lichen Planus**

((Poster No. 70)

Xiuli Liu, MD, PhD; James McMahon, PhD; Keith K. Lai, MD. Department of Anatomic Pathology, Cleveland Clinic, Cleveland, Ohio.

Esophageal lichen planus (ELP) is a rare but underrecognized inflammatory disorder of the esophagus. Direct immunofluorescence (DIF) plays a critical role in diagnosing cutaneous and oral lichen planus, but its use in ELP has not been reported in published ELP cases. A 76-year-old woman presenting with a 5-year history of progressive dysphagia and odynophagia nonresponsive to proton pump inhibitor therapy. Esophagogastroduodenoscopy revealed a proximal esophageal stricture with inflammation, desquamation, and ulceration in the remainder of the esophagus. Biopsy demonstrated bandlike, lymphocytic interface inflammation involving the basal epithelium and superficial lamina propria. Other findings included spongiotic change in the epithelium, many apoptotic keratinocytes, small clefts at the epithelial-lamina propria junction, and rare, scattered collections of intraepithelial eosinophils (<10 per high-power field). Viral cytopathic effect was not identified. Organisms were not seen. DIF studies found shaggy fibrinogen deposition at the epithelial-lamina propria junction (Figure 16) and globular deposition of immunoglobulin (Ig) A, IgM, IgG, and C3. The morphologic and DIF findings established a diagnosis of ELP and a thorough skin and oral cavity examination was recommended. On follow-up 10 weeks after presentation, the patient reported significant improvement of symptoms with flunisolide. Physical examination performed by a dermatologist revealed lesions on the back, occiput, and hard palate consistent with cutaneous and oral lichen planus. Correct diagnosis of ELP is difficult but carries therapeutic and prognostic implications. The DIF findings in this case demonstrate the characteristic pattern seen in cutaneous and oral lichen planus, indicating that DIF may aid differentiation of ELP from other esphaggitides.

**Donor-Derived Small Cell Neuroendocrine Carcinoma of Pulmonary Origin in a Liver Transplant Recipient**

(Poster No. 71)

Adeel Ahmad, MD; Janet Cowan, PhD; Jeffrey Cooper, MD; Monica Pilichowska, MD, PhD. Departments of Pathology and Transplant Surgery, Tufts Medical Center, Boston, Massachusetts.

Donor-derived malignancies in transplant recipients are rare and found in 0.02% to 0.2% of allograft recipients. We report a case of donor-derived small cell neuroendocrine carcinoma in a liver transplant recipient. To the best of our knowledge such a case has not been previously reported. A 44-year-old man with end-stage liver disease secondary to hepatitis C and hepatocellular carcinoma received a cadaveric liver transplant from a 58-year-old female donor. The donor was an active smoker (2 packs per day) for several years with chronic obstructive pulmonary disease but without history of cancer. Donor screening included chest radiograph, which had normal results. Recipient’s clinical course was unremarkable until 8 months posttransplant when he presented with abdominal pain and multiple liver nodules. Computed tomography–guided fine-needle aspiration and core biopsy of the liver revealed sheets and clusters of small cells with high N/C ratio, round nuclei, fine chromatin, and indistinct nucleoli. Tumor cells were positive for pankeratin, cytokeratin 7, thyroid transcription factor 1, and chromogranin and negative for CD45, CD6-2, Hep Par 1, α-fetoprotein, serotonin, somatostatin, vasoactive intestinal peptide, calcitonin, bombesin, and gastrin. The diagnosis of small cell neuroendocrine carcinoma consistent with pulmonary derivation was made. Subsequent workup revealed no primary tumor in the recipient. Fluorescent in situ hybridization analysis of tumor cells revealed a 46,XX chromosome complement consistent with donor origin (Figure 17). The risk of transplant-related tumor xenograft is very low. However, donor-derived small cell carcinoma can occur. A donor’s smoking history could be of interest, and expanded smoking screening of donors might be warranted.

**Cutaneous Manifestations in a Patient With Juvenile Polyposis Syndrome: A Case Report and Review of the Literature**

(Poster No. 72)

Luigi K. Rao, MD (LuigiRao@alumni.nd.edu); Joel T. Moncur, MD, PhD. Department of Pathology and Laboratory Services, Walter Reed Army Medical Center, Washington, DC.

Juvenile polyposis syndrome (JPS), associated with SMAD4 and BMPR1A gene mutations, is defined clinically by at least 6 juvenile colon polyps, multiple gastrointestinal tract juvenile polyps, or any number of juvenile polyps along with a family history of juvenile polyps. Many familial polyposis, including Cowden, Gardner, and Muir-Torre syndromes, have been recognized to have distinct cutaneous manifestations. We present a patient with skin lesions believed to represent cutaneous manifestations of JPS, a phenomenon never previously reported based on our review of the literature. The patient presented at 6 months with rectal bleeding and a lesion protruding from the anus. Subsequent colonoscopy revealed innumerable polyps carpeting the colon with multiple biopsies showing juvenile polyps, and a diagnosis of JPS was rendered. No mutations in SMAD4 or BMPR1A were detected during genetic workup. Continued surveillance discovered multiple gastric and small bowel juvenile polyps. Furthermore, several perianal verrucous polypoid lesions were biopsied on 4 separate occasions beginning at age 2. These polyps ranged in size from 0.3 to 1.5 cm. They exhibited a papillomatous architecture and were lined by an epidermis with varying degrees of acute inflammation with overlying hyperkeratosis and parakeratosis. The dermis dis-
played gaping vessels with prominent lymphocyte and plasma cell-rich chronic inflammation. Parakeratotic spires, keratohyalin granules, or viral cytopathic effect were not identified. In situ hybridization for human papillomavirus was negative. We believe the architecture of these inflamed verruciform fibroepithelial polyps, their recurrent nature, and their proximity to the gastrointestinal tract support the notion that these lesions represent cutaneous manifestations of JPS.

**POSTER SESSION 200: SUNDAY, OCTOBER 11, 2009, 1:00 PM–3:30 PM**

**Clinical Chemistry; Clinical Immunology; Breast Pathology; Gynecologic and Placental Pathology; Pulmonary and Mediastinal Pathology**

**Serum Protein-Bound Thyroxine Induced Biases in Antibody-Based Single-Phase Assays for Free Thyroxine**

*(Poster No. 1)*

Yvette C. Tanhehco, MD, PhD;*yvette.tanhehco@uphs.upenn.edu;* Octavia M. Palmer, PhD;*Linda.S.Derrico@uphs.upenn.edu;* Jorge L. Sepulveda, MD, PhD;*Harry.C.Blair@uphs.upenn.edu;* Department of Pathology and Laboratory Medicine, University of Pennsylvania, Philadelphia; and Department of Pathology, University of Pittsburgh, Pittsburgh, Pennsylvania.

**Context:** Thyroid function is assessed by measuring free thyroxine (fT4) when thyroid-stimulating hormone (TSH) is inconclusive. Interference in single-phase antibody-based assays for free T4 is a major problem. Accurate measurement of free T4 is important when thyroid-binding globulins might vary (eg, during pregnancy). We evaluated the ability of several assays in excluding signal from protein-bound T4.

**Design:** We examined TSH and free T4 in a mostly female population (50% were pregnant) at Magee-Women's Hospital. Protein-bound T4 bias was assessed by dialyzing samples and assaying retentate with increasing amounts of dialysate being added. TSH was measured for all samples.

**Results:** Assays of free T4 using the Vitros ECI platform (Ortho-Clinical Diagnostics, Rochester, New York) were essentially independent from serum protein concentration (R² = 0.009). T4 measurements using Unilab Dx (Beckman Coulter, Fullerton, California), Avia Contaur (Siemens Healthcare Diagnostics, Deerfield, Illinois), and MP radioimmunoassay (MP Biomedical, Irvine, California) were related to serum protein concentration, and dilution curves differed significantly from those with ECI (P < .01; 2-tailed analysis of variance). Degree of interference from protein-bound T4 was similar in these assays, with least squares fits of DxI, Cen毁h/11021; Harry C. Blair, MD.21 Department of Pathology and Laboratory Medicine, University of Pennsylvania, Philadelphia; and 2Department of Medicine, University of Pennsylvania, Philadelphia; and 2Department of Pathology, University of Pittsburgh, Pittsburgh, Pennsylvania.

**Conclusions:** Some single-phase, direct, free T4 immunoassays have important interference from protein-bound T4. The ECI assay was largely unaffected by serum protein. In a mostly female and 50% pregnant population, correlation of TSH to free T4 was poor for all tested assays.

**A New Study of Intravascular Blood for Laboratory Analysis**

*(Poster No. 2)*

Larry J. Miller, MD;*Thomas E. Philbeck, PhD;* (thomas.philbeck@vidacare.com); Diana F. Monteza, RN, BSN;*Cathy J. Spadaccini, MD;* 3Department of Science & Clinical, Vidacare Corporation, San Antonio, Texas; and 3Department of Pathology, Ameripath South, San Antonio.

**Context:** Improved devices that enable providers to deliver critically needed drugs as quickly as central lines have ignited a resurgence in the use of IO space, including drawing IO blood for laboratory analysis. Despite previous favorable studies, some laboratory staff have concerns about the reliability of IO-derived blood for use in laboratory tests. This study validates earlier studies and addresses concerns raised by laboratory staff regarding the use of IO-derived blood.

**Design:** We obtained institutional review board approval. Ten adult volunteers consented to participate, and blood samples were obtained from peripheral veins in the forearm. Within 5 minutes, an IO catheter was placed in the proximal humerus, and 2 sets of IO blood samples were obtained from each participant, one set following 2 mL of marrow/blood waste and one set following 6 mL of waste. At a reference laboratory, all sample sets were analyzed for complete blood count and chemistry profile. Means were compared for each blood value of the drawn samples (intravascular, IO-1, and IO-2), with intravenous blood values serving as controls for IO blood values.

**Results:** IO and intravenous values were clinically similar, except in the case of white blood count and carbon dioxide (Table).

**Conclusions:** We found that IO space is a reliable source of blood for laboratory analysis when conducting tests commonly performed in emergency medicine, such as complete blood count and chemistry profile. Results, however, may be moderately reliable for carbon dioxide and unreliable for white blood count.

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**Variation of Analytic Method for High-Density Lipoprotein Cholesterol Determination Is Clinically Significant**

*(Poster No. 3)*

Stanley J. Podlasek, MD (spodlas2@jhmi.edu). Department of Pathology, Johns Hopkins University, Baltimore, Maryland.

**Context:** High-density lipoprotein cholesterol (HDL-C) is lower in hospitalized patients; this has been attributed to stress or dietary changes related to hospitalization. Because outpatients are tested in commercial laboratories while inpatients are tested in hospital laboratories, we hypothesized that different analytic methods might explain the difference in HDL-C values.

**Design:** We sent 50 random patient samples from physicians’ offices to a commercial laboratory where they were simultaneously assayed on the AU2700 chemistry analyzer (Olympus, Melville, New York) and the LX20 chemistry analyzer (Olympus, Melville, New York) and the LX20 chemistry analyzer (Beckman-Coulter, Fullerton, California) on the day of collection. The EPE Evaluator (David G. Rhoads Associates, Kennett Square, Pennsylvania) was used to calculate means and biases to perform regression analysis.

**Results:** The Olympus method (mean HDL-C, 59.2 mg/dL) had a positive bias of 13.4 mg/dL compared with the Beckman method (mean HDL-C, 45.8 mg/dL). Olympus-based HDL-C equals 1.271 x (Beckman-based HDL-C) + 1 mg/dL.

**Conclusions:** Patients who go from a laboratory that uses the Olympus analyzer to one that uses the Beckman analyzer experience a significant method-dependent decrease in the level of HDL-C, which may change treatment. Manufacturers and laboratories should note the standardized program for HDL-C sponsored by the Centers for Disease Control and Prevention in which the reference range is specified by the National Cholesterol Education Program and not by a population study. Comparing the frequency of race- and sex-matched individuals with low HDL-C values from a particular laboratory with those published for like segments of the US population by the Centers for Disease Control and Prevention would be of value.

**Assessment of Fetal Lung Maturity: Concordance Between TDx-FLM II Values and Lecithin to Sphingomyelin Ratios**

*(Poster No. 4)*

Andrea Wiens, DO (awiens@chsmail.org); Thomas Kocoshis, MD. Department of Pathology, Ball Memorial Hospital, Muncie, Indiana.

**Context:** Respiratory distress syndrome represents a significant disease entity in newborns. Assessment of fetal lung maturity (FLM) is essential when clinicians are determining whether to delay delivery. Several measurements exist to elucidate FLM, including the traditional gold standard ratio of lecithin to sphingomyelin (L/S) and the newer TDx-FLM II assay (Abbott Laboratories, Abbott Park, Illinois). We evaluated concordance be-
tween the TDx-FLM II test kit and the traditional L/S ratio assay (Helena Laboratories, Beaumont, Texas) in predicting FLM.

**Design:** Clinical laboratory values were obtained from 163 consecutive pregnant women whose amniotic fluid was collected from 2005 to 2008 for primary determination of FLM. Concordance values were calculated (n = 140) based on maturity cutoff values of 55 mg/g for TDx-FLM II results and 2.0 for L/S ratios. Comparison was made with the same data using a best apparent TDx-FLM II maturity cutoff value of 45 mg/g, as recent studies demonstrated.

**Results:** Overall concordance between the TDx-FLM II and the L/S ratio was approximately 56% using 55 mg/g as the cutoff value for TDx-FLM II results. Concordance rose to nearly 80% when the cutoff value was lowered to 45 mg/g.

**Conclusions:** Recent studies have shown the TDx-FLM II to be 100% sensitive and 90% specific with a cutoff value of 45 mg/g. We found an overall concordance rate of 78% with this best apparent TDx-FLM II cutoff. We propose implementing a protocol in which the TDx-FLM II test be followed by a reflex L/S ratio for confirmation only when the TDx-FLM II result is interpreted as immature.

**Performance of the Direct Hemoglobin A1c Assay on Ortho-Clinical Diagnostics' VITROS 5600 Integrated System**

**Poster No. 5**

Dean Carlow, MD, PhD1,2 (deancarlow@wwchop.edu); Nancy Kolea, MT1; Department of Laboratory Medicine, Children's Hospital of Philadelphia, Pennsylvania; and 2University of Pennsylvania School of Medicine, Philadelphia.

**Context:** Glycohemoglobin measurement as HbA1c is recommended by the American Diabetes Association and provides the most important marker of time-averaged glycemic status.

**Design:** In this method comparison study of hemoglobin A1c, we used the VITROS 5600 Integrated System (Ortho-Clinical Diagnostics, Rochester, New York) with a National Glycohemoglobin Standardization Program calibrated high-performance liquid chromatography method. Whole blood samples were automatically hemolyzed on the system, and the percentage of A1c was calculated from the measurements of hemoglobin and hemoglobin A1c.

**Results:** The method has a reportable range for hemoglobin, HbA1c, and percentage of A1c of 6.0 to 22.0 g/dL, 0.2 to 2.5 g/dL, and 4% to 14%, respectively. Linearity was demonstrated linearly throughout the entire assay range. Within-run precision (n = 10) was evaluated using 2 levels of quality control materials (mean, 6.4; 11.9%) and yielded coefficients of variation of 1.6% and 1.8%. Between-day precision was evaluated with different quality control materials (mean, 5.4; 9.2%) during a 20-day period using one reagent lot and yielded coefficients of variation of 1.4% and 3.4%, respectively. The accuracy of 53 patient samples ranging in concentration from 4.7% to 14.0% of A1c was tested by correlation of results from the Bio-Rad Variant II ion exchange high-performance liquid chromatography assay (Bio-Rad Laboratories, Hercules, California) and the VITROS assay. The regression analysis of the VITROS System versus high-performance liquid chromatography demonstrated a slope of 1.01 (95% confidence interval; range, 0.9485–1.071) with an intercept of −0.254 (95% confidence interval; range, −0.7245 to 0.2169).

**Conclusions:** The hemoglobin A1c assay on the VITROS System demonstrates rapid, precise, and accurate results for monitoring the percentage of HbA1c levels in patient samples.

**Primary Sternal Cryptococcosis With Dissemination in a Human Immunodeficiency Virus–Negative Patient With Selective Idiopathic CD4-Positive T-Cell Lymphocytopenia**

**Poster No. 6**

Richard H. Siderits, MD1 (richard.siderits@gmail.com); Hong Bing Deng, MD, PhD1; Anup Hazra, MD1; Anamika Patel, MD1; Sujal Singh, RA1; Janusz Godyn, MD1; Osman Ouattara, CT(ASCP)1; 1Department of Experimental Pathology and 2Cytopathology, Robert Wood Johnson University Hospital, Hamilton, New Jersey; and 3Department of Infectious Disease, Infectious Disease Affiliates of Hamilton, New Jersey.

This case study highlights the importance of considering idiopathic CD4-positive lymphocytopenia in nonimmunosuppressed patients present with atypical fungal infections. Medical history was noncontributory for causes of immunosuppression. Findings included a cavitory sternal lesion. Chest x-ray was unremarkable, and human immunodeficiency virus (HIV) testing remained negative. Biopsy of sternum showed granulation tissue with teardrop-shaped, budding yeasts. Culture confirmed Cryptococcus neoformans. Flow cytometry demonstrated selective CD4-positive lymphocytopenia with CD8-positive lymphocytes in the normal range. The patient was diagnosed with idiopathic primary sternal cryptococcoma within a background of CD4-positive lymphocytopenia. Treatment included amphotericin B lipid complex followed by oral fluconazole. Follow-up at 6 months showed persistent CD4-positive lymphocytopenia. The sternal lesion was also persistent. A second cryptococcal hip lesion was identified by computed tomography and was biopsied; results suggested chronic disseminated cryptococcosis with CD4-positive lymphocyctopenia. The patient’s T4 lymphocyte count remained less than 60 cells per microliter for 6 months. Newer treatments may include interleukin 2 to restore T4 levels; prophylaxis for opportunistic infections remains the central treatment. The differential diagnosis may be complicated by false-negative serology in 60% of patients with local cryptococcal infection and by 80% cross-reactivity among blastomyces, histoplasma, and cryptococcal antigens. CD4-positive lymphocytopenia in human immunodeficiency virus–negative patients with no other explanation for immunosuppression has been associated with opportunistic fungal infections. We believe this is the first reported case of primary sternal cryptococcoma in a patient with idiopathic CD4-positive lymphocytopenia. Idiopathic CD4-positive lymphocytopenia is likely underdiagnosed and should be considered in otherwise healthy patients with atypical fungal infections.

**New Multiple Monoclonal Gammapathies Following Autologous Hematopoietic Stem Cell Transplantation in a Patient With Multiple Myeloma:**

**Case Report and Review of Literature**

**Poster No. 7**

Suzzing Xie, MD, PhD1 (suzzing.xie@yahoo.com); Massoud Ahmadnejad, MD1; Sreedhar Katragadda, MD1; Humayun Islam, MD, PhD1; Anthony Deng, MD, PhD1; Janusz Godyn, MD1; Osman Ouattara, CT(ASCP)1; Hong Bing Deng, MD, PhD1; Anup Hazra, MD1; Anamika Patel, MD3; Sujal Singh, RA1; Janusz Godyn, MD1; Osman Ouattara, CT(ASCP)1; 1Department of Pathology and 2Heamatology & Oncology, Westchester Medical Center, Valhalla, New York.

Among treatment options for multiple myeloma, autologous hematopoietic stem cell transplantation (HSCT) is associated with an increased rate of complete remission and an increased rate of survival compared with conventional chemotherapy. HSCT is now considered a choice for patients who are newly diagnosed with multiple myeloma and who are younger than 65 years. We present a case of multiple myeloma in which the patient developed multiple monoclonal immunoglobulins following autologous HSCT. A 41-year-old man presented with anemia. Serum protein electrophoresis and immunofixation found a monoclonal immunoglobulin (Ig) G A band. Morphology and flow cytometry of bone marrow confirmed the diagnosis of multiple myeloma (IgG A monoclonal plasma cells expressing CD38, CD138, CD117, and negative for CD19). Two months after auto-HSCT, immunofixation showed 2 new monoclonal IgG λ bands, in addition to the original malignant IgG lambda band, and a significant decrease in total immunoglobulin. The most recent immunofixation (nearly 6 months after transplantation) showed the same pattern, with a slightly decreased intensity in the 2 extra bands; no lymphadenopathy was noted. Cytogenetics examinations showed no abnormality in bone marrow before or after transplantation. Paraproteinemia may appear in recipients of allogeneic bone marrow transplantation. The origin of immunoglobulin abnormality in these cases might be related to the development of graft-vs-host disease, Epstein-Barr virus and/or cytomegalovirus infection in donor or recipient, malignant lymphoproliferation (lymphoma) secondary to high-dose chemotherapy, or hyperproliferation of some immunosensitized B-cell clones among transplanted cells during bone marrow reconstitution. The latter might be the mechanism in this transplant patient.

**A Systemic Lupus Erythematosus Case With a Wide Spectrum of Autoantibodies and t(1;6)(q25;q23) Translocation**

**Poster No. 8**

Lei Zhang, MD, PhD1 (lei.zhang@hawaii.edu); Timothy Donlon, PhD, FACMG1; Stacey Honda, MD, PhD3; 1Department of Pathology, Hawaii Residency Program, Honolulu; 2Department of The Queen's Genetics Laboratories, Queen's Medical Center, Honolulu, Hawaii; and 3Department of Pathology, Kaiser Permanente Foundation Hospital, Honolulu, Hawaii.

Systemic lupus erythematosus is well known for being difficult to diagnose; diagnosis requires extensive clinical laboratory studies for evidence of autoimmune markers and organ damage. Genetic etiology of this disease also remains elusive. We report a case of a 49-year-old woman who presented with fatigue, shortness of breath for 1 month, and acute menorrhagia. After thorough workup, systemic lupus erythematosus was diagnosed. We detected a wide spectrum of autoantibodies, including...
antinuclear antibody, anti–double-strand DNA antibody, anti-Smith antibody, antineutrophil cytoplasmic antibody (pANCA and cANCA), antithyroid peroxidase antibody, anti–smooth muscle antibody, and serum warm antibody. These findings parallel the patient’s condition, including damage to multiple organs, and highlight her body’s loss of tolerance toward its own antigens. Blood cells are negative for JAK2 mutations.

Cytogenetic analysis on bone marrow and phytomenadione-stimulated blood cells both revealed a 46 XX, t(1;6)(q25;q23) translocation, which has never been seen in any kind of leukemia. Gene translocation is rarely described in systemic lupus erythematosus. Our case is the second report of systemic lupus erythematosus associated with a chromosome translocation.

A Comparison of HLA Crossmatching Methodologies
(Poster No. 9)

Paul J. McGowan, MD (mcgowanp@health.missouri.edu). Department of Pathology and Anatomical Sciences, University of Missouri-Columbia.

Context: The crossmatch is a vital test performed by the transplant or HLA laboratory. Basic/modified microcytotoxicity, anti-human globulin, and flow-based bead/microparticle assay/enzyme immunoassay crossmatching methods are the major techniques used.

Design: Using data collected from the College of American Pathologists’ Proficiency Testing Surveys, we evaluated the relative sensitivities of these 3 major crossmatching methods, changes in sensitivities for each method during a 5-year period, and positive and negative predictive values for each method.

Results: We reviewed 11 College of American Pathologists’ Proficiency Testing surveys (MX1 and MX2 surveys for 2003 and 2008) and analyzed testing surveys (MX1 and MX2 surveys for 2003 and 2008) and showed improved sensitivity during the 5-year period (MX1, P < .001; MX2, P < .001). The other methods showed no improvement or decreased sensitivity during the same period. The flow/enzyme method had higher positive predictive values (87%–94%) than the other methods.

Conclusions: These results strongly suggest that laboratories and their transplant programs that rely on microcytotoxicity (direct, modified, or antigen-specific globulin–augmented) crossmatches may be missing a significant number of clinically significant HLA antibodies. Those laboratories and programs should consider more sensitive methods of antibody detection and crossmatching, such as flow-based bead/microparticle assay/enzyme immunoassay crossmatch methods.

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Abbreviations: AHG, anti-human globulin; DC, basic/modified microcytotoxicity; FC, flow/enzyme method.

Association Between Low Concentrations of Monoclonal and Oligoclonal Gammapathies and Chronic Illness
(Poster No. 10)

Gaofeng Fan, MD, PhD (gfan@numc.edu); Min Guo, MD; Michael Ang-Rabanes, MD; Jen Lin, MD Department of Pathology, Nassau University Medical Center, East Meadow, New York; and School of Medicine, American University of Caribbean, St Maarten, Netherlands Antilles.

Context: We evaluated the significance of low levels of monoclonal and oligoclonal gammapathies in serum.

Design: We reviewed 393 patients of which 18 were typed by immunofluorescence as having a low concentration of monoclonal or oligoclonal bands in serum.

Results: Seven patients (C2, 42-year-old woman with IgG κ; C4, 76-year-old man with IgA λ; C6, 51-year-old woman with IgG λ; C7, 58-year-old man with IgM κ; C10, 80-year-old man with IgA λ; C11, 54-year-old woman with IgG λ; C17, 62-year-old woman with IgG κ) had hypertension, and 4 of these had associated diabetes mellitus (C4, C6, C10, C11). Six patients (C2, C3, 81-year-old woman with IgG κ; C4; C5, 60-year-old man with IgG κ; C12, 60-year-old man with IgG κ; C13, 60-year-old woman with IgG κ and IgG λ) had chronic kidney disease. Five patients (C1, 66-year-old woman with IgG κ; C3, C5, 43-year-old man with Igκ κ; and C15, 85-year-old woman with Igκ κ) had sepsis. Seven patients had malignant tumors, including 3 with colon cancer (C4; C5, 60-year-old man with IgG κ; and C12, 60-year-old man with IgG κ), 1 (C13, 60-year-old woman with Igκ κ and Igκ λ) with chronic lymphocytic leukemia, 1 (C14, 55-year-old man with Igκ κ) with tonsillar carcinoma, and 2 (C15 and C17) with myeloma.

Conclusions: It is plausible that chronic processes with long-standing reaction may have induced immunoglobulin modifications. Further studies should be implemented to correlate the relationship between specific concentrations of monoclonal immunoglobulins and chronic illnesses.

Lobular Carcinoma In Situ With Pleomorphism and Lobular Carcinoma In Situ With Necrosis
(Poster No. 12)

Megan E. Sullivan, MD (msulli7777@yahoo.com); Seema A. Khan, MD; Barbara Susnik, MD, PhD. Departments of Surgery Pathology and Surgery, Northwestern University, Chicago, Illinois.

Context: Lobular carcinoma in situ (LCIS) is a risk marker for breast carcinoma (BC). Its variants, LCIS with necrosis (LCIS-N) and pleomorphic LCIS (LCIS-P), may exhibit more aggressive behavior. We examined clinical and immunohistochemical features of LCIS-N and LCIS-P diagnosed in needle core biopsy (CB).

Design: Core biopsies from January 2003 to August 2008 were reviewed, and 30 cases (LCIS-P, n = 19; LCIS-N, n = 11) met criteria. LCIS-P required pleomorphism and nuclear size greater than 3.5 times a lymphocyte in more than 10% of cells. LCIS-N required classic lobular cytology with necrosis. All were E-cadherin negative. Immunohistochemical
D2-40 Increases Detection of Lymphatic Invasion in Breast Carcinoma
(Poster No. 13)

Kyle L. Eskue, MD (kleskue@utmb.edu); Mahmoud Eltorky, MD, PhD; Basim Mohammed, MD. Department of Pathology, University of Texas Medical Branch, Galveston.

Context: Detection of lymphatic invasion is an important component of complete histopathologic evaluation of primary breast carcinoma for accurate determination of prognosis and management. In addition to the potential for missing lymphatic invasion, another problem occurs when artifactual tissue retraction around tumor (false lumen) is confused with true lymphatic invasion. We hypothesized that using D2-40 antibody, a sensitive marker for lymphatic endothelium, can increase the sensitivity of detecting true lymphatic invasion in breast carcinoma, thus helping to identify patients at higher risk for metastatic disease.

Design: Sixteen cases of lymph node–positive invasive breast carcinoma (14 ductal and 2 lobular) from 2003 to 2007 were retrospectively collected from our institutional archives. In the original pathology reports, all cases were negative for lymphovascular invasion within hematoxylin-eosin–stained tissue sections. Original slides from the cases were reviewed to confirm the study’s inclusion criteria were met, and tissue blocks were selected for D2-40 immunostaining. The original hematoxylin-eosin–stained and D2-40–stained slides were reviewed independently by 2 pathologists. Only cases with unequivocal tumor emboli within positively stained, endothelial-lined, lymphatic vessels were counted as positive.

Results: Four of 16 (25%) cases showed definitive lymphatic invasion within tissue sections that were previously unidentified by hematoxylin-eosin–stained slides alone.

Conclusions: Using D2-40 immunostain on selective tumor sections may increase the diagnostic sensitivity of lymphatic invasion detection in cases of primary breast carcinoma. This study demonstrates the usefulness of D2-40 immunostain as a tool to confirm or reject suspected foci of lymphatic invasion that are questionable in hematoxylin-eosin–stained slides.

Optimal Cutoff Values of Ki-67 as a Proliferative Marker in Breast Cancer
(Poster No. 14)

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Context: Proliferative activity of tumor cells is usually associated with biologic behavior in breast cancer. Ki-67 is the most commonly used proliferative marker; however, no consensus on optimal cutoff values has been defined. Current Ki-67 cutoff values vary in the literature, and this may affect prognosis and management. We attempt to evaluate the correlation among Ki-67 positivity and tumor grade, estrogen receptor, progesterone receptor, and HER2/neu status and to establish rational cutoff values for Ki-67.

Design: We retrospectively reviewed 75 cases of breast carcinoma, including Ki-67, estrogen receptor, progesterone receptor, and HER2/neu data. Immunohistochemical stains were performed following the vendor’s protocols. The Ki-67 positivity cutoff groups were <10%, 10% to 20%, >20%, and <10%, 10% to 29%, and >30%.

Results: Fifty-three percent of tumors in the low proliferative Ki-67 group of <10% were grade 1 tumors. Fifty-two percent of tumors with Ki-67 values of 10% to 20% were grade 2 tumors, and 55% of cases with values >20% were grade 3 tumors. At a cutoff value of >30%, 27% of grade 2 and 28% of grade 1 tumors were excluded from the high proliferative group. All grade 3 tumors were in this high proliferative group.

Conclusions: Our study suggests that Ki-67 cutoff values of <10%, 10% to 29%, and >30% are more closely associated with histologic grade and, therefore, may be more representative of low, intermediate, and high proliferative activity. Ki-67 positivity is not associated with estrogen receptor, progesterone receptor, or HER2/neu status. Further studies with a larger number of cases and correlation of Ki-67 positivity with prognosis are required.

The Role of Fibrinolytic Proteins in Angiogenesis and Tumor Progression
(Poster No. 15)

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Context: Angiogenesis, an essential component of tumor progression, has been studied by various methods. One method is to look for the proteases and protease inhibitors produced in the growth and elongation of existing vessels; another is to look for endothelial cell markers. We used both methodologies to prove that angiogenesis was occurring and to identify the specific sites of angiogenesis in and around mammary carcinoma.

Design: Clinical history, histopathology, and immunohistochemistry results were reviewed for 11 women (range, 41–87 years) with breast cancer who were diagnosed and treated at Hahnemann University Hospital (Philadelphia, Pennsylvania).

Results: Tissue plasminogen activator and annexin II staining were present in both tumor and proximal surrounding tissue, confirming the presence of protease and fibrinolytic/antifibrinolytic protein receptor–regulated steps that are specific to angiogenesis. Additionally, CD105 (endoglin) antibody selectively stained the endothelial cells of angiogenic blood vessels within and adjacent to tumors (Figure 18). Tissue uninvolved by tumor did not show positive staining, thereby serving as an internal control.

Conclusions: Invasive mammary carcinoma and adjacent desmoplastic tissue showed an increased concentration of fibrinolytic proteins and an upregulation of the binding site for proteases and antiproteases. This area of increased fibrinolysis coincides with the area containing blood vessels that stained for CD105, a marker of endothelial cells undergoing angiogenesis. These findings make a strong argument for the existence of the fibrinolytic/antifibrinolytic mechanism of tumor-induced angiogenesis.
Of interest, the finding of CD105-positive blood vessels in desmoplastic stroma suggests that the tumor is priming the blood vessels beyond its periphery for local expansion.

Dr. Sharma received a Department of Defense grant (No. W912566357-N608) in support of this research.

A Rare Case of Bilateral Multinodular Pseudoangiomatous Stromal Hyperplasia in a Patient With Gigantomastia

(Poster No. 16)

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Pseudoangiomatous stromal hyperplasia (PASH) is a benign breast lesion composed of dense collagenous stroma with complex, anastomosing, empty, slitlike pseudovascular spaces that are either acellular or lined by spindled stromal cells. Its appearance mimics a vascular lesion, including angiosarcoma. PASH is usually seen as incidental microscopic foci in normal breast tissue or in association with various benign and malignant breast lesions. Occasionally, it can present as a distinct lesion, either in a diffuse pattern or as a unilateral discrete nodule (nodular PASH). Grossly, the nodule is indistinguishable from fibroadenoma, ranging from 1 to 17 cm. Reports of nodular PASH are rarely present in the literature, and even fewer cases of bilateral nodular PASH are described. We report a case of bilateral multinodular PASH in a 42-year-old woman who has a long history of gigantomastia with progressive enlargement and who has elected to undergo bilateral reduction mammoplasty.

CD1A Expression in Poorly Differentiated Estrogen Receptor– and Progesterone Receptor–Negative Invasive Ductal Carcinoma of the Female Breast

(Poster No. 17)

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Context: Recent studies suggest that primary invasive female breast carcinomas with positive estrogen receptor (ER) and progesterone receptor (PR) have greater dendritic cell infiltration; these patients may also have a better prognosis.

Design: Our study population consisted of patients diagnosed with ER- and PR-negative poorly differentiated invasive ductal carcinoma at Rush University Medical Center between 1975 and 1988. Two distinct groups of patients were compared: group 1 consisted of 16 women who were alive and free of disease for an average of 14 years. Group 2 consisted of 20 women who died of disease within 3 years of diagnosis. The 2 groups were matched for clinical stage and ER/PR receptor status. The following breast cancer marker profile was obtained for all patients: ER (Dako), PR (Dako), and CD1A (Dako).

Results: The average age of group 1 patients was 52.4 years (range, 31–74 years). The average age of group 2 patients was 52.6 years (range, 34–88 years). Evaluation of CD1A did not show a difference between the 2 groups: (group 1, 1 of 16; 8%) versus (group 2, 2 of 20; 10%). CD1A expression was observed in dendritic and tumor cells.

Conclusions: Similar expression of CD1A-positive cells was seen in patients with short- and long-term survival. Strong correlation was found between no expression and/or low expression of CD1A-positive cells and ER- and PR-negative tumors. Tumor cells also expressed CD1A, suggesting a possible costimulatory effect by this molecule on the functional immune response. In patients with ER- and PR-negative invasive ductal carcinoma, lack of expression or low expression of CD1A does not appear to predict survival.

Tissue-Specific Expression of Estrogen Receptor-β Wild Type and Isoforms

(Poster No. 18)

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Context: Estrogen receptor-β (ER-B) has been mostly studied in breast and some prostate cancers and has been shown to be associated with prognosis. We tested ER-B wild type (wt) and its isoforms in different tissues to further elucidate tissue- and cell-specific expression of ER-B.

Design: Tissue microarray slides of 130 normal and 260 malignant tissues from 13 different organs were tested for ER-Bwt (Biogenex, San Ramon, California), 2 clones of ER-B1 (Dako, Carpentaria, California and AbD Serotec, Raleigh, North Carolina), ER-B2 (AbD Serotec), ER-BCT (Upstate, Lake Placid, New York), ER-B NT (Millipore, Billerica, Massachusetts), and ER-A (Dako) using immunohistochemistry procedures. Nuclear staining less than 5% was considered negative.

Results: ER-Bwt and isoforms were detected in nuclei and/or cytoplasm. In normal tissues, ER-Bwt was expressed in 93% (12 of 13) of the organs in the range of 60% to 90% in breast, stomach, kidney, thyroid, endometrium, bladder, pancreas, prostate, brain, and ovary and less than 10% in lung and colon. Hepatocytes showed only cytoplasmic reaction. ER-B1 and ER-B2 isoforms were expressed heterogeneously in only (5 of 13) of the organs. In neoplastic tissues, expression of ER-Bwt, ER-B1, and ER-B2 was decreased in colon, kidney, endometrium, brain, and pancreas and increased in stomach, lung, and ovary. ER-B and ER-A were coexpressed in 30% of normal and malignant endometrium, brain, and ovary tissues.

Conclusions: ER-B is expressed in many normal tissues but variably in neoplastic tissues. ER-B may play a stimulatory or suppressive role in tumorigenesis. Testing ER-B in different tissues may provide further insights on ER-B in tumorigenesis.

Lupus Mastitis: An Unusual and Underrecognized Entity

(Poster No. 19)

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Lupus panniculitis is an infrequent manifestation of systemic lupus erythematosus, occurring in approximately 2% to 3% of patients. Up to 70% of patients with lupus panniculitis have discoid lesions. Lupus mastitis (LM) is a rare manifestation of lupus panniculitis involving the breast, and it clinically and radiologically mimics carcinoma. Approximately 20 cases have been reported in the literature. We add 2 cases of clinical and radiologic findings suspicious for malignancy. The first patient was a 58-year-old African American woman who was diagnosed with systemic lupus erythematosus in 1995. In July 2005, a firm, palpable mass was discovered in the right upper breast. Mammography showed a 2.6-cm, hazy, ill-defined, soft tissue density that was suspicious for malignancy. An excisional biopsy showed a nodular, angiocentric, and angioinvasive lymphoid infiltrate involving fat lobules with associated hyaline fat necrosis and was diagnostic of lupus panniculitis. The patient was started on Plaquenil and showed improvement in her symptoms. However, in November 2006, a new firm, palpable mass was discovered in her left breast. An excisional biopsy again showed LM. The second patient is a 52-year-old African American woman with a diagnosis of discoid lupus. Mammography and ultrasound in November 2008 revealed 2 suspicious left breast masses with associated microcalcifications and an enlarged axillary lymph node. The masses were excised and showed diagnostic changes suggestive of LM. LM has characteristic histologic findings but clinically mimics malignancy and therefore, necessitates tissue biopsy. LM should be considered in the differential diagnosis of breast masses in patients with lupus.

Low-Grade Adenosquamous Carcinoma of the Male Breast

(Poster No. 20)

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Low-grade adenosquamous carcinoma of breast is an uncommon neoplasm in women and is exceedingly rare in men. In the literature, we found only one reported case of low-grade adenosquamous carcinoma in a man. This tumor is known for local recurrence after incomplete excision but also has low metastatic potential. Histologically, the tumor is composed of syringoma-like glandular structures with variable amounts of squamous differentiation in a background of bland spindle cell stroma. Due to its characteristic bland histopathology, this tumor is often confused with infiltrating syringoma of the nipple and tubular carcinoma of breast. We report a case of a 73-year-old man who presented with a 2-cm subareolar left breast hard nodule with increased size and tenderness. Biopsy of the mass revealed the tumor, which was made up of multiple irregular ducts, many of which were curved, convoluted, and irregularly dilated (Figure 19). They were lined by 2 rows of epithelium and squamous cells. The epithelial cells showed bland nuclear morphology. Ductal structures and squamous cell nests were seen infiltrating the muscle bundles of nipple and underlying breast and fibroadipose tissue. Following radical mastectomy, the axillary lymph nodes were negative for metastatic carcinoma. The tumor was positive for HER2/neu and negative for p53. This study reports a rare example of low-grade adenosquamous
Intraoperative Frozen Section on Sentinel Lymph Nodes Is Not Indicated in Patients With Ductal Carcinoma In Situ of the Breast or in Those Undergoing Prophylactic Mastectomy (Poster No. 22)

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Context: The appropriateness and cost-effectiveness of routine intraoperative sentinel lymph node (SLN) assessment remains to be defined. We aim to determine whether routine intraoperative frozen section (FS) examination of SLNs is worthwhile in all patients undergoing surgery for breast cancer.

Intraoperative Axillary Sentinel Lymph Node Evaluation: False-Negative Rate in Neoadjuvant Versus Nonneoadjuvant Cases (Poster No. 24)

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Context: The false-negative (FN) intraoperative interpretation for sentinel lymph nodes may increase the health care cost due to delayed completion axillary dissection. This study evaluates the rates of FN, true positive, true negative, and false positive in patients with and without prior positive correlation.

Laboratory Compliance With the American Society of Clinical Oncology and College of American Pathologists’ Guidelines for HER2 Testing: A College of American Pathologists Survey of 757 Laboratories (Poster No. 23)

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Context: To ensure quality HER2 testing in breast cancer, the ASCO/CAP introduced guidelines with the intent of compliance by 2008. We conducted this survey to assess the effect of these guidelines on pathology laboratories and their ability to address key components.

Design: In late 2008, the survey was distributed with the HER2 immunohistochemistry (IHC) proficiency testing program. It included questions regarding institutional and pathology practice characteristics, assay validation using fluorescence in situ hybridization (FISH) or another IHC laboratory test, and pathologist HER2 scoring competency assessment.

Results: We received 757 of 907 surveys. The median laboratory accessioned 15,000 cases and annually performed 190 HER2 tests. Quantitative computer image analysis was used by 33% of laboratories. In-house FISH was performed in 23% of laboratories. Sixty percent of laboratories addressed the 6- to 48-hour tissue fixation requirement by embedding tissue on the weekend. HER2 testing was performed on the initial biopsy in 40% of laboratories; on the resection specimen in 6%; and either in 56%. Forty-seven percent of laboratories validated with FISH only, 10% with another IHC test only, 13% with both; 12% had not validated; 15% chose “not applicable.” Ninety percent concordance rate with FISH results was achieved in 88% IHC-negative and 81% IHC-positive cases. Ninety percent concordance rate with another IHC test was achieved in 80% negative and 75% positive cases. Ninety-one percent of laboratories had a pathologist competency assessment program.

Conclusions: This survey demonstrates the extent and characteristics of HER2 testing. Although some ASCO/CAP guidelines have been implemented, gaps remain in validation of HER2 IHC testing.
neoadjuvant treatment and compares the differences in the rates for cases evaluated using tumor imprint cytology (TIC) versus TIC and/or frozen section.

Design: We reviewed 174 consecutive cases with intraoperative evaluation of axillary sentinel lymph nodes using both TIC and/or frozen section. The rates of FN, true positive, true negative, and false positive were determined by correlation with permanent hematoxylin-eosin sections. Completion axillary dissection, if performed, was also reviewed.

Results: Thirty-one (18.0%) had neoadjuvant treatment, while 82.2% did not have neoadjuvant treatment (Table). One hundred thirty-three (76.4%) cases were evaluated by TIC only, while 23.6% were evaluated by TIC and/or frozen section (4 cases were evaluated by FS only). There was no false-negative intraoperative diagnosis. Of the 22 total FN, 40.9% had metastasis on permanent hematoxylin-eosin sections larger than 2 mm, while 59.1% had isolated tumor cells (13.6%) and micrometastases (45.5%). For cases with completion axillary dissection, only 7.1% of the FN intraoperative diagnosis had additional positive lymph nodes, compared with 64% in patients with a true-positive intraoperative diagnosis.

Conclusions: The relatively higher rate of FN in patients with prior neoadjuvant treatment may be due to treatment-induced fibrosis. There appears to be a low chance of additional positive lymph nodes on completion axillary dissection with FN intraoperative diagnosis.

### Discordance Between the Immunohistochemical (Estrogen Receptor, Progesterone Receptor and HER2/neu) Characteristics in Primary Breast Cancer Versus Axillary Lymph Node Metastases: Should Lymph Node Metastases Be Retested?

(Poster No. 25)

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**Context:** Patients with stage III breast carcinoma and similar hormone receptor and HER2 gene product status by immunohistochemistry may respond differently to similar therapeutic regimens. The therapy is generally based on the immunohistochemical features of the primary breast tumor, and the metastatic axillary lymph nodes are never tested. We hypothesize that discordance in the immunohistochemical features between the primary tumor and the axillary lymph node metastases might explain different clinical responses to hormonal treatment and/or chemotherapy. In previously published studies, the discordance varied from 0% to 14% for HER2 and from 15% to 37% for estrogen receptor and progesterone receptor.

**Design:** Danbury Hospital’s electronic medical records from the last 2 years were searched to find patients with surgical excisions of primary breast carcinoma and axillary lymph node metastases by axillary lymph node dissection and/or sampling. Only patients who had not received any adjuvant treatment before surgery were included. The paraffin blocks of axillary lymph node metastases were retrieved, cut, and stained for estrogen receptor, progesterone receptor, and HER2/neu by immunohistochemistry, and the results were compared with those for the previously stained primary breast carcinomas.

**Results:** Twenty-nine patients with the previously described tissues were available for study. Discordance percentages were calculated, and a 95% Fisher exact confidence interval was created for each discordance proportion (Table).

### MRE11, RAD50, and NBS1 Gene Expression in Breast Cancer Progression

(Poster No. 27)

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**Context:** MRE11, RAD50, and NBS1 comprise the MRN protein complex involved in DNA double-strand break repair and are reportedly downregulated in invasive breast carcinoma. We compare MRN levels in benign breast tissue, carcinoma in situ, and invasive carcinoma.

**Design:** Western blot analysis was performed on HMT-3522 cell lines (benign S1, preinvasive S3-C, invasive T4-2 cells) grown in 2- and 3-dimenional cultures. Forty-seven randomly selected cases of invasive breast carcinoma with adjacent in situ tumor and benign epithelium were immunohistochemically stained with antibodies to MRE11, RAD50, and NBS1 (BD Biosciences, San Jose, California). Two pathologists independently scored nuclear staining, using a 0 to 3 scale (negative to strongly positive). Cohort analysis was performed to compare staining between tissue types using a linear model with the tissue type and pathologist as explanatory variables. Variance component due to tissue type was tested using F-distribution (SAS Software, Cary, North Carolina). A P value of .01 or less was considered significant.

**Results:** Western blot analysis showed MRN protein levels decreasing progressively between S1, S3-C, and T4-2 cells (Figure 20). There were
significant differences in expression between benign and in situ, in situ and invasive, and benign and invasive tissues for all 3 proteins (P < .01), except for NBS1 when comparing in situ with invasive (P = .07) at 1% significance level and adjusted for interobserver variability.

Reevaluation of Diagnostic Value of p120 catenin in Differentiating Lobular Carcinoma From Low-Grade Ductal Carcinoma of the Breast

(Poster No. 28)

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Context: The confirmation of lobular carcinoma is usually based on negative E-cadherin staining. A recent study reports that p120 catenin is a sensitive and specific positive marker for lobular carcinoma, with strong and diffuse cytoplasmic staining. To our knowledge, there are few follow-up published studies.

Design: Forty-four cases of invasive lobular carcinoma (ILC) and 26 cases of low-grade invasive ductal carcinoma (IDC) were included in this study. Eighteen of 44 ILC cases also contained lobular carcinoma in situ. All ILC cases were negative for E-cadherin, and all IDC cases were positive for E-cadherin. Most cases (n = 65) also contained normal breast tissue. Immunohistochemical staining was performed with monoclonal antibody to p120 catenin (clone 98; 1:200 dilution; BD Biosciences, San Jose, California). The staining intensity was graded as weak, moderate, or strong. The distribution was recorded as negative, 1+, 2+, 3+, and 4+.

Results: All ILC cases were positive for p120 catenin, with strong and diffuse cytoplasmic staining (greater than 3+) in 34 of 44 (77%) cases and moderate to weak staining in 10 (23%) cases. All IDC cases were positive for p120 catenin, with strong and diffuse membranous staining (greater than 3+) in 22 of 26 cases. Four IDC cases showed focal (1+ or 2+) and weak membranous staining.

Conclusions: Our data show that p120 catenin is useful in differentiating ILC from IDC. However, caution should be taken: Twenty-three percent of ILCs showed moderate to weak cytoplasmic and membranous staining, and a small portion of IDCs showed only focal and weak membranous staining.

Detection of Chromosomal Anomalies in Uterine Endometrial Carcinoma Using Fluorescence In Situ Hybridization (UteroFISH)

(Poster No. 30)

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Context: Endometrial cancer is the most common pelvic gynecologic malignancy. The diagnosis of well-differentiated endometrial adenocarcinoma, atypical hyperplasia, and marked hyperplasia is often challenging. We investigated the utility of chromosomal anomalies for the detection of endometrial carcinoma using multitarget fluorescence in situ hybridization (FISH).

Design: Samples were collected by endometrial brush and processed by liquid-based thin-layer cytologic preparation protocol. We collected samples from consecutive cases to include 50 benign, 50 hyperplasia without atypia, 50 atypical hyperplasia, and 50 endometrial cancers. Each was hybridized using fluorescence labeled DNA probes to chromosomes 1, 8, and 10 (UteroFISH). FISH signals were enumerated in 100 cells per case, and the chromosomal anomalies were correlated with pathologic findings, including histologic diagnoses on endometrial tissue samples.

Results: Numeric chromosomal anomalies were found in 0% (0 of 50) of benign, 20% (10 of 50) of hyperplasia, 76% (38 of 50) of atypical hyperplasia, and 86% (43 of 50) of carcinoma specimens. The mean percentage of cells with chromosomal changes was 54% in cancer specimens, which was significantly higher than in nonatypical hyperplasia (13%, P < .001) and atypical hyperplasia (34%, P < .001). The most frequent chromosomal anomaly was gain of chromosome 1. FISH anomalies had an overall sensitivity of 81% and specificity of 90% for the detection of atypical hyperplasia and/or endometrial carcinoma. There was no association with grade of endometrial carcinoma.

Conclusions: Multitarget UteroFISH appeared to be useful for the differential diagnosis of reactive hyperplasia, atypical hyperplasia, and endometrial adenocarcinoma, showing a high level of sensitivity and specificity. Endometrial hyperplasia with chromosomal anomalies may require close follow-up.
lymph nodes were involved by metastatic disease. Histologically, the carcinomatous component was composed of high-grade endometrioid adenocarcinoma, focal clear cell carcinoma, and areas of keratinizing squamous cell carcinoma. A high-grade homologous sarcomatous component was sharply demarcated from the carcinomatous elements. No heterologous sarcomatous component and no lymphatic or vascular invasion were identified. Radiologic imaging included a chest computed tomography scan, which showed multiple pulmonary nodules suspicious for metastatic disease and involving both lungs. Given the complexity and extreme rarity of these tumors and the absence of a large volume of clinical data regarding cervical MMMTs, it is important that all cases be documented as thoroughly as possible to ensure appropriate disease treatment and prognosis.

**Twin Reversed Arterial Perfusion Sequence: A Review of 9 Cases With an Emphasis on the Cord Insertion**

(Roster No. 32)

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**Context:** The etiology of twin reversed arterial perfusion sequence has not been clearly defined, even though it remains one of the most severe consequences of monochorionic twinning. All theories include one main point: intraplacental vascular communication supporting growth of acardiac fetus.

**Design:** We retrospectively reviewed the acardiac accephalus twin gestations during a 19-year period (1990–2008). Nine cases were identified, and the placentas and obstetrical histories were reviewed.

**Results:** Seven of 9 were monoamniotic-monochorionic and 2 of 9 were diamniotic-monochorionic twin placentas. Vascular communications were identified in 7 cases. The other 2 cases were miscarred and inappropriate for vascular communication assessment. Five of 9 demonstrated velamentous umbilical cord insertions; 3 cords were marginally and 1 was eccentrically inserted. Five cords supplying the acardiac fetus had a single umbilical artery; 2 cords had 3 vessels, and 2 cords were severely macrocephalus, meaning the number of vessels could not be accurately assessed.

**Conclusions:** Velamentous cord insertions occur in approximately 1% of placentas and more frequently in multiple gestations. The most serious consequence of velamentous insertions is rupture of unprotected vessels resulting in fetal morbidity and mortality. Twin transfusion syndrome is also associated with velamentous cord insertion. We believe a special type of velamentous cord insertion at the dividing membrane may lead to unidirectional shifting of blood flow from the pump twin to the acardiac cotwin. Characterization of umbilical cord insertion is important in understanding this entity, as there is a need to better assess factors that influence the hemodynamics of vascular communication in the placentas and fetal maldevelopment.

**Cutaneous Heterotropia of Cervix: Use of Molecular Tissue Identity Genotyping to Support Diagnosis**

(Roster No. 33)

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Cutaneous derivatives in cervix is a rare type of cervical heterotropia (CH). Diagnostic certainty depends on definitively excluding preanalytical contamination. We used a molecular tissue identity genotyping method to exclude preanalytical contamination. A 56-year-old postmenopausal woman with negative Papanicolaou tests was referred to the gynecology clinic for evaluation of a small polyp-like lesion on the cervix. We biopsied this lesion, which was at the 9-o’clock position. It contained 2 distinct tissue fragments. The first fragment was unremarkable ectocervix. The second fragment showed squamous epithelium with multiple underlying hair follicle-like structures and surrounding inflammatory infiltrate suggestive of H. To rule out preanalytical contamination, we analyzed both fragments for tissue identity using a pinpoint method for DNA extraction (Zymo Research, Orange, California) and polymerase chain reaction (PCR) amplification of microsatellite markers using ABI AMF/STR Identifier kit (ABI, Foster City, California). PCR products were analyzed by capillary electrophoresis, and allelic assignment was done using Gene Mapper software (ABI). The frequency of randomly matching 2 individuals in the North American population using this method is less than 1 in 82 billion. Complete match of 16 tissue identity alleles was present, confirming identical genotype of both tissue fragments and excluding preanalytical contamination. The colposcopic examination and histologic findings coupled with this information supported the diagnosis of this rare entity. Exclusion of preanalytical contamination by molecular tissue identity genotyping, along with clinical and histologic findings, increases the diagnostic certainty of cutaneous CH. Our findings support this entity being of acquired metastatic inflammatory origin instead of an aberrant embryonic or fetal implantation disorder.

**Squamous Cell Carcinoma Diagnosed by Colonic Biopsy: Case Report of Malignant Transformation of a Mature Cystic Teratoma**

(Poster No. 34)

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Primary squamous cell carcinoma (SCC) of the colon is an exceedingly rare malignancy, occurring in 0.25 to 1 per 1000 colorectal carcinomas. Colorectal SCC most commonly represents metastasis or tumor extension, which is likely from cervical or vaginal carcinomas in female patients. We describe the case of a 72-year-old woman who presented with increased abdominal girth and a 50-lb weight loss. CA 19.9 and carcinoembryonic antigen tumor markers were elevated. A colonoscopy revealed a necrotic mass that was 25 cm from the anal verge. A colon biopsy showed detached fragments of keratinizing SCC. A subsequent computed tomography scan of the abdomen and pelvis showed a 16-cm right adnexal mass that was inseparable from the colon. The patient underwent a hysterectomy with bilateral salpingooophorectomy and partial colectomy. The right ovary showed a 30.5-cm cystic teratoma with hair, sebaceous material, and an 11-cm solid mass that extended to the adjacent colonic wall (Figure 21). Histologically, arising from the mature cystic teratoma was a keratinizing SCC that extended into the colonic submucosa. Immunohistochemistry was positive for p63 and negative for p16. Malignant transformation occurs in less than 2% of ovarian cystic teratomas and is most commonly SCC. In locally advanced tumors, transmural extension into the adjacent colon occurs. This case illustrates a rare example of malignant transformation of cystic teratoma that was first diagnosed by colonic biopsy.

**CD10 Immunoreactivity in Metaplastic and Neoplastic Squamous Lesions of the Endometrium and Cervix and Its Potential Diagnostic Applications**

(Poster No. 35)

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**Context:** The utility of CD10 immunohistochemistry in the differential diagnosis of cutaneous heterotropia of cervix. Use of molecular tissue identity genotyping to support diagnosis.

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**Abstracts**
diagnosis of endometrial stromal lesions and mesonephric glands is established. However, there are limited data available regarding CD10 expression in metastatic and neoplastic squamous epithelial lesions of the female genital tract.

**Design:** We examined the expression of CD10 in a series of 278 cervical lesions (99 invasive squamous cell carcinoma, 14 invasive adenocarcinoma, 118 squamous dysplasia, 12 adenocarcinoma in situ, and 35 squamous metaplasia) and 151 endometrial lesions (104 endometrial carcinoma, 42 complex hyperplasia, and 5 atypical polypoid adenomyoma). CD10 immunoreactivity was analyzed on a 4-tier scale and was correlated with clinicopathologic features, the presence and type of squamous differentiation, and patient outcome.

**Results:** Benign tissues showed no CD10 immunoreactivity. CD10 reactivity was seen in 48 of 118 (41%) squamous dysplasias and in 34 of 99 (34%) invasive squamous cell carcinomas of the cervix; it was also associated with improved recurrence-free survival (P < .03). In contrast, invasive and in situ cervical adenocarcinomas showed no CD10 expression. No CD10 activity was observed in glandular components of endometrial lesions, including adenocarcinomas with keratinizing squamous differentiation. However, strong, diffuse CD10 staining was seen in nonkeratinizing squamous metaplasia present in these lesions.

**Conclusions:** In contrast to squamous metaplasia, CD10 immunoreactivity is present in dysplastic and neoplastic cervical squamous lesions and may be a useful marker in predicting patient outcome. Strong CD10 immunoreactivity in nonkeratinizing squamous metaplasia in endometrial lesions may be a useful marker in their differentiation from solid glandular growth of adenocarcinomas and may aid in tumor grading in difficult cases.

**Adenoid Basal Carcinoma of the Cervix:**

**Two Cases of a Rare Pathologic Entity With Distinctive Ages of Presentation**

(Poster No. 36)

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Adenoid basal carcinoma is a very rare neoplasm of the cervix, classically presenting in postmenopausal women (median age 65) in association with high-grade squamous dysplasia of the cervix. The relative rarity of this lesion has kept it an enigma in regard to its precise biologic evolution, but the lesion has been associated with high-risk human papillomavirus type 16 DNA. The first case of adenoid basal carcinoma encountered at our institution (2004) was an asymptomatic lesion in a 25-year-old woman that was diagnosed on cervical conization subsequent to a previous biopsy demonstrating high-grade squamous dysplasia (CIN III). Smooth irregular nests of bland glandular and mildly atypical squamous cells surrounded by basal epithelium were noted. A p16 stain was focally positive in the tumor. A Ki-67 stain subsequently demonstrated a low proliferation index. The second case of adenoid basal carcinoma (2008) was diagnosed in a 63-year-old woman on cervical conization for severe squamous dysplasia (CIN III). A p16 stain demonstrated strong diffuse positivity within the overlying high-grade epithelial dysplasia and within the deeper well-differentiated adenoid basal carcinoma component. Ki-67 showed a low proliferation index with markedly decreased staining compared with the overlying dysplastic epithelium. Adenoid basal carcinoma is a rare neoplasm of the cervix that usually occurs in association with overlying squamous dysplasia. Although adenoid basal carcinoma appears to be associated with high-risk human papillomavirus, this neoplasm has a low proliferation index and excellent prognosis and may present as an incidental finding in women of any age.

**An Increase in Uterine Natural Killer Cells in First Trimester Miscarriages With Karyotypic Abnormalities: A Flow Cytometry/Cytogenetic Correlation**

(Poster No. 37)

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**Context:** It has been reported that uterine natural killer cells (uNKCs) may play a role in first trimester miscarriages. The function of these cells in human pregnancy is not completely known; however, they are thought to support placentation growth through angiogenesis and immune modulation at the maternal-fetal interface. The most common etiology of miscarriage is karyotypic abnormalities. Therefore, in an effort to understand the relationship of these cells to miscarriage, we determined the percent of uNKCs and compared that with the presence or absence of karyotypic abnormality.

**Design:** Two products of conception specimens from women who miscarried in their first trimester (6–12 weeks) were submitted for cytogenetic analyses and were prospectively studied for CD56+ uNKCs via flow cytometry.

**Results:** Fifteen patients had an abnormal karyotype; findings included both numerical and structural abnormalities. In 5 specimens, the karyotype was normal. The mean uNK percent for cases with karyotypic abnormality was 8.76% (range, 0.18%–38.67%), and the mean uNK percent for cases with no karyotypic abnormality was 0.84% (range, 0%–1.83%; P value = .02).

**Conclusions:** The percent of uNKs found in samples with karyotypic abnormality is significantly statistically higher than in samples with normal karyotypes. To our knowledge, this is the first study that correlates the 2 parameters. This finding may be of benefit, possibly indicating a surrogate marker for early detection of karyotypic abnormalities. Additionally, continued study of uNKs in human products of conception by flow cytometry may help to elucidate the role these cells play in miscarriage.

**Primary Peritoneal Carcinosarcoma in Conjunction With Tubal Intraepithelial Dysplasia**

(Poster No. 38)

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A 62-year-old woman (gravidity 2, para 2) presented with abdominal pain. The abdominal imaging showed bilateral adnexal masses without a definite connection to the uterus. An exploratory laparotomy was performed to establish a diagnosis. The tumor extensively involved the uterine serosa and parametrial tissue as well as 2 foci on the sigmoid colon serosa. Histologically, the tumor was composed of high-grade, pleomorphic, solid nests of epithelial cells with intervening hyaline cartilage. No involvement of the endometrium was seen. The left fallopian tube had diffuse serous tubal intraepithelial carcinoma, while the right fallopian tube had focal serous tubal intraepithelial carcinoma. Immunohistochemical stains for CD5 and WT-1 were positive in the epithelial portion of the carcinosarcoma. The left fallopian tube showed overexpression of both p53 and MIB-1. The right fallopian tube showed focal overexpression of p53. Primary carcinosarcoma of the peritoneum (malignancy mixed Mullerian tumor) is a rare, aggressive entity. Presumably, the tumor arises from cells of the "secondary mullerian system," which is the peritoneal mesothelium and adjacent mesenchyme of the pelvis and lower abdomen. Although previously considered to be a collision tumor, carcinosarcomas are now thought to be metastatic carcinoma with monoclonal epithelial and mesenchymal components. To our knowledge this is the first case of carcinosarcoma with concurrent serous tubal intraepithelial carcinoma, a precursor to pelvic serous carcinoma. Although coincidental concurrence is possible, this case represents a possible link between carcinosarcoma and serous carcinoma, or at least a possible common precursor lesion.

**Comparison of Polymerase Chain Reaction and In Situ Hybridization Methods for Detection of Cervical Human Papillomavirus Infection: Cases That May Not Be Identified by Polymerase Chain Reaction But That May Be Detected by In Situ Hybridization**

(Poster No. 39)

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**Context:** Detection of epithelial cell abnormalities by cervicovaginal cytology screening necessitates human papillomavirus (HPV) testing. Although polymerase chain reaction (PCR) is a very sensitive method for detecting HPV, it still results in some cases being undiagnosed.

Abstracts

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Design: Results from 108 cervicovaginal liquid-based cytology samples analyzed for the presence of HPV DNA by PCR were compared with the results of in situ hybridization (ISH) on 108 cervical biopsies obtained from the same patients using commercial HPV probes and primers.

Results: Positive ISH signals for high-risk, low-risk, and both high- and low-risk HPV types were observed in 70 of 108 (64.8%), 9 of 108 (8.3%), and 5 of 108 (4.6%) cases, respectively, whereas negative signals were found in 24 of 108 (22.2%) cases. By PCR, 52 of 108 (48.2%), 7 of 108 (6.5%), and 5 of 108 (4.6%) cases were positive for the respective HPV risk types. Eight (7.4%) patients were positive for unknown HPV risk types, and in 36 (33.3%) patients, PCR was negative. The degree of concordance between PCR and ISH was 69.4% (75 of 108) for all samples (Table). Interestingly, 16 of 108 (14.8%) cases were negative for HPV by PCR but positive by ISH in cervical biopsies.

Conclusions: A higher number of positive results were detected by ISH in tissue biopsies (84 of 108; 77.8%) than by PCR in liquid-based cytologic specimens (73 of 108; 67.6%). In our series, ISH was an adequate method for detecting HPV in high-grade lesions with similar efficacy to PCR. Patients with abnormal cervicovaginal cytology and undetectable HPV on testing with PCR could be tested by ISH on biopsy specimens.

### Comparison of Detection of Different Risk Types of HPV DNA Using PCR and ISH

<table>
<thead>
<tr>
<th></th>
<th>High-Risk Type HPV DNA (PCR), No. (%)</th>
<th>Low-Risk Type HPV DNA (PCR), No. (%)</th>
<th>High- and Low-Risk Type HPV DNA (PCR), No. (%)</th>
<th>Negative (PCR), No. (%)</th>
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</thead>
<tbody>
<tr>
<td>High-risk type HPV DNA (ISH), No (%)</td>
<td>47 (43.5)</td>
<td>3 (2.8)</td>
<td>0 (0)</td>
<td>13 (12)</td>
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<td>Low-risk type HPV DNA (ISH), No (%)</td>
<td>2 (1.9)</td>
<td>4 (3.7)</td>
<td>1 (0.9)</td>
<td>2 (1.9)</td>
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<tr>
<td>Low- and high-risk type HPV DNA (ISH), No (%)</td>
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<td>0 (0)</td>
<td>4 (3.7)</td>
<td>1 (0.9)</td>
</tr>
<tr>
<td>Negative (ISH), No (%)</td>
<td>3 (2.8)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>20 (18.5)</td>
</tr>
</tbody>
</table>

### PAX8: An Immunohistochemical Marker for Endometriosis

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Conclusions: We observed PAX8 expression in all 22 cases of endometriosis, which may be a marker for the mullerian system and that PAX8 immunohistochemistry may be a sensitive method for diagnosing endometriosis.

### Invasive Paget Disease of the Vulva With Concurrent Basal Cell Carcinoma

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We report a case of an 81-year-old woman who had a granular, red-vulvar lesion that she had noticed for more than a year. The vulvectomy specimen showed invasive vulvar Paget disease with concurrent basal cell carcinoma (BCC). This is the first reported case of BCC associated with invasive vulvar Paget disease and the second reported case of concurrent vulvar Paget disease and BCC. The epidermis showed nests of cells with abundant clear cytoplasm, large pleomorphic nuclei with vesicular chromatin, and conspicuous nucleoli. These malignant cells were also seen infiltrating the dermis in direct continuity with the intraepidermal component. The overlying and adjacent epithelium showed extensive pseudoepitheliomatous hyperplasia and several foci of BCC arising immediately adjacent to Paget disease. The intraepidermal nests of malignant cells showed immunoreactivity for cytokeratin (CK) 7 and were negative for CK20, S100 protein, Melan-A, and HMB-45. The infiltrating component showed the same immunoprofile. The diagnosis of invasive Paget disease was based on cytologic similarities and intimate association of the intraepidermal and invasive components as well as their shared immunoprofile. The overlying squamous epithelium and pseudoepitheliomatous hyperplasia were positive for high-molecular-weight cytokeratin and negative for CK7. The BCC was weakly positive for CK7. Because the BCC in this case arose in an ulcerated reactive epidermis with pseudoepitheliomatous hyperplasia, it is possible that Paget disease was the predisposing factor for the development of BCC. However, we cannot rule out the possibility that the 2 lesions developed independently.

### Severe Dysplasia and Adenocarcinoma In Situ Within an Endocervical Polyp

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Endocervical polyps, the most common benign neoplasia of the uterine cervix, are frequently seen in multigravid women during the fourth to sixth decades of life. The polyps can present with vaginal discharge or bleeding. In situ and invasive carcinoma arising in endocervical polyps is extremely rare. The incidence of squamous dysplasia in polyps is estimated between 0.5% and 2%. The association between adenocarcinoma in situ and squamous dysplasia of the cervix is well known; however, the coexistence of squamous dysplasia and adenocarcinoma in situ within an endocervical polyp has not been previously described. We present a case of an endocervical polyp with severe dysplasia and associated adenocarcinoma in situ. We searched Tufts Medical Center’s archival files from 1998 to 2008 (1004 cases) for the diagnosis of dysplasia and adenocarcinoma in situ arising in cervical polyps. We found 9 (0.89%) cases with...
squamous dysplasia, including CIN 1 (0.39%), CIN 2 (0.09%), and CIN 3 (0.39%). No other cases of severe dysplasia with adenocarcinoma in situ were found. A 58-year-old woman presented with episodic postmenopausal spotting. Pelvic examination revealed atrophic changes in the external genitalia and vagina and a 1.5-cm reddish polyp at the cervical os. Histologic findings showed an endocervical polyp with focal severe squamous dysplasia (CIN 3) (Figure 22, A) and focal adenocarcinoma in situ (Figure 22, B). Carcinoma arising in endocervical polyps is very uncommon and carries an excellent prognosis if limited to the polyp. A subsequent hysterectomy revealed no residual tumor or dysplasia.

**Immunohistochemical Study of Squamous Morules and Stromal Changes in Endometrial Hyperplasia**  
*(Poster No. 43)*

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**Context:** Morules are nonkeratinizing squamous metaplasia that frequently occur in association with endometrial hyperplasia; their histogenesis and role in the development of endometrial hyperplasia are unknown.

**Design:** Hematoxylin-eosin–stained glass slides of 247 consecutive cases of endometrial hyperplasia were reviewed for the presence of squamous morules. Cases with squamous morules were stained with CD10 (marker of endometrial stromal cells) and α-smooth muscle actin (αSMA) immunostains. Immunoreactivity was assessed based on the topographic location of the proteins and intensity of immunoreactivity.

**Results:** Squamous morules were detected in immunostained sections of 19 cases, and they stained strongly positive for CD10 and negative for αSMA in 18 of 19 cases. This finding was associated with complete loss of CD10 expression in the stroma immediately adjacent to the CD10-expressing squamous morules. There was also an overall decrease in CD10 expression in the stromal cells of endometrial hyperplasia, regardless of whether it was simple or complex hyperplasia. The decrease in CD10 expression ranged from reduction in the intensity of the immunoreactivity to negative immunohistochemical reaction in some areas. In endometrial hyperplasia, patchy to diffuse expression of αSMA was noted in the stromal cells, especially in the peripheral areas.

**Conclusions:** The expression of CD10 by the squamous morules suggests squamous metaplasia in endometrial hyperplasia to be of stromal origin. The downregulation of CD10 in the stroma of endometrial hyperplasia and the concurrent acquisition of αSMA expression by the stromal cells supports the hypothesis that changes in the endometrial stroma may play a very significant role in the pathogenesis of endometrial hyperplasia.

**Placental Chorioangioma Associated With Diffuse Fetal Vascular Malformations**  
*(Poster No. 44)*

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Chorioangioma is the most frequently occurring nontriphloblastic tumor of the placenta. Vascular anomalies of the placenta associated with fetal vascular malformations are rarely described. We report on a fetoscopy case in which a chorioangioma of the placenta was associated with vascular malformations of the adrenals, bladder, heart, liver, lungs, spleen, and soft tissue of a 21-week-old fetus. We studied the expression of CD34, CD31, vimentin, factor VIII, and cytokeratin in these lesions. The same expression patterns were seen in the lesions of both the placenta and the fetus. The vascular anomalies in the fetus may be related to the chorioangioma of the placenta.

**Thyroid Transcription Factor–Positive Primary Endocervical Adenocarcinoma**  
*(Poster No. 45)*

Siem Khelifa, MD; Daniela Mihova, MD (damihova@yahoo.com); Marietta Kintiroglou, MD. Department of Pathology, St Barnabas Medical Center, Livingston, New Jersey.

**Context:** Thyroid transcription factor 1 (TTF-1) is considered a reliable marker in distinguishing primary and metastatic adenocarcinomas of the lung from metastatic tumors of other origin. A challenging case of TTF-1–positive primary endocervical adenocarcinoma metastatic to the mediastinum in a 63-year-old patient interested us, leading us to conduct a study exploring the expression of TTF-1 in primary endocervical adenocarcinoma cases diagnosed at our institution.

**Design:** Twenty cases of primary endocervical adenocarcinoma with no previously known history of any cancer were retrieved from our archived data and matched against 20 negative control cases of benign endocervical biopsies/excisions. Cases were matched using age and date of exploration as criteria. TTF-1 staining was performed on the 40 cases. TTF-1 positivity was defined by a nuclear pattern (scored from 0 to 3+).

**Results:** Of 20 cases of primary endocervical adenocarcinoma, 1 (5%) case was TTF-1 strongly positive (nuclear score 3+). Of 20 cases of negative controls, 0 (0%) cases were TTF-1 positive. The TTF-1–positive case was a primary noninvasive endocervical adenocarcinoma in a 37-year-old patient with no history of malignancy.

**Conclusions:** In our study, 1 of 20 (5%) of the selected primary endocervical adenocarcinomas were TTF-1 positive, whereas none of the benign cervical tissues were positive. The mechanism behind TTF-1 positivity in tumors of other origin than lung or thyroid is not well understood. While waiting for larger studies exploring TTF-1 in different kinds of tumors we should be overly cautious when dealing with a TTF-1–positive metastasis, especially in the absence of clinical pulmonary and thyroid history.

**Morphoproteomic Evidence of a Constitutively Activated and Overexpressed Signal Transducer and Activator of Transcription-3 Pathway With Interleukin 8 Coexpression in Cervical Cancer and High-Grade Dysplasia**  
*(Poster No. 46)*

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**Context:** Interleukin 6 (IL-6) is known to be associated with cervical cancer, promoting tumor growth via activation of the signal transducer and activator of transcription 3 (STAT3) pathway. Recent literature also describes increased levels of IL-6 transfection by human papillomavirus type 16, E6 and E7 genes. Both IL-6 and IL-8 levels are increased in cervicovaginal secretions of patients with cervical cancer. IL-8 is a target gene of STAT3. In this study, we apply morphoproteomics to investigate the STAT3 pathway in cervical cancer and dysplasia.

**Design:** A tissue microarray comprised of benign cervical tissue, high-grade dysplasia, and invasive squamous cell carcinoma was assembled. Immunohistochemical probes using monoclonal antibodies to STAT3 phosphorylated (p-STAT3) on tyrosine 705 and to IL-8 were applied. Results were graded according to intensity of staining (0–3+) and percentage of cells stained (0%–100%).

**Results:** Our data showed no immunoreactivity for IL-8 and only rare nuclear expression of p-STAT3 in basal cells of the benign squamous epithelium. Ninety-five percent of cancer and dysplasia cases showed strong positivity (2+–3+) for nuclear p-STAT3. Additionally, all cases of carcinoma and dysplasia were strongly positive for IL-8. There was no difference in the intensity or quantity of staining between high-grade dysplasia and invasive squamous carcinoma for these protein analytes.

**Conclusions:** Morphoproteomic analysis showed constitutive activation and overexpression of the STAT3 pathway in invasive squamous cell carcinoma and high-grade dysplasia versus nonneoplastic cervical mucosa by virtue of p-STAT3 (Tyr 705) nuclear expression and correlative expression of IL-8.
Adenoid Cystic Carcinoma of the Bartholin Gland: Case Report and Review of Literature (Poster No. 47)

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Primary adenoid cystic carcinoma of the Bartholin gland is a very rare neoplasm, which is characterized by slow growth, perineural invasion, and a high propensity for recurrence. We report a case of a 65-year-old woman who presented with complaints of vaginal pressure and an enlarging cystic-like structure in her vagina. A partial deep vulvectomy was performed. Pathologic examination revealed an ovoid portion of pink-tan soft tissue that measured 2.5 x 16 cm. Microscopic examination revealed numerous sheets and nests of small, uniform, polygonal to rounded neoplastic cells, displaying a predominantly cribriform pattern with variable sized spaces. Focally, some of these spaces contained amorphous eosinophilic material. Also present were single cords of malignant cells infiltrating the stroma. There were rare foci of perineural invasion, as well as foci suspicious for lymphovascular invasion by the neoplasm. The tumor was extensively present at the peripheral surgical margins of the specimen. Currently, due to the small number of cases and lack of well-defined prognostic parameters, there is no consensus regarding the optimal treatment for primary adenoid cystic carcinoma of the Bartholin gland. A review of cases in the literature from 1985 to the present revealed that infiltrated the stroma. There were rare foci of perineural invasion, as well as foci suspicious for lymphovascular invasion by the neoplasm. The tumor was extensively present at the peripheral surgical margins of the specimen. Currently, due to the small number of cases and lack of well-defined prognostic parameters, there is no consensus regarding the optimal treatment for primary adenoid cystic carcinoma of the Bartholin gland. A review of cases in the literature from 1985 to the present revealed that margin status does not appear to play a significant role in outcome. Additionally, the use of adjuvant radiation therapy may be beneficial when coupled with local excision, partial vulvectomy, or hemivulvectomy, regardless of margin status.

Validation of a Novel Fluorescence In Situ Hybridization Assay and Comparison to p16, Topoisomerase II, and MDM2 Protein Status in Cervical Squamous Intraepithelial Neoplasia (Poster No. 48)

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Context: Human papillomavirus is important for the development of cervical carcinoma. Parallel diagnostic immunohistochecmical assays were developed, including p16 test and ProExC (topoisomerase II and MDM2) kits, to differentiate dysplastic lesions and their mimickers. Comparative genomic hybridization has identified genetic and chromosomal alterations as early events in the progression of cervical dysplasia to carcinoma. Several genes and chromosome-targeted probes have been developed. We assessed a novel fluorescence in situ hybridization (FISH) probe set and other gene/chromosome probes for their diagnostic utility.

Design: Forty-three cervical tissue samples were tested against p16 (clone JC8), ProExC testing kit, and 7 FISH probes against p16, chromosome 3 centromere, TERC gene, chromosome 7 centromere, chromosome 8 centromere, MYC gene, and chromosome 17 centromere. Diagnoses ranged from reactive to high-grade lesions.

Results: p16 showed excellent positive predictive value (95%) and negative predictive value (98%) for high-grade cervical intraepithelial lesions. ProExC had 100% positive predictive value and 100% negative predictive value. Only grade 2 and 3 lesions (65%) showed CEP8 triploidy, MYC triploidy, TERC triploidy, and CEP3 triploidy. The p16 gene status did not correlate with the protein status.

Conclusions: Abnormal p16 protein in high-grade lesions showed no relationship to p16 gene status. The most common genetic/chromosomal anomaly in cervical dysplasia was trisomy, confirming earlier studies. Among all evaluated DNA sequences, TERC, CEP6, and MYC showed the most common abnormalities in high-grade dysplasia. Most grade 1 lesions showed normal genetic findings. Our study also showed that the combination of ProExC and p16 provides more sensitive and specific results.

Primary Heterologous Carcinosarcoma or Malignant Mixed Mesodermal Tumor of the Vulva: A Clinicopathologic Case Study (Poster No. 49)

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Carcinosarcoma of the vulva is a very rare neoplasm. Only 2 vulvar carcinosarcomas in which the carcinomatous component was squamous carcinoma have been reported. The sarcomatous component in one case was osteosarcoma, and in the other case, it was leiomyosarcoma. We present the first case of a primary vulvar adenocarcinomatous carcinosarcoma with homologous leiomyosarcomatous and heterologous osteosarcomatous differentiation. A 51-year-old African American woman presented with a labial mass. She underwent right radical vulvectomy, received whole pelvic radiation therapy, and has been without evidence of disease for 6 months. The multicentric cystic tumor, measuring 7.5 x 6.5 x 3.1 cm, contained papillary excrescences and necrosis, and invaded underlying soft tissue. Microscopically, the adenocarcinomatous component was positive for cytokeratin AE1/AE3 and epithelial membrane antigen; the sarcomatous component contained osteosarcoma and pleomorphic poorly differentiated cells that expressed CD10 and smooth muscle actin. Some of the poorly differentiated sarcomatous cells were also positive for cytokeratin AE1/AE3, which may support the hypothesis that the carcinomatous and sarcomatous components of carcinosarcoma are clonally related; however, further investigation of this tumor is needed. Carcinosarcomas in the female genital tract are usually highly aggressive malignancies with poor clinical prognosis. Therefore, in our case, even though no lymph nodes were available for evaluation and the surgical margins were free of tumor, the patient still underwent whole pelvic radiation therapy postoperatively. Additionally, due to the different histopathologic characteristics, continuous patient follow-up is warranted to monitor clinical outcome for anything unusual and for clinical management.

Endometrial Adenocarcinoma: Intratumor Variability in Estrogen Receptor and Progesterone Receptor Immunostain Results (Poster No. 50)

Sonya Hwang, MD1 (sohwang@notes.cc.sunysb.edu); Harry Hwang, MD1; Allen Gown, MD1; Michael Pearl, MD1; Carmen Tomos, MD2; Departments of Pathology and Obstetrics/Gynecology and Gynecology Oncology, Stony Brook University Medical Center, Stony Brook, New York; and 1Department of Pathology, Phenopath Laboratory, Seattle, Washington.

Context: Estrogen receptor (ER) status and progesterone receptor (PR) status are used as prognostic and treatment indicators for endometrial adenocarcinomas. Many studies have reported variable results regarding correlation among prognosis, clinical stage, and histologic grade. Intratumor differences in receptor status have not been well characterized; this was the purpose of our study.

Design: Twenty-five cases of endometrioid adenocarcinoma with noninvasive and invasive areas were used, with a range of International Federation of Gynecology and Obstetrics grades (10 grade 1, 12 grade 2, and 3 grade 3) and depths of invasion (17 cases ≤50% invasion, 8 cases >50% invasion). Immunostain for ER and PR were performed using an optimized biotin-free, polymer-based immunoperoxidase methodology. The stains were scored as positive (≥10% staining) or negative (<10% staining). In a subset of cases, percentage of tumor and staining intensity (weak, moderate, strong) were evaluated (Table).

Results: In 21 (84%) cases, ER and PR were positive in both noninvasive and invasive areas. In these cases, morphology was similar in the noninvasive and invasive areas. Four cases showed quantitative and qualitative differences in areas of different morphologies; these were analyzed in more detail (Table).

Conclusions: We found no intratumoral differences in ER and PR status in invasive versus noninvasive areas when morphology was the same. However, we did see intratumoral differences in ER and PR immunostains, depending on tumor differentiation. Because ER and PR status may indicate prognosis and treatment, we feel immunostains should be done on the least differentiated areas of tumors to provide the most accurate analysis.
Expression of Thyroid Transcription Factor 1 and Loss of Expression of Estrogen Receptors in Endometrial Adenocarcinoma

(Poster No. 51)

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Context: Thyroid transcription factor 1 (TTF-1) is a relatively sensitive and specific marker for carcinomas of lung and thyroid. In recent studies, TTF-1 expression was observed in tumors other than lung and thyroid, such as small cell carcinoma of the bladder and endometrial and endo-cervical adenocarcinomas. We investigate the expression of TTF-1 and estrogen receptor in endometrial adenocarcinomas.

Design: We immunohistochemically evaluated the expression of TTF-1 on conventional tissue sections in 80 cases of endometrioid adenocarcinoma, including 25 cases of grade I, 35 cases of grade II, and 20 cases of grade III tumors. Two TTF-1 monoclonal antibodies were used (1:25, 8G7C3/1, Cell Marque Corporation, Rocklin, California and 1:50, sc-56606, Santa Cruz Biotechnology, Santa Cruz, California). We recorded staining intensity (weak or strong) and distribution (negative, 1+, 2+, 3+, and 4+).

Results: Strong and diffuse (4+) nuclear staining for TTF-1 was demonstrated in 2 of 80 (2.5%) cases, with identical patterns for both antibodies. Both cases were grade II endometrioid adenocarcinomas, with a positive cytokeratin 7 and negative estrogen receptor profile. In 1 of the 2 cases, a lung metastasis developed 4 years after a hysterectomy.

Conclusions: Our data confirm previous findings with 2 different antibodies against TTF-1; however, the positive percentage is significantly lower than in a previous study (2.5% vs 19%). Caution should be taken when working on an unknown primary because a small portion of endometrioid adenocarcinomas may carry an immunophenotype of cytokeratin 7 positive, TTF-1 positive, and estrogen receptor negative, which is similar to the immunophenotype of a primary adenocarcinoma of lung.

Primary Small Cell Carcinoma of the Endometrium: Case of a Rare and Aggressive Tumor

(Poster No. 52)

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Primary small cell carcinomas of the female genital tract constitute less than 2% of all gynecologic malignancies. Small cell carcinomas of the endometrium are very rare. Most patients present with vaginal bleeding. Macroscopically, the lesions are large, occupying most of the uterus and often showing evidence of an intraabdominal spread. Microscopy shows nests and sheets of small cells with scant cytoplasm, evenly dispersed chromatin, and inconspicuous nuclei. Immunohistochemical stains demonstrate positivity for one or more neuroendocrine markers. Electron microscopy can be used to demonstrate neurosecretory granules. The patient is a 60-year-old postmenopausal woman who presented with vaginal spotting.

Endometrial biopsy was diagnostic of a small cell carcinoma. Gross examination showed an enlarged uterus (770 g) that was almost entirely occupied by a soft, red to brown, ill-defined mass. Microscopy demonstrated an infiltrative lesion composed of small blue cells with scant cytoplasm and a high nuclear-to-cytoplasmic ratio. Vascular invasion was frequent. Immunohistochemical stains for synaptophysin and chromogranin were positive. Malignant cells were negative for cytokeratin, estrogen receptor, and progesterone receptor.

Conclusions: Our data confirm previous findings with 2 different antibodies against TTF-1; however, the positive percentage is significantly lower than in a previous study (2.5% vs 19%). Caution should be taken when working on an unknown primary because a small portion of endometrioid adenocarcinomas may carry an immunophenotype of cytokeratin 7 positive, TTF-1 positive, and estrogen receptor negative, which is similar to the immunophenotype of a primary adenocarcinoma of lung.

Histologic Type, Stage of Disease, and Tumor Grade Are Unrelated Racial Disparity Among Blacks and Whites for Endometrial Cancer

(Poster No. 53)

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Context: It is well known that endometrial cancer varies by race; however, the reason for this disparity remains unclear. Adjusting for clinical pathologic factors may clarify endometrial cancer racial disparities.

Design: Endometrial cancer data were obtained from Surveillance, Epidemiology and End Results registry data (1990-2005). Invasive cancers in blacks and whites were stratified by histologic type and adjusted for stage and grade. Descriptive techniques included age-adjusted temporal trends, age-specific incidence rates, incidence rate ratios, Kaplan-Meier plots, and hazard rates for endometrial cancer-specific deaths. Statistical significance was assessed (α = .05).

Results: There were 81 620 endometrial cancer cases, including 93.0% white individuals and 7.0% black individuals. Age-adjusted incidence rates were higher for whites (incidence rate ratio white to black, 1.38; 95% confidence interval: 1.34, 1.42) and have decreased during the past 15 years, whereas incidence rates for blacks have increased. Despite decreasing rates in mortality, mortality rates for blacks remain significantly higher than for whites (P < .001). Compared with whites, blacks have significantly higher incidence rates of more aggressive histologic types, such as serous carcinoma, clear cell carcinoma, and carcinosarcoma, and higher rates of late-stage and high-grade cancers. Kaplan-Meier plots and hazard rates showed survival was worse for blacks than whites, even after stratifying for histologic type and adjusting for stage and grade.

Conclusions: Endometrial cancer survival rates were worse for blacks than whites, and racial survival disparities persisted even after adjustment for clinical pathologic factors. Histologic type, stage, and tumor grade are not the only determinants that contribute to the disparity seen in endometrial cancer among blacks and whites.

Clinical and Histopathologic Features Differentiating Benign and Malignant Solitary Fibrous Tumors of the Thorax

(Poster No. 54)

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Context: Solitary fibrous tumor of the thorax (SFT) is a rare tumor that may occur benign or malignant. SFTs have a variety of histologic patterns, including patternless pattern and hemangiopericytoma-like and cellular patterns. We investigated the clinicopathologic features differentiating benign SFT from malignant SFT in a series of SFTs excised during a 14-year period at 2 hospitals.

Design: We searched surgical pathology databases (1994-2008) of 2 hospitals, identifying 24 patients with SFT. The surgical pathology reports were reviewed, and the following demographic and histologic features were analyzed: age, gender, location, size, histologic patterns, mitosis, necrosis, nuclear pleomorphism, and immunohistochemistry.

Results: The group consisted of 17 (71%) patients with benign SFT and 7 (29%) patients with malignant SFT. The average age of patients with benign SFT was 48.5 years (range, 20-77 years), whereas the average age of patients with malignant SFT was 69 years (range, 62-76 years). Female to male ratio was 11:6 for benign SFT and 2:5 for malignant SFT. Average tumor size was 4.5 cm for benign SFT and 11.5 cm for malignant SFT. Histologic patterns in benign SFT were 71% patternless pattern, 23% hemangiopericytoma-like pattern, and 6% cellular pattern. Histologic patterns in malignant SFT were 0% patternless pattern, 72% hemangiopericytoma-like pattern, and 28% cellular pattern.

Conclusions: In our series, malignant SFT occurred in patients older than 60 years, tended to have a large tumor size, and had a predominantly hemangiopericytoma-like pattern. Benign SFT occurred in a wide age range (20-76 years), with a slightly female predominance and a predominantly patternless pattern.

Solitary Fibrous Tumor of Pleura: A Rare Macrocytotic Form

(Poster No. 55)

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A 75-year-old woman presented with shortness of breath for 2 months. Respiratory system findings were suggestive of a mass lesion in the left hemithorax. Thorax computed tomography scan showed a soft tissue mass with several macrocysts in the left pleural cavity that was compressing the left lower lobe. Posteroanterior thoracotomy was done for exploration. The tumor was attached to the visceral pleura of lung by a pedicle. Grossly, the surface was smooth and had a shiny, tan-red multilobular appearance. Sectioning revealed a large lobulated tumor (20 × 15 × 15 mm).
Primary Adenoid Cystic Carcinoma of the Bronchus: A Case Report and Review of the Literature

(Poster No. 56)

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Primary salivary gland–like lung cancers are rare neoplasms, constituting less than 0.5% of all respiratory malignancies in the United States. In particular, adenoid cystic carcinoma has been described in the trachea and more rarely in the mainstem bronchus. This carcinoma usually presents clinically as an endobronchial mass lesion, causing obstructive symptoms and pneumonia. We present a rare case of an 82-year-old man who was previously diagnosed with bladder and renal pelvis urothelial carcinomas and an obstructive 1.2-cm endobronchial mass in the left main bronchus. Biopsy and subsequent subtotal resection of the mass showed adenoid cystic carcinoma. Computed tomography showed a noncalcified 1.2-cm nodule within the left main bronchus and arising from the superior wall of the bronchus. The lesion almost completely occluded the bronchus; atelectasis did not occur. The tumor was biopsied and subsequently resected. The tumor was positive for CD34. The staining intensity was graded as weak, moderate, or strong. A value less than 0.5 was considered statistically significant.

Results: Twenty-five of 36 (69%) MMs (21 epithelioid and 4 biphasic) and 2 of 15 (13%) SFTs were positive for D2-40. No D2-40 positivity was detected in pleomorphic carcinomas (n = 13) or synovial sarcomas (n = 3). The difference of D2-40 positivity between MMs and SFTs was significant (P < .001).

Conclusions: D2-40 was highly positive in MM, but it was also positive in a small percentage of SFTs. These findings indicate that D2-40 is a useful marker for MM, but caution should be taken in diagnosing small biopsy specimens of D2-40–positive pleural spindle cell neoplasms, especially in rendering the differential diagnosis between SFT and MM.

An Unusual Presentation of Pulmonary Talcosis in a 55-Year-Old Woman

(Poster No. 58)

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Repetitive inhalational exposure to talc can lead to chronic pulmonary disease. This condition has been reported in millers, miners, and drug abusers but has rarely been associated with exposure to cosmetic talc-containing products. A 55-year-old woman presented with a 3- to 4-month history of progressive dyspnea and cough. She had a history of alcohol and cocaine abuse, which was discontinued approximately 10 years ago. There was no known exposure to occupational dusts, pets, or travel. Chest computed tomography scan revealed evidence of interstitial lung disease. Based on this presentation, differential diagnosis included bronchiolitis obliterans-organizing pneumonia, sarcoidosis, and hypersensitivity pneumonitis. A transbronchial biopsy of the right middle and lower lobes was performed. On microscopic examination, biopsy revealed fragments of lung parenchyma with alveolar septal expansion by non-necrotizing, foreign body–type granulomas. There were scattered multinucleated giant cells, many of which contained polarizable, birefringent, platelike and needle-shaped talc particles. The granulomas and talc particles were not identified in association with blood vessels, ruling out exposure related to intravenous drug abuse. Questioning of the patient revealed no known exposure to talc-containing products, and she admitted only to using a cornstarch-based powder, which she routinely applied to her body after showering. Given her remote history of cocaine abuse, the possibility of talc exposure via inhalation of crushed talc-containing pills was considered. We report a rare case of inhalational pulmonary talcosis with an unclear source of exposure in a 55-year-old woman. This chronic pulmonary disease can progress to interstitial fibrosis, emphysema, and chronic respiratory failure (Figure 24).
Squamous Cell Carcinoma of the Lung Secreting Human Chorionic Gonadotropin and β-Human Chorionic Gonadotropin in a Young Female Smoker
(Poster No. 60)

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A 43-year-old woman presented with dysfunctional uterine bleeding for approximately 1 year. She had a human chorionic gonadotropin level of 14000 mIU/mL (normal upper limit, 0.7 mIU/mL) and a β-human chorionic gonadotropin level of 20132 mIU/mL (normal upper limit, 0.5 mIU/mL). Pelvic examination and ultrasonography showed no abnormal findings and no signs of pregnancy. At that time, the patient developed pain in the left upper quadrant, which was aggravated by deep breathing. She also reported weakness, intermittent night sweats, and an unintentional 12-lb weight loss during the past year. She denied shortness of breath or cough. A computed tomography scan of the thorax showed a 7-cm right lower lobe lung mass and a 1.2-cm left apex nodule contiguous with pleura. A positron emission tomography scan showed potential metastatic lesions throughout the right and left lobes of the liver, spleen, and left kidney and a left frontal brain lesion. A fine-needle aspirate of a liver mass showed a tumor composed of sheets of round to oval cells with a delicate connective tissue stroma. Admixed with the tumor cells were multinucleated giant cells without atypia. An occasional mitotic figure was identified. Cytokeratins were negative in tumor cells. The patient underwent resection of the right lower lobe and has been without evidence of disease for the past 1.5 years. Microscopically, this tumor resembled a GCT of the lung. This is the 11th case reported in the literature. Giant cell tumors (GCTs) are primarily regarded as tumors of the bone. Despite their potential to metastasize to the lung and other organs, GCTs are commonly benign. Although cases of GCT have been reported in the pancreas, thyroid, skin, lung, and soft tissue, few GCT primary in organs other than bone are included in the literature. We report a primary GCT of the lung in a patient without bone involvement. A 75-year-old man presented with a history of heavy smoking, chronic obstructive pulmonary disease, hypertension, hyperlipidemia, glaucoma, and cerebrovascular disease. He had a chronic unproductive cough and was found to have a solitary 1.7-cm right lower lobe lung mass. A transbronchial biopsy of the mass showed a tumor composed of sheets of round to oval cells with a delicate connective tissue stroma. Admixed with the tumor cells were multinucleated giant cells without atypia. An occasional mitotic figure was identified. Cytokeratins were negative in tumor cells. The patient underwent resection of the right lower lobe and has been without evidence of disease for the past 1.5 years. Microscopically, this tumor resembled a GCT of the bone. This is the 11th case reported in the literature to date of a primary GCT of the lung. Pathologists should be aware that GCT may occur as a primary neoplasm in the lung.
**Context:** Secondary bronchiolitis obliterans with organizing pneumonia (BOOP) is a reaction to injury, forming granulation tissue within airspaces. Idiopathic cryptogenic organizing pneumonia (COP) and secondary BOOP are histologically similar. COP has been reported to show increased collagen in the granulation plugs and fewer myofibroblasts and capillaries. Using CD34 for capillaries and α-smooth muscle actin for myofibroblasts, we assessed these stains to differentiate COP from secondary BOOP.

**Design:** We retrieved and reviewed 21 biopsies diagnosed as secondary BOOP to verify they met criteria for secondary BOOP. Next, they were stained for CD34 and α-smooth muscle actin. Based on the intensity of staining, they were classified as either COP or secondary BOOP. Clinical data were reviewed for evidence of a specific condition to confirm a diagnosis of secondary BOOP. In the absence of such data, the case was clinically classified as COP.

**Results:** From the α-smooth muscle actin and CD34 staining, 6 of 21 cases were diagnosed as COP. The clinical records revealed a cause in 1 of 6 cases. Thus, 5 of 6 cases were correctly classified as COP. We diagnosed 15 of 21 cases as secondary BOOP. A case was determined in 9 cases (7 chemoradiation, 1 local effects of cancer, 1 illicit drugs). No cause was found in 6 cases.

**Conclusions:** Fourteen of 21 cases were correctly classified histologically as COP or secondary BOOP. One case was inappropriately classified; the remaining 6 were classified as secondary BOOP without an apparent clinical etiology. The data suggest that CD34 and α-smooth muscle actin are useful in distinguishing COP from secondary BOOP.

**Sclerosing Mediastinitis Presenting as Superior Vena Cava Syndrome in a Patient With History of Coccidioides Pneumonia**

(Hannah H. Wong, MD) (Poster No. 64)

**Abstracts**

**Invasive Ductal Carcinoma of the Breast With Metastasis to Primary Adenocarcinoma of the Lung**

(Elizabeth N. Pavlisko, MD) (Poster No. 65)

**Atypical Proteinosis: A Pathologic Disorder Mimicking Pulmonary Alveolar Proteinosis**

(Michiya Nishino, MD, PhD) (Poster No. 66)

**Abstracts**
**Diffuse Thymic Fibrosis Mimicking Neoplasia: Report of 4 Cases**

**Poster No. 67**

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**Context:** Extensive thymic fibrosis in the absence of a primary thymic lesion (neoplasm or cyst) is unusual. We describe 4 cases of diffuse thymic fibrosis presenting as mass lesions.

**Design:** We identified 4 cases of diffuse thymic fibrosis referred to our consultation service between 2001 and 2004. Clinical features, gross reports, and histologic slides were reviewed. Immunohistochemical studies were performed using commercial antibodies to pancytokeratin, CD3, CD1a, and IgG4 (Dako, Carpinteria, California).

**Results:** The 4 cases included 2 men and 2 women ranging in age from 28 to 62 years (mean, 48 years). Both women had myasthenia gravis; 1 man presented with fever and dyspnea; the mass was discovered incidentally in 1 man. The masses measured 5.5 to 16.5 cm (mean, 9.75 cm) in greatest dimension. The lesions were confined to the thymus/anterior mediastinum by imaging or as determined from intraoperative notes. They were well demarcated and lobulated. There were 3 to 15 (mean, 11) hematoxylin-eosin-stained sections available for review on each case. Microscopically, the fibrosis was diffuse and dense and resembled the fibrosis of fibrosing mediastinitis. No granulomas were identified. There were small residual islands of involuted thymic tissue with paucity of lymphocytes in all cases. One case showed increased IgG4-positive plasma cells.

**Conclusions:** To the best of our knowledge, the observed diffuse thymic fibrosis is unique and not previously documented in the literature. Although the etiology of the fibrosis is undetermined, the history of myasthenia gravis and the histology resembling fibrosing mediastinitis raise the possibility of autoimmune or infectious causes. Alternatively, the lesions may be idiopathic in nature.

**Clinicopathologic Correlation of Pulmonary Dirofilariasis**

**Poster No. 68**

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Human pulmonary dirofilariasis (HPD) is a rare vector-borne parasitic infection that is a clinical simulator of malignant lung neoplasm. Dogs and cats are the usual natural hosts of Dirofilaria immitis. Transmission to humans occurs through mosquito bites. Humans are a dead-end host because larvae cannot develop into adult form. HPD develops when the larva dies in circulation, embolizes to the lung, lodges in a small pulmonary artery branch, and releases antigens. These antigens lead to endarteritis with subsequent thrombosis and pulmonary infarction of a size larger than expected. A 59-year-old man presented with complaints of cough, sputum production, and wheezing. He was found to have a peripheral 1.2-cm mass in the upper lobe of the left lung and left hilar lymphadenopathy. The patient had a long history of smoking and alcohol abuse. Wedge resection of the mass revealed necrotizing granuloma on frozen section, and permanent sections demonstrated a discrete necrobiotic granulomatous nodule with a centrally placed thrombosed artery containing a parasitic worm characteristic of D immitis (Figure 27). The preoperative diagnosis of HPD is difficult because of a lack of characteristic clinical symptoms, laboratory results, and roentgenographic findings. The probability of definitely diagnosing HPD on either biopsy or fine-needle aspiration biopsy is low. Extensive sampling of necrobiotic granulomas, with attention specifically directed toward detection and examination of a central supplying artery, is recommended.

**Hematopathology; Kidney and Genitourinary Pathology**

**Composite Classic Hodgkin Lymphoma and Langerhans Cell Histiocytosis Arising in the Mediastinum of a Pediatric Patient**

**Poster No. 1**

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Langerhans cell histiocytosis (LCH) is a neoplastic process defined by a proliferation of Langerhans cells. Rarely, LCH is found to occur asynchronously and synchronously with classic Hodgkin lymphoma (CHL) and other neoplasms. Synchronous occurrences of LCH and CHL have been reported in different anatomic locations (eg, CHL in a lymph node and LCH in the bone) and as composite tumors (eg, CHL and LCH occurring in the same lymph node). Most cases of composite CHL and LCH involve adults and are found in peripheral lymph nodes. We describe a case of a previously healthy 15-year-old adolescent boy who presented to the emergency department with a 2- to 3-week history of progressive superior vena cava syndrome symptoms. A computed tomography scan demonstrated a 22 × 14 × 8-cm heterogeneous mediastinal mass with associated mediastinal and right cervical lymphadenopathy. Core biopsies of the mediastinal mass revealed a composite CHL and LCH. By immunohistochemistry, the CHL component was positive for CD30, CD15, and Pax-5 and negative for CD1a, CD20, and S100 protein. The LCH component was positive for CD1a and S100 protein and negative for CD30, CD15, CD20, and Pax-5. While composite CHL and LCH has been described in the literature, this is the youngest patient reported so far to have a composite LCH and CHL and the first case reported to arise in the mediastinum.

**Signet Ring Follicular Lymphoma Presenting as a Soft Tissue Mass**

**Poster No. 2**

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Signet ring follicular lymphoma is a rare morphologic variant of follicular lymphoma. It has been reported in lymph nodes, bone marrow, and various extranodal sites. We report a case of a 54-year-old woman who presented with a palpable mass. Magnetic resonance imaging performed on the patient's knee showed an oval mass in the posterior subcutaneous tissue that measured 2.8 cm in greatest dimension with no other evidence of disease. Microscopically, the lymphoma showed signet ring features. The lymphoma grade 3/3 with areas of diffuse large B-cell lymphoma (Figure 28). By immunohistochemistry, the tumor was positive for CD20, CD10, Bcl-2, and Bcl-6 and negative for CD5, CD23, CD43, Bcl-1, IgG, IgA, IgM, IgD, κ, and λ. Fluorescence in situ hybridization (FISH) demonstrated a translocation with the BCL-2 gene on chromosome 18q21 and IgH gene on chromosome 14q32. Gene rearrangement by polymerase chain reaction showed that the tumor was positive for clonal Ig heavy chain and Ig light chain rearrangements. To our knowledge, this is the first reported case of a signet ring follicular lymphoma with a documented presence of t(14;18) by FISH and with a presentation of a soft tissue mass clinically mimicking a sarcoma. This case serves to illustrate that follicular lymphoma may morphologically mimic a soft tissue neoplasm and the diagnosis should be considered when other studies do not support a sarcoma or carcinoma.
Primary Cardiac Lymphoma Should Be Included in the Differential Diagnosis of a Right Atrial Mass (Poster No. 3)

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A 63-year-old woman with no significant past medical history presented to the emergency room in October 2008 complaining of dyspnea on exertion and chest pain of 3 weeks’ duration. Echocardiogram showed a large right atrial mass that extended and prolapsed into the right ventricle. The mass was attached to the interatrial septum with right ventricular inflow obstruction. Preoperative cardiac catheterization showed mild coronary artery disease and a 60% left ventricular ejection fraction. Presumptive diagnosis of large blood clot versus atrial myxoma was made and the patient underwent open chest exploration. Needle core biopsies of the mass were obtained and a frozen section was requested that showed atypical lymphoid infiltrate suggestive of lymphoma. The mass was not resected. Permanent section evaluation displayed diffuse infiltrates of large atypical lymphocytes with moderate mitotic activity. Fresh tissue sent for cell surface analysis by flow cytometry revealed the presence of monoclonal B-cell population with light chain restriction. Immunohistochemical studies showed B-cell markers CD20 and CD79a to be positive to the large atypical cells. Proliferative fraction, as measured by Ki-67 IHC, was 90%. The immunophenotype of the large atypical lymphoid cells was consistent with diffuse large B-cell lymphoma. The right atrium and right ventricle were then explored, and resection of the mass was performed. Permanent section evaluation displayed diffuse infiltrates of large atypical lymphoid cells with moderate mitotic activity. Fresh tissue sent for cell surface analysis by flow cytometry revealed the presence of monoclonal B-cell population with light chain restriction. Immunohistochemical studies showed B-cell markers CD20 and CD79a to be positive to the large atypical cells. Proliferative fraction, as measured by Ki-67 IHC, was 90%. The immunophenotype of the large atypical lymphoid cells was consistent with diffuse large B-cell lymphoma.

Bone Marrow Infiltration of Non-Hodgkin Lymphoma (Poster No. 5)

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Context: The pattern of bone marrow (BM) involvement and combination of immunophenotyping are important in BM biopsy specimens to establish diagnosis of lymphoma or to determine the extent of disease dissemination for staging purposes.

Design: We retrospectively reviewed 231 BM biopsy specimens obtained from January 2006 to December 2008 in Kings County Hospital Center and investigated the histologic patterns of non-Hodgkin lymphoma (NHL) according to World Health Organization 2008 classification. BM involvement patterns are divided into categories of paratrabecular, diffuse, nodular, interstitial, sinusoidal, and mixed. Immunohistochemistry (IHC) and flow cytometry data were also analyzed.

Results: Of the 231 BM biopsy specimens, 23 cases (10%) with NHL involvement were identified; 11 cases were T-cell lymphomas and 12 cases were B-cell lymphomas. In T-cell lymphomas, the majority (lymphoblastic leukemia/lymphoma, adult T-cell leukemia/lymphoma, peripheral T-cell lymphoma, NOS, and NK/T cell lymphoma, nasal type) showed diffuse or interstitial pattern of infiltration; anaplastic large cell and hepatosplenic lymphoma were characterized by sinusoidal infiltration. In B-cell lymphomas, the majority (plasmablastic lymphoma, lymphoblastic leukemia/lymphoma, hairy cell leukemia, and marginal zone cell lymphoma) showed interstitial infiltration, sometimes admixed with sinusoidal infiltration; small lymphocytic lymphoma/chronic lymphocytic leukemia presented as nodular or diffuse patterns; and Burkitt lymphoma demonstrated diffuse pattern. Immunophenotyping by IHC or flow cytometry can assist classification and recognize some infiltration patterns, such as interstitial and sinusoidal infiltrations.

Conclusions: Recognition of infiltration pattern is important in the diagnosis and staging of patients with NHL. The combination of histology, IHC, and/or flow cytometry aid the diagnosis and subtyping of NHL BM infiltration.

Subdural Hematoma and Associated Accelerated Phase of BCR/ABL1-Positive Chronic Myelogenous Leukemia Occurring in the Setting of Long-Standing JAK-2V617F-Positive Polycythemia Vera (Poster No. 6)

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A 74-year-old male patient with a long-standing history of polycythemia vera, pulmonary hypertension, congestive heart failure, and left ventricular thrombus presented with marked shortness of breath and left-sided weakness at the emergency room. A head computerized tomography examination revealed an acute and chronic right subdural hematoma. The complete blood count showed white blood cell count 51.1 × 10^11/L; absolute neutrophil count 36.3 × 10^9/L; signs of monocytoanalysis 2.6 × 10^9/L; eosinophilia 1.5 × 10^9/L; and slight basophilia 0.5 × 10^9/L; mean corpuscular volume 92.7 μm³; hemoglobin 6.5 g/dL; and platelets 10 × 10^12/L. A leukocytolytic pictures was noted on the peripheral blood smear, with circulating dysplastic neutrophils. The hypercellular bone marrow had increased trilineage hematopoiesis, dysmegakaryopoiesis, dyserythropoiesis, increased reticulin deposition, and absent iron stores. By immunohistochemistry, there were 5%-6% CD34^- and approximately 20% CD117^- nucleated bone marrow cells. While a 46,XY karyotype was noted, molecular studies detected the BCR/ABL translocation in both the peripheral blood and the bone marrow aspirate. The bone marrow was positive for the JAK2-V617F mutation. The findings were in keeping with an accelerated phase of chronic myelogenous leukemia, BCR/ABL positive, which evolved in a background of long-standing polycythemia vera. The unusual occurrence of chronic myelogenous leukemia in the setting of polycythemia vera has been rarely reported in the medical literature and should be of consideration in the differential diagnosis of so-called myeloid metaphasias in patients with long-standing polycythemia vera. Whether these findings represent disease evolution or just a random association remains to be discovered.

A Rare Case of Moyamoya Disease with Sickle Cell Trait (Poster No. 7)

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Moyamoya disease is a rare, idiopathic cerebrovascular disorder primarily affecting children. It features bilateral narrowing/occlusion of the distal internal carotid arteries and presence of a fine network of collateral channels at the base of the brain (moyamoya means “ puff of smoke” in Japanese and describes the angiographic appearance). It can be fatal because of intracerebral hemorrhage. We report a rare case of an adult with moyamoya disease and sickle cell trait (HbAS). A 44-year-old East Indian man presented with left-sided weakness. A magnetic resonance angiogram revealed moyamoya disease (Figure 30). Preneurosurgery workup found normal white blood cells (9.6 × 10^11/L); red blood cells (RBC) (4.70 × 10^12/μL); hemoglobin (13.5 g/dL); hematocrit (38.8%); mean corpuscular volume (82.6 fL); mean corpuscular hemoglobin (28.6 pg/cell); mean corpuscular volume (82.6 fL); mean corpuscular hemoglobin concentration (34.7 g/dL); and platelet count (259 × 10^9/μL); high red cell distribution width (15.6%); normal iron (79 μg/dL); transferrin (381 μg/dL); transferrin saturation (21%); and high ferritin (394 ng/mL). The differential count and RBC morphology were normal. Soluble test result for sickling was positive and hemoglobin electrophoresis by high-performance liquid chromatography showed 40% HbS, <1% HBF (remaining being HbA and HbA2), confirming a diagnosis of sickle cell trait. He had no family history of sickle cell disorder and is doing well postoperatively. Although HbSS, HbSC, HbS-thalassemia, HbSO (Arab), HbF/thalassemia, and HbH-thalassemia have all been reported in children with moyamoya disease, the association is distinctly rare in adults and in “hematologically benign” conditions like sickle cell trait (HbAS). The possible pathogenesis of cerebrovascular disorder in such a case remains unclear.

Simultaneous Chronic Lymphocytic Leukemia and Chronic Myeloid Leukemia: Identification of Two Distinct Clones by Fluorescence In Situ Hybridization (Poster No. 8)

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Chronic lymphocytic leukemia (CLL) and chronic myeloid leukemia (CML) are the most common chronic lymphoid and myeloid leukemias, respectively. However, their simultaneous occurrence is rare. We present a case of simultaneous CLL and CML in which fluorescence in situ hybridization (FISH) was used to determine whether the 2 leukemias derive from 1 common clone or 2 distinct clones. A 76-year-old man without significant history presented with leukocytosis. Physical examination was unremarkable. Peripheral blood examination revealed a hemoglobin of 17.0 g/dL, white cell count of 37.5 × 10^9/L (70% neutrophils, 1% eosinophils, 1% basophils, 2% monocytes, and 26% lymphocytes), and platelet count of 288 × 10^12/L. Bone marrow examination revealed a markedly hypercellular marrow with myeloid predominance and scattered nonparatrabecular lymphoid aggregates. Flow cytometric characterization of the peripheral blood and bone marrow showed a monoclonal B-cell population expressing CD5, CD11c (dim), CD19, CD20 (dim), CD23, and Ig light chain restriction, consistent with CLL. Karyotyping done on the bone marrow revealed 46,XY(t(9;22)(q34;q11). FISH done on the bone marrow confirmed the presence of a BCR/ABL rearrangement and additionally showed 13q14 deletion (the most common cytogenetic abnormality in CLL). To ascertain the presence of 1 common or 2 distinct clones, the bone marrow was hybridized with 3 separate probes in a single cocktail: BCR, ABL, and 13q14 (D13S319). The FISH results identified one clone (66%) with only a BCR/ABL rearrangement and the other (27%) with only 13q14 deletion, indicating the presence of 2 distinct clones in this rare case of simultaneous CLL and CML.

Utility of Bone Marrow Examination in Systemic Lupus Erythematosus (Poster No. 9)

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Context: Autoimmune-mediated cell destruction has been considered the most frequent cause of cytopenias in systemic lupus erythematosus (SLE). Both central and peripheral mechanisms may contribute to peripheral cytopenia in most cases of SLE. Since bone marrow examination is not routinely performed for patients with SLE, reported data on the subject are scarce.

Design: The frequency and features of bone marrow abnormalities were studied in 18 patients with systemic lupus erythematosus. Bone marrow aspiration and biopsy were performed to assess the hematopoietic activity and to rule out infectious and infiltrative disorders. Hematologic and peripheral blood findings showed pancytopenia in most (10/18) of the cases.

Results: Quantitative hematopoietic abnormalities were common including hypocellularity in 8 patients and hyperplasia of erythroid or myeloid lineage in each of 4 patients. Stromal changes included cellular depletion, edema, and infiltration by lymphocytes, plasma cells, and macrophages in 10 cases. Focal increase in reticulin fibers was seen in 3 cases. One case showed presence of lymphoid aggregates and epithelioid cell granuloma without demonstrable microorganisms. In one case extensive bone marrow necrosis was present; test results for the patient were found to be negative for anti-phospholipid antibody. In this brief series, we observed hemophagocytic syndrome or overt myelodysplastic changes.

Conclusions: All these features provide persuasive evidence that the
bone marrow is a common target organ affected in SLE. Hematopoietic alterations and bone marrow stromal changes may both contribute to peripheral cytopenia in most cases of SLE.

An Unusual Human Herpesvirus-8–Negative Primary Effusion Lymphoma-like Lymphoma With Biphenotypic Features: A Case Report and Review
(Poster No. 10)

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Primary effusion lymphoma (PEL), as defined by the World Health Organization, is a B-cell neoplasm universally associated with human herpesvirus-8 (HHV-8) and most often occurs in the setting of immunodeficiency. We present a case of a primary effusion lymphoma (PEL)-like large cell lymphoma of undetermined lineage in the ascitic fluid of a 74-year-old man with human immunodeficiency virus (HIV)–negative status, hepatitis C virus (HCV) cirrhosis, and no lymphadenopathy or lymphomatous masses by physical examination or computed tomography scan. From 1997 to 2004 there have been 5 reported cases of HIV-negative patients with chronic HCV infection who had primary lymphomatous effusions involving the abdominal cavity and who were HHV-8 and Epstein-Barr virus (EBV) negative. Unlike the 5 previously reported cases, our case shows evidence of T-cell immunophenotype in addition to large cell lymphoma of undetermined lineage. The CD45 immunostain result was negative. B- and T-cell lineage specific markers should be routinely performed in undifferentiated tumors when the CD45 immunostain result is negative.

Abstracts

<table>
<thead>
<tr>
<th>Source, y</th>
<th>HIV HHV-8</th>
<th>Phenotype</th>
<th>TCR Rearrangement</th>
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<td>Said et al, 1999</td>
<td>P</td>
<td>CD2+, CD5+, CD7+, CD3-</td>
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<td>N</td>
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<td>P</td>
<td>CD3+, CD43+, CD45RO+, CD30+</td>
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</table>

Abbreviations: N, negative; P, positive; TCR, T-cell receptor rearrangement.

Is CD45 a Reliable Marker to Rule Out Aggressive Non-Hodgkin Lymphomas? (Poster No. 11)

Joanna J. Xie, MD (joanna.xie@chs.org); Randa Alsabeh, MD. Department of Pathology, Cedars-Sinai Medical Center, Los Angeles, California.

Context: Aggressive lymphomas can mimic other neoplastic processes and are considered in the evaluation of undifferentiated malignancies. Except for anaplastic large cell lymphoma (ALCL), CD45 is thought to be consistently expressed in most non-Hodgkin lymphomas (NHLs), and therefore a negative immunostain result is thought to exclude this diagnosis. The aim of this study is to evaluate expression of CD45 in a large number of aggressive lymphomas.

Design: One hundred forty-six cases of aggressive lymphomas were stained with CD45 antibody (1:100; Dako) by using the Dako Autostainer. Cases included 124 diffuse large B-cell lymphomas (DLBCLs), 6 lymphoblastic lymphomas (LBLs), 5 anaplastic T-cell lymphomas (T-ALCLs), and 11 anaplastic B-cell lymphomas (B-ALCLs). The intensity of CD45 staining for each case was evaluated by 2 pathologists. Grades of 0 (negative), 1 (weak), 2 (moderate), and 3 (strong) corresponded to <5%, 5%–25%, 26%–50%, and >50% positivity, respectively.

Results: See the Table.

<table>
<thead>
<tr>
<th>Grade, No. (%)</th>
<th>DLBCL</th>
<th>LBL</th>
<th>T-ALCL</th>
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<tr>
<td>0</td>
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<td>97 (78)</td>
<td>4 (67)</td>
<td>2 (40)</td>
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</table>

Conclusions: The largest percentage of cases with negative to weak staining occurred in lymphoblastic lymphoma (33%) followed by T-ALCL (20%) and DLBCL (15%). These findings are especially important in small-needle core biopsies of undifferentiated tumors, as NHL may be falsely excluded when only a minority of cells show CD45 expression and are missed with sampling. Although CD45 can be used as a screening marker for NHL in most cases, a negative CD45 stain result should not be considered as sole evidence for a nonhematopoietic tumor. Additional B- and T-cell lineage specific markers should be routinely performed in undifferentiated tumors when the CD45 immunostain result is negative.

Cutaneous Marginal Zone B-Cell Lymphoma Six Years After Initial Presentation with IgM Monoclonal Gammopathy
(Poster No. 12)

Jason Schallheim, MD (jmschal@gwu.edu); Alison Huppmann, MD; Minling Liu, MD, PhD.1 Department of Pathology, George Washington Hospital, Washington, District of Columbia; 2 Department of Pathology, Washington, DC VA Medical Center, Washington, District of Columbia.

Marginal zone B-cell lymphoma may be associated with monoclonal gammopathy. However, cases with significant IgM paraprotein years before the emergence of marginal zone B-cell lymphoma are rarely reported in the literature. A 65-year-old man presented with a 2-year history notable for IgM-A monoclonal protein (2.3 g). He had no evidence of lymphadenopathy and a bone marrow biopsy result was negative. A diagnosis of Waldenström macroglobulinemia was clinically rendered. The patient received 1 course of rituximab and the paraprotein amount decreased to 0.5 g. Several months later, the patient experienced lower extremity palpable purpura and an increase of paraprotein to 2.6 g. A biopsy revealed leukocytoclastic vasculitis. Rituximab therapy was repeated, resulting in a decrease of paraprotein that remained stable at 0.5 g. Four years later, he presented with multiple subcutaneous nodules measuring up to 3 cm located on the lower back and upper chest. These nodules were hypermetabolic on positron emission tomography scan. Biopsy of a lower back nodule showed subcutaneous tissue with a diffuse lymphoid infiltrate of heterogeneous small to medium lymphocytes including centrocytes, mono-
consistent with extranodal marginal zone B-cell lymphoma with plasma­cytic differentiation. This case illustrates an unusual marginal zone B-cell lymphoma presenting with multifocal subcutaneous nodules and diagnosed years after IgM paraproteinemia.

Diagnosis of Hodgkin Lymphoma in a Young Child Contributing to a Diagnosis of Ataxia Telangiectasia
(Poster No. 13)

Jennifer M. Hummel, MD, MPH (jenhummel@med.umich.edu); Diane A. Hall, MD, PhD; Megan S. Lim, MD, PhD. Department of Pathology, University of Michigan Health System, Ann Arbor.

Ataxia telangiectasia is associated with neurologic impairment, immunodeficiency, and chromosomal instability. Ten percent of patients develop malignancies at an early age, predominantly leukemias and non-Hodgkin T-cell lymphomas. We report the clinical, pathologic, and molecular features of a child who presented with stage IV Hodgkin lymphoma, which led to the diagnosis of ataxia telangiectasia. A 6-year-old boy with developmental delay and “clumsiness” presented with abdominal pain, fever, and fatigue. A computed tomography scan detected enlarged mediastinal, periaortie, and supraclavicular lymph nodes. The peripheral blood smear showed neutropenia and anemia. The lymph node biopsy revealed scattered large lacunar Reed-Sternberg cells in a background of sclerosis with small lymphocytes and eosinophils. The bone marrow revealed nonne­cro­tizing granulomas, eosinophilia, and large atypical lymphocytes with prominent nuclei (Figure 3). These atypical lymphocytes and lacunar Reed-Sternberg cells expressed CD30, PAX5 weakly, and CD15 in a subset, leading to the diagnosis of Hodgkin lymphoma. Subsequent neuro­logical examination revealed oculomotor apraxia, hand dysmetria, and gait disturbance. Serum α-fetoprotein was elevated, IgG2 was reduced, and cytogenetic evaluation of the blood demonstrated 10% of cells with chromosomal breakage, including 7;7 and 14;14 translocations consistent with ataxia telangiectasia. In situ hybridization for Epstein-Barr virus ribonu­cleic acid (EBER-1) was performed on the lymph node biopsy and demonstrated numerous positive cells. Although chemotherapy resulted in remission, the patient experienced a relapse 26 months later and had had persistent disease. This case documents a rare presentation of early-onset Hodgkin lymphoma with bone marrow involvement contributing to a diagnosis of ataxia telangiectasia.

Dural Extranodal Marginal Zone Lymphoma Mimicking a Meningioma
(Poster No. 14)

Luis Brandi, MD (luis.brandi@tulane.edu); Safaa Labib, MD; Hari B. Bockman, MD; BS.2 Department of Pathology and Texas Tech University School of Medicine, Texas Tech Health Sciences Center, Lubbock.

Extranodal marginal zone lymphomas primary to the central nervous system are extremely rare, are typically dural based, and are known to mimic meningiomas. They typically present with single or multiple extra­axial masses that enhance diffusely with additional contrast material and can be easily confused with a meningioma. MALT lymphomas compose 7%–8% of all B-cell lymphomas and up to 50% of primary gastric lym­phomas. A 52-year-old woman presented with a complaint of a severe headache that was not responsive to medication. Magnetic resonance imaging demonstrated a 1.1 × 4.7 × 2.3-cm extra-axial enhancing mass through the interhemispheric falx, near the vertex just right of the midline in the right parafalcine region, radiologically consistent with meningio­nia. Frozen section biopsy results were positive for a lymphocytic infiltrate in a fibrous background, possibly dural. Microscopic examination of hematoxylin-eosin-stained sections revealed dural tissue with focal psammomato­sis, including numerous positive cells. Although chemotherapy resulted in remission, the patient experienced a relapse 26 months later and had had persistent disease. This case illustrates an unusual marginal zone B-cell lymphoma with plasma­cytic differentiation. This case illustrates an unusual marginal zone B-cell lymphoma presenting with multifocal subcutaneous nodules and diagnosed years after IgM paraproteinemia.

Nonsecretory, Nonproducing Plasma Cell Myeloma Presenting with Clinical Features of Hairy Cell Leukemia
(Poster No. 15)

Crystal L. Rose, MD, MS (crose@chsmail.org); Janet Roepke, MD, PhD. Department of Pathology, Ball Memorial Hospital, Muncie, Indiana.

Plasma cell myeloma is not an uncommon diagnosis and 97% of cases demonstrate the presence of an M-spike on immunofluorescence electro­phoresis. Of the 3% of cases that fail to do so, 85% demonstrate clonal light chains in the cytoplasm of the neoplastic cells by immunohistochemistry and are therefore termed nonsecretory. Of the nonsecretory cases, 15% do not have cytoplasmic immunoglobulin synthesis and are termed nonpro­ducing. Consequently, nonsecretory, nonproducing plasma cell myeloma constitutes less than 0.5% of cases. The presence of this entity as a mimic of hairy cell leukemia has yet to be reported. In our case, a 69-year-old man presented with diarrhea, anorexia, and weight loss. Peripheral blood showed numerous lymphoid cells with oval nuclei and pale blue cytoplasm with circumferential projections best characterized as classic hairy cells. Periph­eral blood flow cytometry showed an immunophenotype of CD19+, CD20, CD56+, CD5, CD79a+, and CD138+. The bone marrow showed an abnormal population of cells containing 92%, of which were positive for CD4, CD38, CD56, and CD79a. Cytogenetic analysis demonstrated multiple abnormalities including 11;14, k/λ light chains by in situ hybridization showed a clonal k population of cells. In conclusion, nonsecretory, nonproducing plasma cell myeloma is rare and can mimic hairy cell leukemia; therefore it constitutes a unique entity that warrants increased awareness.

Systemic Mastocytosis Presenting With Chronic Monocytosis and Osteoblastic Lesions in a Patient With History of Breast Cancer
(Poster No. 16)

Karimireddy J. Reddy, MD (karimireddy.reddy@ucdmc.ucdavis.edu); Prashanti Reddy, MD; Edward C. Larkin, MD. Department of Pathology, UC Davis Medical Center, Sacramento, California.

We present an interesting case of an 80-year-old woman with a remote history of breast cancer who presented to an outside hospital with weakness, weight loss, fatigue, loss of appetite, dyspepsia, and loss of muscle tone. Imaging showed sclerotic lesions in the abdomen, pelvis, and thorax that were suggestive of metastases. An extensive workup yielded negative results for bone marrow biopsy, JAK2-2 mutation, and BCR/ABL (fluores­cence in situ hybridization) and normal cytogenetics. The patient was seen...
A Retrospective Review of Pathologic Diagnosis of Bone Marrow Biopsy in Hospitalized Patients
(Poster No. 17)

Ming Xie, MD (mingxie@yahoo.com); Emily E. Volk, MD. Department of Pathology, William Beaumont Hospital, Troy, Michigan.

Context: Bone marrow biopsy is indicated in the evaluation of a broad variety of diseases including both hematologic lesions and nonhematologic lesions with bone marrow involvement. Many hospitalized patients with abnormal complete blood cell count (CBC) findings undergo bone marrow evaluation. This study evaluates the necessity of the bone marrow biopsy in hospitalized patients by reviewing the bone marrow biopsy reports and related clinical information.

Design: During 2007 a total of 138 bone marrow samples were collected from 133 hospitalized patients. The pathological reports were retrospectively reviewed. Patient's information, including age, sex, clinical diagnosis for hospitalization, and the clinical indication for bone marrow biopsy were recorded.

Results: The patients consisted of 65 males and 68 females (mean age, 64 years). Hematologic diseases were detected in 64 patients (48.1%). Three patients (2.3%) showed nonhematologic diseases. Another 66 patients (49.6%) showed nonspecific histologic findings without specific pathologic diagnosis. Among these patients, 61 were hospitalized because of nonhematologic diseases, mainly respiratory failure, cardiovascular diseases, and diabetes; 5 because of lymphoma/plasma cell neoplasm with bone marrow involvement, and 6 because of osteosclerotic bone, in light of the patient's history of breast cancer, warranted the consideration of a myeloproliferative disorder and/or radiation-induced fibrosis with osteosclerosis. However, the typical morphology of paratrabecular infiltrates of spindle cells resulted in an unexpected diagnosis of systemic mastocytosis (Figure 33). This was confirmed by tryptase immunostaining and elevated serum tryptase levels (505 μg/L). Systemic mastocytosis is a rare disease and diagnosis requires a high degree of suspicion. Our case is unusual in its presentation with chronic mononcytosis, vague constitutional symptoms, and absence of clear clinical symptoms of mast cell degranulation in the context of remote breast cancer. This case also emphasizes the importance of a meticulous bone marrow examination before resorting to more extensive diagnostic testing.

Conclusions: In this retrospective study, nearly half (49.6%) of the bone marrow biopsy samples collected from the hospitalized patients showed nonspecific histologic findings without specific pathologic diagnosis. Although the nonspecific or negative bone marrow findings can be important information for patient care during hospitalization, in some patients, the bone marrow biopsy may be performed at an outpatient clinic after discharge for the evaluation of abnormal CBC parameters.

Aberrant Expression of T-Cell Antigens in Diffuse Large B-Cell Lymphoma of the Testis
(Poster No. 18)

Jay L. Patel, MA (jay.patel@hsc.utah.edu); Albert K. Ho, MD, PhD; David Y. W. Bailey, MD, PhD. Department of Pathology, University of Utah School of Medicine, Salt Lake City.

The aberrant expression of T-cell antigens in B-cell non-Hodgkin lymphoma occurs rarely. We report the case of a 78-year-old man with a history of diffuse large B-cell lymphoma (DLBCL) in the left testicle that was diagnosed in 1995. He was treated with unilateral orchietomy plus multiagent chemotherapy and radiation therapy and achieved complete remission. Recently, however, he presented with a contralateral testicular mass. Hematoxylin-eosin-stained sections showed displacement of residual testicular tissue by sheets of atypical lymphoid cells, consistent with recurrence of DLBCL. On further immunophenotypic characterization by 5-color flow cytometry, a monoclonal B-cell population was identified that expressed dim λ light chains, CD19, CD20, and the T-cell antigens CD5 and CD7 without CD3, CD10, CD22, CD30, CD45, FMC-7, or any additional T-cell markers. Immunohistochemical staining for the proliferation marker MIB-1 was performed and showed positivity in approximately 50% of the neoplastic cells. The patient went on to receive multiple cycles of chemotherapy and has achieved complete remission. The occurrence of T-cell markers in DLBCL is unusual and appears to be primarily of diagnostic relevance. No unusual or aggressive clinical behavior was observed in this case. B-cell non-Hodgkin lymphoma may express 1 or more T-cell antigens. One or more pan-B-cell antigens, such as CD22 in this case, may be absent. Awareness of these possibilities is necessary to avoid diagnostic errors.

Nasopharyngeal Hodgkin Lymphoma With Necrosis and Fungal Proliferation: A Challenging Diagnosis
(Poster No. 19)

Melissa M. Rodgers-Ohlau, MD1 (melissa.rogers-ohlau@ucdmc.ucdavis.edu); Michelle McNamara, MD; Thomasina Bailey, MD; Peter Banks, MD; David Harrison, MD; Denis Dywe, MD.1 Department of Pathology, University of California Davis Medical Center, Sacramento; 2Department of Pathology, Carolinas Medical Center, Charlotte, North Carolina; 3Department of Hematology and Oncology, University of California Davis, Sacramento.

Classic Hodgkin lymphoma (CHL) is a lymphoid neoplasm with at least some B-cell differentiation, typically arising in lymph nodes. Extranodal presentation is unusual; when it occurs, spleen or bone marrow is commonly affected. We report the case of a 41-year-old woman with primary nasopharyngeal CHL. She presented with progressive superficial skin lesions and a large mass. Hematoxylin-eosin–stained slides of nasal biopsies revealed extensive surface necrosis with fungal hyphae. Beneath the necrosis was acute chronic inflammation with lymphohistiocytic proliferation. Large cells with polylobated nuclei and macronucleoli were also noted. Immunohistochemical staining revealed that the large cells were variably positive for CD20, CD79a, Ki67, and Bcl-2 and negative for CD3, CD5, CD10, and MUM-1. Systemic mastocytosis is a rare disease and diagnosis requires a high degree of suspicion. In this case, tryptase immunostaining and elevated serum tryptase levels confirmed the expected diagnosis of systemic mastocytosis (Figure 33). This was confirmed by tryptase immunostaining and elevated serum tryptase levels (505 μg/L). Systemic mastocytosis is a rare disease and diagnosis requires a high degree of suspicion. Our case is unusual in its presentation with chronic mononcytosis, vague constitutional symptoms, and absence of clear clinical symptoms of mast cell degranulation in the context of remote breast cancer. This case also emphasizes the importance of a meticulous bone marrow examination before resorting to more extensive diagnostic testing.

Histiocytic Necrotizing Splenitis: Kikuchi-Fujimoto-like Splenic Findings in Patients With Chronic Autoimmune Disorders
(Poster No. 20)

Thomas A. Summers, Jr, MD (thomas.a.summers@verizon.net); Aaron Auerbach, MD; Nadine S. Aguilera, MD.1 Department of Pathology, Walter Reed Army Medical Center, Washington, District of Columbia; 2Department of Hematopathology, Armed Forces Institute of Pathology, Washington, District of Columbia.

Autoimmune diseases are associated with enlarged lymph nodes and
splenomegaly in many cases. The histologic findings in these lymph nodes have been described as follicular hyperplasia, with similar findings in the splenic white pulp being described less commonly. Histiocytic necrotizing lymphadenopathy has also been reported in autoimmune diseases, but a similar counterpart in the spleen has not been documented. We report 2 cases of histiocytic necrotizing spleenitis (Kikuchi-Fujimoto-like) findings in spleens from patients with chronic autoimmune disorders. The patients’ medical histories were significant for systemic lupus erythematosus. Splenectomy was performed secondary to thrombocytopenia in one case and to rule out a lymphoproliferative disorder in the other. Both exhibited features characteristic of histiocytic necrosis without acute inflammation similar to Kikuchi-Fujimoto disease described in lymph node specimens. Splenic involvement was extensive and diffuse and centered predominantly in the red pulp or nonwhite pulp areas. Fibrinoid necrosis was present in all cases (Figure 34). The most striking features of the cases were the marked extracellular and intracellular karyorrhectic nuclear debris (apoptotic debris) that was present without an associated neutrophilic or eosinophilic response. Surrounding these necrotic areas were benign histiocytes, immunoblasts, and plasmacytoid mononuclear cells. Plasma cells (a normal splenic constituent) were present in all cases and hematoxylin bodies were not identified. Staining results for infectious organisms were negative in all cases. Splenomegaly in autoimmune disease is rarely studied and is assumed to be hyperplastic in most cases, but we present rare cases of histiocytic necrotizing splenitis, which calls into question that assumption.

**Primary Amyloidosis of the Glans Penis: A Painful κ-Positive Lesion**

(Poster No. 21)

Joo Y. Song, MD† (joosong@gwu.edu); Suman Chauhan, MD; Washington, District of Columbia; 2Department of Pathology, Veterans Affairs Hospital, Washington, District of Columbia.

Primary amyloidosis is uncommon and extremely rare when localized to the glans penis. We report a case of a 53-year-old uncircumcised man with a history of diabetes and hypertension presenting with a broad-based flat lesion of the glans penis. The patient had complaints of penile pain for 1 month. The penile biopsy under microscopic examination revealed flat lesion of the glans penis. The patient had complaints of penile pain for 1 month. The penile biopsy under microscopic examination revealed a pink homogenous subepithelium stroma with thickened blood vessel walls. Congo red-stained section showed apple-green birefringence with polarizing light microscopy in the areas of eosinophilic positivity for κ light chains. Immunoperoxidase staining was performed on the specimen and found to be positive only for κ light chains. Further workup for systemic amyloidosis was performed (chest x-ray, serum protein electrophoresis, urine protein electrophoresis, immunofixation); the results were normal. Clinical and pathologic correlation rendered a diagnosis of primary amyloidosis localized to the glans penis. Rare cases of localized amyloidosis of the penis present as a painless lesion composed of κ light chains, which have a particular “amyloidogenicity.” Here we illustrate the first case reported in the literature that was painful and positive for κ light chains.

**A Nodal Marginal Zone Lymphoma With Bright CD10 Expression Mimicking Follicular Lymphoma**

(Poster No. 23)

Dava S. West, MD (dava.west@duke.edu); Endi Wang, MD, PhD. Department of Pathology, Duke University Medical Center, Durham, North Carolina.

Nodal marginal zone lymphoma (NMZL) is a small B-cell neoplasm.
that lacks a unique immunophenotype. It is thus, in part, a diagnosis of exclusion that must be differentiated from other small B-cell lymphomas, including follicular lymphoma (FL). Previous studies have demonstrated a high specificity for CD10 expression in FL in comparison to other small B-cell neoplasms. Here, we report a CD10- NMZL in a 62-year-old man who presented with weight loss, night sweats, and anemia. Imaging revealed widespread lymphadenopathy without splenomegaly. Histologic sections of inguinal lymph node showed a nodular lymphoid proliferation with an interfollicular infiltrate of small/medium-sized lymphocytes with a “monocytoid” appearance. Flow cytometry detected a monoclonal B-cell population with bright CD10 expression. Immunohistochemical staining confirmed CD20 and CD10 positivity in both follicle center and interfollicular lymphocytes, with brighter CD10 staining in neoplastic interfollicular areas (Figure 37). Bcl-2 immunohistochemical staining highlighted a marginal zone growth pattern. Interphase fluorescence in situ hybridization for t(14;18)(IGH/BCL2), a genetic hallmark for FL, was performed on paraffin-embedded tissue. No fusion signal was observed. Rare hybridization for t(14;18)(IGH/BCL2), a genetic hallmark for FL, was performed on paraffin-embedded tissue. No fusion signal was observed. Rare cases of MZL with weak CD10 expression have been described in the literature. However, to our knowledge, this is the first case of a strongly CD10- NMZL in which FL was definitively excluded by molecular studies. The case underscores the importance of recognizing architectural and cytomorphic features of NMZL even when CD10 expression suggests FL. Immunohistochemical analysis for B-cell markers and Bcl-2 can be used to highlight NMZL morphologic pattern. Molecular studies can then be used for definitive diagnosis.

CD58 Expression Remains Elevated in Recurrent and Residual Precursor B-Cell Acute Lymphoblastic Leukemia and Decreases in Remission as Nonmalignant B cells Mature in the Bone Marrow

(Poster No. 24)

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Context: Previous studies have demonstrated that CD58 is overexpressed on leukemic blasts in precursor B-cell acute lymphoblastic leukemia (B-ALL) when compared to benign B-cell precursors. However, CD58 expression in B-ALL after treatment has not been evaluated. This study sought to measure the levels of CD58 expression in B-ALL at initial diagnosis, to compare these results to levels found in subsequent post-treatment bone marrows, and to examine CD58 expression in active disease compared to expression in remission.

Design: Diagnostic and follow-up bone marrows from 8 patients with B-ALL with either recurrent or residual disease were included. For comparison, 37 cases of previously diagnosed B-ALL with no evidence of disease were selected. Multivariate flow cytometric analysis was performed by using panels of informative markers. CD58 mean fluorescent intensity was measured on the neoplastic blasts and maturing B-cell precursors.

Results: Diagnostic bone marrows and subsequent bone marrows with recurrent or residual disease had statistically similar levels of CD58 expression on leukemic blasts (P = .69). Mean fluorescent intensity of CD58 on leukemic blasts for patients with active leukemia was significantly higher than the corresponding intensity for maturing nonmalignant B-cell precursors for cases lacking evidence of leukemia (P < .001).

Conclusions: Our results indicate that CD58 is significantly and consistently overexpressed in B-ALL patients with active disease when compared to its expression in B-ALL patients lacking evidence of ongoing leukemia. The expression of CD58 on leukemic lymphoblasts appears to be a useful biomarker for detecting minimum residual or recurrent disease because it remains elevated in positive cases and is decreased in absence of active leukemia.

CD3+ Primary Mediastinal Large B-Cell Lymphoma in a 42-Year-Old Woman

(Poster No. 25)

Maggie Stoeker, MD; Endi Wang, MD, PhD (endi.wang@duke.edu), Department of Pathology, Duke University Medical Center, Durham, North Carolina.

Primary mediastinal large B-cell lymphoma (PMBCL), a subtype of diffuse large B-cell lymphoma (DLBCL), arises in the anterior mediastinum, presumably from thymic B cells. Whereas aberrant expression of antigens of other lineages is frequently observed in lymphomas, DLBCL with aberrant expression of CD3, a T-cell specific antigen, is rare. We report the case of a 42-year-old woman with chest pain radiating to the left arm that developed during a 2-month period. Radiographs showed a 9.9-cm, anterior mediastinal mass, which was fluoroscopically biopsied. Hematoxylin-eosin–stained sections demonstrated a diffuse proliferation of mixed small and large lymphocytes in a background of fibrosis. The large cells formed cohesive clusters with few intermingled small lymphocytes. Immunohistochemical stains demonstrated homogeneous positive staining in large cells for CD45, CD20, CD79a, Pax-5, bcl-2, bcl-6, and MUM-1. Many large cells had weak-moderate membranous staining with CD3 and CD4. Other T-cell–associated antigens, CD3, CD2, CD7, CD4, and CD8, were negative in large cells. CD30 was positive in a subset of large cells (15%-20%), but CD15 was essentially negative. Polymerase chain reaction–based immunoglobulin (Ig) gene and T-cell receptor (TCR) gene rearrangement studies were performed on paraffin-fixed tissue that revealed a clonally rearranged Ig κ light chain gene without clonal rearrangement of TCR. While rare cases of conventional DLBCL with aberrant CD3 have been recently described, aberrant expression of CD3 in PMBCL has never been reported, to the best of our knowledge. We emphasize application of immunohistochemical antibody panels and the value of molecular tests for definitive diagnosis of uncommon lymphomas with ambiguous phenotype.

Recurrent Classic Hodgkin Lymphoma—Type Posttransplant Lymphoproliferative Disorder

(Poster No. 26)

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The least common subtype of posttransplant lymphoproliferative disorder (PTLD) is classic Hodgkin lymphoma type (cHL), an entity most often described in renal transplant patients. We present a case of a 17-year-old cardiac transplant recipient with cervical lymphadenopathy, 11 years after transplant. Lymph node biopsy revealed complete effacement of nodal architecture by large, atypical Hodgkin/Reed-Sternberg (HRS) cells against a background of small lymphocytes. The HRS cells expressed Epstein-Barr virus on in situ hybridization and CD30, CD15, Pax-5 weakly, but not CD20 or CD45. The diagnosis of cHL-PTLD was made. Complete remission was achieved following immunosuppression withdrawal. Six years later, the patient died following unrelated multiorgan failure. Autopsy revealed cHL-PTLD in the mediastinal lymph nodes and liver, identical morphologically and immunohistochemically to the lymph node biopsy 4 years earlier. The main differential diagnosis for cHL-PTLD is Hodgkin-like PTLD. Until recently, both were considered the same entity because of their similar morphology. They can be distinguished as follows: HRS cells in cHL-PTLD express CD30, CD15, and Epstein-Barr virus (EBV) in both HRS-like cells and bystander small lymphocytes and demonstrate Ig gene rearrangement. It is important to distinguish between these 2 entities because cHL-PTLD responds to chemotherapies targeted for Hodgkin lymphoma, while Hodgkin-like PTLD responds to non-Hodgkin lymphoma therapies. To the best of our knowledge, recurrent cHL-PTLD is extremely rare in pediatric cardiac transplant patients. An accurate diagnosis is vital for optimal management.
A Case of Primary Omental Peripheral T-Cell Lymphoma Presenting With Marked Hypereosinophilia, Omental Caking, a Tubo-Ovarian Mass, Ascites, and Elevated CA125: An Illustration of Anchoring Bias in Clinical Decision-Making (Poster No. 27)

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A 53-year-old Asian woman with peripheral blood eosinophilia (126,300/μL) presented with left upper-quadrant pain and lethargy. Stool examination for parasites was negative. Bone marrow with molecular and cytogenetic analysis along with flow cytometry was negative for chronic eosinophilic leukemia, chronic myelogenous leukemia, acute leukemia, malignant lymphoma, and other malignancies. Computerized tomography did not show lymphadenopathy but showed a large omental cake, a small amount of ascites, and a small left tubo-ovarian mass. Serum levels of CA125 were elevated (368 U/mL). A clinical diagnosis of metastatic ovarian carcinoma was made. Hysterec tomy with bilateral salpingo-oophorectomy, omentectomy, and bilateral iliac lymphadenectomy were done without a preoperative or intraoperative biopsy. Malignant lymphoma was suspected from the postsurgery frozen section done to select tissue for chemotherapy sensitivity testing. Flow cytometric analysis of omental tissue showed only CD57+/CD11c+ cells. Hematoylin-eosin sections showed medium to large lymphoid cells with brisk mitotic activity, angiocentricity, intense eosinophil infiltrate (Figure 38), and focal necrosis in the removed tissue, mass-forming only in omentum. The neoplastic infiltrate was seen only in the serosa and subserosa of bilateral adnexa and uterus. Iliac lymph nodes were negative for lymphoma. Paraffin immunohistochemistry was positive for CD3, CD7, CD43, granzyme, TIA-1, perforin, TCRαβ, and Ki-67 (about 80%). Results for CD56, CD57, EBV-LMP1, and EBER were negative. Polymerase chain reaction for T-cell receptor gene rearrangement yielded positive results. Primary omental peripheral T-cell lymphoma, not otherwise specified, was diagnosed because of a large mass in omentum and lack of any other mass. This represents a good example of anchoring bias in clinical decision-making.

LMP1 expression in MEGs has not been previously reported. CD79a expression has been previously recognized, but has not been extensively studied. We compared these markers to better-known MEG markers.

Design: Forty cases were examined: 29 bone marrow (5 myeloproliferative disease [MPD]), 3 myeloproliferative disease/myelodysplastic syndrome (MPD/MDS), 21 various diagnoses, and 11 EMH (8 spleen, 3 lymph node). Tests with CD61, LMP1, Factor VIII, and CD79a were performed on paraffin-embedded sections (Table). In situ detection of EBV-encoded RNA was performed in 5 cases that were immunoreactive for LMP1 to exclude Epstein-Barr virus infection. Each stained slide was graded for the percentage of MEGs stained, intensity, and background. Each parameter was given a numerical score from 0–3. The average scores are reported.

Results: LMP1 staining was observed in 39 of 40 cases and the overall staining profile for the 3 characteristics was 2.8/2.05/0.80. CD79a staining was observed in 32 of 38 cases (2.84/2.58/0.89); Factor VIII staining in 39 of 39 cases (3.0/2.92/2.08); and CD61 staining in 39 of 40 cases (2.90/2.50/1.75). The presence of EBV-encoded RNA was negative in all cases.

Conclusions: LMP1 staining was not as intense but was consistently positive with a cleaner background. CD79a performed comparably except in extramedullary tissues because of background. LMP1 and CD79a were expressed in dysmorphic MEGs of MPD and MDS. The mechanism for expression of CD79a and LMP1 is unknown. Use of CD79a and LMP1 increases the repertoire of immunohistochemical stains available for megakaryocytes; in addition, recognition of their expression is helpful in excluding hematopoietic disease and misidentification.

Unusual Immunohistochemical Markers for Megakaryocytes: A Comparison of the Novel Markers LMP1 and CD79a to the More Traditional Markers CD61 and Factor VIII (Poster No. 28)

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Context: Megakaryocytes (MEGs) can be difficult to recognize in cases of extramedullary hematopoiesis (EMH) or when MEGs are dysmorphic.

LMP1 to exclude Epstein-Barr virus infection. Each stained slide was graded for the percentage of MEGs stained, intensity, and background. Each parameter was given a numerical score from 0–3. The average scores are reported.

Results: LMP1 staining was observed in 39 of 40 cases and the overall staining profile for the 3 characteristics was 2.8/2.05/0.80. CD79a staining was observed in 32 of 38 cases (2.84/2.58/0.89); Factor VIII staining in 39 of 39 cases (3.0/2.92/2.08); and CD61 staining in 39 of 40 cases (2.90/2.50/1.75). The presence of EBV-encoded RNA was negative in all cases.

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Streck Cell Preservative Reagent Stabilizes Bone Marrow Cells and Their Antigen Expression Profiles for Extended Analysis by Flow Cytometry (Poster No. 29)

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Context: Streck Cell Preservative (SCP, formerly Cyto-CheX Reagent) is a cell and tissue preservative used to stabilize samples for analysis by flow cytometry. Current flow cytometry protocols require analysis of bone marrow samples within 24 hours of collection.

Design: The goal of this study was to determine whether bone marrow is preserved beyond 24 hours by using SCP, thus avoiding the rejection of samples delayed during shipping and eliminating the need for weekend staffing.

Results: We report that SCP can preserve bone marrow samples for flow cytometric analysis for 72 hours. Bone marrow samples drawn from patients were mixed 1:1 with SCP and evaluated by flow cytometry at 6 hours and 72 hours after isolation. We reported on the stabilization of bone marrow samples from 13 patients. Now we report on a total of 23 patient samples that were stabilized by diluting into SCP and tested for CD marker expression by using standard leukemia and lymphoma panels. The SCP-diluted bone marrow sample results were compared to bone marrow samples collected in K2EDTA tubes. We have tested samples with a presumptive clinical diagnosis of myelodysplastic syndrome, chronic lymphocytic leukemia, or acute myeloid leukemia. Results indicate that regardless of the leukemia and lymphoma panel type, the samples diluted in SCP and tested at 6 hours and 72 hours yielded results phenotypically comparable to samples collected in K2EDTA tubes and tested at 6 hours.

Conclusions: We conclude that bone marrow samples diluted in Streck Cell Preservative are stable for immunophenotyping analysis for up to 72 hours.
Flow Cytometry in Predicting Morphologic Patterns of Lymphoma (Poster No. 30)

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Context: Flow cytometry (FC) is generally considered a reliable supplement to tissue diagnosis of lymphomas. However, its use as a stand-alone diagnostic tool for predicting morphologic patterns has been cautiously considered.

Design: FC cases performed in our institution (2003–2008) were reviewed by 4- and 6-color methods. Lymph nodes (LN) or solid tissue biopsies with corresponding definitive diagnosis were selected. Cases were reviewed by FC in blinded fashion to the final diagnosis and findings were then correlated by using tissue diagnosis as the gold standard.

Conclusions: FC pattern can reliably predict reactive or non-H lesions and can be used to morphologically subtype B-cell non-Hodgkin lymphomas. Although the use of FC has limitations in HLs, the pattern can predict certain subtypes such as NLP-HL. The application of multiparametric FC may be of greater value in predicting morphologic lesions than previously thought.


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Blastic plasmacytoid dendritic cell neoplasm is a rare and aggressive hematodermic tumor with distinct clinical, pathologic, and immunophenotypic features. Patients usually present with a cutaneous lesion followed by dissemination to involvement of bone marrow, blood, and lymph nodes and the central nervous system. Clinical course is aggressive with median survival of 14 months. The history of this entity dates back to 1994 when Adachi et al reported the first case. Since then, approximately 150 cases have been reported in literature by using a gamut of names such as blastic NK cell lymphoma, CD4+/CD56+ hematodermic neoplasm, and aggressive agranular NK cell leukemia. For many years, it was believed to be derived from NK cells because of its unique B, T, and myeloid lineage-negative CD4+, CD56+, and myxovirus A by tumor cells provided strong evidence that the precursor of the plasmacytoid dendritic cell may be the cell of origin for this rare neoplasm. Incorporation of these data lead to the renaming of this entity as blastic plasmacytoid dendritic cell neoplasm in the revised WHO (2008) classification for hematopoietic and lymphoid neoplasms. We present here 2 cases of blastic plasmacytoid dendritic cell neoplasm recently diagnosed at our institution (Table), along with a review of the literature highlighting its unique clinical, histopathologic, and immunophenotypic features. Awareness and recognition of this rare entity by pathologists is vital for early diagnosis and aggressive treatment of this lethal neoplasm.

<table>
<thead>
<tr>
<th>Case</th>
<th>Age, y/ Sex</th>
<th>Extracutaneous Sites Involved</th>
<th>Flow Cytometry</th>
<th>IHC</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>68/M</td>
<td>Central nervous system</td>
<td>Blast population 40% of all cells; positive for dim CD45, HLA-DR, CD4, CD56, partial CD33, and partial CD7; negative for CD3, CD5, CD8, CD19, CD20, CD13, CD34 and CD117</td>
<td>Positive for CD123, CD4, CD56, CD43, CD68, LCA, Bcl2, CD33, CD79a, and TdT</td>
</tr>
<tr>
<td>2</td>
<td>59/M</td>
<td>Bone marrow</td>
<td>Blast population 83% of all cells; positive for HLA-DR, TdT, CD4, CD56, CD2, CD7, CD33, CD38; negative for CD5, CD10, CD19, CD20, CD13, CD34, and CD117</td>
<td>Positive for CD3, CD4, CD56, LCA, and TdT</td>
</tr>
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</table>

Abbreviation: IHC, immunohistochemistry.

Primary Pulmonary Adult T-Cell Lymphoma Presenting With Recurrent Spontaneous Pneumothorax (Poster No. 32)

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Primary pulmonary lymphoma is a very rare condition in adults, accounting for less than 0.5% of all primary lung malignancies. Most of these lymphomas are B-cell type and the incidence of other non-B-cell type of pulmonary lymphomas is unknown. Human T-cell lymphotropic virus types 1 and 2 (HTLV-1 and HTLV-2), and human immunodeficiency virus-1 (HIV-1) have been associated with pulmonary lymphomas. Herein, we present a case of a 36-year-old man who presented with recurrent spontaneous pneumothorax with bullae formation and a history of HTLV-1 seropositivity. Diagnosis of lymphocytic interstitial pneumonitis (LIP) was considered initially. However, pathologic examination of a pleural biopsy and a bilateral bullectomy specimen showed a cytologically atypic...
ical small T-cell lymphocytic population immunoreactive to CD3 and CD5 antibodies (Figure 39). Gene rearrangement studies performed on the paraffin-embedded tissue demonstrated rearrangement of the T-cell receptor. These findings, in addition to the HTLV-1 seropositivity, pointed to a diagnosis of a primary pulmonary adult T-cell lymphoma. Infection with HTLV-1 has been associated with other pulmonary conditions such as lymphocytic interstitial pneumonitis (LIP) and diffuse panbronchiolitis (DPB). In our case it is unclear whether LIP or DBP existed as a prema-
ligant condition that predisposed to the development of the lymphoma or if the macroscopic pulmonary changes were secondary to the presence of pulmonary lymphoma.

**An Unusual Case of Near-Tetraploid Early B-Precursor Acute Lymphoblastic Leukemia With Multiple Chromosomal Abnormalities**

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In childhood acute lymphoblastic leukemia, gene rearrangement, blast cell DNA content, and ploidy have important prognostic implications. Approximately 1% are near-tetraploid clonal populations. Of these, the median number of chromosomes is 55 with >65 chromosomes being of rare occurrence. ETV6/RUNX1 (TEL/AML1) gene rearrangement is a known favorable prognostic factor. We describe the case of a 15-year-old adoles-
cent female who presented with a 1-month history of fatigue, shortness of breath, and headache. Her initial white blood cell count was 4800/mm³, with 25% blast count and hemoglobin level of 4.7g/dL. The blast cells were markedly enlarged with unusual nuclear configuration. Bone mar-
row examination revealed increased cellularity with almost complete re-
placement of the normal marrow elements by the blast cells. These blast cells expressed CD19, TdT, and aberrant coexpression of CD13. DNA plo-
dy revealed a near-tetraploid population with a DNA index of 1.87. Chro-
mosomal analysis (Figure 40) revealed multiple chromosomal abnormal-
ities and confirmed the near-tetraploid karyotype (87 chromosomes) with loss of chromosomes X, 7, 8, and 14; gain of chromosome 22; and struc-
tural rearrangement of 1p, 5q, 12p, 15q, 20p, and 22q. Fluorescence in situ hybridization (Figure) analysis showed ETV6/RUNX1 (TEL/AML1) gene rearrangement. The patient began chemotherapy and the day 8 bone mar-
row contained 15%–20% blasts, but by day 15 there was no residual dis-
ease. She subsequently had good clinical outcome despite multiple che-
motherapeutic complications. We will review literature on whether the presence of near-tetraploid population, and subsequently several copies of ETV6/RUNX1 (TEL/AML1) gene, would have had an influence on a patient’s clinical outcome.

Concomitant Chronic Lymphocytic Leukemia and Acute Lymphoblastic Leukemia at Initial Presentation: Report of 2 Cases

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mayun K. Islam, MD, PhD. Department of Pathology, Westchester Medical Center/New York Medical College, Valhalla, New York.

Chronic lymphocytic leukemia (CLL) has been reported as concurrently presenting with other hematopoietic and nonhematopoietic malignancies, including acute myeloid leukemia, multiple myeloma, systemic mastocytosis, large granular lymphocytic leukemia, and renal cell carcinoma. However, it has never been reported with acute lymphoblastic leukemia (ALL). We describe 2 unique cases of CLL concurrently presenting with ALL and discuss their clinical, immunophenotypic, cytogenetic, and bio-
logic features. Case 1 was that of a 63-year-old man who presented with pancytopenia, while case 2 was that of a 74-year-old man with bicyto-
penia. Complete hematologic workup was done in both cases, including flow cytometry of peripheral blood (PB) and bone marrow (BM). Both cases had relative lymphocytosis and increased blast counts in PB. BMs were hypercellular in both and essentially packed with blasts. Immunophenotypic analysis by flow cytometry and/or immunohistochemistry re-
vealed that the blasts were precursor B cells expressing CD19, CD22, CD10, and TdT. In addition, flow cytometry on PB showed a u-
lation of mature CD5- B cells expressing CD19, CD20, CD22, and CD23. The latter also focally involved the BM in the second case. Cytogenetics showed normal karyotype in both cases. True incidence of concurrent CLL and ALL might be underestimated and may be increasingly detected with simultaneous immunophenotypic analysis of PB and BM. Synchro-
 nous ALL and CLL represents either a clonal evolution of the initial asymtomatic CLL clone or simultaneous presence of 2 separate clones, a distinction which remains to be confirmed in future studies.

**Intratumor Myeloid Sarcoma Occurring Within Glioblastoma Multiforme**

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versity of California at Davis, Sacramento.

A tumor occurring within other malignancies is a rare occurrence. We report a case of myeloid sarcoma (MS) occurring within a primary CNS glioblastoma multiforme (GBM). In this case, the patient's history included acute myelogenous leukemia (AML-M1) with normal cytogenetics. She was treated with cytarabine and an anthracycline, and remission was ul-
timately achieved after a second induction. Three years later, she had a re-
lease of AML, which was successfully treated with induction chemother-
apy. Later, she had neutropenic and infectious complications that re-
quired prolonged hospitalization, and she therefore did not receive con-
solidation chemotherapy. During the prolonged hospitalization, there were changes in her mental status. Subsequent magnetic resonance imag-
ing showed a right temporal lobe lesion. Biopsy of the brain lesion showed GBM with prominent perivascular intratumoral nodules. The GBM stained positively for glial fibrillary acidic protein, while the nodule staining results were negative. Additional staining revealed that the nodule were positive for myeloperoxidase and chloroacetate esterase, consist-
tent with intra-tumor MS. This is the first report of intratumoral MS. Determination of the MS component is critical, as the presence of intra-
cranial relapse has important implications in the decision to offer further treatment. MS most often affects bone, nodes, and skin. Intraparenchymal brain AML relapse is unusual. This report demonstrates not only that the brain microenvironment can be hospitable for leukemic blasts but also that GBM tumor and vascularity are also areas where tumor cells can proliferate, possibly because of the interrupted blood brain barrier.

**Unusual Presentation of a Hepatosplenic T-Cell Lymphoma**

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A 42-year-old man presented with 4 months of weight loss, night sweats, pruritic skin rash, and arthralgia for which he was taking large amounts of acetaminophen. Initial clinical examination identified an ex-

tensive contiguous skin rash, fever, and hepatosplenomegaly. No periph-
eral adenopathy was detected. Laboratory data showed the following: white blood cell count, 1.7 x 10⁷/mm³; hemoglobin, 12.7 g/dL; platelets, 17 x 10⁹/mm³; lactate dehydrogenase, 1349 U/L (reference range, 63–200 U/L); alanine transaminase, 1158 U/L (reference range, 0–30 U/L); as-
partate transaminase, 1270 U/L (reference range, 10–32 U/L); alkaline phosphatase, 262 U/L (reference range, 30–120 U/L); and normal levels of creatinine. Computed tomographic scans showed no lymphadenopathy but confirmed the splenomegaly. Results of viral hepatitis and human immunodeficiency virus screen were negative; skin biopsy was nondiagnostic. A bone marrow aspirate showed a predominance of inter-
mediate to large-sized cells with blastic morphology. The bone marrow biopsy showed infiltration by lymphoid cells located in the sinusoidal and interstitial spaces. Flow cytometry showed the infiltrate was predomi-

cantly T cells, with virtually all expressing TCR α-β and most with loss of CD5. The abnormal cells were positive for CD7; CD3, CD8, CD56, and Ki-67 (50%) and negative for CD5, CD20, CD19, CD30, and CD15. A diagnosis of hepatosplenic γ-δ T-cell lympho-

Arch Pathol Lab Med—Vol 133, October 2009
been responsible for hepatomegaly, might obscure the diagnosis.

**Idiopathic Neutropenia in a Cocaine User: A Case Report and Review of the Literature**

(Poster No. 37)

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Idiopathic neutropenia is a rare benign disorder of granulopoiesis characterized by an unexplained reduction in the absolute neutrophil count below the lower limit of the reference range for a prolonged period. Laboratory testing for anti-neutrophil antibodies is technically challenging and not widely available. Neutropenia associated with levamisole contamination of cocaine is becoming a public health hazard. A young male with a history of cocaine use and neutropenia presented with fever, skin lesions, and lymphadenopathy in 2007. The bone marrow was evaluated and showed arrested granulopoiesis at the myelocyte stage and dysplastic megakaryocytes (Figure 41). Anti-neutrophil antibody testing was positive. The patient has been followed up for 2 years and has demonstrated continued cocaine use. The bone marrow morphology is suggestive of chronic idiopathic neutropenia, but the case illustrates the need for adequate history and communication between pathologist and hematologist. This case presents a diagnostic challenge and emphasizes the need for clinicopathologic correlation.

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**Detecting CML in the Blood of a Patient with Idiopathic Neutropenia**

(Poster No. 38)

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As a prototype of myeloproliferative neoplasms, chronic myelogenous leukemia (CML) is constantly associated with the BCR-ABL1 translocation, and often presents with typical morphologic findings. We report 2 cases with unusual morphologic features that were not recognized as CML before the cytogenetic results were available. The first case is that of a 64-year-old woman with history of hypertension and hypercholesterolemia. She presented with an increased blast count in her peripheral blood. The bone marrow biopsy demonstrated a hypercellular marrow with increased numbers of myeloblasts (10%–15%), myeloid and erythroid hyperplasia, multilineage dysplasia, and reticulin fibrosis. The presence of blasts was confirmed by flow cytometry and immunohistochemistry. These findings were interpreted as refractory anemia with excess blasts. However, the cytogenetic results revealed the BCR-ABL1 translocation in 95% of cells, in addition to other abnormalities: t(6;18) and trisomy 19. The second case is that of a 51-year-old woman who received a renal transplant in 1996. In 2008, she presented with weakness and mid-epigastric abdominal pain. Workup revealed a mass along the greater curvature of the stomach. A biopsy was diagnosed as carcinoid tumor because of synaptophysin and CD56 positivity. Subsequently, the patient developed upper-gastrointestinal bleeding and underwent subtotal gastrectomy. Gross examination showed a 6-cm, exophytic mass extending through the entire thickness of the stomach. Microscopic examination showed an infiltrative lesion composed of atypical plasmacytoid cells. One perigastric lymph node was involved. Immunohistochemistry showed strong positivity for CD45, MUM-1, and CD138 (Figure 42), supporting the initial impression of a plasma cell neoplasm. The tumor also showed a predominance of light chain production. Tumor cells were strongly positive for EBV-RNA by fluorescence in situ hybridization. PTLD encompasses a broad range of lymphoid proliferations that develop in transplant recipients. The World Health Organization divides PTLD into early, polymorphic, and monomorphic PTLDs. Early and polymorphic lesions are relatively benign. Monomorphic PTLDs represent a variety of lymphomas and are morphologically similar to corresponding entities occurring in an immunocompetent host. Most cases are EBV-induced. Plasmacytoma-like PTLDs are very rare, with only a few reported cases.
seminoma. Computed tomography of chest, abdomen, and pelvis were unremarkable. Laboratory study (α-fetoprotein, LDH, HCG-β subunit) results were all within normal levels. Patient underwent right radical orchiectomy. Grossly, the testis showed a well-circumscribed, homogeneous yellow mass measuring 3.5 cm in greatest diameter. Histologically, the tumor was confined to the testis and composed of spindle cells in fascicular growth pattern with focal epithelioid areas that appeared to form abortive tubular structures (Figure 43). Immunohistochemistry showed coexpression of S100 and smooth muscle markers and negativity for cytokeratins and desmin. The tumor expressed the gonadal stromal tumor coexpression of S100 and smooth muscle markers and negativity for cytoplasm, and mitotic activity of 3/HPF focally in the current case favor a stromal tumor of low malignant potential. To our knowledge, this is the first case of sex cord/gonadal stromal tumor classified as incompletely differentiated with low malignant potential.

Is Digital Planimetry Preferable to Visual Estimate in Routine Evaluation of Prostate Carcinoma?
(Poster No. 41)

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Context: Tumor volume (TV) is an important determinant of clinical outcome after radical prostatectomy. Recently, various studies have discussed the digitized methods for estimating TV. We sought to measure TV by digital planimetry (DP) and compare the values with visual estimate (VE).

Design: TV was determined from whole-mount hematoxylin-eosin slides by using VE as well as DP from 70 consecutive patients with prostate carcinoma, Gleason score 8–10. MacroPATH Imaging System was used for digital planimetry. Additionally, correlation of TV by both methods with various parameters such as Gleason grade, margin positivity, extraprostatic extension, seminal vesicle invasion, and angiolymphatic invasion were assessed by Pearson correlation.

Results: TV by DP is statistically significantly correlated to that by VE ($r^2 = 0.64, P < .001$). Mean TV by VE differs significantly between extraprostatic extension negative (16.7) and extraprostatic extension positive (37.3) cases ($P = .02$) and in angiolymphatic invasion negative (33.2) versus angiolymphatic invasion positive (45) cases ($P = .05$) (Figure 44). Gleason grade, margin positivity, and seminal vesicle invasion does not show statistically significant association with TV by both methods.

Conclusions: Our findings differ from the previous studies in that we found that both methods (digital planimetry and visual estimate) had positive correlation in estimating tumor volume. Visual estimate can serve as a reliable, inexpensive prognostic indicator in predicting extraprostatic extension and angiolymphatic invasion. Digital planimetry, which is potentially expensive, time consuming, and labor-intensive, may not yield much additional benefit.

Mass-Forming IgG4-Related Tubulointerstitial Nephritis: A Clinical and Radiologic Mimicker of Malignancy
(Poster No. 42)

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IgG4-related autoimmune pancreatitis is a well recognized mass-forming lesion of the pancreas. Tubulointerstitial nephritis has been recently described as one of the extrapancreatic manifestations in these patients. A 29-year-old man with past history of type 1 diabetes mellitus, Grave disease, sclerosing cholangitis, and ulcerative colitis presented to our hospital for management of bilateral enhancing hypodense renal masses on computed tomography (CT) scan workup. CT-guided needle biopsy from 1 of these masses showed tubulointerstitial nephritis with eosinophils and lymphoplasmacytic infiltrate. Flow cytometry results were negative for B-cell lymphoproliferative disorder. T- and B-cell gene rearrangement study results were also negative. Since the clinical and radiologic suspicion for malignancy was high, a partial nephrectomy was performed. Histologic findings of the mass-forming tissue consisted of tubulointerstitial nephritis with extensive interstitial fibrosis and tubular atrophy with focally thickened tubular basement membranes. The infiltrate consisted of numerous eosinophils, lymphocytes, plasma cells, and few histiocytes. Adjacent nonlesional renal parenchyma appeared unremarkable and had a sharp demarcation from the inflamed and fibrotic tissue. Immunohistochemistry for lymphoproliferative disorders and histiocytic malignancies was negative. The plasma cells were polyclonal in nature and strongly expressed IgG4 antibody. Serum IgG4 levels were
also high (864 mg/dL). IgG4-related tubulointerstitial nephritis can present as a mass-forming lesion and is a clinical and radiologic mimic of malignancy. It should be included in the differential diagnosis as one of the pseudotumors in kidney biopsies and resection specimens (Figure 45).

Low-Grade Adenocarcinoma Arising in Nephrogenic Metaplasia at Urinary Bladder Neck of an Adolescent Female
(Poster No. 43)

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Nephrogenic metaplasia is a rare benign condition of urothelium that displays tubulo-cystic, papillary-polyoid, or rarely, diffuse growth patterns. Its most important differential diagnosis is clear cell adenocarcinoma, a high-grade carcinoma considered to be its malignant counterpart. Here we report an unusual adenocarcinoma with growth patterns resembling both conditions. The patient had a history of recurrent urinary tract infection and lower back pain for 3 months. Preoperative workup identified a 3.2-cm solid mass at the urinary bladder neck. The cystectomy specimen contained a poorly defined firm tumor involving the anterior wall of bladder neck and the adjoining proximal urethra. Microscopically, the tumor diffusely infiltrated from lamina propria to the perivesical fat. It had a tubulo-cystic pattern lined by a single layer of low cuboidal or hobnail cells with dense eosinophilic luminal secretion in some tubules. Intermingled were areas of solid growth made up of cells arranged in cords or nests, many with intracytoplasmic lumen (Figure 46). Areas of nephrogenic metaplasia were noted in the overlaying urothelium and histologic transition to the invasive carcinoma was identified. Mitoses were rare, and areas of necrosis absent. Ki-67 staining varied, up to 15% in focal areas; p53 staining was weak and diffuse. Results with CK7, EMA, vimentin, CA-125, luminal CD10, and nuclear PAX2 were positive. The malignant tumor differs from nephrogenic metaplasia and clear cell adenocarcinoma in that it is deeply invasive, has low mitotic rate, and lacks areas of necrosis. We believe that the tumor represents an unusual low-grade adenocarcinoma arising in nephrogenic metaplasia.

Demonstration of Lower Expression of BRMS1 in Primary Prostatic Adenocarcinoma Than in Normal Prostatic Glandular Tissue
(Poster No. 44)

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Context: Breast cancer metastasis suppressor 1 (BRMS1) has been implicated as an important gene in preventing multiple steps of the metastatic cascade from occurring in various tumor xenograft models, notably in breast, melanoma, and ovarian models. Evaluation of the expression of BRMS1 in prostatic adenocarcinoma has not been performed. Our purpose was to determine expression of BRMS1 in the evolution of prostatic adenocarcinoma from normal gland to metastatic adenocarcinoma.

Design: A tissue microarray (Biomas, Rockville, Maryland) containing formalin-fixed, paraffin-embedded prostatic tissue was stained with a monoclonal antibody (Clone 3a1.21). Fifteen cores of normal prostatic tissue, 66 cores of prostatic adenocarcinoma, and 4 cores of benign prostatic tissue from a prostate intraepithelial neoplasia (PIN) were evaluated for BRMS1 protein expression. Some cores with absent cellularity were excluded from the study. The intensity of nuclear BRMS1 staining was graded on a scale of 0–3.

Results: BRMS1 was strongly expressed in all cases of normal prostate tissue, with an average staining intensity of 2.73±0.1. Staining was diffuse, intense, and nuclear. There was no statistical difference observed between staining intensity of PIN lesions (2.75±0.25) and normal prostate tissue. The prostatic adenocarcinoma group demonstrated a significant decrease in staining intensity (2.04±0.1) compared to that in normal and PIN lesions (P <0.003).

Conclusions: The staining results are consistent with a decrease in expression of BRMS1 in prostatic adenocarcinoma as compared to that in normal prostate tissue and high-grade PIN lesions, which suggests a role for BRMS1 in prostate tumor progression. Further study of the role of BRMS1 in the regulation of tumor progression is necessary.

Plasmacytoid Urothelial Carcinoma: Two Case Reports Demonstrating CD138 and VS38c Positivity
(Poster No. 46)

Elizabeth Plocharczyk, MD (elizabeth.plocharczyk@osumc.edu); Gang He, MD, PhD. Department of Pathology, Ohio State University Medical Center, Columbus.

Plasmacytoid urothelial carcinoma is a rare, recently described entity, with fewer than 60 cases reported in the literature. Histologically, tumor cells of this variant appear plasmacytoid with eccentric nuclei, abundant eosinophilic cytoplasm, and a discohesive or Indian-filing pattern, reminiscent of lobular carcinoma of the breast. Immunohistochemistry demonstrated positivity for cytokeratins, confirming the cells’ epithelial origin. Positivity for the plasma cell marker CD138 is variable and staining characteristics for another plasma cell marker, VS38c, have not been reported. Herein, 2 cases of plasmacytoid urothelial carcinoma positive for CD138 and VS38c are reported. Case 1 involved a 67-year-old white man who presented to his urologist for worsening dysuria. A computed tomography scan demonstrated a bladder mass. Biopsy revealed poorly differentiated urothelial carcinoma. Final pathology of the cystoprostatectomy specimen demonstrated a poorly differentiated urothelial carcinoma with areas of plasmacytoid differentiation infiltrating the muscularis propria. Case 2 was that of a 71-year-old white woman who developed dysuria...
and polyuria, and cystoscopy demonstrated a bladder mass. Biopsy of the mass revealed sheets of discohesive malignant cells with abundant, eosinophilic cytoplasm and eccentrically placed large nuclei infiltrating the muscularis. Immunohistochemical staining in both cases was positive for AE1/3, Cam5.2, CK7, CD10, CD138, and VS38c and negative for CK20, CD79a, and CD45, confirming the diagnosis of plasmacytoid urothelial carcinoma. Figure 47 shows a hematoxylin-eosin photomicrograph at ×40 magnification (a), as well as immunohistochemical staining for AE1/3 (b), CD138 (c), and VS38c (d).

Renal Oncocytic Neoplasms: Molecular and Immunohistochemical Analysis With an Emphasis on the Birt-Hogg-Dube\'e Gene and Mammalian Target of Rapamycin-Related Proteins
(Poster No. 47)

Stephen M. Rohan, MD (rohan@mskcc.org); Maria E. Dudas, MD; Samson W. Fine, MD; Anuradha Gopalan, MD; Victor E. Reuter, MD; Satish K. Tickoo, MD. Department of Pathology, Memorial Sloan-Kettering Cancer Center, New York, New York.

Context: Patients with Birt-Hogg-Dube\'e (BHD) syndrome develop renal tumors, wherein renal oncocytic neoplasms (RONs) are overrepresented. Alterations of the BHD gene on chromosome 17 (ch17) have been documented in sporadic renal tumors. The protein product of the BHD gene interacts with the mammalian target of rapamycin (mTOR) pathway. We evaluated the mutational status of the BHD gene, ch17 copy number by fluorescence in situ hybridization (FISH), and immunohistochemistry (IHC) expression of mTOR pathway activation markers (p-S6, p-4EBP1) in sporadic RONs.

Design: Fifty-four RONs (9 oncocytes [ROs], 26 chromophobe carcinomas [CRs], and 19 renal cell carcinomas, unclassified, oncocytic type [URCCs]) were examined. The unclassified category included oncocytic tumors with features that precluded their inclusion among RO or CR. IHC for CK7, CD117, TFE3, p-S6, and p-4EBP1 was performed. Staining was graded as absent/weak (0 or 1+), 0%–25% cells positive) or strong (2+ or 3+, 26%–100%). The BHD gene was sequenced and mutational analysis was performed. FISH was done using a ch17 centromeric probe.

Results:

<table>
<thead>
<tr>
<th>Marker</th>
<th>CHR, No. (%)</th>
<th>RO, No. (%)</th>
<th>URCC, No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CD117</td>
<td>22 (85)</td>
<td>8 (89)</td>
<td>15 (79)</td>
</tr>
<tr>
<td>CK7</td>
<td>18 (69)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>p-4EBP1</td>
<td>0</td>
<td>3 (34)</td>
<td>3 (15)</td>
</tr>
<tr>
<td>p-S6</td>
<td>1 (4)</td>
<td>0</td>
<td>3 (15)</td>
</tr>
<tr>
<td>TFE3</td>
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</tr>
</tbody>
</table>

Most tumors expressed CD117. CK7 was expressed in most CHRs, but in none of the ROs or URCCs. No mutations of the BHD gene were detected. Most (15/25, 60%) CHRs showed loss of ch17. Ch17 loss was seen in 1 URCC. No ROs showed ch17 loss. There was no correlation between ch17 copy number and mTOR marker expression.

Conclusions: Our data suggest that URCCs are more closely related to ROs than CHRs. Mutations of the BHD gene and mTOR marker expression appear to be infrequent in sporadic RON.

p63 Is Not Expressed in Most Micropapillary Urothelial Carcinomas
(Poster No. 48)

Liset Pela\'ez, MD (lpelaez@med.miami.edu); Carmen Gomez-Fernandez, MD; Merce Jordi, MD, PhD. 1 Department of Pathology, Jackson Memorial Hospital, Miami, Florida; 2 Department of Pathology, Jackson Memorial Hospital/University of Miami/Sylvester Comprehensive Cancer Center, Miami, Florida.

Context: Carcinomas with micropapillary features have been described in urinary bladder, ovary, breast, lung, and salivary gland. They are characterized by small papillary clusters of cells located within a lacuna and associated with high pathologic stage with early vascular invasion, metastasis, and high mortality. Micropapillary urothelial carcinoma (MPUC) represents approximately 1% of all bladder urothelial cancers. Because of its aggressive behavior, metastasis may be the initial presentation. p63, a member of the p53 family, is expressed in the nucleus of squamous and urothelial cells and in their carcinomas. However, loss of expression of p63 occurs in a subset of high-grade urothelial carcinomas. The objective was to identify the expression of p63 immunohistochemistry in MPUC and its potential role in distinguishing MPUC from other carcinomas with micropapillary morphology.

Design: Six cases of MPUC were identified in a period of 10 years (1998–2008). Four cases corresponded to transurethral resection of bladder tumor, 1 case to a radical cystectomy, and 1 case to a nephrectomy/ureterectomy. Immunohistochemical analysis for p63 (1:50; M7247, Dako) was performed in all cases by using the LSAB method.

Results: p63 positivity was defined as strong nuclear staining. All cases but one were negative for p63.

Conclusions: p63 is not expressed in most MPUCs. Lack of expression of p63 in MPUC can be associated with a possible glandular differentiation or to a loss of expression of p63 due to the tumor’s higher grade. p63 immunostain is not useful in distinguishing MPUC from other micropapillary carcinomas of nonurothelial origin when metastasis is the initial presentation.

Use of Image Analysis for Interpretation of PIN-4 Immunohistochemical Staining in Prostate Needle Biopsies
(Poster No. 49)

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Context: Immunohistochemistry markers routinely used in the interpretation of prostate biopsies include P504S, p63, and high-molecular-weight cytokeratins. The combination of these in the PIN-4 cocktail can be useful in the distinction between adenocarcinoma, high-grade prostatic intraepithelial neoplasia, and benign glands, particularly in cases with limited tissue. However, interpretation of multiple markers staining different subcellular compartments of different cell types can be challenging. An image analysis algorithm was therefore developed to assist in the interpretation of PIN-4–stained tissue.

Design: Fifty prostate needle biopsy cases, each consisting of corresponding hematoxylin-eosin– and PIN4-stained slides, were selected. Slides were scanned at ×20 magnification on the BioImagene iScan Scanner. Manual interpretation was performed on a computer monitor that permitted the viewing of whole slide images at magnifications from ×1 to ×40. After a 2-week wash-out period, the same cases were reviewed by using image analysis for selected regions of interest in the PIN-4 study. For both manual and automated scoring, cases were categorized as adenocarcinoma or benign (includes PIN). A high degree of concordance (>95%) was observed between manual and automated interpretation of benign and malignant biopsies. The algorithm correctly distinguished benign from malignant glands based on PIN-4 staining in almost all cases. PIN was more frequently diagnosed by image analysis than by manual review.

Conclusions: Image analysis can accurately distinguish between benign and malignant prostate glands in PIN4-stained tissue, without assistance from the pathologist. To our knowledge, this is the first example of image analysis of multicolor immunohistochemistry for interpretation of prostate biopsies.
Obstructive Uropathy Secondary to Familial Mediterranean Fever-Related Amyloidosis (Poster No. 50)

Erin Morris, MD (emorris@tuftsmedicalcenter.org); Pushkar A. Phadke, MD, PhD; Monika E. Pilchowska, MD, PhD. Department of Pathology, Tufts Medical Center, Boston, Massachusetts.

Familial Mediterranean fever (FMF) is a rare hereditary autosomal disorder characterized by recurrent paroxysmal febrile episodes and serosal inflammation. Secondary amyloidosis, most commonly involving the kidney, is a well-known long-term complication and significant source of morbidity and mortality in FMF. We report a case of a 76-year-old male renal transplant recipient who underwent a renal biopsy for increased creatinine 3 years posttransplant. The biopsy revealed tubular epithelial cell injury suggestive of calcineurin inhibitor toxicity and vascular mural eosinophilic deposits positive for amyloid by Congo red staining and apple green birefringence under polarized light. There was no evidence of cellular or antibody-mediated rejection. Direct immunofluorescence did not reveal light chain restriction. Immunohistochemical studies for AA amyloid revealed deposition in blood vessel walls and interstitium. These findings were diagnostic of renal allograft involvement by AA amyloidosis. Detailed history revealed that the end-stage renal disease was due to obstructive uropathy secondary to prostatic hypertrophy. Retrospective immunohistochemical examination of the prostate resection specimen revealed prominent interstitial deposits of AA amyloid. Additionally, the patient and his brother had suffered from episodes of chronic episodic diarrhea. Based on the history and clinical findings, a diagnosis of FMF was made. The patient’s presentation in this case is unusual because renal failure was caused by obstructive uropathy secondary to amyloid-related prostatic hypertrophy, as opposed to primary renal involvement, which is the usual case in FMF. Furthermore, this case highlights that AA amyloidosis can recur in a kidney allograft, thereby complicating the clinical course.

Adult Testicular Granulosa Cell Tumor: A Case Report and Review of the Literature (Poster No. 51)

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Adult testicular granulosa cell tumors are rare sex cord-stromal tumors of which only 28 have been reported. As compared to their ovarian counterparts, these tumors follow a more aggressive course and the proportion of malignant cases is higher. To date, there are no features that definitively predict malignancy. We present the 29th case of an adult testicular granulosa cell tumor and review the literature in an attempt to identify features that may predict its malignant potential. Our patient is a 21-year-old man who was referred to his urologist for a painless left testicular mass. Orchiecotomy revealed a 1.0-cm, well-circumscribed mass abutting the tunica albuginea. Histologic sections showed a solid to focally trabecular pattern of medium-sized cells with grooved ovoid nuclei and scant cytoplasm. The cells displayed mild pleomorphism and showed distinct nuclear molding. The mitotic count was 15/10 high-power fields. There was no hemorrhage, necrosis, or lymphovascular invasion. Immunohistochemistry was strongly positive for inhibin, and focally positive for calretinin. At 16 months follow-up, the patient was free of disease. A review of all 29 reported adult testicular granulosa cell tumors shows that size (>5 cm) is the only significant predictor of malignancy (Mann-Whitney, \( P = .02 \)). Although the mitotic rate in our patient is high, he has a favorable prognosis because of the small size of his tumor.

Bladder Urothelial Carcinoma Metastatic to the Testicle (Poster No. 52)

Matthew D. Geller, DO (mgeller327@yahoo.com); Nicole M. Durie, MD; Robert D’Esposito, MD; Andrea Flieder, MD. Departments of Pathology and Urology, Winthrop University Hospital, Mineola, New York.

Most testicular neoplasms are primary in nature; however, an estimated 3.6% are metastatic from distant sites. Numerous cases of neoplasms metastatic to the testicle have been reported. Of these, the most common organs of origin are prostate, lung, kidney, stomach, skin (melanoma), and colon. There have been few reports of bladder urothelial carcinoma metastasizing to the testis. We add to the small repertoire of published reports of this rare occurrence. Our patient is an 87-year-old man with a history of infiltrating, poorly differentiated bladder urothelial carcinoma who presented with a hard right testicle. His testicular tumor was found to be histomorphologically identical to his prior bladder tumor. In addition, his primary and metastatic tumors both showed squamous differentiation, a finding that, to our knowledge, has not been reported.

Collision Angiomyolipoma and Renal Cell Carcinoma in an Elderly Woman: A Case Report and Review of the Literature (Poster No. 53)

Anna T. Vischio, MD, MPH (annavischio@gmail.com); Jeet Sandhu, MD; Hani El-Fanek, MD. Departments of Pathology and Laboratory Medicine and Radiology, Danbury Hospital, Danbury, Connecticut.

The coexistence of a renal cell carcinoma and an angiomyolipoma is quite rare, with only 31 cases cited in the literature. Renal angiomyolipoma is a relatively benign retroperitoneal tumor. Histologically, it is a choristoma composed of an intimate admixture of fat, smooth muscle, and vessels. Despite the lack of cellular anaplasia, angiomyolipomas represent a significant aberration in normal development that cause hematuria, flank pain, renal failure, or even spontaneous hemorrhage and shock, if symptomatic. Angiomyolipomas are highly associated with the hereditary disease tuberous sclerosis; therefore, all patients with renal angiomyolipomas should be evaluated. We present the case of an 80-year-old woman who initially presented with painless hematuria in 2005. An abdominal computed tomography (CT) showed a 2.8-cm left renal mass containing fatty elements and soft tissue suggestive of an angiomyolipoma. In 2008 the patient re-presented with recurrent painless hematuria. A heterogeneously enhancing 4.4 × 4.4 × 3.6-cm mass in the upper pole of the left kidney was seen on CT. An ultrasound-guided core needle biopsy was performed. Histologic examination of the core needle biopsy of the renal mass demonstrated a collision tumor of a well-differentiated renal cell carcinoma, clear cell type, and an associated angiomyolipoma (Figure 48). The angiomyolipoma was composed mainly of smooth muscle fibers without the adipose tissue component. Immunoperoxidase stains demonstrated strong positivity for HMB-45. The patient is scheduled for a radical nephrectomy. These tumors are rare and usually have a good prognosis if detected and excised early.

<table>
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<td>2</td>
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<td>20</td>
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<tr>
<td>Size</td>
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<td></td>
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<tr>
<td>&lt;5 cm</td>
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<td>8</td>
<td>3</td>
<td></td>
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<td>&gt;10 cm</td>
<td>5</td>
<td>2</td>
<td>3</td>
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<tr>
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<td>18</td>
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</tr>
</tbody>
</table>

Abbreviation: NS, not significant.
Infiltrating Urothelial Carcinoma May Be of the Clear Cell Variant
(Poster No. 54)

Stewart Nash, MD1 (Stewart.Nash@ttuhsc.edu); Allan Haynes, MD; Mitchell Wachtel, MD; Dale Dunn, MD.1 Departments of Pathology and Urology, Texas Tech University Health Sciences Center, Lubbock.

A 62-year-old white man presented with hematuria. A computed tomography scan revealed a thickened urinary bladder with a 7.46 × 5-cm, lobulated, intraluminal mass with obstruction of both ureters and bilateral hydronephrosis, without any other tumor. The patient underwent cystoscopic resection. Received were 11.8 g of tissue chips. A solid tumor, with rare foci of non–clear cell change, which invaded perivesicle parenchyma into a pseudocapsule. At microscopy (Figure 49), the tumor contained monotonous small cells with “salt-and-pepper” chromatin, and negative for prostate-specific antigen and vimentin. The cystoprostatectomy specimen showed the same tumor, with rare foci of non–clear cell change, which invaded perivesicle fat. One lymph node was partly replaced by non–clear cell urothelial carcinoma. The prostate tissue was benign. The patient remains alive, 1 ½ years after cysto-prostatectomy. From this case, one might hypothesize that a predominantly clear cell variant of urothelial carcinoma can arise from urothelial carcinoma in situ. Because the lymph node metastasis was of non–clear cell type, it can be further hypothesized that urothelial tumor cells with clear cytoplasm are less aggressive than are those that lack clear cytoplasm (Figure 49).

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Plasma Copper in Leukopenic Dialysis Patients
(Poster No. 55)

Claude Burdick, MD (claude.burdick@fmc-na.com); Nabat K. Wadhwa, MS. Spectra Laboratories, Milpitas, California.

Context: Deficiency of copper is unusual, but occasionally occurs in infants or adults fed a copper deficient enteral formula. In these subjects, the blood displays leukopenia with myelodysplastic changes. Recently, there have been reports of sporadic copper deficiency manifested by neurologic symptoms. Clinical laboratories serving hemodialysis patients receive occasional specimens showing leukopenia resembling that described in copper deficiency. We thought it possible that copper might be lost in the hemodialysis process and tested these specimens for copper deficiency. Previous studies had shown that peritoneal dialysis does not remove copper from the blood. There are no hemodialysis studies.

Design: Plasma copper was measured by inductively coupled plasma emission spectroscopy. Three studies were done. Copper was measured from 27 volunteers, from 29 dialysis patients with normal white blood cell counts, and from 39 dialysis patients who had white blood cell counts of 2000/µL or lower.

Results: Copper levels in normal subjects ranged from 67–247 µg/dL, with a mean of 105 µg/dL and a standard deviation of 38 µg/dL. Copper levels in dialysis patients with normal white counts ranged from 67–152 µg/dL with standard deviation of 23 µg/dL. Copper levels in leukopenic dialysis patients ranged from 44–139 µg/dL, with a mean of 86 µg/dL and standard deviation of 23 µg/dL.

Conclusions: Patients described in the literature with a dysplastic leukopenia due to hypocupremia have copper values in the range of 0–9 µg/dL. No leukopenic patient approached these levels, so that hypocupremia is not an explanation for their dysplastic leukopenia. Hemodialysis does not remove copper from blood.

Primary Renal Carcinoid:
A Case Report and Review of the Literature
(Poster No. 56)

Heather Baldwin, MD (hbaldwin@mailshroud.com); Amer Mahmoud, MD; Amanda Mullins, MD; Nadeem Zafar, MD. Department of Pathology and Laboratory Medicine, University of Tennessee Health Science Center, Memphis.

Primary renal carcinoid is a rare tumor, mostly reported as isolated cases in the literature. We report the case of a 52-year-old man who presented with abdominal pain and an abdominal mass at clinical examination. At computed tomography, a solid enhancing mass was seen in the right renal pelvis, which prompted right nephrectomy. At gross pathologic examination, the renal hilum contained a well-circumscribed, 3.5-cm, yellow-tan tumor that compressed the neighboring renal parenchyma into a pseudocapsule. At microscopy (Figure 50), the tumor contained monotonous small cells with “salt-and-pepper” chromatin, arranged in anastomosing trabeculae, cords, and some solid sheets. Extensive lymphovascular involvement was present. The working differential diagnoses included carcinoid tumor, small cell neuroendocrine carcinoma, primitive neuroectodermal tumor, paraganglioma, Wilms tumor, and neuroblastoma. Cellular monomorphism with typical architectural arrangement, immunoactivity with neuron-specific enolase, chromogranin, synaptophysin, and CD56, as well as no other site evidence for carcinoid tumor, clinched the diagnosis of primary renal carcinoid in this case. Tumor cells also did not immunoreact with EMA, TTF-1, WT-1, CD99 and F104S. Carcinoid tumors are distinct entities within the 2004 World Health Organization classification scheme of renal tumors, with similar features to carcinoid tumors found elsewhere. Awareness for primary renal carcinoid is likely to lead to an accurate diagnosis.
Combined Neoplasm of the Urinary Bladder: Case Report With Review of Literature (Poster No. 57)

Vlad A. Alexeeva, MD (vladlogon@msn.com); Sambit K. Mohanty, MD; Matthew D. Geller, DO; George K. Turi, MD. Department of Pathology, Winthrop University Hospital, Mineola, New York.

Small cell carcinoma of the urinary bladder is a rare tumor known to have a dismal prognosis. This neoplasm often coexists with high-grade invasive transitional cell carcinoma and, in up to 40% of cases, with transitional cell carcinoma in situ. Currently, only a few cases of large cell neuroendocrine tumor of the urinary bladder have been reported in the literature. In our case report, we describe the coexistence of small cell carcinoma of the urinary bladder with large cell neuroendocrine tumor, as well as an invasive transitional cell carcinoma with an in situ component in a 79-year-old male patient. We also show the tumor's immunohistochemical profile, showing the presence of the multiple lines of differentiation in 1 neoplasm raises significant questions about the molecular events of this neoplastic process.

Pathologic Correlation of Radiologically Detected Prostate Cancer Lesions by a Novel Technique (Poster No. 58)

Haresh Mani, MD; Baris Turkbey, MD; Marcellino Bernardo, MS; Vijay Shah, PhD; Tom Pohida, PhD; Peter Pinto, MD; Peter Choyke, MD; Maria J. Merino, MD (mjerino@mail.nih.gov). 1National Cancer Institute and Center for Information Technology, National Institutes of Health, Bethesda, Maryland; 2SAIC-Frederick, National Institutes of Health, National Cancer Institute-Frederick, Maryland.

Context: Whole mount sections of prostates allow pathologic-radiologic correlations and tumor volume determination, factors that are important in patient management. However, whole mount sectioning often results in gland distortion and an inability to achieve these aims.

Design: To alleviate the problems of specimen distortion and for precise sectioning of prostatectomy specimens, we used a novel technique. Eight consecutive patients with biopsy-proven prostate cancer were accrued. Based on preoperative magnetic resonance imaging (MRI), a 3-D prostate model was generated to create a customized mold for each patient. Prostate specimens were differently fixed and sectioned in their respective molds at 6 mm intervals (to facilitate comparison with the 3 mm-interval MRIs). Tumor foci were mapped on whole mount hematoxylin-eosin–stained sections and correlated with MRI findings.

Results: Sectioning in the mold yielded uniform slices, without distortion, and excellent quality histologic results. There were 2 to 5 (mean 2.8) foci of tumor per specimen with tumor volumes up to 11.9 cc. One case showed focal extraprostatic extension. Preoperative imaging had overall detection sensitivity of 69% and specificity of 61%; the sensitivity improved to 90% when central gland tumors and tumors less than 0.125 cc were excluded from analysis. Imaging detected both gland-rich and infiltrating foci of tumors but overestimated extraprostatic extension.

Conclusions: This novel technique of sectioning prevents specimen distortion and allows precise measurement and mapping of prostate cancer. The high correlation of preoperative imaging with histopathologic findings suggests that this technique will aid in directed tissue procurement for research to better understand pathology of prostate cancer.

Lymphovascular Invasion in Micropapillary Urothelial Carcinoma (Poster No. 59)

Elizabeth B. McQuitty, MD (emcquitty@tmhs.org); Luân D. Truong, MD; Steven S. Shen, MD, PhD; Jae Y. Ro, MD, PhD; Alberto G. Ayala, MD; Philip T. Cagle, MD; Qhui’ Jin” Zhai, MD. Department of Pathology, The Methodist Hospital, Houston, Texas.

Context: Micropapillary urothelial carcinoma (MPUC) is characterized by clusters of tumor cells floating in lacunar spaces that are conventionally understood to represent retraction artifact. This morphology is associated with high frequency of lymph node metastasis and low survival; reasons for this aggressiveness remain unclear. We hypothesize that some lacunar spaces were immunostained with D2-40 and CD34 for comparison with routine hematoxylin-eosin–stained sections.

Results: Of 25 patients, 22 were men with a median age of 70 (range, 56–85 years). All cases were associated with high-grade urothelial carcinoma (transitional cell carcinoma grade 3/3). Stage grouping was available in 9 cases; 7 of these (78%) presented with stage III disease and greater. Tissue was available for immunostaining in 22 cases. Lacunar spaces were almost uniformly identifiable for D2-40 and CD34. However, lymphovascular invasion was present in 21/22 cases (95%), a rate significantly higher than for conventional urothelial carcinoma (28% in previous work at our institution).

Conclusions: Our results confirm that most lacunar spaces are not lymphovascular channels. However, nearly all MPUC tumors (95% in this series) show evidence of lymphovascular invasion. The high incidence of lymphovascular channels in MPUC tumors partially explains MPUC’s tendency to present with higher rates of lymph node metastasis than conventional urothelial carcinoma. Our data support the use of MPUC as a morphologic marker for aggressive disease.

Epithelioid Angiomyolipoma of the Kidney With a Unique t(6;11)(q13;p15) Chromosome Translocation (Poster No. 60)

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Epithelioid angiomyolipoma is a potentially malignant, rare variant of renal angiomyolipoma, characterized by proliferation of predominantly or exclusively of epithelioid cells. It often presents as a part of a tuberous sclerosis complex. Peculiar pattern of immunoreactivity includes expression of melanocytic differentiation markers such as human melanoma black-45/Melanin-A, and microphthalmia transcription factor and variable expression of smooth muscle markers. Expression of epithelial markers is always negative. Histologic characteristic of epithelioid angiomyolipoma with cells having enlarged nuclei and prominent nucleoli may lead to misdiagnosis of high-grade carcinoma especially renal cell carcinoma. Perivascular cellular arrangement, focal features of otherwise classic angiomyolipoma, and characteristic immunoprofile are clues to the correct diagnosis. Cytogenetic abnormalities include allelic loss of chromosomal arm 16p16 in classic, epithelioid, and sarcomatoid areas and TP53 mutation mostly detected in epithelioid areas. We report the case of a 76-year-old man with history of left renal mass who subsequently developed local recurrence and distant metastasis to the liver. Histologically, all of the lesions appeared similar and characterized by proliferation of large, bizarre, epithelioid cells with abundant clear to deep eosinophilic cytoplasm, vesicular nuclei, and prominent nucleoli. Multinucleated giant cells, coagulative tumor necrosis, mitosis, and atypical mitotic figures are easily discernable. Immunohistochemical staining revealed positivity of neoplastic cells for human melanoma black-45 and melan A and negative staining for S100, pancytokeratin, vimentin, and CD10. Genotypic analysis, with standard GTG banding technique, revealed a unique, previously unreported t(6;11)(q13;p15) chromosome translocation. In conclusion, we present this case because of its rarity and detection of a new, unique chromosome translocation.

Interobserver Agreement for Extracapsular Extension of Prostatic Adenocarcinoma (Poster No. 61)

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Context: Extracapsular extension (EPE) of adenocarcinoma beyond the prostate capsule is a common occurrence and an important factor determining tumor stage but may be difficult to interpret even by experienced urologic pathologists. We measured expert interobserver agreement (multirater κ) from responses to 6 questions that pathologists face when evaluating EPE.

Design: Routinely processed, hematoxylin-eosin–stained slides (n = 46) of prostatectomy cases were reviewed by 14 pathologists independently. Each pair of slides and, for each slide, they recorded their responses, limited to “yes,” “no,” or “equivocal.” The following questions were given: (1) is tumor present in fat; (2) is tumor present with EPE present; (3) is the tumor stage pT3; (4) is the capsule identified; (5) is extraprostatic fat present; and (6) are deeper levels necessary.
Results: See Table.

Conclusions: Our results demonstrate moderate agreement between expert urologic pathologists on the presence of prostatic adenocarcinoma with EPE and the assignment of tumor stage pT3. As expected, there was only slight agreement when characterizing the capsule and peri-prostatic soft tissue, with diversity between pathologists regarding the necessity of deeper levels to complete the diagnostic workup. These findings reflect the subjectivity inherent in evaluating adenocarcinoma with EPE and suggest a need for consensus definitions and guidelines to improve agreement, the clinical significance of which has yet to be prospectively determined.

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**Morphometric and Ultrastructure Study of Peritubular Capillaries in Renal Biopsies of Childhood Idiopathic Nephrotic Syndrome**

(Poster No. 62)

Kamaljeet Singh, MD1 (kisingh@lifespan.org); Ruma Ray, MD, FRCPATH; Arvind Bagga, MD; Amit K. Dinda, MD, PhD2; Department of Pathology, Brown University, Providence, Rhode Island; Department of Pathology, All India Institute of Medical Sciences, New Delhi, India.

Context: Peritubular capillary (PTC) loss is present in tubulointerstitial damage in adult glomerulonephritis. PTC rarefaction correlates with decreased renal function in kidney transplants. PTC status is not known in childhood idiopathic nephrotic syndrome (CINS).

Design: We performed (1) quantification of PTCs in kidney biopsies of CINS; (2) correlation of PTC number with tubular atrophy, interstitial fibrosis, and renal function; and (3) transmission electron microscopic study of PTCs. Kidney needle biopsies of 30 cases and 7 controls (autopsy) were studied with immunohistochemistry for CD34 (IgG1, monoclonal, Dako), Masson trichrome, and transmission electron microscopy. PTC number and interstitial fibrosis were calculated by Image-Pro Plus (Media Cybernetics, USA) image analysis software. Glomerular filtration rate was calculated by Schwartz formula.

Results: Mean PTC number/mm² was as follows: control (n = 7), 604±16 (Figure 51); minimal change disease (n = 13), 540±55 (P = .02); focal segmental glomerulosclerosis (n = 10), 461±54 (P = .001); and mesangioproliferative glomerulonephritis (n = 7), 564±55 (P = .06). For interstitial fibrosis, the results were as follows: control, 5.24±0.93; minimal change disease, 7.25±2.3 (P = .04); focal segmental glomerulosclerosis, 16.63±6.0 (P = .005); mesangioproliferative glomerulonephritis, 7.73±3.7, (P = .08). There was a significant positive correlation between PTC number and glomerular filtration rate (P = .04, r² = 0.15). Transmission electron microscopy showed widening, splitting, and multilayering of endothelial basal lamina in 3/10 cases of focal segmental glomerulosclerosis.

Conclusions: PTC loss is present in CINS. PTC loss is significant in minimal change disease and focal segmental glomerulosclerosis. PTC loss correlates positively with interstitial fibrosis and negatively with renal function. Basal lamina splitting and multilayering consistent with PTC damage was present in focal segmental glomerulosclerosis.

**Seminoma With Rete Testis Hyperplasia Mimicking Mixed Germ Cell Tumor: An Entity Every Pathologist Should Be Aware of**

(Poster No. 63)

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Lesions of the intratesticular excretory ducts are rare and include adenocarcinoma, adenofibroma, cystic dysplasia, and nodular proliferation of connective tissue involving the rete testis. A more frequently encountered scenario is that of infiltration of the rete testis by adjacent infiltrating testicular tumors, particularly seminoma. We present a case of seminoma with extension into the rete testis in which secondary hyperplasia and secretory change of the rete testes were identified. Microscopic examination revealed a proliferation of arborizing glandular structures with bland nuclear features infiltrating between the seminomatous lesion. The glandular structures were filled with eosinophilic colloid-like material, simulating a yolk sac tumor. We performed tests with a panel of immunohistochemical stains to help differentiate rete testis hyperplasia from yolk sac tumor and from stroma ovarii. Immunohistochemical results revealed vimentin and cytokeratin positivity with lack of staining for alpha-fetoprotein, TTF-1, and thyroglobulin, supporting the diagnosis of rete testis hyperplasia. Rete testis hyperplasia is a rarely seen lesion and is usually detected as an incidental microscopic finding. It is hypothesized to be a pseudoneoplastic reaction to secondary invasion of the rete testes by tumor. The histologic features of this lesion mimic the well-recognized features of yolk sac tumors. Because of the difference in treatment protocols between seminomatous and nonseminomatous germ cell tumors, it is important to avoid misdiagnosis of this lesion as a mixed germ cell tumor with seminomatous and yolk sac components from a pure seminoma.

**Utility of Immunohistochemical Markers to Confirm the Presence of Vas Deferens in Vasectomy Specimens**

(Poster No. 64)

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Context: Vasectomy-related cases are one of the most frequent types of malpractice claims filed by urologists. As such, many urologists routinely send vas deferentia (VD) for histologic confirmation. However, in certain cases histology is indeterminate for the presence of VD because of innate properties of the specimen or processing errors. CD10 has recently been described as a marker that can distinguish Wolffian duct derivatives from Mullerian remnants but has yet to be tested in vasectomy specimens.

Design: We determined whether CD10, as well as nonspecific epithelial marker pan-keratin (PK), could corroborate the presence of VD. Our dataset included three consecutive vasectomy specimens subjected to immunohistochemical analysis for CD10, PK, and CD31. Luminal and basal layer cells were semiquantitatively analyzed.

Results: In all cases with optimal epithelial histology (92/103), CD10 demonstrated intense apical membranous expression in all VD and weak basal cytoplasmic staining in 98% of cases. PK demonstrated cytoplasmic and membranous expression in both apical and basal layers in 99% of cases. CD31 did not show apical or basal reactivity in any VD. In cases with suboptimal epithelial histology (11/103), the detection of epithelia was 100% for CD10 and PK. Similar CD10 and PK expression was seen in the glandular epithelium of prostate, vas deferens, seminal vesicle, and ejaculatory ducts of radical prostatectomy samples.
Bilateral Synchronous Testicular Tumors in a 31-Year-Old Man

(Marker No. 65)

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Simultaneous bilateral germ cell tumors of the testis are relatively rare, having an incidence of approximately 1%–2%. In most cases, the histology is classic seminoma. Seminomas are largely found in an older group of men (mean, 40 years), whereas nonseminomatous germ cell tumors are found in a younger group (mean, 25 years). We present a case of seminoma and embryonal carcinoma occurring simultaneously in the bilateral testes of a 31-year-old man. The patient complained of right testicular enlargement and left testicular pain. The serum \\( \alpha \)-fetoprotein level was 34.3 ng/mL (reference range, 0–8 ng/mL), serum \( \beta \)-human chorionic gonadotropin level was 2780 mIU/mL (reference range, 0–6 mIU/mL), and serum lactate dehydrogenase level was 512 IU/L (reference range, 98–192 IU/L). Ultrasonography showed echogenic masses in both testes. The patient had bilateral congenital undescended testes, of which one later descended and the other was surgically corrected. The patient subsequently underwent bilateral orchidectomy. Gross examination of the right testis revealed a 3.5 \( \times \) 2.5 \( \times \) 2.4 cm, poorly demarcated yellow mass with areas of hemorrhage and necrosis on cut surface. Microscopic and immunohistochemical staining pattern was consistent with embryonal carcinoma (Figure 52, left). The left testis revealed a 1.5 \( \times \) 1.0 \( \times \) 1.0 cm, well-demarcated white mass with a 0.5 \( \times \) 0.5 \( \times \) 0.5 cm cystic area on cut surface. The microscopic and immunohistochemical staining pattern was consistent with classical seminoma (Figure, right). Our case represents the third reported in the English literature of bilateral synchronous testicular tumors of seminoma and embryonal carcinoma histology.

Isolated Testicular Relapse of Acute Myeloid Leukemia

7 Years After Initial Diagnosis

(Poster No. 66)

David D. Grier, MD\(^1\) (dgrier@wfubmc.edu); Andrew Eskew, MD; Thomas White, MD\(^3\); Thomas W. McLean, MD\(^2\); Departments of Pathology and Pediatrics, Wake Forest University School of Medicine, Winston-Salem, North Carolina; Department of Urology, High Point Regional Hospital (Piedmont Urological Associates), High Point, North Carolina; Department of Pathology, High Point Regional Hospital (North State Pathology), High Point, North Carolina.

Isolated testicular relapse in acute myeloid leukemia (AML) is a rare event in children. We report a case of an 18-year-old man who had an isolated testicular relapse 86 months after the initial diagnosis and 81 months after finishing chemotherapy. He was originally diagnosed with AML with minimal differentiation at age 11. He was treated with cytarabine-based chemotherapy and did well until age 18 when he presented with a left testicular mass. He had no other signs or symptoms and the results of his hematologic workup were unremarkable. An inguinal orchectomy was performed and he was diagnosed with a myeloid sarcoma. There was no evidence of bone marrow involvement by morphology, immunohistochemistry, flow cytometry, or cytogenetics. The cerebrospinal fluid and a positron emission tomography–computed tomography scan were also negative for disease. The original AML and the myeloid sarcoma were immunophenotypically (CD34, CD117, CD33, myeloperoxidase negative, terminal deoxynucleotidyl transferase negative) and cytogenetically (trisomy 8) identical except for loss of CD15 expression in the myeloid sarcoma. To our knowledge, this is the longest reported interval between remission and an isolated testicular relapse in AML. This case also demonstrates the use of immunophenotyping and cytogenetic studies to differentiate AML relapse from a secondary AML or a de novo myeloid sarcoma. The optimal management of patients with late extramedullary recurrence of AML is unknown.

The Nonneoplastic Kidney in Tumor Resections:

Tumor-Related Alterations and Their Clinical Significances

(Poster No. 67)

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Context: The nonneoplastic changes of kidney are often not reported in tumor nephrectomies. There are 2 published studies on nonneoplastic changes in nephrectomies that focused on glomerular and arterial lesions. Significant diabetic glomerulopathy and arterial sclerosis were common and predicted renal failure. This study investigated peritumoral alterations and their clinical significances in nephrectomies for renal cell carcinoma (RCC).

Design: Nephrectomy specimens from 75 patients with RCC, 60 cases of clear cell RCC, and 15 cases of papillary RCC were reviewed. Tumor-related alterations in the peritumoral cortex were identified and correlated with clinical information.

Results: Sixty-nine of 75 tumors formed a 0.5–5 mm pseudocapsule. Sixty-nine RCCs lacked a pseudocapsule. Within the pseudocapsule were atrophic tubules, sclerotic glomeruli, and compressed arteries with marked fibrointimal thickening. These changes appeared unrelated to tumor size or stage and occurred in clear cell and papillary RCC. The pseudocapsule was inflamed and associated with lymphangiogenesis in a prior study. In 14/22 cases with follow-up, the creatinine level was elevated (mean, 0.34). Two cases showed postnephrectomy creatinine level >3 mg/dL. The change in creatinine level after nephrectomy did not correlate with peritumoral changes of the kidney.

Conclusions: Tumor-related alterations in renal cell carcinoma include a peritumoral pseudocapsule representing nephron atrophy and fibrosis, likely a consequence of tubular and vascular obstruction. Peritumoral inflammation is invariably present and associated with lymphangiogenesis. These tumor-related alterations did not correlate with size or staging of the tumor and do not predict deterioration of renal function after nephrectomy.

Atypical Glomus Tumor of Uncertain Malignant Potential in the Urinary Bladder:

Case Report and Literature Review

(Poster No. 68)

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We present a case of atypical glomus tumor of uncertain malignant potential arising in the urinary bladder of an 84-year-old woman with recurrent low-grade noninvasive papillary urothelial carcinoma of the bladder, which was previously resected in June 2006. Glomus tumors are mesenchymal neoplasms characterized by small size, benign nature, and location often in the dermis or subcutis of extremities. Histologic features include uniformly round cells with pale eosinophilic cytoplasm and central round to oval nuclei. Immunostaining demonstrates muscle-specific actin and desmin positivity and usually CD34 negativity. Specifically, atypical glomus tumors of uncertain malignant potential are defined by lack of criteria for malignant glomus tumor and the following: high mitotic count (>5/50 HPF) and superficial location or large size only or deep location only. Microscopically, this case has an abnormal proliferation of ovoid cells in the lamina propria, uniform ovoid nuclei with indistinct eosinophilic cytoplasm, sheet-like growth pattern with a prominent capillary network, mild nuclear atypia, and high mitotic rate (2/HPF). This case showed smooth muscle actin and smooth muscle myosin positivity and CD34 negativity. A PubMed search revealed 1 reported case of a malignant glomus tumor and no cases of atypical glomus tumors in the urinary bladder. A recent follow-up, 6 months after the initial diagnosis, did not show recurrences of this lesion. This unique case of atypical glomus tumor of uncertain malignant potential represents a challenging, rare neoplasm occurring in an unusual location. Distinction of this entity from the adjacent noninvasive papillary urothelial carcinoma is important.
A Case of a Collision of Renal Cell Carcinoma and Transitional Cell Carcinoma

(Poster No. 69)

Monica I. Ruiz, MD (miruz@bcm.edu); Linh M. Dang, MD; Chris J. Finch, MD. Department of Pathology, Baylor College of Medicine, Houston, Texas.

Renal cell carcinoma accounts for up to 90%–95% of all neoplasms of the kidney, while transitional cell carcinoma is the most common tumor of the renal pelvis, accounting for more than 90% of renal pelvis tumors. A collision of renal cell carcinoma and transitional cell carcinoma in the kidney is very rare. There have been only 26 cases reported in the English literature. We report an unusual case of a collision of transitional cell carcinoma and renal cell carcinoma in the kidney. The patient was a 57-year-old woman who initially presented with flank pain. Upon imaging studies, a left upper pole renal mass and a left necrotic hilar mass with a staghorn calculus was found. Subsequently, the patient underwent a total left nephrectomy and splenectomy. Grossly, the mass in the upper pole of the kidney was golden-yellow with areas of hemorrhage. The renal pelvis lesion appeared tan-brown with a friable surface. The upper pole mass and the hilar mass appeared to merge together into a single tumor measuring 8 cm in greatest dimension. Microscopically, the upper pole mass showed a high-grade unclassified renal cell carcinoma and the adjacent pelvic mass showed a grade 2 papillary transitional cell carcinoma. Cases of renal cell carcinoma and transitional cell carcinoma found in the same kidney are extremely rare. This case illustrates the importance of a thorough and generous sampling of surgical specimens to ensure the correct diagnoses and treatment of combined renal malignancies.

The Unproportional Number of Reports on Coexisting Adenocarcinoma and Carcinoïd Tumor in the Urinary Bladder

(Poster No. 70)

Jiong Zhang, MD, PhD (pathdoc.zhang@gmail.com); Vivekanand Datla, MD, PhD. Department of Pathology, The University of Tennessee Health Science Center at Memphis.

We encountered a rare case of 2 neoplastic processes coexisting in the urinary bladder. These neoplastic processes consist of an adenocarcinoma and a carcinoid tumors. The mucinous adenocarcinoma is positive for cytokeratin-20 and carcinoembryonic antigen and negative for cytokeratin-7, neuron-specific enolase, prostate-specific antigen, synaptophysin, CDX-2, and chromogranin A. The carcinoid lesion is positive for cytokeratin-7, carcinoembryonic antigen, neuron-specific enolase, synaptophysin, and chromogranin and negative for cytokeratin-20, prostate-specific antigen, and CDX-2. This is the fifth reported case of carcinoid tumors coexisting with another carcinoma in the urinary bladder. Among urinary bladder carcinomas, urothelial carcinomas are more than 10 times more frequent than adenocarcinomas. Therefore, we would normally expect that if another malignancy co-occurs with carcinoid tumor in the urinary bladder, it would most often be urothelial carcinoma by chance alone. Interestingly, only 1 of 5 of these reported mixed tumor cases involved urothelial carcinoma. Four of them involved adenocarcinomas, as in our case. This prompts us to suspect that the co-occurrence of these 2 different tumors in the bladder may have 1 underlying pathogenesis pathway, such as a novel tumor syndrome.

Mucinous Cystadenocarcinoma of the Testis

(Poster No. 71)

Alina C. Iuga, MD (aiuga@chpnet.org); Jason Mull, MD; William Miller, MD. Department of Pathology, St.Luke's Roosevelt Hospital Center, New York, New York.

Ovarian-type surface epithelial carcinomas of the testis are a rare primary testicular malignancy, and most of the previously reported cases are of the serous variety. We present a case of unilateral invasive intratesticular cystadenocarcinoma with mucinous differentiation. Extensive literature review revealed only 3 similar reported cases. The patient is a 71-year-old man with a history of melanoma who presented with a left testicular hydrocele secondary to a mass. Imaging studies and colonoscopy revealed no other suspicious lesion. Gross examination of the orchietomy specimen revealed a 3.5 cm, white, soft, glistening, well-delineated mass with a 0.1 cm yellow undulating border, completely replacing the testicular parenchyma. Microscopically, the mass was a well-differentiated cystic neoplasm with elongated fine pseudopapillary structures lined by columnar epithelium with alternating goblet and ciliated cells. Mitotic activity was rare. Foci of neoplastic epithelial lining overlying fibrous stroma in the testicular mediastinum were identified as a possible in situ component. The tumor invaded into but not through the fibrous capsule. The cyst wall showed extensive inflammatory and xanthogranulomatous reactive, dystrophic calcification, and areas of dystrophic calcification. No involvement of the tunica albuginea, rete, or appendage testis was identified. No teratomatous elements were identified. Immunohistochemical studies showed positivity for cytokeratin 20 and carcinoembryonic antigen, negativity for cytokeratin 7 and vimentin, and focal positivity for estrogen receptor. We discuss the histopathologic findings of this unusual testicular neoplasm with a particular immunophenotypic profile and review the existing literature on the subject.

Discrepancy in Cancer Localization Between Prostate Biopsy and Radical Prostatectomy Specimens in Patients With Unilateral Positive Biopsy Cores: Implications for Focal Ablative Therapy

(Poster No. 72)

Michael Sinnott, MD (sinnomt@cf.org); Sara M. Falzarano, MD; Ming Zhou, MD, PhD; Cristina Magi-Galluzzi, MD, PhD. Department of Anatomic Pathology, Cleveland Clinic, Cleveland, Ohio.

Context: Ablative treatment has gained acceptance as treatment strategy for patients with prostate cancer (PCA) who are not candidates for prostatectomy (RP). The success of unilateral ablation strategy depends on the reliable prediction of unilateral PCA by biopsy.

Design: A total of 1326 men had PCA on 12-needle biopsy (12Bx). In 439 (32.8%), PCA was detected only in 1 side. RP was available for 183 patients. All specimens were reviewed by a pathologist who mapped the tumor outline, determined the number of PCA, their volume (TV), zone of origin, Gleason score (GS), and tumor stage.

Results: Mean age, preoperative prostate-specific antigen (PSA) level, and prostate weight were 59 years, 6.1 ng/mL, and 53 g, respectively. In 50 men, 12Bx findings correlated with RP extractions (unilateral PCA). In the remaining 133 patients (72.7%), 1–5 PCA foci/RP were detected in the contralateral side. In 110/133 patients, 173 significant PCAs (>5 mm2 and GS ≥ 6) were missed. The contralateral PCAs were GS6 (72%), GS7 (26%), and GS7 with pattern 5 (2%); their TV ranged from 6 to 274 mm3. Stage was T1a (n = 3), T2+ (n = 2), and T2 (n = 168). PCA location was distributed as follows: apex (14.4%), mid (46.2%), base (4%), apical-mid (26%), apical-base (5.2%), and mid-base (4%). Thirty percent of PCAs involved transitional/20 and 70% involved peripheral zone.

Conclusions: Most men with unilateral positive biopsies have pathologically proven bilateral PCA and focal treatment is unlikely to be curative. Additional biopsies of the mid/apical-mid prostate could be suggested before considering focal ablative therapy.

POSTER SESSION 400: MONDAY, OCTOBER 12, 2009, 1:00 PM–3:30 PM

Autopsy and Forensic Pathology; Bone and Soft Tissue Pathology; Transfusion Medicine and Coagulation; Administrative and Regulatory Affairs

Bile Acid Pneumonitis in a Neonate Born to a Mother With Intrahepatic Cholestasis of Pregnancy: An Emerging Entity to Consider in the Differential Diagnosis of Neonatal Respiratory Distress

(Poster No. 1)

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Bile acid pneumonitis is a recently described entity affecting neonates born to mothers who have developed intrahepatic cholestasis of pregnancy. This disease was first described by Zecca et al in 2004. They suggested that maternally derived bile acids enter the fetal lungs by aspiration or circulatory uptake, resulting in inhibition of surfactant activity and consequent respiratory distress syndrome. Very few cases of neonatal bile acid pneumonitis have been reported since then. We present a case of bile acid pneumonitis in a neonate born at 38 weeks' gestation by induced vaginal delivery to a 35-year-old woman who was group B streptococci–positive and was diagnosed with intrahepatic cholestasis of pregnancy (generalized pruritus and increased serum bile acid levels of 22 μmol/L). After birth, Apgar scores were 9 and 9 at 1 and 5 minutes, respectively. Soon after delivery, the baby developed respiratory distress with significant oxygen desaturations. Despite adequate respiratory support, intravenous therapy was initiated..Initially, a high index of suspicion for sepsis was entertained. Owing to the clinical presentation and the maternal history, a thorough evaluation was performed to rule out bile acid pneumonitis. The work-up included a chest X-ray, blood and sputum cultures, and a bronchoscopy. The chest X-ray revealed bilateral opacification, and the cultures and bronchoscopy were unremarkable. Further investigation revealed a positive bile acid level of 22 μmol/L, confirming the diagnosis of bile acid pneumonitis. The baby was treated with respiratory supportive therapy, including supplemental oxygen, sedation, and intravenous fluids. Despite these interventions, the baby's respiratory distress persisted. The attending neonatologist and pediatrician were consulted, and a decision was made to change the ventilator settings to a lower fraction of inspired oxygen (FIO2) and to increase the tidal volume. After these adjustments, the baby's respiratory distress improved, and the oxygen saturation improved to 90%. The baby was discharged home on the 10th day of life on supplemental oxygen and scheduled for follow-up in the neonatal intensive care unit (NICU). The baby continued to do well, and follow-up appointments were arranged in the NICU. The baby was discharged home on the 28th day of life in good condition with no respiratory issues.

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potential cause of respiratory distress. 

Infectious hepatitis. The patient was scheduled for liver transplantation, but he died before the transplant could be performed.

The patient was referred for a thymectomy because of clinical hyperthyroid symptoms. Serum autoantibody studies showed high titers of thyroglobulin antibody (25250 U/mL) and thyroid peroxidase antibody (2204 U/mL). At autopsy, the thymus was found to be markedly enlarged, weighing 19 g (reference range, 2.3–4.1 g). It showed thymic hyperplasia on histology; it occupied most of the chest cavity, encompassing the anterior heart. There was also evidence of cardiovascular compromise, including severely congested hepatosplenomegaly and severe congestion in the umbilical cord vein. This is the first reported case of intrauterine fetal demise due to thymic hyperplasia in which the mother was diagnosed with hypothyroidism. Thymic hyperplasia is relatively common in patients with hyperthyroidism and Graves disease, and thyroid autoantibody can cause thymic hyperplasia. Thyroid tropin receptors have been identified in human thymus. However, thymic hyperplasia is rare in patients with hyperthyroidism. There is one report of thymic enlargement during thyroxine treatment for primary hypothyroidism. The etiology of the severe thymic hyperplasia in this case merits further investigation.

Transfusion-Related Iron Overload in Diamond-Blackfan Anemia: An Autopsy Case Report

Abstracts

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Sclerosing encapsulating peritonitis, also known as “abdominal cooon,” is a rare entity. We describe a case of generalized idiopathic sclerosing peritonitis affecting not only peritoneum but also pericardium and pleura. Besides anecdotal reports of prolonged ß-blocker therapy-associated idiopathic sclerosing peritonitis, we did not find any cases in the literature. A 66-year-old man was followed up for 9 years for presumptive alcohol-induced liver cirrhosis with low serum albumin, recurrent ascites, pleural effusions requiring paracentesis and thoracentesis. He received transjugular intrahepatic portosystemic shunt procedure for increasing ascites. Past serologic workup was negative for autoimmune diseases and infectious hepatitis. The patient was scheduled for liver transplantation. He presented with unstable condition, lethargy, confusion, drowsiness, and orthopnea and was transferred to intensive care unit where he died after complicated course. Autopsy showed that all organs of the abdominal and thoracic cavity were encased in a thick, hyalinized fibrous tissue. Histologic findings revealed bland panacinar subserosal fibrocollagenous tissue with focal chronic inflammation (Figure 53). Liver showed chronic passive congestion without evidence of cirrhosis. A stable radiologic abnormality in the upper lobe of left lung was a 0.8-cm, well-differentiated pulmonary adenocarcinoma with no evidence of metastases. Massive upper gastrointestinal bleeding was the terminal event. Cases of sclerosing encapsulating peritonitis have either silent clinical course or acute presentation with intestinal obstruction. In our case, the process was insidious, restrictive-causing multiorgan failure due to the constrictive effect of fibrosis. We term this case idiopathic sclerosing polymyositis in view of the above findings and absence of recognized clinical causes of sclerosing encapsulating peritonitis.
A Case of Otocephaly-Agnathia Complex (Poster No. 9)

Rashmi Kanagal Shammanna, MD (rshaman1@fhhs.org); Frederick Meier, MD. Department of Pathology and Laboratory Medicine, Henry Ford Hospital, Detroit, Michigan.

Otocephaly-agnathia complex is a rare, lethal malformation, including hypognathia or agnathia, synoectasia, microstomia, and hypoglossia. Estimated prevalence is 1/70,000, with 80 published cases. A 17-year-old GIPO adolescent girl presented at 32 weeks' gestation with ruptured membranes and chorioamnionitis. Results from a 21-week obstetrical ultrasonography were normal. She gave birth to a premature male infant with low birth weight (1260 g). Because of multiple head and neck anomalies, he died within an hour. Postmortem imaging and autopsy focused on the pattern and extent of anomalies. Autopsy revealed absent mandibular arch, hemipalate, hypoplastic facial bones, low-set ears, microstomia, and microglossia. Imaging showed malformed hyoid bone, wide sella turcica, and multiple vertebral and rib abnormalities. Dissection demonstrated unusual rostral insertion of neck musculature and inferiorly displaced eustachian tubes. Anterior pituitary was present; nasopharynx and salivary glands were absent. Cardiac atrial septal defect was present. Neuropathologic examination showed arrhinecephaly, lissencephaly and Arnold-Chiari type 1 malformation associated anomalies, including synostia, external nose malformation, and situs inversus, were absent. Other findings included hypoplastic lungs, vesical hemorrhages, and dilated heart with normal cytogenetic study (Figure 55: clockwise: absent mandible, upon fetogram and gross examination; arrhinecephaly; vertebral rib abnormalities). This rare finding demonstrated the importance of otocephaly-agnathia complex associated with atrial septal defect. Developmentally, maxillary process derived from 1st pharyngeal arch. Failure in

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We present a case of peripartum aortic dissection, a rare but documented entity in the literature. The deceased was a 37-year-old white woman (G2P2) with no history of miscarriage or abortion. Shortly after delivery of a healthy, male infant at 32 5/7–week gestational age, she was found unresponsive in bed in asystole. Autopsy findings revealed an extensive descending aortic dissection with left hemithorax, 1400 mL; left subpleural hematoma, 100 mL; and hematoperitonium, 100 mL. Microscopic examination revealed acute aortic dissection with no evidence of inflammation. Fragmentation of the elastic fibers was noted in the site of rupture with minimal or no medial degeneration. The absence of connective tissue disease, Marfan syndrome and Ehlers-Danlos syndrome indicates that the rupture may have occurred in the peripartum period with no apparent predisposing factors. The cardiovascular system undergoes important adaptation during pregnancy to accommodate fetal and maternal requirements. These changes may weaken the aorta, with the possible surge in blood pressure during the delivery probably acting as an initiator for the dissection. Complaints of chest and back pain during the peripartum period warrant consideration of an aortic dissection.

We report a case of aggressive T-cell lymphoma that diffusely infiltrated all major organs, causing multiorgan failure and death in a previously healthy 4-year-old boy. The patient presented with acute onset of abdominal pain and vomiting. A computed tomography scan suggested acute appendicitis with perforation. The patient underwent emergent appendectomy. Postoperatively, he developed abdominal distension, respiratory distress, and hypotension. He was intubated; however, sufficient oxygenation could not be maintained, and he died on postoperative day 4. At autopsy, there were discrete hyperemic areas along the small-bowel serosa that corresponded to raised mucosal plaques. Extensive lymphadenopathy was most prominently noted in the mesentery. Microscopic evaluation showed diffuse infiltration of virtually all organs by monomorphic atypical lymphocytes. Flow cytometry analysis was performed on tissue after a postmortem interval of 25 hours. We identified an abnormal T-cell population with the following immunophenotype: CD3+, CD4+, CD8+, TcRα–, and TcRβ–. Molecular testing of the appendix showed a monoclonal T-cell receptor–γ gene rearrangement. Microarray comparative genomic hybridization was performed. It showed 3 segmental deletions in chromosomes 6q and 9p, including a homozygous 9p21 deletion, which has been associated with an aggressive natural history and poor prognosis in lymphoproliferative diseases. γ/δ T-cell lymphomas are typically aggressive; however, this type of fulminant presentation is unprecedented. Moreover, the molecular alterations we observed have not been previously described in this disease and likely contributed to the rapidly fatal course. This study underscores the importance of using all available techniques for postmortem evaluation of challenging cases.
Epithelioid angiosarcomas (EASs) of the adrenal gland are extremely rare neoplasms. The diagnosis is difficult due to lack of conclusive radiographic and endocrinologic findings, unusual location, and histologic features. The differential may involve epithelial neoplasms, and metastatic disease. Because of the small number of reported cases, we know little about clinical course and prognosis. Our case of adrenal EAS had an unusual clinical presentation and was diagnosed at autopsy. The patient was a 65-year-old woman with a history of melanoma. During evaluation for lower back pain, we discovered a 5-cm, nonfunctioning adrenal mass. The patient underwent laparoscopic adrenalectomy; however, she died postoperatively before diagnosis of the surgical specimen. Microscopic examination of the hemorrhagic retroperitoneal tissue revealed residual adrenal gland with nests and cords of pleomorphic epithelioid cells demonstrating prominent nucleoli and high mitotic activity throughout the cortex and medulla and interspersed with anastomotic vascular spaces. Metastatic foci with identical morphology were also identified in multiple retroperitoneal lymph nodes and in bone marrow. Tumor emboli were noted in the lungs. Immunohistochemical analysis was negative for Melan-A, HMB-45 and S100 and positive for vimentin, CD31, CD34 and factor VIII. We report a case of adrenal EAS that was diagnosed at autopsy. Immunohistochemical analysis helped to rule out metastatic melanoma and to diagnose EAS. The presence of extensive metastatic foci indicates an extremely aggressive course. This report contributes to a better understanding of the natural history of this rare entity.

Agnathia-Otocephaly With Alobar Holoprosencephaly and Visceral Anomalies: A Case Report and Immunohistochemical Study

(Poster No. 12)

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Agnathia-otocephaly with alobar holoprosencephaly and visceral anomalies is a very rare and lethal congenital disorder. Since 1717, less than 30 cases have been reported in the literature. Most cases are sporadic and of normal karyotype. Etiology is unknown and might be related to a mutation of sonic hedgehog, ZIC2, SIX3, and paired-related homeobox genes. The current case is that of a male infant who was born at 35 weeks' gestation to a 16-year-old G2P2 mother. The infant died shortly after birth. We performed autopsy and cyto genetic examinations and immunostaining for chromogranin and inhibit on adrenal glands. Macroscopically, facial dysmorphosis showed trigonocephalic microcephaly, cyclopia with anophthalmia, tiny central skin tags, absence of nose and nostrils, microstomia and microglossia, agnathia and hypoplasia of the maxilla, and centrally displaced low-set ears. Alobar form, pancake like holoprosencephaly showed pachygyria with an 80-ml fluid-filled dorsal sac and undivided thalami and corpora striata. We found no olfactory tracts and bulbs, optic nerves, chiasm and optic tracts, pituitary gland and pineal gland, or corpus callosum. Medulla showed olivary hypertrophy and pyramidal hypotrophy. Both lungs were hypoplastic with massive hemorrhage. Spleen was bilobed and accessory. Microscopically, adrenal glands demonstrated cortical hypoplasia and medullar hypertrophy and were positive for inhibitin and chromogranin. The thyroid gland was hypoplastic, and the testes were small and undescended. Cytogenetics indicated normal male karyotype 46, XY. This rarely reported phenotype suggests that temporal and spatial damage of the anterior embryonic disc occurs during early embryonic development (Carnegie stage 10, embryonic days 22 or 23).

Hyphal Coccidioidomycosis of the Brain in a Patient With Central Nervous System Lymphoma

(Poster No. 13)

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Coccidioidomycosis is an opportunistic infection caused by the dimorphic fungi Coccidioides immitis and Coccidioides posadasii. At body temperature, the organism almost always assumes a characteristic spheroidal morphology. The hyphal morphology has been observed in human tissue, but almost exclusively in the lung. A review of the literature revealed 3 previously reported cases of parenchymal brain disease. We describe the first known case occurring with concurrent lesions of diffuse large B-cell lymphoma of the brain. The patient was a 22-year-old Hispanic woman who presented with dyspnea, weight loss, and fatigue. A workup revealed diffuse large B-cell lymphoma involving the bone marrow, mediastinum,
and brain. She was treated with chemotherapy, radiation, and ultimately matched-unrelated stem cell transplantation. She developed multiple infectious complications and died 1 month later. Postmortem examination showed lymphoma of multiple organs, including the left frontal lobe of the brain. Disseminated coccidioidomycosis was observed in the lungs, lymph nodes, kidneys, and brain. Microscopic examination of the left frontal lobe adjacent to the tumor showed sphered nuclei admixed with characteristic hyphae and barrel-shaped alternating arthroconidia. Several small arteries were occluded by thrombi with mural invasion by a coccolid mold. Hyphal coccidioidomycosis is exceedingly rare in tissue other than the lung. Only 3 cases of parenchymal brain infection have been previously reported. They include 2 men (ages 26 and 43) with human immunodeficiency virus and one 46-year-old woman with a history of kidney transplantation due to diabetic nephropathy. This is the first known case associated with central nervous system lymphoma and bone marrow transplantation.

Characterization of Triamcinolone in Formalin-Fixed and Paraffin-Embedded Tissue Specimens by Using Infrared Micro-Spectroscopy (Poster No. 14)

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Corticosteroid injection sites have to be differentiated microscopically from other conditions, including rheumatoid nodules, gouty tophi, myxomas, and injection sites of other materials. Infrared microspectroscopy is a noninvasive technique that allows for the molecular characterization of unidentified materials in histopathology specimens. We evaluated 2 specimens for the presence of steroids. In case 1, we received formalin-fixed wet tissue from a postavasectomy spermatic cord stump that contained a pale nodule that was sampled for infrared microspectroscopy. In case 2, we received a formalin-fixed, paraffin-embedded shave biopsy of skin. Consecutive unstained sections were placed on an aluminized glass slide, a carbon disc, and a glass slide. The latter was hematoxylin-esoin-stained, and the areas of interest were located for analysis of the unstained sections, which were deparaffinized and examined by infrared microspectroscopy and by scanning electron microscopy with energy dispersive x-ray analysis. In both cases, infrared spectra characteristics of triamcinolone acetone were obtained. A clinical history of multiple prior triamcinolone injections was provided for case 1 but not for case 2. In case 2, scanning electron microscopy with energy dispersive x-ray analysis identified carbon, oxygen, and fluorine in an area of interest. Fluorine is a constituent of triamcinolone. Triamcinolone may be identified by infrared microspectroscopy in both formalin-fixed wet tissue and in formalin-fixed, paraffin-embedded tissue. Fluorine may be identified by scanning electron microscopy with energy dispersive x-ray analysis. This analysis can help in the differential diagnosis of steroid injection sites and can have broader applications in forensics and medico-legal investigations.

Generational Differences in Coronary Artery Atherosclerosis in Women: An Autopsy-Based Study (Poster No. 15)

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Context: Heart disease remains the leading cause of death for women in the United States, with coronary disease being the most common form. Many studies characterize coronary artery atherosclerosis by autopsy and by in vivo methods, but very few studies in the recent literature focus on women.

Design: This was a retrospective review of autopsy reports from 2003–2008. We abstracted patient age, sex, height, weight, and cause of death and heart weight and degree of coronary atherosclerosis in the left anterior descending coronary artery, left circumflex coronary artery, and right coronary artery. All autopsies included histologic examination of coronary arteries with grading of stenosis (1 = <25%, 2 = 26%–50%, 3 = 51%–75%, 4 = >75%). These data were compared to similar data compiled at our institution and published in 1950.

Results: We included 726 women ranging in age from 30–99. Cases with at least 1 grade 3 lesion in at least 1 coronary artery included 49% of women aged 30–39, 61% aged 40–49, 55% aged 50–59, and 71% aged 60–69. Of these groups, 12%, 15%, 18%, and 18%, respectively, had grade 3 lesions in all 3 arteries. Patients older than 70 years had comparatively lower grade lesions occurring in fewer arteries; this trend was not statistically significant. In 1950, less than 30% of women under age 70 had 1 grade 3 disease in any vessel.

Conclusions: Potentially significant (>50%) coronary stenosis was found at autopsy in a surprisingly high number of premenopausal women dying from any cause. This represents a major shift from data published 60 years ago.

Abdominal lymphomatosis (Poster No. 16)

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Confronted with a gross pathologic finding of massive tumor infiltration of the omentum as shown in the figure below (Figure 56) and a radiologic diagnosis of abdominal carcinomatosis, most pathologists would be very confident that this is an epithelial or mesothelial malignancy; this, however, was a disseminated peritoneal B-cell lymphoma in a 51-year-old woman who presented with severe abdominal pain. Computed tomography showed extensive peritoneal infiltration of tumor, bilateral adrenal masses, and right pleural effusion, results which prompted the radiologic diagnosis of peritoneal carcinomatosis with possible ovarian primary tumor. The patient died of massive pulmonary thromboembolism before biopsy could be performed. Microscopic examination revealed sheets of intermediate-sized blastlike cells with scant cytoplasm and round nuclei with a fine chromatin pattern. Immunoreactivity was demonstrated for B-cell markers, CD10, CD22, and CD79a, with little to no expression of T-cell or epithelial markers, leading to the diagnosis of B-cell lymphoid neoplasm with high-grade features. This case serves to raise awareness of the entity, abdominal lymphomatosis, which is radiologically difficult to differentiate from peritoneal carcinomatosis.

Postmortem Demonstration of the Source of Pulmonary Thromboembolism: The Importance of the Autopsy (Poster No. 17)

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Pulmonary thromboembolism is a major cause of death. Most emboli have been shown to originate in the veins of the legs. However, recent data have shown an increasing number of thromboemboli arising from the pelvic veins, namely from the periprostatic and periuterine plexuses. Other sites of clot origin, such as the atrial appendage of the right heart or the vessel wall at the tip of a venous catheter, may be identified on the basis of clinical presentation. However, for a group of patients, the site of clot origin remains a clinical enigma. In these cases, an autopsy is critical. We present the case of 2 patients for whom autopsy demonstrated periprostatic venous thrombi as the source of pulmonary emboli. The pathways for emboli migration from periprostatic veins may be through drainage into the inferior vena cava or via Batson plexus into the superior vena cava (Figure 57). This report highlights a rarely considered source of pul-

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monary thromboemboli that is usually identified by postmortem examination. In such cases, the autopsy also helps determine the possible pathways of clot migration (Figure 57). The periprostatic plexus primarily drains into the internal iliac veins via the vesical veins to reach the inferior vena cava and eventually the pulmonary circulation. Alternatively, this plexus communicates with the Batson vertebral plexus, which reaches pulmonary agenesis and severely hypoplastic lungs, agenesis of the external iliac veins, a poorly formed lumbosacral spine, Potter phenotype with complete renal agenesis, and pulseless electrical activity cardiac arrest, leading to the patient's death. Exploration of his family history revealed a mother who died before the age 50 of amyloidosis and 2 aunts who also likely had the disease. The major finding at autopsy was diffuse amyloid deposition in nearly all organs examined. Congo-red staining of representative slides confirmed the diagnosis of amyloidosis. A genetic mutation of serine to arginine at position 50 (S50R) in transthyretin was identified. This mutation has not been previously reported only 3 times and in Japanese and European patients. Mutations in transthyretin are the most common cause of hereditary amyloidosis, and there are more than 80 amyloidogenic mutations identified, each of which is associated with particular clinical features and geographic regions. This mutation involves the complex pathophysiology and genetics of HFE-associated HH.

Severe Phenotype of HFE-Associated Hemochromatosis

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Hereditary hemochromatosis (HH) is the most common inherited disorder in individuals of Northern and Central European ancestry, affecting approximately 1 in 100. Left untreated, HH can result in widespread tissue injury and early death. We describe the case of a 37-year-old man with a 2-year history of progressive fatigue, darkening skin, intermittent leg swelling, and occasional heart palpitations. He had cardiomegaly, atrial fibrillation, and hepatosplenomegaly. Pertinent laboratory data were as follows: serum iron levels 194 μg/dL (reference range, 50–160 μg/dL); serum transferrin saturation 99% (reference range, 25%–45%); and serum ferritin levels 3260 μg/dL (reference range, 27–285 μg/dL). A liver biopsy disclosed cirrhosis and grade 4 iron deposition. Genetic testing revealed homozygosity for Cys282Tyr in the HFE gene. No mutation was detected in the HAMP, HIV, TJR2, and FRN genes. The patient was treated with frequent phlebotomies, digoxin, amiodarone, spironolactone, and furosemide. After brief clinical improvement, he suffered rapid decline and fatal cardiac complications. Autopsy findings included massive hemosiderin deposition in myocardial fibers, hepatocytes, pancreas, follicular epithelial cells of the thyroid, adrenal zona glomerulosa, and gastric mucosa. HFE mutations are associated with most HH cases. However, many individuals with HFE mutations do not express clinical disease, and early fatalities of HFE-associated HH are very rare. The latter are often associated with hepatotoxic insults, such as alcohol abuse, hepatitis B, or hepatitis C. This case is significant for absence of confounding environmental factors and mutations in other known HH-associated genes. This case highlights the persistent gap in our understanding of the complex pathophysiology and genetics of HFE-associated HH.

Hereditary Systemic Amyloidosis With a Novel Arg50 Mutation in an African American Man

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A 44-year-old African American man was newly diagnosed with systemic amyloidosis, which was initially thought to be of light-chain origin. He presented with chronic diarrhea, peripheral neuropathy, and lower extremity edema. The hospital course was complicated by S. aureus infection and pulseless electrical activity cardiac arrest, leading to the patient's death. Exploration of his family history revealed a mother who died before the age 50 of amyloidosis and 2 aunts who also likely had the disease. The major finding at autopsy was diffuse amyloid deposition in nearly all organs examined. Congo-red staining of representative slides confirmed the diagnosis of amyloidosis. A genetic mutation of arginine at position 50 (S50R) in transthyretin was identified. This mutation has been previously reported only 3 times and in Japanese and European patients. Mutations in transthyretin are the most common cause of hereditary amyloidosis, and there are more than 80 amyloidogenic mutations identified, each of which is associated with particular clinical features and geographic regions. This mutation involves the complex pathophysiology and genetics of HFE-associated HH.

A Case Report on Sirenomelia: Theories of Pathogenesis

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Sirenomelia is a congenital birth defect that is defined as a fusion of the lower extremities. Sirenomelia is also associated with other anomalies. It is a rare defect that has an incidence of approximately 1 in 60,000 to 1 in 100,000 births. There is a male predominance of nearly 3:1. Some consider that sirenomelia represents the most severe end of the spectrum known as caudal dysgenesis. A full autopsy was performed on a non-macerated, stillborn, female fetus born at 31 weeks’ gestation by induced labor. We found multiple anomalies, including a fused single inferior limb with a poorly formed lumbar sacral spine, Potter phenotype with complete renal agenesis and severely hypoplastic lungs, agenesis of the external genitalia, agenesis of the vagina and uterus, anorectal atresia, a persistent left superior vena cava, and a single umbilical artery with an aberrant abdominal aorta connection. These findings represent many of the classic features associated with sirenomelia. There are 2 main hypotheses regarding the pathogenesis of sirenomelia. One hypothesis involves an axial mesoderm defect and the other a vascular developmental defect. The axial mesoderm hypothesis suggests that sirenomelia arises from a blastogenesis or developmental field defect. The vascular hypothesis suggests that the single umbilical artery is a remnant of the vitelline artery and contributes to caudal vascular steal syndrome. However, there is still disagreement as to whether the vascular anomaly is the cause or consequence of the sirenomelia sequence because an axial mesoderm defect could preclude the development of normal umbilical arteries.
Congenital Intracranial Teratoma: A Case Report With Autopsy Findings and Literature Review
(Poster No. 21)

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Congenital intracranial teratoma is extremely rare and accounts for 0.5% to 1% of all pediatric brain tumors. These tumors grow rapidly, are destructive, and have a poor prognosis. We report a case of congenital intracranial teratoma in a 5-week-old female neonate who was born with normal Apgar scores at 38 weeks’ gestation by elective cesarean delivery. At birth, she was macrocephalic with increasing hydrocephalus. Cranial ultrasonography and magnetic resonance imaging showed a large heterogeneous cystic and solid midline tumor with multiple calcifications and obstructive hydrocephalus. The lesion was unresectable, and she received palliative care until her death. Autopsy findings showed significantly increased occipitofrontal circumference (greater than 98th percentile) with wide open anterior and posterior fontanelles. An 8 × 8 × 6-cm, gray-tan, solid and cystic midline tumor with areas of necrosis and hemorrhage occupied most of the supratentorial compartment. The epicenter of the tumor was in the region of the third ventricle and hypothalamus. The tumor stretched and attenuated the corpus callosum, inferiorly displaced the cerebellum, and caused massive obstructive hydrocephalus in both lateral ventricles. Histologic findings showed a teratoma with mature elements and abundant immature neuroepithelium showing prominent abortive tubular/telodendriose-like structures. Mesenchymal elements present included mature cartilage, bone, glands, and squamous epithelium. Although immature teratoma is a rare pediatric brain tumor, it is the most common congenital central nervous system tumor presenting at birth and is typically in a supratentorial location. This entity should be included in the differential diagnosis of congenital or neonatal hydrocephalus with a calcified intracranial mass.

Inner Ear and Eye Pathology in Wolfram or DIDMOAD Syndrome: Clinicopathologic Correlation
(Poster No. 22)

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Wolfram or DIDMOAD syndrome is a neurodegenerative disease that is characterized by diabetes mellitus and optic atrophy leading to blindness. Most patients also suffer from some degree of diabetes insipidus and deafness. While blindness and deafness are major aspects of this syndrome, previous histopathologic studies have not described the eye and inner ear. We present postmortem neuropathologic findings, including histologic examination of retinas and ears, for a man with Wolfram syndrome. His disease course included blindness, high-frequency hearing loss, diabetes insipidus, diabetes mellitus, and episodes of central hypoventilation leading to aspiration pneumonia and eventually death at the age of 24 from acute respiratory distress syndrome. Findings on histologic examination of the brain were similar to previously reported neuropathologic descriptions of Wolfram syndrome, including atrophy and loss of myelinated axons in the optic tracts and nerves and loss of neurons in the pontine base and lateral geniculate, paraventricular, supraoptic, and inferior olivary nuclei. Histologic examination of the cochlea revealed bilateral loss of the organ of Corti in the basal turns and focal atrophy of the stria vascularis (Figure 58). These findings correlate clinically with the high-frequency hearing loss seen in our patient and typically seen in Wolfram syndrome. Histologic examination of the retina revealed marked loss of neurons in the retinal ganglion layer, suggesting that neuron loss in the retina leads to subsequent degeneration of the axons in the optic nerves and tracts. These findings provide new insight into the underlying pathology of blindness and hearing loss in Wolfram syndrome.

Hepatocerebral Syndrome With Mitochondrial DNA Polymerase γ Compound Heterozygous Missense Mutations
(Poster No. 23)

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Mitochondrial DNA polymerase γ mutation is related to several disorders of mitochondrial metabolism that have a broad range of clinical presentations. We report the case of a female infant with compound mitochondrial DNA polymerase γ mutations. Clinical presentation was consistent with hepatocerebral syndrome (Alpers syndrome). At 7 months of age, the patient started having seizures, failure to thrive, hypotonia, and renal tubular acidosis. She subsequently developed fulminating liver failure with significant coagulopathy, and she died 3 months later. An autopsy revealed massive liver necrosis with diffuse hepatocyte dropout and marked bile ductular proliferation with parenchymal fibrosis. Occasional glial nodules were noted in the brain stem, and there was significant loss of Purkinje cells in the cerebellum. There were degenerative changes in the cerebral gray matter. The thymus was atrophied, and bone marrow was hypocellular with diffuse erythroid precursor dysplasia. Scattered bilateral cryptomegalovirus-positive cells were identified in the lungs. Electron microscopy showed no specific inclusion bodies associated with mitochondrialopathies. Premortem blood molecular tests revealed heterozygous mitochondrial DNA polymerase γ mutation A467T, which has been previously linked to Alpers syndrome, and heterozygous R807H mutation, which is a novel missense mitochondrial DNA polymerase γ polymorphism. Because heterozygous A467T mutation is unlikely to cause clinically significant disease, R807H is probably a relevant novel mutation contributing to this clinical syndrome; however, the type and extent of the contribution is not clear. This case shows the important diagnostic role that autopsy pathologists can have in cases of infant death preceded by a metabolic syndrome when premortem workup was incomplete.

Congenital Cerebral Arteriovenous Malformation Identified at Autopsy: Associated Findings and Implications for Prenatal Screening
(Poster No. 24)

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Cerebral arteriovenous malformations are uncommon phenomena that can present at any age, but they rarely occur during the perinatal period. We present a case of unexpected perinatal death secondary to asystole that occurred after emergency cesarean delivery due to fetal heart rate abnormalities. Prenatal ultrasonography showed no anatomic anomalies. At autopsy, the heart was found to occupy nearly the entire thoracic cavity with subsequent pulmonary hypoplasia. Upon opening the cranium, a 3.0-cm arteriovenous malformation was identified, connecting the basal artery and the vein of Galen with vessels completely encircling the midbrain. Subarachnoid and subdural hemorrhages were also present. Identification of such a lesion is imperative because it may indicate hereditary disease, such as the autosomal dominant capillary malformation-
been of significant value in elucidating the unusual etiology of this patient's progressive neurologic disorder. Therefore, diagnosis of such a lesion at autopsy may aid the family's bereavement. It may also encourage closer prenatal monitoring in future pregnancies and allow for early intervention if necessary.

**Black Esophagus With Histopathologic Description and Characterization**

(Poster No. 25)

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Black esophagus, or acute necrotizing esophagitis, is a blackening of the esophagus that is usually distal with a sharp demarcation at the gastroesophageal border. On histology, the mucosa is necrotic with underlying deranged muscle fibers in the absence of causative agents. Black esophagus is known to the gastroenterology community and carries a 36% mortality rate according to its literature; however, it is virtually unknown in the pathology literature with only 1 instance described in 1967. Black esophagus is thought to occur as a poorly elucidated ischemic phenomenon. Our patient was a 45-year-old woman who had a past history of cocaine and alcohol abuse. She was found unresponsive after a 2-day illness. Emergency medical services responded; she was pronounced dead at the scene. External examination was significant for nasal septal perforation. On internal examination, the esophagus was black with ischemic necrosis of the mucosa, submucosa, and muscularis, including a diffuse acute inflammatory infiltrate and brown pigmentation limited to the mucosa. Results were positive for periodic acid–Schiff with diastase and negative for iron stains, suggesting that the pigment was lipofuscin and likely secondary to ischemia. The nature of the pigmentation has not been previously described. A Masson trichrome stain showed fibrosis around the muscle fibers, placing them at approximately 24 hours post-ischemic event. The liver showed steatosis and increased fibrosis, which is consistent with chronic alcohol use. Toxicology showed cocaine metabolism occurring during all-trans retinoic acid (ATRA) therapy for relapsed acute promyelocytic leukemia. No significant thrombotic events had been documented during her initial induction with ATRA and idarubicin 1 year earlier. After a month of ATRA therapy for relapse, the patient's platelet count increased from less than 20,000 to 252,000. She subsequently experienced sudden cardiopulmonary arrest the day after an ultrasonography revealed a nonoclusive jugular vein thrombus. A complete autopsy revealed the following: multiple right pulmonary thromboemboli with occlusion of the right main pulmonary artery, bilateral internal jugular venous thromboses, a remote portal vein thrombus, and leukemic cells throughout the marrow and in other organs. ATRA is now widely accepted as a first line induction therapy for acute promyelocytic leukemia, and it greatly reduces bleeding complications. However, low-grade disseminated intravascular coagulation and procoagulant activity may persist during ATRA therapy. With the recovery of peripheral blood platelets, the chance of thrombotic events increases, presenting an underrecognized, potentially fatal risk in clinically promising induction therapy. This case suggests that close monitoring of the hypercoagulative state might be required during ATRA induction therapy.

**Deep Vein Thromboses and Fatal Pulmonary Thromboembolism During All-Trans Retinoic Acid Induction Therapy for Relapsed Promyelocytic Leukemia**

(Poster No. 27)

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Coagulopathy with a tendency toward severe bleeding is a well-recognized complication of acute promyelocytic leukemia. However, deep vein thromboses and fatal thromboembolism are rarely associated with acute promyelocytic leukemia. We report an autopsy case of a 36-year-old woman with multiple deep vein thromboses and a fatal pulmonary embolism occurring during all-trans retinoic acid (ATRA) therapy for relapsed acute promyelocytic leukemia. No significant thrombotic events had been documented during her initial induction with ATRA and idarubicin 1 year earlier. After a month of ATRA therapy for relapse, the patient's platelet count increased from less than 20,000 to 252,000. She subsequently experienced sudden cardiopulmonary arrest the day after an ultrasonography revealed a nonoclusive jugular vein thrombus. A complete autopsy revealed the following: multiple right pulmonary thromboemboli with occlusion of the right main pulmonary artery, bilateral internal jugular venous thromboses, a remote portal vein thrombus, and leukemic cells throughout the marrow and in other organs. ATRA is now widely accepted as a first line induction therapy for acute promyelocytic leukemia, and it greatly reduces bleeding complications. However, low-grade disseminated intravascular coagulation and procoagulant activity may persist during ATRA therapy. With the recovery of peripheral blood platelets, the chance of thrombotic events increases, presenting an underrecognized, potentially fatal risk in clinically promising induction therapy. This case suggests that close monitoring of the hypercoagulative state might be required during ATRA induction therapy.

**Adult-Type Gangliosidosis Diagnosed at Autopsy**

(Poster No. 26)

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Gangliosidoses (GM), a group of autosomal recessively inherited lysosomal storage diseases, are characterized by the accumulation of gangliosides primarily in neurons. Two types have been described: GM1 results from a deficiency of acid β-galactosidase, and GM2 results from defects in the β-hexosaminidase A or β-sulfotransferase or the GM2 activator protein. An enzyme assay on peripheral blood leukocytes demonstrating decreased acid β-galactosidase or hexosaminidase A activity is diagnostic of GM1 or GM2, respectively. We report a case of gangliosidosis diagnosed at autopsy. Our patient was a 37-year-old white woman with a history of developmental delay that was first noted at 5 years of age. She developed slowly progressive dementia, proximal muscle weakness, dysphagia, and ataxia, with acceleration of her symptoms 3 years before her death from pneumonia. The clinical differential diagnosis included Huntington disease, fragile X–associated tremor/ataxia syndrome and spino-cerebellar ataxia, each of which had negative genetic evaluations. A central nervous system–only limited autopsy revealed moderate cerebral atrophy with histologic demonstration of numerous swollen neurons containing periodic acid–Schiff–positive, granular storage material in the brain and spinal cord (Figure 59). Ultrastructural studies demonstrated multiple small, electron-dense inclusions containing concentrically arranged and curved lamellar structures in the swollen perikarya of the affected neurons. The clinical, histologic, and ultrastructural findings were consistent with adult-type GM1 or GM2 gangliosidosis. Although a central nervous system–only histologic, and ultrastructural findings were consistent with adult-type dense inclusions containing concentrically arranged and curved lamellar acid-Schiff–positive, granular storage material in the brain and spinal cord.
Correlation of Proliferation and Apoptotic and Glucose Utilization Markers With [18F]fluorodeoxyglucose Positron Emission Tomography Uptake in Peripheral Nerve Sheath Tumors

(Poster No. 29)

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Context: [18F]fluorodeoxyglucose positron emission tomography identifies malignant tumors with high accuracy. However, tumor [18F]fluorodeoxyglucose uptake by standardized uptake value (SUV) misclassifies some tumors. We analyzed benign peripheral nerve sheath tumors (BPNSTs) and malignant peripheral nerve sheath tumors (MPNSTs) and correlated our findings with [18F]fluorodeoxyglucose emission tomography SUV.

Design: We analyzed 24 tumors (12 MPNSTs and 12 BPNSTs). The SUV-positive group had 11 MPNSTs and 2 schwannomas; the SUV-negative group had 1 MPNST, 2 neurofibromas, and 8 schwannomas. We studied histologic features (necrosis and intratumoral hemorrhage), proliferative indices (mitotic rate, Ki-67, and skp2), apoptotic rate by terminal deoxynucleotidyl transferase–mediated dUTP-biotin end labeling of fragmented DNA (TUNEL), and expression of glucose utilization markers including glucose transporter (GLUT-1) and hexokinase II. Ki-67, p53, and TUNEL indices were estimated and quantified by automated image analysis software. Established scoring systems were used for GLUT-1 and hexokinase II staining. Tumors with more than 10% staining were classified as high (skp2) or positive (p53).

Results: Necrosis and hemorrhage were not statistically different between groups. Proliferative indices were higher in the SUV-positive group. Apoptotic rate was higher in the SUV-negative group. SUV-positive tumors had more GLUT-1 staining; hexokinase II stained all but 1 SUV-positive tumor. The difference in mitotic rate and TUNEL was significant on 2-way analysis of variance. GLUT-1 score and SUV status demonstrated significant correlation. SUV-positive and SUV-negative BPNSTs showed no differences in the above factors.

Conclusions: Compared to SUV-negative tumors, SUV-positive peripheral nerve sheath tumors were associated with higher mitotic rate and GLUT-1 scores and lower apoptotic rate.

A Framework for Computer-Assisted Pathologic Diagnosis of Well-Differentiated Liposarcomas

(Poster No. 30)

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Context: Increased digitalization of microscopic images provides a unique opportunity for studying the utility of image analysis as an adjunct to microscopic diagnosis. In particular, image analysis may facilitate arriving at diagnoses that are dependent on identification of relatively rare cytologic or histopathologic features. By using MATLAB software (The MathWorks, Inc, Natick, Massachusetts) to identify atypical lipoblasts in well-differentiated liposarcomas, we hope to determine if screening by image analysis could provide diagnostically useful information.

Design: We identified 10 cases of benign lipoma and 10 cases of well-differentiated liposarcoma in the surgical pathology and consultation files at East Carolina University. Glass slides were digitized using the Aperio system (Aperio Technologies, Inc, Vista, California). MATLAB software was used to identify cells with enlarged, hyperchromatic nuclei by using k-means segmentation and subsequent filtering based on size and color. Images from 20 cells, selected by software screening from each case, underwent blind review. A diagnosis was rendered in each case, and then was compared to the light microscopic diagnosis. Sensitivity, specificity, and predictive values were calculated.

Results: Ten of 10 liposarcomas were correctly classified. One of 10 lipomas was misclassified as a liposarcoma. Sensitivity was 100% and specificity 90%. Negative predictive value was 100% and positive predictive value was 91%. The difficulty associated with ink or fibromuscular tissue caused difficulty with software screening and interpretation in some cases.

Conclusions: Screening by image analysis can assist in diagnosis through identification of infrequent cytologic or histopathologic features of selected pathologic processes.

Leiomyosarcoma Arising From the Pancreatic Duct: A Case Report and Review of Pancreatic Sarcomas

(Poster No. 31)

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Leiomyosarcomata are rare malignant smooth muscle tumors that may arise in any organ or tissue that contains smooth muscle. They are most commonly found in the stomach, large and small intestine, and retroperitoneum. Primary pancreatic leiomyosarcoma is extremely rare. To the best of our knowledge, only 30 cases have been reported in world literature since 1951. However, no cell of origin has ever been clearly shown. The prognosis is poor, and treatment consists of alleviating symptoms and pain management. In this case, a pancreatic tail mass was identified by computed tomography scan. Histopathologic evaluation showed large pleomorphic and spindle-shaped areas of the Immunohistochemistry for vimentin and smooth muscle actin was positive. Results with all remaining immunohistochemical markers used were negative. There was a clear origination from the pancreatic duct, with expansion of the wall by a tumor with overlying benign duct epithelium lining the constricted lumen. This case represents the first reported pancreatic leiomyosarcoma to clearly arise from the main pancreatic duct wall.

Sclerosing Rhabdomyosarcoma as a Metastasis of Embryonal Variant or Vice Versa: A Clinicopathologic, Immunohistochemical, and Molecular Case Study

(Poster No. 32)

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Sclerosing rhabdomyosarcoma (SRMS) is a recently described rare variant of rhabdomyosarcoma that is characterized by extensive hyaline fibrosis. We report a case of a 37-year-old man with coexisting tumors: a 2-cm soft tissue tumor located in the right elbow and a 3-cm right testicular tumor. Histopathologically, the tumor in the right elbow was located in the deep soft tissue, with a richly collagenized matrix corresponding to an SRMS and a microscopic focus of embryonal rhabdomyosarcoma. The testicular tumor was reported as a pure embryonal rhabdomyosarcoma. Both tumors were immunohistochemically negative for desmin and positive for MyoD1. In both tumors, genomic study results with reverse transcription–polymerase chain reaction were negative for alveolar rhabdomyosarcoma–mutated genes PAX3, PAX7, and K-RAF wild type. Six months after tumor resection, the patient presented with metastatic disease in lung and bone. We present a rare case of 2 coexisting subtypes of rhabdomyosarcoma: embryonal rhabdomyosarcoma and SRMS. Despite their different locations, it was difficult to determine the primary tumor from the metastatic one. This case shows a clear relationship between SRMS and embryonal rhabdomyosarcoma. Furthermore, our case suggests that SRMS is a subtype of embryonal rhabdomyosarcoma and that they share a common origin, with one being the primary tumor and the other being the metastatic one.

Metastatic Osteosarcoma Presenting 28 Years After Primary Diagnosis

(Poster No. 33)

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We report an unusual case of metastatic osteosarcoma presenting in the lungs 28 years after the primary diagnosis. The patient was a 45-year-old woman who presented with a persistent cough for 3 months. She also had a past medical history of low-grade osteosarcoma of the right proximal tibia, which occurred at the age of 17 and was treated with a right-above-the-knee amputation only. Computed tomography scan revealed an approximately 16 × 12-cm, large, multiseptated, predominately solid mass occupying the right lung and extending into the right hilum with encasement of the bronchus. Bronchoscopy and endobronchial biopsy were performed. Histologic sections of the biopsy revealed infiltrating, poorly differentiated, highly pleomorphic neoplastic cells. Immunohistochemical staining was performed on the biopsy specimen, and the neoplasm was strongly positive for vimentin and very focally and weakly positive for desmin. Results with pan-cytokeratin, CAM 5.2, thyroid transcription factor-1, epithelial membrane antigen, and S100 were negative, and sarcoma was favored. A pneumonectomy with node dissection was subsequently performed. Consistent with metastatic osteosarcoma, the histologic appearance of the mass was that of a highly cellular pleomorphic sarcoma with focal osteoid production and extensive necrosis. The patient revealed a 12.1-cm GCT with atypical features (Figure 60), such as large areas of coagulative necrosis, focal areas of mild nuclear pleomorphism, and tensinhomolog mutation analysis was negative. The excision specimen revealed a cartilaginous neoplasm of low cellularity that was felt represented a low-grade chondrosarcoma on the basis of the radiographic features and location. Gross examination of the subsequent resection specimen revealed a well-circumscribed cartilaginous mass with scattered foci of dark brown discoloration. The lesion involved the humeral metaphysis and epiphysis with focal, mild, endosteal erosion. Microscopic examination of the lesion demonstrated a low-cellularity cartilaginous tumor that was consistent with an enchondroma. Sections also revealed the presence of a metastatic papillary thyroid carcinoma, a morphologic diagnosis supported by immunohistochemical positivity for thyroglobulin and thyroid transcription factor-1. Our knowledge, only one prior case report of a collision tumor involving an enchondroma and carcinoma exists. That case report described an enchondroma and metastatic lung carcinoma. Prior cases of enchondroma receiving a metastatic papillary thyroid carcinoma have not been reported in the literature.

Electron Microscopy Ultrastructural Study as an Adjunct to Fine-Needle Aspiration Biopsy in Establishing a Definitive Diagnosis of Soft Tissue Tumor (Poster No. 35)

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Context: Making a specific diagnosis by fine-needle aspiration biopsy (FNA) is often difficult; nevertheless, the screening role of FNA cannot be overemphasized because of its low cost, quick turnaround time, and low incidence of complication. The use of FNA on soft tissue tumors is becoming more widespread because of advanced immunohistochemistry and molecular and cytogenetic techniques. However, electron microscopy (EM) ultrastructural studies of FNA material have mainly been reported in case studies.

Design: Cytopathology files from 2001 to 2007 were searched for cases of soft tissue FNA with corresponding EM ultrastructural studies. We retrieved the results of cytology and EM and reviewed the corresponding tissue diagnosis of cases.

Results: Ten soft tissue FNA materials were submitted for EM during this period. Six cases had an EM diagnosis; 3 cases had no malignant cells; and 1 case yielded only degenerated tumors cells. EM was subsequently performed on 2 of the 4 unsuccessful cases by using histology materials. The EM lesions included 2 Ewing sarcomas, 1 monomorphic synovial sarcoma, 1 lymphoma, 1 osteosarcoma, and 1 poorly differentiated carcinoma. Except in 1 case, the EM diagnosis was confirmed by histologic analysis.

Conclusions: Ultrastructural study by EM can be helpful in the diagnosis of problematic soft tissue tumor cases with FNA material. Procurement of material by FNA and subsequent EM processing can be done without much difficulty. Using immunohistochemistry, molecular and cytogenetic techniques, and EM on FNA material can greatly improve the accuracy of soft tissue tumor diagnosis by FNA.

Solitary Intraosseous Rosai-Dorfman Disease Involving the Humerus (Poster No. 36)

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Rosai-Dorfman disease, or sinus histiocytosis with massive lymphadenopathy, is a rare, benign, and usually self-limited disease of unknown etiology that was first described by Rosai and Dorfman in 1969. With classic Rosai-Dorfman disease, the patient presents with lymph node involvement; however, extranodal involvement is common. The most common sites of extranodal disease include skin, upper respiratory tract, and bone. Isolated involvement of medullary bone without lymphadenopathy has rarely been reported in the literature. We report a case of Rosai-Dorfman disease in the proximal humerus of a 50-year-old woman who presented with 3 months of worsening right shoulder pain. She was found to have a single lytic lesion in the right proximal humerus with significant surrounding edema. The patient had no evidence of lymphadenopathy or other foci of systemic disease. The clinical and imaging features indicated infection, and the patient subsequently underwent an open biopsy and curettage of the lesion. Intraoperative frozen section of the lesional tissue revealed sheets of histiocytic cells with emperipolysis, and a preliminary diagnosis of Rosai-Dorfman disease was rendered. Permanent sections confirmed the frozen section results. The histiocytic cells showed positive immunohistochemical staining for S100 protein and negative staining for CD1a. Oil red O preparation on frozen section material showed positive staining in the histiocytic cells. Special stain results for organisms and cultures were negative. Although classic Rosai-Dorfman disease presents with lymphadenopathy, this case illustrates that it can present as a solitary intraosseous lesion that mimics infection. Rosai-Dorfman disease should be considered in the differential diagnosis of solitary bone lesions.

Familial Form of Granular Cell Tumor With Atypical Features and Widespread Metastases (Poster No. 37)

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Malignant granular cell tumors (GCTs) are extremely rare. We report a rare case of familial, multicentric GCT with borderline malignant features and widespread metastases. A 32-year-old African American woman presented with a large soft tissue mass in the lumbar region. She had a history spanning more than 3 decades of multiple GCTs with benign morphologic features in the vulva, back, neck, elbow, and larynx. Family history was significant for GCTs in her siblings and father. Phosphatase and tensin homolog mutation analysis was negative. The excision specimen revealed a 12.1-cm GCT with atypical features (Figure 60), such as large areas of coagulative necrosis, focal areas of mild nuclear pleomorphism, and cells with vesicular nuclei and prominent nucleoli. However, the mitotic rate was less than 1 per 10 high-power fields, and the mitotic labeling index was low. There was no evidence of spindling of cells, high nuclear to cytoplasmic ratio, or increased mitotic rate, and the tumor did not meet the published criteria for malignant GCT. A year later, the patient presented with widespread metastasis. Bilateral inguinal lymph node sampling showed 4.7-mm lymph node metastases and was confirmed by metastatic GCTs. The metastatic GCTs had features that met the criteria for malignant GCT. In addition, computed tomography revealed wide-
Ossifying Fibromyxoid Tumor of Soft Parts Presenting as a Parapharyngeal Mass

(Poster No. 38)

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Ossifying fibromyxoid tumor of soft parts (OFTSP) is a rare mesenchymal neoplasm of intermediate malignant potential. The tumor is of possible Schwann cell origin and commonly occurs in adult men with preferential localization to the subcutis of upper and lower extremities. Nine cases of OFTSP occurring in submucosal and subcutaneous tissues of the head and neck region have been previously reported. A 35-year-old man presented with a right neck mass that slowly grew during the course of 3–4 years. Radiographic images, including magnetic resonance imaging, showed that the mass originated in the right parapharyngeal space, displacing the internal and external carotid arteries anteriorly and the jugular vein posteriorly. He underwent a transcervical resection of the right parapharyngeal mass. Grossly, the tumor was a focally calcified and partially cystic, 6-cm, well-circumscribed, encapsulated mass with a whorled cut surface. Histologically, the tumor had a lobulated growth pattern, with lobules separated by hyaline fibrous strands containing a delicate capillary meshwork. Some lobules were hypocellular and consisted of cytologically uniform cells with ovoid nuclei and indistinct cytoplasm within a myxoid matrix, demonstrating transitions toward hyaline fibrosis. Other areas were distinctly hypercellular, showing mitotic activity and neoplastic ossification within tumor lobules (Figure 61). The tumor showed diffuse positive staining for vimentin and focal positivity for S100 and desmin; results for cytokeratin, smooth muscle actin, epithelial membrane antigen, and glial fibrillary acidic protein were negative. OFTSP was diagnosed. This case illustrates that the clinical and radiographic differential for a parapharyngeal mass is broadened by this unusual case of an OFTSP.

Activation of Mammalian Target of Rapamycin in Soft Tissue and Bone Tumors: Study of 141 Cases

(Poster No. 39)

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Context: Malignant target of rapamycin is a serine/threonine kinase of the PI3K/AKT signaling pathway that is known to play an important role in tumor growth. It is also a potential therapeutic target. Phosphoribosomal S6 protein is a downstream molecule and a surrogate marker for mammalian target of rapamycin activation. Several mammalian targets of rapamycin inhibitors are in clinical trials. We examined phosphoribosomal S6-protein reactivity in a wide variety of sarcomas and mesenchymal tumors.

Design: We reviewed 141 cases of sarcomas. Cases included 19 categories of soft tissue and bone tumors: synovial sarcoma (10), Ewing sarcoma (5), chordoma (8), leiomyosarcoma (20), pleomorphic undifferentiated sarcoma (5), malignant solitary fibrous tumor (5), low-grade fibromyxoid sarcoma (5), clear cell sarcoma (2), alveolar soft part sarcoma (3), angiosarcoma (12), desmoplastic small round cell tumor (3), liposarcoma (12), malignant peripheral nerve sheath tumor (14), chondrosarcoma (5), extraskeletal myxoid chondrosarcoma (8), osteosarcoma (5), desmoid type fibromatosis (7), rhabdomyosarcoma (3), and angiomylipoma (9). Sections were stained with antibody to phosphoribosomal S6 protein and were scored on a 3-point scale: 0 (negative), 1+ (less than 25%), 2+ (less than 50%), 3+ (greater than 50%). High expression was defined as tumors with at least 50% of 2+ or 3+ staining; low expression was defined as a 1+ score.

Results: Expression pattern was stratified naturally into high and low expressors (Table).

Conclusions: High expression of phosphoribosomal S6 protein was observed in several sarcoma subtypes, suggesting a potential benefit from targeted mammalian target of rapamycin therapy. Clinical trials are needed to confirm clinical utility.

<table>
<thead>
<tr>
<th>pS6rp Expression in Soft Tissue and Bone Tumors</th>
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<tbody>
<tr>
<td><strong>High Expressors</strong> (2+ or 3+ score), Tumor (%)</td>
</tr>
<tr>
<td><strong>Rhabdomyosarcoma (100)</strong></td>
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<tr>
<td>Leiomysarcoma (80)</td>
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<tr>
<td>Pleomorphic undifferentiated sarcoma (80)</td>
</tr>
<tr>
<td>Angiomyolipoma (78)</td>
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<tr>
<td>Chordoma (75)</td>
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<td>Liposarcoma (75)</td>
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<tr>
<td>Alveolar soft parts sarcoma (67)</td>
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<tr>
<td>Osteosarcoma (67)</td>
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<td><strong>Chondrosarcoma (20)</strong></td>
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High-Grade Sarcoma Arising in an Ossifying Fibromyxoid Tumor

(Poster No. 40)

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Ossifying fibromyxoid tumor of soft parts is an uncommon neoplasm that typically has a benign to uncertain or low-grade behavior. However, atypical and malignant forms that potentially behave more aggressively have been described. Conventional ossifying fibromyxoid tumors have the potential for local recurrence, but they pose little to no risk for metastasis. We present a rare case of a high-grade sarcoma arising from a conventional ossifying fibromyxoid tumor with multiple lung metastases. A 34-year-old man was being evaluated for sudden abdominal pain when mul-
tiple incidental bilateral lung nodules were identified. Physical examina-
tion and further radiologic evaluation revealed a large intramuscular mass 
in his left axilla, with distinctive peripheral and focal cental bone for-
mation. After resection, we identified a firm, white, well-circumscribed, 
encapsulated mass that had a white, fibrous cut surface and that was 
partially encapsulated (50%) by hard bone. Microscopically, cords of me-
dium round cells arranged within a hyaline background and surrounded 
by a shell of lamellar bone were present (Figure 62, A and B); these find-
ings were consistent with an ossifying fibromyxoid tumor of soft parts. In 
other areas, the sections resembled a sclerosing osteosarcoma (Figure 
62, C) and a high-grade round cell sarcoma. The metastatic lesions in 
the lung were clearly high grade, consisting of undifferentiated round cells 
with prominent mitoses and areas of necrosis (Figure 62, D). This case 
provides the first reported clinical and pathologic evidence that high-
grade transformation can occur in ossifying fibromyxoid tumors and that 
the risk for metastasis is present, albeit only after transformation.

Williams syndrome (WS) is an autosomal dominant disorder caused by 
deletion of chromosome 7q11.23, which encodes the elastin gene. Pheno-
typic manifestations include abnormalities in epidermal and subcutane-
ous tissues; however, no known tumor predisposition is currently recog-
nized. We report on a patient with WS who developed a proximal-type 
epithelioid sarcoma. A 26-year-old man who was diagnosed with WS by 
metaphase fluorescence in situ hybridization analysis, which identified a 
deletion at the WS critical region, presented with a firm, painless peritonal 
mass of 8 weeks' duration. His medical history was significant for aortic 
and renal artery stenosis. A computed tomography scan showed a solid 
3.2 × 2.9-cm soft tissue mass located between the scrotum and anus. 
Needle-core biopsy demonstrated poorly differentiated tumor cells that were 
strongly immunoreactive against broad spectrum cytokeratin, epithel-
ial membrane antigen and myoglobin and focally positive for calre-
tinin, p53, and CK7. The cells were negative for p63, TTF-1, desmin, my-
ogenin, MART-45, and CK20. Ki-67 labeled 25% of nuclei. These find-
ings are consistent with the diagnosis of proximal-type epithelioid sarcoma. 
The patient received neoadjuvant radiation with evidence of tumor necro-
sis, and then, underwent an excision with administration of intraoperative 
radiation. Rarely have tumors been reported in patients with WS. These 
include epithelial and hematologic malignancies. A case of fibrous ham-
artoma of infancy has also been reported in a patient with WS, suggesting 
a link between abnormal elastin synthesis and development of certain soft 
tissue tumors. To our knowledge, this is the first report of a sarcoma of 
any type in a patient with WS.

Expression of MTA1, FIP1, RBM9, and CTR9 in Small 
Blue Cell Tumors in Children 
(Poster No. 43)

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York.

Context: Metastasis-associated protein 1 (MTA1) is an oncogene that 
regulates epithelial to mesenchymal transition and metastasis and may 
indicate progression to metastatic state. Factor interacting with poly(A) 
polymerase (FIP1), RNA-binding motif protein 9 (RBM9), and Paf1/RNA 
polymerase II complex component homolog Ctr 9 (CTR9) are c-myc path-
way oncogenes that are important in controlling tumor growth. The pur-
pose of this study was to evaluate the expression of these novel growth 
tumor markers in small blue cell tumors in children.

Design: A tissue microarray was constructed using paraffin-embedded 
samples from 7 Ewing sarcomas, 6 rhabdomyosarcomas, 6 neuroblasto-
mas, 2 Wilms tumors, and 2 desmoplastic small round cell tumors. Im-
munohistochemistry was performed with rabbit polyclonal antibodies to 
MTA1, FIP1, RBM9, and CTR9. Immunoreactive scoring was based on 
stain intensity (2+ to 3+ were positive) and percentage of positive tumor 
cells.

Results: MTA1 and RBM9 were moderately to strongly expressed in 
most of the small blue cell tumors. FIP1 had stronger expression in des-

moplastic small round cell tumors and Wilms tumor. CTR9 had stronger 
expression in Wilms tumor than in other small blue cell tumors (Table).

Conclusions: FIP1 is a potential diagnostic marker for desmoplastic 
small round cell tumors, and CTR9 is a potential diagnostic marker for

<table>
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<tr>
<th>Expression of MTA1, FIP1, RBM9, and CTR9 in Small Blue Cell Tumors</th>
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<tr>
<td>Score Positive</td>
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<tr>
<td>MTA1, No./Total, (%)</td>
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<tr>
<td>FIP1, No./Total, (%)</td>
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<td>RBM9, No./Total, (%)</td>
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<td>CTR9, No./Total, (%)</td>
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<tr>
<td>Ewing Sarcoma (n = 7)</td>
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<td>7/7 (100)</td>
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<td>5/7 (70)</td>
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<td>0/7 (0)</td>
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<td>Wilms Tumor (n = 2)</td>
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<td>Neuroblastoma (n = 6)</td>
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<td>Desmoplastic small round cell tumors (n = 2)</td>
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Amyloidoma of Bone and Peripheral Nerve: Report of 2 Cases and Review of Literature

(Poster No. 44)

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Amyloidosis is the extracellular deposition of the fibrous protein amyloid with resultant tissue damage. Amyloidosis may be systemic, organ limited, or localized. Amyloidoma, also known as tumoral amyloidosis, is defined as a solitary localized deposit of amyloid in the absence of plasma cell dyscrasia or abnormal serum proteins. Although uncommon, amyloidomas have been reported in various anatomic sites, including respiratory, genitourinary, and gastrointestinal tracts. We report 2 distinct cases of amyloidomas in very unusual locations. The first case was that of a 42-year-old man who presented with a mass lesion in his arm. At the time of surgery, the peripheral nerve seemed to be encased in a sheath of abnormal firm tissue, which was submitted for pathologic evaluation. Both of the lesions were diagnosed as amyloidoma. Involvement of peripheral nerves by amyloidoma is extremely uncommon. Most prior cases of amyloidomas of the central nervous system have involved the trigeminal nerve. Tumoral amyloidosis of bone is even rarer, with only 34 cases reported in the literature. Previously reported cases often involved the spine and skull. To our knowledge, this is the only report of amyloidoma with involvement of the pelvis. Additionally, there are no reports of amyloidomas of such large size. We discuss the clinical and pathologic findings of the amyloidomas in these 2 patients and review the prior literature.

Rare Metastatic Site for a Malignant Fibrous Histiocytoma

(Poster No. 45)

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Of the soft tissue sarcomas that occur in adults, malignant fibrous histiocytoma is the most common. The 2 main sites of metastases are lung and bone. The brain is a rare and unusual site for metastasis. We report a case of a 52-year-old man who presented with a 1-week history of left arm weakness and dizziness. The patient’s medical history was significant for hypertension and hyperlipidemia. The patient was noted to have left lower extremity weakness, sleep disturbance, and hyporeflexia. On examination, the patient was noted to have left leg weakness and a left foot drop. Imaging studies revealed a large heterogeneous mass in the region of the left lateral ventricle. The lesion was biopsy-proven malignant fibrous histiocytoma. The patient developed respiratory distress and was intubated. He died shortly thereafter. Autopsy revealed a large left lateral ventricular mass causing obstructive hydrocephalus and death. Malignant fibrous histiocytoma is a rare sarcoma, and metastases to the central nervous system are exceedingly rare. This case is unusual because of the site of metastasis and the rapid clinical course.

A Rare Case of Adrenal Cavernous Hemangioma

(Poster No. 46)

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Cavernous hemangiomas of the adrenal gland are extremely rare, benign, vascular lesions composed of large cavernous blood vessels lined by endothelial cells. Patients may present with complaints of dull pressure or mass-related symptoms. Microscopic sections showed a malignant neoplasm containing pleomorphic nuclei with multiple mitotic figures suggestive of metastatic malignant fibrous histiocytoma. The neoplasm was immunoreactive for vimentin but not for glial fibrillary acidic protein. Postoperative magnetic resonance imaging showed resection of the cavernomatous mass with residual tumor burden signal along the inferior and lateral aspect of the right lateral ventricle. The patient gradually improved neurologically. He also showed improvement in left upper extremity weakness and was ambulatory at discharge 4 days after surgery. Although the diagnosis of cerebral metastasis is a terminal event, this case represents early detection of a rare metastatic site, with successful tumor decompression as a reasonable therapeutic approach.

The Utility of Perivascular Lymphocytic Infiltrates as a Diagnostic Feature of Atypical Lipomatous Tumor

(Poster No. 48)

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Context: Atypical lipomatous tumor (ALT), also known as well-differentiated liposarcoma, is an uncommon tumor with predilection for the thigh and retroperitoneum. Morphologically, ALT is differentiated from lipoma by the presence of atypical cells with hyperchromatic nuclei. The diagnosis can be missed when diagnostic cells are inconspicuous or unidentifiable.

Spondyloepiphysial dysplasia congenita is a rare disorder that is characterized by short limbs, large head, flattened facies, retinal detachment, hearing loss, cleft palate, and inguinal hernias. This primarily autosomal dominant condition is due to defects in type II collagen and has a genetic linkage to COL2A1 (12q13.11-q13.2). We report a case of spondyloepiphysial dysplasia congenita that was first diagnosed in a 3-month-old, 46, XY male infant who presented at birth with rhizomelia, platyspondyly, short neck, flattened facies, retrolental fibroplasia, Pierre Robin sequence, protuberant abdomen, bilateral inguinal hernias, bilateral simian creases, and a tracheoesophageal fistula that was repaired early in life. The diagnosis was established by radiographic findings and genetic testing that showed a defect in the transition of amino acids involving exon 20 of the COL2A1 gene. Unfortunately, the patient developed Pseudomonas and Serratia culture-positive bronchopneumonia, and his condition deteriorated. Additional findings at autopsy included poor ossification of the calvarium and pubic bones. Microscopic examination of the vertebrae and femur were remarkable for disorganization of the physis growth zone and scattered cytoplasmic inclusions in chondrocytes. These findings were consistent with established descriptions of this disease. This is the first reported case of spondyloepiphysial dysplasia congenita with concomitant bilateral simian creases and tracheoesophageal fistula, findings which may indicate additional manifestations and clinical implications of this disorder.
Design: We tested the sensitivity and specificity of perivascular lymphocytic infiltrates as a novel histologic feature for differentiating ALT from lipoma. We assessed 30 ALTs and 68 lipomas for the presence or absence of perivascular lymphocytic infiltrates. This feature was defined as the presence of at least 15 lymphocytes surrounding at least two-thirds of one or more blood vessels. The ALTs included specimens from 6 biopsies and 24 resections that were selected from cases diagnosed at our institution since 2001. All selected lipomas were resected specimens.

Results: Among ALTs, 23 of 24 resected specimens (95.8%) and 3 of 6 biopsy specimens (50%) contained perivascular lymphocytic infiltrates. Among lipomas, 3 of 68 cases (4.4%) contained perivascular lymphocytic infiltrates. In cases of perivascular lymphocytic infiltrate, all ALTs showed multiple foci of perivascular lymphocytic infiltrate, while only 1 lipoma showed multiple foci. In most cases, the number of perivascular lymphocytic infiltrates was directly proportional to the number of atypical cells present.

Conclusions: Perivascular lymphocytic infiltrates are a useful diagnostic feature when differentiating lipoma from ALT. One should strongly consider a diagnosis of ALT when perivascular lymphocytic infiltrates are present in a fatty tumor. In such cases, additional sections, deeper sections, or immunohistochemical staining to search for atypical cells is warranted.

Extranodal Rosai-Dorfman Disease of Right Calcaneus Without Lymphadenopathy in a 2.5-Year-Old Girl (Poster No. 49)

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Rosai-Dorfman disease (RDD) is characterized by massive painless cervical lymphadenopathy, which is caused by accumulation of proliferating histiocytes in the sinusoids of lymph nodes. We present a unique case of extranodal RDD without systemic lymphadenopathy in the right calcaneus of a 2.5-year-old girl. Imaging studies demonstrated a fairly defined lytic focus involving the posterior portion of the right calcaneus with no adjacent periosteal reaction or soft tissue swelling. There were no other distant lesions. Based on imaging, the differential diagnosis included osteogenic sarcoma, eosinophilic granuloma, bone cyst, or chondroblastoma. ExCISIONal curettage was performed, and histologic examination demonstrated bone fragments with polymorphous inflammatory cell infiltrate composed of lymphocytes, plasma cells, neutrophils and large vacuolated histiocytes with intracytoplasmic lymphocytes, and neutrophils (emperipolesis). The foamy histiocytes were S100 positive and CD1a negative by immunohistochemical staining. This combination of morphology and immunohistochemical findings is characteristic of RDD histiocytes. To our knowledge, only 12 cases, 7 of which were pediatric (Table), have been reported to date of extranodal RDD as a solitary lesion in bone without systemic lymphadenopathy. Our case is the first reported case in the right calcaneus in the pediatric population. There is no specific therapy for RDD; however, a solitary lesion in the bone may be treated with local excision or corticosteroid therapy.

Rosai-Dorfman Disease as Solitary Bone Lesions in Pediatric Population: Case With Literature Review

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Source</th>
<th>Age/Sex</th>
<th>Location</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Allgrana et al</td>
<td>14 y/F</td>
<td>Pariet temporal</td>
</tr>
<tr>
<td>3</td>
<td>Hamels et al</td>
<td>1.5 y/M</td>
<td>Radius</td>
</tr>
<tr>
<td>4</td>
<td>Lewin et al</td>
<td>7 y/F</td>
<td>Metacarpal</td>
</tr>
<tr>
<td>5</td>
<td>Nawroz et al</td>
<td>11 y/M</td>
<td>Radius</td>
</tr>
<tr>
<td>6</td>
<td>Paterson et al</td>
<td>17 y/M</td>
<td>Tibia</td>
</tr>
<tr>
<td>7</td>
<td>Rasool et al</td>
<td>10 mo/F</td>
<td>Right index finger</td>
</tr>
<tr>
<td>8</td>
<td>Present case</td>
<td>2.5 y/F</td>
<td>Calcaneus</td>
</tr>
</tbody>
</table>

Spinal Bone Tumors: A Review of 100 Cases Collected From 2000 to 2009 (Poster No. 50)

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Context: We reviewed 100 spinal bone lesions that were biopsied from 2000-2009 in the musculoskeletal section. We present histopathologic findings of common and uncommon spinal lesions with a review of the pertinent radiographic findings.

Design: Lesions fell into 6 general categories based on frequency and pathologic and radiographic findings: infections, benign and malignant bone lesions, metastatic bone lesions, traumatic bone lesions, and neural neoplasms.

Results: Metastatic lesions included breast (8), squamous cell (5), thyroid (5), prostate (1), lung (1), hepatocellular (1), and gastrointestinal/genitourinary (1). Benign bone lesions included aneurysmal bone cyst (1), giant cell tumor (1), brown tumor (1), osteoid osteoma (1), osteoblastoma (5), giant cell granuloma (1), hemangioma (5), and traumatic lesions (19). Neural lesions included schwannoma (5), ganglieneuroma (1), and epiphondroma (1). Primary malignant bone lesions included osteosarcoma (1), lymphoma (3), treated lymphoma (1), multiple myeloma/plasma cell dyscrasia (8), chondrosarcoma (1), osteosarcoma (1), chondroma (5), and possible yolk sac tumor (1). Pathologic findings for infectious cases (13) were nonspecific or showed mild acute or chronic inflammation. Cultures yielded results for Staphylococcus aureus (1), tuberculosis (1), and Pneumococcus osteomyelitis (1). Positive culture results were obtained in 23% of cases.

Conclusions: Benign lesions (34) were most numerous and were commonly posttraumatic. Metastases (25) were the most common spinal bone tumor, with breast tumor being the most common followed by squamous carcinoma. Primary malignant lesions (21) accounted for 21% of cases, with myeloma and chordoma being the most common. Neural lesions (7) were mostly schwannomas. Histopathologic appearance and correlation with clinical history and radiographs is paramount for diagnosis.

Malignant Granular Cell Tumor: Case Report With a Novel Karyotype (Poster No. 51)

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Granular cell tumor is an uncommon benign neoplasm that arises in all body sites with predilection for the head and neck region. Rare case reports and small series describe the metastatic potential and adverse prognosis of malignant granular cell tumors. To our knowledge, no specific karyotype characterizes these tumors. We report a case of malignant granular cell tumor arising in the subcutaneous tissue of the thigh in a 56-year-old woman. There was metastasis to the abdominal wall and both lungs, and the patient experienced dyspnea. Grossly, the tumor was ulcerated, homogeneously gray-white, ill-defined, and firm. Microscopically, it was composed of sheets and nests of pleomorphic epithelioid and spindle cells with eosinophilic and granular cytoplasm. There was scattered karyorrhexis. Mitotic count was up to 7/10 high-power fields. Immunohistochemically, the tumor cells were diffusely and strongly positive for S100. Sixty per cent of tumor cells displayed the following karyotype: 46,XX, + 4,5 dic(5;15)(p14;q25). Malignant granular cell tumor is a rare and difficult tumor to diagnose and treat. The histologic criteria of malignancy proposed by Fanburg-Smith et al are still debated among pathologists, with metastasis being the only criterion unanimously agreed upon. We report an interesting case of malignant granular cell tumor with multiple metastases and a novel karyotype. Detecting characteristic cytogenetic alterations in these tumors is important because they might serve as an aid in diagnosis or therapy.

Retropertioneal Fibrosis Associated With Widely Disseminated Anaplastic Large Cell Lymphoma Identified at Autopsy (Poster No. 52)

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Retropertitoneal fibrosis is a fibroinflammatory condition involving the abdominal aorta, iliac vessels, and ureters. This rare phenomenon, with an incidence of 0.1 cases per 100,000 people, carries a strong correlation with autoimmune conditions, such as scleroderma, polymyositis, sarcoidosis, and systemic lupus erythematosus. Our case was idiopathic; however, as many as one-third of cases can be attributed to a secondary cause. We present a case of secondary retropertitoneal fibrosis arising in a 29-year-old woman with anaplastic large cell lymphoma identified at autopsy. The patient presented with a 2-month history of early satiety, abdominal discomfort, constipation, and progressive fatigue. Abdominal
magnetic resonance imaging revealed a peripancreatic soft-tissue mass, which on open biopsy revealed fibroadipose tissue with acute inflammation and fat necrosis. A bone marrow biopsy was unremarkable. Despite steroid therapy, the patient declined during the ensuing 8 months, experiencing failure to thrive and then death. At autopsy, diffuse fibrosis surrounded the abdominal aorta from the level of the renal arteries to the origin of the iliac vessels. The fibrosis encased the pancreas, bilateral ureters, and the inferior mesenteric artery. Histologic examination revealed a CD2/3/4/7/8/25/43-negative and CD30/ALK-1–positive infiltrate of large lymphoid cells with wreath-shaped nuclei infiltrating most organs and fibrotic areas. To our knowledge, this represents the first association between anaplastic large cell lymphoma and retroperitoneal fibrosis reported in the English literature. This case illustrates the importance of both patient demographics and adequate surgical sampling for patients with retroperitoneal fibrosis.

A Case and Review of Osseous Sarcoidosis of the Distal Clavicle and Proximal Humerus

(Poster No. 53)

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A 51-year-old white man with known pulmonary sarcoidosis presented with a 1-year history of right shoulder pain during strenuous activity. Plain radiographs of the right shoulder were unremarkable, but a magnetic resonance imaging study showed multiple low-intensity foci in his right proximal humerus, acromium, and distal clavicle. Shoulder arthroscopy with open distal clavicle excision was performed. Histologic evaluation of the right distal clavicle and right acromium revealed multiple noncaseating granulomas composed of compact epithelioid histiocytes and multinucleated giant cells. Special stains for acid-fast bacilli and fungi were negative. Given the patient’s history, these lesions were consistent with osseous sarcoidosis. Bone involvement in patients with sarcoidosis can occur in up to 30% of cases and typically affects the vertebrae and bones of the hand and foot. Bone involvement is often asymptomatic and discovered incidentally by radiographic studies. Plain radiographs may fail to reveal the osseous lesions, which are identified on magnetic resonance scan or nuclear scintigraphy. Histologic evaluation of the involved bone established the diagnosis and demonstrated aggregates of epithelioid histiocytes, multinucleated giant cells, and macrophages surrounded by lymphocytes and fibroblasts with no evidence of caseating necrosis. In this patient, the clinical history, in conjunction with the radiographic and histologic findings, was consistent with osseous sarcoidosis limited to the distal clavicle and proximal humerus. This is a previously undocumented isolated osseous location for this disease.

Autoimmune Hemolytic Anemia After Small-Bowel Transplantation May Represent Graft Versus Host Disease

(Poster No. 54)

Srividya Sathiyamoorthy, MBBS, MS; Rachel Edwards, MB, MT(ASCP); Purviben Jariwala, MT(ASCP); Karen W. Eldin, MD; Trung C. Nguyen, MD; Jun Teruya, MD, DSc.

After observing 2 cases of autoimmune hemolytic anemia after small-bowel transplants, we reviewed Transfusion Service records of all solid organ transplants during the prior 12 months for serologic evidence of autoimmune hemolytic anemia. Positive direct antiglobulin test results were identified for 3/21 patients with multorgan transplants including small bowel, 0/90 patients with liver transplants, and 0/6 patients with kidney transplants (+/- pancreas). A 1-year-old boy with microvillous inclusion disease received liver, pancreas, and small-bowel transplants. On day 137 posttransplant, we observed a positive direct antiglobulin test (anti-IgG: 2+ / anti-C3d: 1+) and an eluate panagglutinin (hematocrit = 32.9%) for the first time. A 4-year-old boy with microvillus inclusion disease received small bowel, liver, pancreas, and spleen transplants. On day 141 posttransplant, we detected a positive direct antiglobulin test (anti-IgG: 3+ / anti-C3d: 1+) and an eluate panagglutinin (hematocrit = 28.0%) for the first time. These cases of autoimmune hemolytic anemia appear to distinguish small-bowel transplants from other solid organ transplants. In theory, all transplanted organs have the potential for expressing graft versus host disease by cellular and/or humoral immune mechanisms. However, the presence of a major site of the donor’s humoral immunity (Peyer patches) in transplanted small bowels distinguishes these solid organ transplants from others. We hypothesize that autoimmune hemolytic anemia after small-bowel transplants may represent a humoral variant of graft versus host disease. In our cases, the relatively uncommon presence of IgG autoantibody and complement (C3d) on red blood cell counts may reflect the unique donor tissue origin of these autoantibodies.

Utility of the Disseminated Intravascular Coagulation Scoring System by International Society on Thrombosis and Haemostasis in a Pediatric Setting

(Poster No. 56)

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We reviewed 2136 DIC panels and 25 autopsy reports in which DIC was suspected. The patients were monitored by using a panel of coagulation assays that included prothrombin time, activated partial thromboplastin time, fibrinogen levels, thrombin time, D-dimer, and platelet count. Difference in diagnosis was compared between the ISTH scoring system and our hospital by isolating data specific to ISTH criteria from the DIC panels and then entering it in the ISTH algorithms.

Results: Our hospital and ISTH showed 59.4% concordance for suspected DIC diagnosis. The autopsy reports confirmed that 96% of patients suspected of having DIC did have DIC (Table). The three autopsy cases with significantly elevated prothrombin time, positive D-dimer, and low platelet
counts scored below a 5 under ISTH guidelines. The ISTH scoring system more closely represented D-dimer and platelet counts but underrepresented elevated prothrombin time and higher levels of fibrinogen when indicating DIC. ISTH criteria suggest fibrinogen counts lower than 100 mg/dL are significant; however, these values are rarely seen in DIC cases at our hospital.

Conclusions: We recommend comparative analysis of all DIC-related assays until the ISTH system is revised.

Risk of Hemolytic Transfusion Reactions After Emergency Release Red Blood Cell Transfusion (Poster No. 57)

Pamela P. Goodell, MD (ppgoodell@udmc.harvard.edu); Lynne Uhl, MD; Monique T. Mohammed, MS(ASCP) SBB; Amy Powers, MD. Department of Pathology, Division of Laboratory and Transfusion Medicine, Beth Israel Deaconess Medical Center, Boston, Massachusetts.

Context: Patients requiring urgent red cell blood (RBC) transfusion may receive one by using emergency release (ER) RBCs before completion of routine blood bank testing. To avoid ABO-incompatible hemolytic transfusion reactions (HTRs), group O RBCs are typically issued. Identification of antigen-incompatible antibodies was identified in 17/29 (6.4%) ER episodes. The remaining upon completion of testing in 29 episodes (10.9%). Clinically significant HTRs (0.4% of ER episodes) and receipt of antigen-incompatible antibodies were identified in 17/29 (6.4%) ER episodes. The remaining 12 included warm autoantibodies (6) and clinically insignificant antibodies (2). Four others were inconclusive. Seven recipients with clinically significant antigen-incompatible antibodies received a transfusion, with a total of 15 antigen-incompatible units. One incompatible unit resulted in a clinically apparent HTR due to anti-c.

Conclusions: Transfusion of ER RBCs before completion of routine blood bank testing carries a low but real risk of non-ABO antigen-mediated HTRs (0.4% of ER episodes) and receipt of antigen-incompatible RBCs (2.6% of ER episodes).

Management of Membranoproliferative Glomerulonephritis Type II–Related Complement-Mediated Glomerular Injury With Plasmapheresis Postrenal Transplant (Poster No. 58)

Christina M. Bagby, DO1 (Christina.Bagby@UHhospitals.org); Joshua J. Augustine, MD2; Greta H. Jacobs, MD; Katharine A. Downes, MD. Departments of Pathology and Nephrology, University Hospitals Case Medical Center, Cleveland, Ohio.

Membranoproliferative glomerulonephritis type II (MPGN II) is a rare kidney disease that is characterized by ribbonlike electron-dense deposition within the glomerular basement membrane. More than 80% of patients with MPGN II have circulating C3 nephritic factor (C3NF), an autoantibody directed against the C3bBb convertase involved in the complement cascade. We present the case of a 36-year-old man who was diagnosed with MPGN II at age 16 and who had bilateral native nephrectomies and a failed cadaveric renal transplant because of rapid recurrence of disease. After 17 years of dialysis, he received a second cadaveric renal transplant in November 2008 and required dialysis for persistent oliguria (>10 cc/d) posttransplant. Ten days posttransplant, a renal biopsy revealed abnormal C3 immunofluorescent staining, which was suggestive of early recurrence of MPGN II, however, electron-dense deposition was not seen. High levels of C3NF were detected, and plasmapheresis (PE) was initiated for possible removal of this autoantibody. PE was performed in 1-volume exchanges by using fresh frozen plasma daily for the first 4 days. PE was progressively decreased to once a week after clinical improvement. C3NF levels were assayed pre-PE and post-PE (Table). A second renal biopsy performed 41 days after initiating PE showed glomerulosclerosis with negative C3 immunofluorescent staining. The patient was maintained on 1-volume daily dialysis therapy for 6 months. At the initiation of PE, Post-PE he has maintained urine output greater than 1000 cc/d and negative or equivocal C3NF levels weekly. Although the role of PE in MPGN II remains unclear, it may assist in maintenance of renal function posttransplant.

Severe Hemolytic Disease of Newborn Due to ABO Incompatibility (Poster No. 59)

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ABO incompatibility is now the most common cause of hemolytic disease of newborn (HDN). Symptoms of ABO-HDN are typically mild and could include jaundice within 24 hours of birth and mild anemia with spherocytosis but little or no increase in nucleated red cells on peripheral smear. The current case demonstrates an unusually severe presentation of ABO-HDN. An African American male infant was delivered at 37 4/7 weeks of gestation to a G1P0 mother after an uneventful pregnancy. The mother’s blood type was O positive; an antibody screen was negative. At birth, the neonate was blood type B positive and was jaundiced (bilirubin 9.6 mg/dL) and anemic (hematocrit 27.7%); the direct antiglobulin test on the infant’s red cells was weakly positive. A peripheral smear revealed a large number of nucleated red cells and marked reticulocytosis (20%). Despite phototherapy, his bilirubin continued to rise, and an exchange transfusion was performed on day 2 of life. This case demonstrates several unusual features. While jaundice is common in ABO-HDN, rapidly rising bilirubin levels (>12 mg/dL) are uncommon, and exchange transfusion is rarely required (<1:100 in 1 series). Additionally, while spherocytosis is a relatively common finding in ABO-HDN, hemolysis is rarely so severe as to result in marked reticulocytosis (4%–6% of ABO-HDN cases), and nucleated red cells in the peripheral blood are distinctly unusual. Finally, ABO-HDN is more common when the mother is type O and the neonate is type A. This case emphasizes that ABO-HDN is occasionally severe and may require aggressive postnatal care.

Are Optical Density Readings of an Enzyme Immunoassay for Heparin-Induced Thrombocytopenia Antibodies Predictive of Serotonin Release Assay Results in Clinical Practice? (Poster No. 60)

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Context: The serotonin release assay (SRA) is considered the gold standard for identification of antibodies that cause heparin-induced thrombocytopenia. Because of technical difficulty and expense, our laboratory outsources to BloodCenter of Wisconsin. In-house, we use the PFA Enhanced qualitative enzyme immunoassay (EIA) (GTI Diagnostics, Waukesha, Wisconsin). Because physicians sometimes order both tests, paired results were studied to assess whether the EIA results were predictive of SRA results.

Design: Patients who underwent an EIA and SRA within 7 days of each other between January 1, 2006, and February 5, 2009, were identified in our data files. Cases were stratified by EIA OD values, and the percentage agreement of EIA and SRA qualitative results was calculated for each stratum. EIA OD less than 0.400 was considered negative.

Results: Of 1753 EIA tests, 10% met the inclusion criteria. Of those, 123 EIA tests were positive, and 30 SRA tests were positive. Overall agreement
was 46%. A negative EIA predicted a negative SRA with 96% accuracy. The average OD per stratum was correlated with percentage of positive SRA results ($r^2 = 0.991$). However, the percentage of agreement between positive EIA and positive SRA ranged from only 7% to 67%, depending on the OD stratum (Figure 64).

**Conclusions:** As used clinically in our setting, the OD of the EIA correlates with the percentage of positive SRA results. However, the degree of correlation is not sufficient enough to override clinical judgment when an SRA is felt to be indicated.

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**Prospective Review Improves Compliance for Blood Component Transfusion**

**Poster No. 63**

Christina M. Mancini-Flegel, BS (cmancin1@jhmi.edu); Bonnie K. Hammond, BS; Stanley J. Podlasek, MD. Department of Pathology, Johns Hopkins University, Baltimore, Maryland.

**Context:** Life-saving blood component therapy still has residual risk of immune reactions, clerical accidents, mechanical or thermal damage to components either before or during transfusions, and transmission of infectious contaminants. Despite vast improvements in transfusion safety, clinicians must weigh benefits against these risks. To assure best practice, protocols have been implemented, and blood transfusions have been reviewed retrospectively on the basis of well-established transfusion indications.

**Design:** We hypothesized that prospective review of transfusion indications would lead to improved compliance with protocols in comparison to retrospective review. Indications for packed red blood cells, frozen plasma, apheresis platelets, and cryoprecipitate were simplified and adjusted to comply with former transfusion indications at Howard County General Hospital and The Johns Hopkins Hospital. We collected data on retrospective compliance by medical chart review from a representative sample of blood transfused in 2007–2008. For prospective review, the same indication criteria for each blood component were displayed as choices on a physician order sheet, which was completed by the ordering physician and was sent to blood bank before blood was issued. Prospective review was introduced in September 2008.

**Results:** Prospective blood review demonstrated 194/194 (100%) compliance with the transfusion protocol indication criteria. In contrast, retrospective blood review showed that 36/39 (92.3%) of blood components transfused in 2008 and 142/146 (97.3%) of blood components transfused in 2007 successfully met the protocol criteria. Prospective blood review gives better compliance with transfusion indications than does retrospective blood review. American Association of Blood Banks designated our procedure as a commendable practice.

**Conclusions:** Prospective blood review gives better compliance with transfusion indications than does retrospective blood review. American Association of Blood Banks designated our procedure as a commendable practice.

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**Burkitt Lymphoma Mimicking Thrombotic Thrombocytopenic Purpura in a Woman With Postpartum Gigantomastia**

**Poster No. 64**

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A 35-year-old gravida 1, para 1 woman with a medical history of migraines presented 10 days postpartum with unexplained thrombocytopenia, anemia, and elevated levels of hepatic transaminases. Her pregnancy was complicated during the third trimester by preeclampsia and progressive breast enlargement attributed to gigantomastia. Physical examination revealed bilateral massive breast enlargement with prominent purple discoloration and exquisite tenderness requiring narcotic analgesia. Breast ultrasonography showed no hemorrhage or other abnormality. Peripheral blood smear was nonspecific, with 1 to 2 possible schistocytes/high-power field, markedly diminished platelets, and no abnormal or im-
mature leukocytes. A few days into the hospitalization, she developed mild confusion, headaches that were not consistent with her previous migraines, and left facial numbness. The initial differential diagnosis was HELLP syndrome versus postpartum thrombotic thrombocytopenia purpura. Her platelet count continued to decline after 3 days. 1.5-volume plasma exchanges with fresh frozen plasma. Given her worsening symptoms, lack of response to plasma exchange, low reticulocyte count in the presence of anemia, and return of a normal ADAMTS13 activity, bone marrow biopsy and aspirate were performed with findings diagnostic for Burkitt lymphoma. Chemotherapy was begun with rapid diminishment of breast enlargement. This case illustrates the importance of having a high index of suspicion in diagnosing these rare cases. The role of plasma exchange is not clearly established for atypical HELLP. However, since the differential diagnosis of HELLP in the postpartum period includes thrombotic thrombocytopenia purpura, plasma exchange may have a role in these cases, especially when thrombocytopenia lasts more than 3 days postpartum.

**Familial Combined Factor V and Factor VIII Deficiencies**

(Poster No. 65)

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A 6-year-old girl presented with minor head trauma with bleeding that responded to intravenous desmopressin. She bruised easily but had no complaints of epistaxis or mucosal bleeding. No other bleeding problems were noted; she never had surgery. Revealing a prothrombin time of 15.6 seconds, an international normalized ratio of 1.4, and an activated partial thromboplastin time of 64.1 seconds. Further workup for the prolonged activated partial thromboplastin time revealed a corrected mixing study. Factor assays were significant for a factor VIII level of 12% and a factor V level of 13%. Other factors were within normal reference ranges. Her 4-year-old sister had a history of easy bruising but no significant bleeding history. Testing revealed a prothrombin time of 17.0 seconds, an international normalized ratio of 1.5, and an activated partial thromboplastin time of 78.4 seconds. This girl's mixing studies corrected with normal plasma and factor assays were significant for a factor VIII level of 6% and a factor V level of 8%; other factors were normal. Low factor VIII levels in females may indicate a rare hemophilia A, which is caused by a particular lyonization or a carrier mother and affected father, resulting in a homozygous state. Type 2N von Willebrand disease is a consideration. The prolonged prothrombin time suggested a possible defect in the common pathway as well. Combined factor V and VIII deficiencies are a rare autosomal recessive bleeding disorder that is associated with plasma levels of coagulation factors V and VIII that are approximately 5%–30% of normal.

**Applications of Sanctions by the Centers for Medicare and Medicaid Services and Accrediting Organizations for Proficiency Testing Failure: A 7-Year Study**

(Poster No. 66)

Amy B. Karger, MD, PhD (karger026@umn.edu); Anthony A. Killeen, MD, PhD, FACP. Department of Laboratory Medicine and Pathology, University of Minnesota, Minneapolis.

**Context:** Proficiency testing (PT) is a requirement for laboratories that hold certificates for nonwaived testing under the Clinical Laboratory Improvement Amendments of 1988. There has been little published analysis regarding sanctions levied against laboratories with unsuccessful PT performance.

**Design:** Data from the Laboratory Registry, which are published annually by the Centers for Medicare and Medicaid Services (CMS), were examined for a 7-year period (2001–2007) to determine the incidence of sanctions by CMS or an accrediting organization for unsuccessful PT performance. We reviewed the type of sanctions that were imposed on laboratories that failed PT. In addition, the current certification status of these laboratories was determined by searching the CMS Laboratory Diagnostic Information Report database.

**Results:** During the period examined, 272 laboratories were sanctioned for unsuccessful PT performance. Of these laboratories, 67 received a principal sanction, the most severe penalty imposed by CMS. Of the laboratories receiving a principal sanction, 24% are no longer operating. Of the laboratories that received a sanction, 6.3% now have a Certificate of Waiver. PT failures have increased in recent years, and most laboratories cited were penalized with a principal sanction.

**Conclusions:** Most laboratories that failed PT received a principal sanction, most are currently operating with CMS Certificates of Compliance or Accreditation. Therefore, most laboratories took the required corrective actions to regain a CLIA Certificate of Operation. Further investigation is needed to determine whether the increasing application of sanctions is the result of deteriorating laboratory performance in PT or increased enforcement by CMS or accrediting agencies.

**POSTER SESSION 500: TUESDAY, OCTOBER 13, 2009, 7:00 AM–9:30 AM**

**Cytologypathology; Dermatopathology; Neuropathology; Practice Management; Cardiovascular Pathology**

**Fine-Needle Aspiration Biopsy of Salivary Gland Lesions: Comparing On-Site Rapid Interpretation with the Final Cytology Diagnosis**

(Poster No. 1)

Ami Bhalodia, MD (abhalodi@sluhsc.edu); Jessica Bagby, BS; Fleurette Abreo, MD; Songlin Zhang, MD, PhD. Department of Pathology, Louisiana State University Health Sciences Center, Shreveport.

**Context:** Fine-needle aspiration biopsy (FNAB) has been used for evaluation of salivary gland lesions during the past several decades, and FNAB has been documented to have very good sensitivity and accuracy for differentiating neoplastic lesions from reactive processes. Most FNABs were performed in outpatient clinics by clinicians without on-site rapid interpretation, so the accuracy and efficiency of on-site rapid interpretation has not been documented in the literature.

**Design:** We searched our cytopathology files from 2003 to 2007 for salivary gland aspiration and the corresponding surgical resection reports. The on-site rapid interpretation, the final cytology diagnosis, and the corresponding histology diagnosis were compared.

**Results:** One hundred ninety salivary gland FNABs were performed during the 5-year period; 94 cases had surgical resection follow-up (49.5%). A total of 168 cases had on-site cytology evaluation (88.4%), 159 cases had on-site rapid diagnosis, and 9 cases were deferred for permanent diagnosis (deferring rate 5.4%). One hundred forty-one (88.7%) cases had both on-site and final diagnosis, and 18 (11.3%) cases had variable-degree differences. Thirteen cases were upgraded, and 5 cases were downgraded in final diagnosis. Eleven of the 18 cases had surgical follow-up, and final diagnosis was confirmed in 9 cases.

**Conclusions:** On-site rapid interpretation has a high (88.7%) diagnosis agreement with final cytology diagnosis, and only a few cases (5.4%) were deferred for the permanent diagnosis. We encourage providing on-site rapid interpretation, and the advantage of on-site cytology evaluation includes decreases patient’s anxiety and waiting time, providing training opportunity for pathology residents/fellows, and increasing interaction and trust between pathologists and clinicians.

**Deletion of 9p21 Is a Rare Finding in Urine Specimens Collected From Patients With a History of Hematuria and Bladder Cancer**

(Poster No. 2)

Junqi Qian, MD; Mililani Medina, MS; Karen Crewell, MS; Deena Weber, MS; Deloar Hossain, MD; David G. Bostwick, MD, MBA (mmdonald@bostwicklaboratories.com). Bostwick Laboratories, Glen Allen, Virginia.

**Context:** Fluorescence in situ hybridization (FISH) of voided urine is a sensitive and specific test for the detection of urothelial carcinoma. Common FISH testing consists of 4 DNA probes to chromosomes 3, 7, and 17 and to band 9p21. We sought to determine the incidence of these chromosomal anomalies in urine specimens because their patterns are not well documented.

**Design:** Urine samples from 13284 patients with a history of hematuria and/or bladder cancer were studied. FISH was performed using probes to chromosomes 3, 7, and 17 and to band 9p21; cytology was also performed.

**Results:** The FISH positive rate was 5.7% (691 of 12 163) of the samples sufficient for FISH. Gains of chromosomes 3 and 7 (56.5%), 7 and 17 (51.6%), and 3 and 17 (36.9%) were most frequent. Deletion of 9p21 was observed in 12% of cases, but such deletions were more sensitive than cytology for the detection of urothelial carcinoma (77.4% vs 53.5%, respectively; P = .03), but specificity was nearly equal (68% vs 71.6%, respectively; P > .05).

**Conclusions:** Gains of chromosomes 3 and 7 were the most common anomalies detected, whereas deletions of 9p21 only was rare and never seen in isolation. FISH was significantly more sensitive than cytology for the detection of urothelial carcinoma with equivalent specificity.
Primary Intrathyroid Paraganglioma Mimicking Hürthle Cell Neoplasm on Fine-Needle Aspiration Cytology: Unique Cytomorphologic Presentation in a Rare Entity
(Poster No. 3)

Arvind Rishi, MBBS (arishi@nshs.edu); Yan Shi, MD, PhD; Patricia Wasserman, MD. Department of Pathology, North Shore Long Island Jewish Health System, New Hyde Park, New York.

Primary intrathyroid paraganglioma of thyroid is extremely rare and offers significant diagnostic challenges on fine-needle aspiration cytology (FNAC). Cytologic features are diverse, and important differential diagnosis includes Hürthle cell neoplasm, paraganglioma-like medullary carcinoma, hallowing trabecular adenoma, follicular carcinoma, parathyroid gland lesions, and carcinoid tumor. We report an unusual case of primary intrathyroid paraganglioma, mimicking Hürthle cell neoplasm on FNAC, in a 21-year-old euthyroid woman presenting with a solitary left thyroid nodule. Cytology showed moderately cellular specimen composed of polygonal, round to spindle cells with moderate amounts of amphiphilic finely granular cytoplasm, focal intracytoplasmic vacuoles, eccentrically located nuclei with mild nuclear pleomorphism, and conspicuous eosinophilic nuclei. FNAC was suggestive of Hürthle cell neoplasm. Histology on partial thyroidectomy specimen showed nests of polygonal to round cells arranged in a characteristic “zellballen” neuroendocrine pattern. Mitosis, necrosis, or capsular infiltration was absent. The tumor cells were immunopositive for CD56, chromogranin and synaptophysin, and immunonegative for TTF-1 and calcitonin. S100 protein and literature review, the most helpful cytomorphologic features for differential diagnosis include the color of cytoplasmic granules, intracytoplasmic vacuoles, admixed spindle cells, and background of bare nuclei (Table). Also discussed are the other cytomorphic features reported in primary thyroid paraganglioma and the diagnostic pitfalls of paraganglioma in all body sites.

Cytologic Features of Hailey-Hailey Disease in an Anal ThinPrep: Pitfalls in the Diagnosis of Squamous Intraepithelial Lesions in Liquid-Based Cytology Specimens
(Poster No. 4)

Sarah E. Frost, MD1 (sarah.frost@mssm.edu); Marie A. Ramer, DDS1; Jeffrey S. Freed, MD2; Arnold H. Szporn, MD.1 Departments of Pathology and Surgery, The Mount Sinai School of Medicine, New York.

Pemphigus has long been known as a pitfall in the diagnosis of squamous intraepithelial lesions arising in squamous mucosa, but its presentation in liquid-based cytologic preparations is not well described. Hailey-Hailey disease (benign familial chronic pemphigus) is a rare, dominantly inherited dermatosis not previously described in the cytology literature. We present the case of a 36-year-old woman with a known personal and family history of Hailey-Hailey disease and previous high-risk human papilloma virus–positive tests who was diagnosed by another laboratory as having a “high-grade squamous intraepithelial lesion with gland involvement” in an anal ThinPrep. We received for review one Papanicolaou-stained ThinPrep slide originally prepared from an anal brushing. Low-power examination revealed many dyscohesive to loose clusters of cells with metaplastic features and apparent high nuclear to cytoplasmic ratios. However, at high-power, many of these cells demonstrated bichromatic cytoplasm, which was peripherally soft but centrally dense, closely surrounded the nucleus, and had a relatively low nuclear to cytoplasmic ratio. It is this dense cytoplasmic zone that gave the false low-power impression of a high nuclear to cytoplasmic ratio. The centrally located nuclei had relatively fine chromatin, usually one or more nucleoli, and relatively round, thin, and smooth nuclear membranes lacking any neoplastic features. In one such cluster, acantholysis was seen, exemplified by the presence of intercellular bridges (Figure 65). Familiarity with the cytologic presentation of lesions of the Pemphigus family on liquid-based specimens, as well as conventional smears and clinical history, are keys in avoiding the pitfall diagnosis of a squamous intraepithelial lesion.

Cytomorphologic Comparison of Hürthle Cell Neoplasm and Paraganglioma

<table>
<thead>
<tr>
<th>Cytologic Features</th>
<th>Hürthle Cell Neoplasm</th>
<th>Paraganglioma</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cellularity and arrangement</td>
<td>Moderate to high, single cells, sheets and clusters</td>
<td>Low to moderate, single cells, loosely cohesive clusters</td>
</tr>
<tr>
<td>Cell shape</td>
<td>Polygonal to round</td>
<td>Polygonal to round with wispy cytoplasm</td>
</tr>
<tr>
<td>Cell borders</td>
<td>Usually well defined</td>
<td>Usually poorly defined</td>
</tr>
<tr>
<td>Cytoplasm Amount</td>
<td>Moderate to abundant</td>
<td>Moderate to abundant</td>
</tr>
<tr>
<td>Granules Staining</td>
<td>Coarse, eosinophilic</td>
<td>Fine, variable</td>
</tr>
<tr>
<td>Vacuoles</td>
<td>Usually absent</td>
<td>Mostly present</td>
</tr>
<tr>
<td>Nuclear features</td>
<td>Usually absent</td>
<td>Mostly present</td>
</tr>
<tr>
<td>Number</td>
<td>Frequent binucleation</td>
<td>Usually single</td>
</tr>
<tr>
<td>Location Pleomorphism</td>
<td>Mostly central</td>
<td>Mostly eccentric</td>
</tr>
<tr>
<td>Nucleoli</td>
<td>Usually monomorphic</td>
<td>Abrupt, mild to moderate</td>
</tr>
<tr>
<td>Chromatin</td>
<td>Finely granular, uniformly</td>
<td>Occasional/conspicuous</td>
</tr>
<tr>
<td>Inclusions</td>
<td>Usually absent</td>
<td>Finely granular, uniformly</td>
</tr>
<tr>
<td>Grooves</td>
<td>Usually present</td>
<td>Occasionally present</td>
</tr>
<tr>
<td>Background Colloid</td>
<td>Present in benign lesions</td>
<td>Absent</td>
</tr>
<tr>
<td>Bare nuclei</td>
<td>Absent</td>
<td>Present</td>
</tr>
<tr>
<td>Neutrophils</td>
<td>Absent</td>
<td>Variable</td>
</tr>
<tr>
<td>Necrosis</td>
<td>Present in malignancy</td>
<td>Variable/does not indicate malignancy</td>
</tr>
</tbody>
</table>

Granulosa Cell Tumors of the Ovary: Cytologic Findings in 7 Cases
(Poster No. 5)

Renuka Kulkarni, MBBS (rkulkarni@mcc.edu); Sravankumar Kavuri, MBBS; Preetha Ramalingam, MBBS; Michelle Reid-Nicholson, MBBS. Department of Pathology, Medical College of Georgia, Augusta.

Context: The cytology of adult (AGCT) and juvenile granulosa cell tumors (JGCT) is only rarely described. Accurate cytologic diagnosis is important for appropriate staging and management. We describe cytologic findings in 6 AGCTs and 1 JGCT, emphasizing differences between recurrent/metastatic (REC) and nonrecurring (NREC) AGCTs.

Design: Tumor imprints and pelvic washings/aspirate fluids from 7 patients were evaluated for hypercellularity, CALL-EXNER bodies (CEB), sheets, single cells/naked nuclei (SCNN), nuclear grooves, single cell necrosis,
and histologic features of cellular atypia in AGCT (>3 mitoses, pleomorphism, hyperchromasia, and prominent nucleoli [PN]).

Results: Fluids had lower cellularity and fewer clusters, grooves, and SCNN than imprints, but no CEBs, necrosis, or vacuoles were seen. Hyperchromasia and PN were more obvious in fluids and more striking in JGCT than in AGCT. CEBs and grooves were only seen in AGCTs. Only RECs had vacuoles, and PN were 3 times more common in RECs than NRECs (Table).

| Cytologic Findings for Adult (Recurring and Nonrecurring) and Juvenile Granulosa Cell Tumors |
|-----------------------------------------------|---|---|---|
| Hypercellularity | 100 | 100 | 100 |
| Grooves | 100 | 100 | 100 |
| CEB | 66 | 66 | 0 |
| Sheets | 66 | 66 | 100 |
| Vacuoles | 100 | 0 | 0 |
| Pleomorphism | 0 | 0 | 100 |
| Hyperchromasia | 100 | 100 | 100 |
| PN | 66 | 33 | 100 |
| Necroses/mitoses | 33 | 0 | 0 |

Conclusions: Although AGCTs and JGCTs show many similarities, CEBs and grooves are only seen in AGCTs. Cellular atypia is more striking in JGCT than AGCTs (REC or NREC). Careful evaluation is necessary when examining fluids because tumor cells of AGCTs can be easily overlooked. Our series suggests that AGCTs with cytoplasmic vacuoles, PN, increased mitoses, and necrosis correspond to clinically aggressive behavior and should, therefore, be conveyed in cytology reports of ovarian tumors.

Endoscopic Ultrasound-Guided Fine-Needle Aspiration of Pancreatic Mucinous Neoplasm: Diagnostic Accuracy and Pitfalls

Ilke Nalbantoglu, MD*(inalbantoglu@yahoo.com); Mohammad Barawi, MD; Basim M. Al-Khafaji, MD† Departments of Pathology and Internal Medicine, St. John Hospital and Medical Center, Detroit, Michigan.

Context: Pancreatic mucinous neoplasms (PMNs) are rare tumors, characterized by a mucin-producing epithelium, which includes intraductal papillary-mucinous neoplasm, mucinous cystic neoplasms, and mucinous adenocarcinoma. Most PMNs are evaluated with endoscopic ultrasound-guided fine-needle aspiration (EUFNA). The diagnostic accuracy of the cytomorphologic criteria of PMNs is evaluated.

Design: Our institution's files from January 2003 to March 2009 were reviewed to identify EUFNA of PMN. Two independent reviewers evaluated the cytologic features: background, cellularity, and nuclear and cytoplasmic features, noting the corresponding histologic diagnosis and/or clinical follow-up when available.

Results: Four hundred sixty-six FNAs of pancreatic lesions were identified, 25 had a cytologic diagnosis of PMN, all obtained by EUFNA, and 13 had a histologic diagnosis. Patients' age ranged between 33 and 80 (average 58), including 6 women and 7 men. There were 10 true-positive (6 PMNs, 2 ductal adenocarcinoma, 1 adenoma with high-grade dysplasia, and 1 metastatic renal cell carcinoma), and 2 false-positives (chronic pancreatitis). True-positive cases showed a thin mucinous background in all 10, whereas 3 had areas of thick mucin. Most (9 of 10; 90%) were moderately to densely cellular. However, review of the 2 false-positives showed similar features, except for the lack of thick mucin, epithelial sheets of cells, and increased cellularity.

Conclusion: The presence of a thin/thick mucinous background, honeycomb sheets, and increased cellularity should raise the possibility of a PMN. Samples obtained by EUFNA were adequate in reaching a cytologic diagnosis. Additional studies are suggested to identify further cytologic criteria to differentiate false-positive cases.

Reconsidering Human Papillomavirus Triage for Low-Grade Squamous Intraepithelial Lesion in Women Older Than 30 Years

Michael J. Thrall, MD (mjthrall@tmhs.org); Debbie A. Smith, CT(ASCP); Dina R. Mody, MD. Department of Pathology, The Methodist Hospital, Houston, Tex.

Context: High-risk human papillomavirus (HR-HPV) testing for colposcopy triage of the Papanicolaou test (PT) category of low-grade squamous intraepithelial lesion (LSIL) is not cost effective in young women because of high positive rates (~8%). It remains unclear whether HR-HPV may be a useful test for triage of older women.

Design: We compiled HR-HPV data for women aged 30 years and older with LSIL who were seen in clinics requesting adjunctive HR-HPV testing from April 1, 2006, to March 31, 2008. Follow-up cervical biopsy information was collected for the period April 1, 2006, to August 15, 2008. The annual PT volume for the clinics used in this study is about 30,000. Dysplasia clinics were excluded. HR-HPV tests were ordered either adjunctively or for reflex testing of a different PT. We used the Hybrid Capture 2 test performed on residual material from liquid-based PT (98% ThinPrep, 2% SurePath).

Results: Women positive for HR-HPV had a significantly greater likelihood of high-grade dysplasia than LSIL women who were HR-HPV negative (P = .01) or who were not tested (P = .01; Table). The overall HR-HPV positive rate in women aged 30 years and older with LSIL was 56.7%. The ages of the HR-HPV positive women (mean, 43.4; median, 41.3) were similar to the untreated women (mean, 43.4; median, 41.9).

C-MYC Protein Is a Useful New Diagnostic Marker for Prostate Cancer

David G. Bostwick, MD, MBA (mmbconald@bostwicklaboratories.com); Deloar Hossain, MD; Justin Peters, MS; Junqui Qian, MD. Bostwick Laboratories, Glen Allen, Virginia.

Context: The contemporary, standard immunohistochemical profile for the diagnosis of prostate cancer in needle biopsies includes racemase (P504S), high molecular weight keratin 34BE12, and p63. However, race- mase is negative in up to 20% of cancer cases. The aim of this study was to determine whether the expression of c-myc protein was sufficiently specific to provide assistance in the diagnosis of needle biopsies in which racemase staining is marginal or absent.

Design: Fifty sets of prostatic needle biopsies were stained by routine methods for racemase, keratin 34BE12, p63, and c-myc, including 33 with adenocarcinoma, 47 with benign tissue, and 9 with high-grade prostatic intraepithelial neoplasm (PIN). The percentage of stained cells and staining intensity was recorded for each biopsy.

Results: Intense nuclear staining of c-myc was identified in epithelial cells in 15%, 100%, and 97% of cases of benign tissue, PIN, and cancer, respectively: mean percentage of c-myc* cells was 0.2% (range, 0%–5%), 34.4% (range, 10%–50%), and 32.3% (range, 5%–70%), respectively. In 9 cancer biopsies (27%), there were acini with negative racemase staining but positive c-myc staining (mean, 29.6% of acini; range, 5%–100%). The percentage of c-myc* cells was associated with a Gleason score (P = .02), unlike racemase (P = .52).

Conclusions: C-myc protein was highly overexpressed in prostate cancer cells, especially in those with negative racemase staining. This overexpression was associated with a Gleason score, suggesting that c-myc staining may be useful for both diagnosis and prognosis of prostate cancer.

Biliary Brushing Cytology Combined With Immunocytochemical Staining for IMP3 Provides Superior Diagnostic Sensitivity in the Detection of Pancreaticobiliary Malignancies

Meena S. Parab, MD (meenaparah1@hotmail.com); Daniza Mandich, MS; Richard W. Cartun, PhD; Saverio Ligato, MD. Department of Pathology, Hartford Hospital, Hartford, Connecticut.

Results: Most PMNs are evaluated with endoscopic ultrasound-guided fine-needle aspiration (EUFNA) to determine whether the expression of c-myc protein was sufficiently specific to provide assistance in the diagnosis of needle biopsies in which racemase staining is marginal or absent.

Design: Fifty sets of prostatic needle biopsies were stained by routine methods for racemase, keratin 34BE12, p63, and c-myc, including 33 with adenocarcinoma, 47 with benign tissue, and 9 with high-grade prostatic intraepithelial neoplasm (PIN). The percentage of stained cells and staining intensity was recorded for each biopsy.

Results: Intense nuclear staining of c-myc was identified in epithelial cells in 15%, 100%, and 97% of cases of benign tissue, PIN, and cancer, respectively: mean percentage of c-myc* cells was 0.2% (range, 0%–5%), 34.4% (range, 10%–50%), and 32.3% (range, 5%–70%), respectively. In 9 cancer biopsies (27%), there were acini with negative racemase staining but positive c-myc staining (mean, 29.6% of acini; range, 5%–100%). The percentage of c-myc* cells was associated with a Gleason score (P = .02), unlike racemase (P = .52).

Conclusions: C-myc protein was highly overexpressed in prostate cancer cells, especially in those with negative racemase staining. This overexpression was associated with a Gleason score, suggesting that c-myc staining may be useful for both diagnosis and prognosis of prostate cancer.

Follow-up Biopsy Results for Women 30 Years and Older With LSIL

<table>
<thead>
<tr>
<th>HR-HPV Results</th>
<th>CIN 2–3, No. (%)</th>
<th>HPV/CIN 1, No. (%)</th>
<th>Negative, No. (%)</th>
<th>No Biopsy, No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive</td>
<td>11 (7.6)</td>
<td>54 (37.5)</td>
<td>14 (9.7)</td>
<td>65 (45.1)</td>
</tr>
<tr>
<td>Negative</td>
<td>1 (0.9)</td>
<td>12 (10.9)</td>
<td>15 (13.6)</td>
<td>82 (74.5)</td>
</tr>
<tr>
<td>Not done</td>
<td>11 (2.3)</td>
<td>114 (23.7)</td>
<td>67 (13.9)</td>
<td>259 (58.7)</td>
</tr>
<tr>
<td>Total</td>
<td>23 (3.1)</td>
<td>180 (24.5)</td>
<td>96 (13.1)</td>
<td>436 (59.3)</td>
</tr>
</tbody>
</table>
Biliary brush cytology is an important diagnostic tool in the evaluation of patients with bile duct strictures. In this study, we evaluated the immunocytochemical expression of insulin-like growth factor (IGF) mRNA-binding protein 3 (IMP3), also known as k-homology domain-containing protein overexpressed in cancer (KOC/L523S), to assess the performance of this marker for the detection of malignant cells in bile duct-brushing specimens.

**Design:**Sixty-four patients who underwent endoscopic retrograde cannulation of the pancreatic and bile duct and bile duct brushing for bile duct stricture were studied. Diagnoses were 37 cases negative for malignancy; 14 cases atypical, not diagnostic for malignancy; and 13 cases suspicious/positive for malignancy. Alcohol-fixed, Papanicolaou test–stained slides were immunostained with monoclonal antibody to IMP3 (Dako). Results were recorded as negative (<5% cells positive) or positive (>5% cells positive). The atypical, not diagnostic cytology cases were considered negative for statistical analysis.

**Results:**Thirty-nine of the 64 patients were diagnosed with malignancy based on biopsy, fine-needle aspiration, or clinical progression of disease. The sensitivity of routine cytology for the detection of malignancy was 33.3% (13 of 39), immunocytochemical-IMP3 expression was 64.1% (25 of 39), and the combined sensitivity was 71.8% (28 of 39) (P < .001). The specificity of both tests was 100%.

**Conclusions:**Our study shows that IMP3 improves significantly the sensitivity of routine cytology for the detection of malignancy in bile duct specimens. The combined use of biliary brushing cytology and IMP3 provides the highest yield for diagnosing malignancy in the pancreaticobiliary system.

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**Quantification of Atypical Squamous Cells of Undetermined Significance (ASC-US) on ThinPrep and SurePath Papanicolaou Tests:** Is Total Number of ASC-US Cells/Clusters per Slide or One ASC-US Cell/Cluster Significant?

(Chart No. 10)

Ognjen Kosarac, MD* (okosarac@tmhs.org); Debora A. Smith, CT(ASC-P)*; Hidehiro Takei, MD, PhD; Dina R. Modly, MD*; Department of Pathology, The Methodist Hospital, Houston, Texas; Department of Pathology, Weill Cornell Medical College, Houston.

**Context:**Few reports are available on a quantitative analysis of atypical squamous cells of undetermined significance (ASC-US) on Papanicolaou (Pap) tests.

**Design:**ASC-US Pap tests were compared for the mean of ASC-US c/c between the following groups: age, high-risk (HR) human papilloma virus (HPV) status, presence (+) versus absence (−) of bacterial vaginosis, Candida, and inflammation, and ThinPrep versus SurePath Pap methods.

**Results:**ASC-US cases (184 cases; mean, 40.9 y/o) consisted of 138 ThinPrep and 46 SurePath Pap tests. Forty-seven (25.6%; mean, 33.5 y/o) and 137 (mean, 43.5 y/o) cases were HR-HPV− and HR-HPV+, respectively. Bacterial vaginosis, Candida, and inflammation were present in 37 (20.1%), 20 (10.8%), and 121 (65.7%) cases, respectively. The total number of ASC-US c/c per slide was 2.5 on average (range, 1–14) with no significant association with HR-HPV status, presence or absence of microorganisms, or inflammation. ASC-US c/c were significantly more present on ThinPrep slides (average, 2.8) than on SurePath slides (average, 1.6) (P = .001). Results of ASC-US cases with one c/c per slide are summarized in the Table.

<table>
<thead>
<tr>
<th>Analysis of Number of Cases With One ASC-US Cell/Cluster Per Slide</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>No. of Cases With One cell/cluster ASC-US, %</strong></td>
</tr>
<tr>
<td><strong>No.</strong></td>
</tr>
<tr>
<td><strong>(%)</strong></td>
</tr>
<tr>
<td><strong>(PP%)</strong></td>
</tr>
</tbody>
</table>

**Abbreviations:** ASC-US, atypical squamous cells of undetermined significance; PPV, positive predictive values; HR-HPV+, high PPV for HR-HPV+ status; one ASC-US c/c is clinically significant, particularly in patients who are 30 years old or younger.

**Type-Specific Human Papilloma Virus Testing on Liquid-Based Cytology Samples in Routine Clinical Practice**

(Poster No. 11)

Brian J. Sutton, MD; Jennifer Laudadio, MD (jlaudadi@wfubmc.edu). Department of Pathology, Wake Forest University, Winston-Salem, North Carolina.

**Context:**Routine type-specific human papilloma virus (HPV) testing, as opposed to pooled high-risk detection, can be useful in monitoring the persistence of HPV infections and is increasingly important for patient management. The purpose of this study is to determine the positivity rate, type-specific prevalence, and number of persistent HPV infections detected in routine clinical testing of cytology samples.

**Design:**DNA extracted from liquid-based cytology samples was amplified using consensus HPV primers. Positive samples were typed by restriction enzyme digestion. HPV test results were retrospectively correlated with cytologic diagnosis, biopsy result, and prior Papanicolaou test result.

**Results:**During a 10-month period, 765 HPV tests were performed on cytology samples from 747 patients aged 14 to 85 years. Of the 765 HPV tests, 377 (49.3%) were positive: 273 high risk (72.4%), 52 low risk (13.8%), and 52 unclassified risk (13.8%). HPV positivity rate was 51.6% in atypical squamous cells of undetermined significance (ASC-US) cases versus 21.8% in cytology-negative cases (P < .001). Almost 65% (64.9%) of patients younger than 30 years old were positive for HPV compared with 35.9% of patients 30 years old and older (P < .001). Overall, 35 different HPV types were detected with types 16 and 52 being most common; 273 single-type HPV infections were detected. Twenty-eight persistent infections, 27 of which were high risk, were identified with corresponding dysplasia on 50% of the available biopsies.

**Conclusions:**Of cytology samples routinely sent for HPV testing, 49% were positive, with HPV types 16 and 52 being the most common; 28 persistent infections were identified.

**Cytologic Analysis of Residual Fixative From Prostate Biopsy Vials**

(Poster No. 12)

Deloar Hossain, MD; Harpreet Singh, MS; Suman Banerjee, MD; Junqi Qian, MD, David G. Bostwick, MD, MBA (mmdonald@bostwicklaboratories.com). Bostwick Laboratories, Glen Allen, Virginia.

**Context:**Malignant cells may be shed into the transport media from prostate biopsy specimens, and cytologic evaluation may increase the cancer yield. We studied the yield of cytologic examination of residual-transplant fixative in prostate biopsy vials.

**Design:**Prostate biopsies were routinely collected and processed from 64 previously untreated patients, in vials containing StatFix (BBC Biochemical, Seattle, Washington), an alcoholic/formalin fixative. All residual-transplant fixative in vials from the left and right sides were separately pooled and processed through cytocentrifugation and acid hematoxylin staining, creating 2 slides per case. Two cytopathologists, blinded as to biopsy findings, evaluated the cytology slides, and results were correlated with the biopsy findings. Triple stains (34BE12, p63, and racemase) were used in all cases with atypical cytologic findings.

**Results:**In total, 25 of 64 patients (39%) were diagnosed with prostate cancer on routine biopsy review by pathologists; 14 had unilateral cancer, and 11 had bilateral cancer. An additional 6 cases (9.4%) had high-grade prostatic intraepithelial neoplasias (PIN) and/or atypical small acinar proliferation (ASAP) suspicious for cancer, and 33 cases (51.6%) were benign. Cellularity in the cytologic preparations was invariably low. After triple stain, 8 of 64 cytologic cases (12.5%) had at least 1 of 2 slides diagnosed as abnormal (at least suspicious for malignancy). Correlation with biopsy findings (assuming PIN and cancer findings are positive) revealed sensitivity of 16.6% and specificity of 100%, with a false-positive rate of 0%.

**Conclusions:**Cytologic analysis of residual fixative from prostate biopsy vials has 100% specificity and 0% false-positive rate for the detection of prostate cancer.

**Fine-Needle Aspiration Biopsy of Thyroid Nodules in the Pediatric Population: A 10-Year Experience**

(Poster No. 13)

Lori A. Anderson, DO (LAnderson@nshs.edu); Yan Shi, MD; Daniel Soto, CT; Melissa Klein, CT; Chiara Sugrue, MS, CT; Patricia Wasserman,
MD. Department of Pathology, North Shore/Long Island Jewish Medical Center, Glen Oaks, New York.

**Context:** Thyroid nodules are uncommon in the pediatric population, and the prevalence of malignancy is higher than in adults. The clinicopathologic studies in the pediatric population are limited. The National Cancer Institute (NCI) recently published a 6-tier thyroid fine-needle aspiration (FNA) classification scheme for cytologic diagnosis of thyroid lesions. The purpose of the present study was to analyze our thyroid FNA experience in the pediatric population.

**Design:** Thyroid FNA performed in patients younger than 21 years from January 1998 through December 2008 were reviewed retrospectively. The cytologic diagnoses were classified according to the new NCI diagnostic categories, and clinical follow-up information was reviewed.

**Results:** From 1998 to 2008, 11,178 cases of thyroid FNA were received. One hundred sixty-seven cases (1.5%) were from patients younger than 21 years. These cases were classified into one of following NCI diagnostic categories: Nondiagnostic (9.6%), benign (69%), atypical follicular cells of undetermined significance (5.4%), suspicious for follicular neoplasm (22.2%), suspicious for malignancy (1.8%), and malignant (13.2%). Fifty-five patients had surgical follow-ups, including 5.5% nondiagnostic, 14.5% with benign FNA, 5.5% with atypical follicular cells of undetermined significance, 40% with suspicious for follicular neoplasm, 9% with suspicious for malignancy, and 59% with malignant results. The sensitivity and specificity of thyroid FNA for malignancy in pediatric population were 100% and 100%, respectively.

**Conclusions:** Thyroid FNA provides a sensitive and specific diagnostic tool for the evaluation of thyroid nodules in the pediatric population. NCI classification standardizes the diagnostic terminology, which is beneficial for clinical management of pediatric patients.

**Clinicopathologic Investigation of Metastatic Tumors to the Liver Diagnosed by Fine-Needle Aspiration**

**Poster No. 14**

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**Context:** Colorectal adenocarcinoma is generally regarded as the most common secondary hepatic tumor. The data supporting this assertion are (34 of 140; 24.3%), lung (29 of 140; 20.7%), colorectal (25 of 140; 17.9%), unknown (17 of 140; 12.1%), and breast (7 of 140; 5.0%) (Figure 66). Adenocarcinomas were the most common metastases (93 of 140; 66.4%), followed by neuroendocrine (22 of 140; 15.7%), undifferentiated (6 of 140; 4.3%), melanomas (5 of 140; 3.6%), and squamous cell carcinomas (4 of 140; 2.9%). Secondary hepatic adenocarcinomas most frequently originated from the pancreas (25 of 93; 26.9%), whereas secondary neuroendocrine and squamous cell carcinomas most frequently originated from the liver (12 of 22; 54.5% and 2 of 4; 50.0%, respectively; Figure). The incidence of metastatic pancreatic cancer was significantly higher in our study compared with the combined incidence of the 3 prior autopsy series (24.3% vs 6.2%; P < .001).

**Conclusions:** In our sample, pancreas and lung cancers were more common secondary hepatic tumors than colorectal cancers. The incidence of secondary hepatic tumors originating from the pancreas is significantly higher than previously reported.

**Interobserver and Intraobserver Variability in the Measurement of Colombo Index: Implications for the Evaluation of Aspiration in Children**

**Poster No. 15**

Renuka Kulkarni, MBBS; rskulkarni@mcg.edu; Bamidele Adeagbo, MBBS; John Crosby, MD; Stephen Looney, PhD; Michelle Reid-Nicholson, MBBS; Departments of Pathology and Statistics, Medical College of Georgia, Augusta.

**Context:** Chronic aspiration in children is a diagnostic challenge with no gold standard for assessment. The Colombo index (COLIN) is a quantitative test that measures lipid-laden macrophages in bronchial washings/lavages in cases of suspected aspiration. It is not universally accepted and can be tedious to perform. We evaluated interobserver (IROV) and intraobserver variability (IAOV) in calculating COLIN and correlated the results with clinical findings.

**Design:** Using established COLIN measurement standards, 49 oil red O-stained bronchoalveolar lavages were scored (twice) by 3 pathologists at 2-week intervals and by a cytotechnologist (once). Lipid content/l00 macrophages was quantified and graded, and data were entered into a log form. Based on clinical diagnosis patients were classified as group 1 (no diagnosis), group 2 (dyspnea/ cough/cardiac or immune dysfunction), group 3 (reflux disease/cystic fibrosis/asthma or recurrent pneumonia), and group 4 (any 2 diagnoses from group 3). Interobserver and intraobserver agreement was measured using intraclass correlation coefficient (ICC; 95% confidence interval [CI]). Mean COLIN values between groups were also compared.

**Results:** There was no IAOV between pathologists (ICC, 0.84; 95% CI, 0.78–0.89). There was significant IROV between pathologists, with (ICC, 0.67, 95% CI, 0.56–0.77) and without (ICC, 0.77, 95% CI, 0.61–0.84) cytootechnologists included. There was no significant difference in the mean COLIN between groups (smallest P = .20; group 2 vs group 3).

**Conclusions:** Although there was no IAOV in COLIN measurement, there was significant IROV both between pathologists and between cytootechnologists. This challenges the reproducibility and reliability of COLIN at predicting aspiration in children. COLIN measurement does not reliably correlate with clinical diagnosis.

**CD10 Expression in Metastatic Prostatic Carcinoma to the Liver**

**Poster No. 16**

Alicia Calderon, DO; amcalder@uci.edu; Banafsheh Rashidi, MD; Jane Ellaine Tongson-Ignacio, MD. Department of Pathology, University of California Irvine, Orange.

Although the loss of CD10 expression is a common early event in human prostate cancer, its expression appears in lymph node metastasis and in a subset of cases with high Gleason scores. Furthermore, studies suggest that prostate tumors with high Gleason scores express high levels of CD10, have a more aggressive biology, and frequently metastasize to the lymph nodes. CD10 positivity offers potential clinical utility for stratifying prostate cancer to predict the biologic behavior of the tumor. We recently encountered an unusual case of a prostatic carcinoma metastasizing to the liver, diagnosed by cytology via computed tomography (CT)-guided fine-needle aspiration biopsy. This is a case of a 53-year-old man with a past history of poorly differentiated prostatic adenocarcinoma, Gleason score 8, with local recurrence, including metastasis to the lymph nodes. He presented to our institution with a liver lesion and underwent a CT-guided liver biopsy. Cytomorphologically, the aspirated smears and cell block showed clusters of malignant cells with prominent nuclei and acinar formation. Immunohistochemical stains showed the malignant cells to be positive for protein-specific antigen, PSA, and CD10 (Figure 67). Primary liver or possible metastatic lesions from the kidney, lung, and gastrointestinal tract were ruled out. Awareness that CD10 expression by...
Disseminated Blastomycosis Diagnosed by Fine-Needle Aspiration of the Thyroid
(Poster No. 17)

Aaron M. Harvey, MD (amharvey@tmhs.org); Dina R. Mody, MD; Morgan Amrikachi, MD. Department of Pathology, The Methodist Hospital, Houston, Texas.

Blastomycosis is an uncommon disease caused by the dimorphic fungus Blastomyces dermatitidis. It can manifest as chronic pulmonary symptoms or disseminated disease. Only 3 previous cases of blastomycosis involving the thyroid have been reported, of which only 2 were diagnosed by fine-needle aspiration. We present a case of disseminated blastomycosis initially diagnosed by thyroid fine-needle aspiration. Our case involved a 47-year-old man, with past medical history significant for diabetes, hyperlipidemia, and chronic pancreatitis, who presented with a 2-week history of fever, chills, rigors, constipation, and 10-pound weight loss. Abdominal computed tomography (CT) revealed chronic pancreatitis and a calcified mass in the pancreas. Chest CT revealed a single 1.5 to 2 cm thyroid mass and innumerable small (2–3 mm) pulmonary nodules bilaterally. Fine-needle aspiration of the thyroid demonstrated 10–20 µm, broad-based, budding yeasts with thick-walled, refractile capsules amidst a background of granulomatous inflammation and was diagnosed as a fungal infection consistent with blastomycosis. The patient was started on treatment with itraconazole based upon the fine-needle aspiration diagnosis. Concurrent lung biopsy demonstrated rare possible yeast forms on hematoxylin-eosin, and the other was used for FISH analysis. Disseminated blastomycosis rarely involves the thyroid. However, the thyroid is amenable to fine-needle aspiration. Fungal and mycobacterial cultures and special stains for fungal organisms should be requested on all thyroid fine-needle aspiration biopsies with granulomatous inflammation.

Efficacy of Cell-Block Preparations of Thyroid Fine-Needle Aspiration Biopsies
(Poster No. 18)

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Context: Fine-needle aspiration biopsies (FNABs) are routinely used in the initial evaluation of thyroid lesions. The objective of the study was to determine the usefulness of cell-block preparations of thyroid fine-needle aspirates.

Design: Papanicolaou smears were made, and cell blocks were made on 343 FNABs performed by clinicians between January 2007 and January 2009. The cases were divided into 4 groups: (1) the cell block was not contributory; (2) the cell block provided information when the smear was insufficient for analysis; (3) the cell block provided a diagnosis of atypia, which was not seen on the smear; (4) the smear demonstrated atypia, but the cell block showed only benign tissue.

Results: Cell blocks were contributory in 7% of thyroid FNABs. In 2 of these cases (0.6% of all cases), the cell block changed a benign diagnosis from the smear to a diagnosis of atypia. The surgical specimens for these cases were benign. There were 54 smears that were nondiagnostic. In 38.9% of these cases (n = 21; 6.1% of all cases), the cell blocks contributed to the diagnosis. In 1.2% of cases (n = 4), the smear showed atypia, and the cell block showed only benign tissue. Two of these cases were diagnosed as carcinoma on histologic sections.

Conclusions: We conclude that it is not cost effective to routinely prepare a cell block for every thyroid FNAB. It would be cost effective to order a cell block on insufficient smears only.

Does Polyomavirus Infection in Urine Specimens Cause False-Positive Fluorescence In Situ Hybridization Results?
(Poster No. 19)

David Hull, MD; Deloar Hossain, MD; Milliani Medina, MS; Karen Crewell, MS; Harpreet Singh, MS; Janqi Qian, MD; David G. Bostwick, MD, MBA (mmcdonald@bostwicklaboratories.com). Bostwick Laboratories, Glen Allen, Virginia.

Context: In urine specimens, polyomavirus-infected cells (decoy cells) may be misinterpreted as malignant. Urine cytology alone, although specific, suffers from suboptimal sensitivity. Multicolor fluorescence in situ hybridization (FISH) assay allows separation of diploid and nondiploid (aneuploid) cells. We sought to characterize the coincidence of polyoma-virus and positive FISH results in urine specimens and to identify whether polyoma cells specifically were aneuploid by FISH analysis.

Design: The study group consisted of 101 urine specimens with polyomavirus-infected cells. Cytology slides were prepared in duplicate: one set was stained with hematoxylin-eosin, and the other was used for FISH assay to chromosomes 3, 7, and 17, and to band 9p21 (p16/CDKN2A gene).

Results: Among the 101 specimens with polyomavirus infection, the mean number of decoy cells per case was 4.1 (range, 1–31), with a mean of 2.5 urothelial cells per high power field (HPF, 400×; range, 1–16). Ninety-eight of 101 specimens (97%) had normal diploid FISH results, whereas 3 (3%) had abnormal, nondiploid FISH results. These 3 specimens consisted of 2 with urothelial cancer cells and 1 with abnormal suspicious urothelial cells. FISH was invariably negative in polyoma-infected cells.

Conclusions: Polyomavirus infected cells were not a source of false-positive FISH results using FISH criteria. Polyomavirus infection does not appear to involve findings of abnormal or malignant urothelial cells.

An Improved, Buffered, Alcoholic Fixative for Urine Cytologies
(Poster No. 20)

Harpreet Singh, MS; Karen Crewell, MS; Milliani Medina, MS; David G. Bostwick, MD, MBA (mmcdonald@bostwicklaboratories.com). Bostwick Laboratories, Glen Allen, Virginia.

Context: The sensitivity and specificity of urine cytology for bladder cancer detection are improved by multitarget fluorescence in situ hybridization (FISH). We previously described an improved method for preparing urine FISH slides in Saccomanno fixative (Arch Pathol Lab Med. 2007; 131:1574–1577). One limitation of this method was filter clogging in cases with abundant particulate debris. To overcome this limitation, we investigated using a different fixative.

Design: Urine samples from 36 healthy individuals were split into a traditional, nonbuffered, alcoholic fixative (Saccomanno) or a novel, buffered, alcoholic fixative (NuCyte, QC Sciences). Samples were routinely processed for bright-field microscopy. One hundred twenty-five additional urine specimens were collected in the novel fixative and analyzed by FISH using probes to chromosomes 3, 7, and 17 and to band 9p21. FISH slides were screened using the Metafer automated-image-capture system (Meta systems, Inc.). Results were compared with 125 sequential FISH cases received in traditional fixative.

Results: Bright-field slides were evaluated by a cytotechnologist blinded to the fixative. The novel fixative showed reduction of crystals compared with the additional fixative (0% vs 33% of cases, respectively, P < .001), reduction in background (3% vs 22%, P = .01), and improved staining contrast (69% vs 0%, P < .001); also, FISH results showed a reduction in insufficient cases (6 vs 10) and an increase in the number of cases readable by automated imaging (82 vs 69).

Conclusions: The new, buffered, alcoholic fixative was superior to traditional Saccomanno fixative for bright-field and FISH analyses by virtually eliminating crystals, reducing background, and improving the overall diagnostic value of difficult urine specimens.
Soraya Rorriguez, MD; John Lew, MD; Stephen E. Vernon, MD (svernon@med.miami.edu). Departments of Pathology and Surgery, University of Miami/Jackson Memorial Hospital, Miami, Florida.

Context: Fine-needle aspiration (FNA) is the standard procedure for evaluation of thyroid nodules. Cytologic aspirates containing predominantly Hürthle cells are often problematic for both cytopathologists and clinicians. Large oncocytic cells may be present in nonneoplastic conditions or in benign or malignant neoplasms. Because many clinicians regard all Hürthle cell lesions as at least potentially malignant, most patients with Hürthle cell neoplasm (HCN) by FNA are referred for surgical excision. This study examines the final histologic findings in 30 patients who underwent surgical resection after FNA diagnosis of Hürthle cell neoplasm.

Design: We reviewed reports from FNAs of thyroid lesions examined by the Department of Pathology, University of Miami/Jackson Memorial Hospital during a 5-year period. Thirty patients with HCN subsequently underwent surgical excision. HCN was defined by FNA when Hürthle cells comprised at least 70% of the cellularity. Slides and reports were reviewed, and the final diagnoses and results of special stains and immunohistochemistry were noted.

Results: Among the 30 FNA cases designated as HCN, there were 13 Hürthle cell adenomas, 10 carcinomas, and 7 nonneoplastic thyroid lesions. Thyroid carcinomas included 3 Hürthle cell carcinomas, 2 oncocytic variant papillary carcinomas, 2 medullary carcinomas, 2 insular carcinomas, and 1 squamous cell carcinoma. Nonneoplastic benign lesions were 3 cases of chronic lymphocytic thyroiditis, 3 cases of nodular hyperplasia, and 1 case with both features.

Conclusions: HCN by FNA may indicate Hürthle cell adenoma or carcinoma. Papillary and medullary thyroid carcinomas may also show oncocytic features on FNA smears. Surgical resection remains essential for definitive classification.

The Role of Multimodality Approach in a Bone Fine-Needle Aspiration of a Patient With Lymphoma (Poster No. 22)

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A 62-year-old woman presented with left leg pain. Computed tomography (CT) scan showed a lytic lesion in the left femur and diffuse lymphadenopathy. Fine-needle aspiration (FNA) of the right paratracheal lymph node was performed. Flow cytometry (FC) using cluster analysis revealed CD5+/CD10−; k-restricted, large B-cell lymphoma (red cluster, Figure 68) in addition to a lesser population of CD5+/CD10−, γ-restricted, B-cell chronic lymphocytic leukemia/small lymphocytic lymphoma (blue). Morphologically, variously sized atypical lymphocytes were present. CT-guided FNA and core biopsy of the lytic lesion in the left femur was performed. FC showed the B-cell chronic lymphocytic leukemia/small lymphocytic lymphoma. The large B-cell lymphoma component present in the prior FC was not identified. Morphology and an extensive immunohistochemical panel revealed only the diffuse large B-cell lymphoma component. The small CD5+ B-cell population identified by both the accompanying and the previous FC was not apparent. A staging bone marrow showed involvement by the B-cell small lymphocytic lymphoma/chronic lymphocytic leukemia by both morphology and FC. The relatedness between the 2 processes may represent Richter syndrome or 2 independent diseases, in light of the synchronous presentation and opposite light chain restriction. In addition, we discuss the sensitivity of FC and FNA in bone samples. The case reinforces the understanding that an accurate pathologic diagnosis is a multimodality approach, and a clinically significant component may be potentially missed when a single modality is employed.

Primary Cerebrospinal Fluid Diagnosis of Pineal Germinoma (Poster No. 23)

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A 29-year-old man presented with a 6-week history of left-sided facial numbness, facial droop, and symptoms of diabetes insipidus. Magnetic resonance imaging revealed a 2.5-cm, hyperdense mass, with calcifications in the pineal region, and diffuse intraventricular, subependymal, and subarachnoid metastatic disease. Surgical biopsy was precluded because of the perceived high risk of the procedure, and a diagnostic lumbar puncture was performed. Cytospin slides prepared from the cerebrospinal fluid were hypercellular and showed a discohesive population of large, atypical cells with moderate amounts of clear cytoplasm, vesicular chromatin, and prominent nucleoli, in a lymphocytic background (Figure 69, Diff-Quik stain, ×400). A cell block was prepared from the residual fluid, and immunohistochemical staining revealed that the atypical cells were positive for placent al alkaline phosphatase. A diagnosis of pineal germinoma was made, and a course of targeted chemotherapy and cerebrospinal fluid irradiation was commenced. Follow-up imaging studies performed 6 weeks later showed a marked decrease in the size of both the primary pineal tumor and the metastatic deposits, and a repeat cerebrospinal fluid specimen was negative for malignant cells. Pineal germinomas are the most common primary intracranial germ cell tumors, accounting for 60% of pineal neoplasms. Morphologically, these tumors are indistinguishable from their gonadal counterparts. Although surgical biopsy remains the gold standard for diagnosis, this case demonstrates that, in the appropriate clinical setting and with the selective use of ancillary studies, a primary diagnosis of germinoma by cerebrospinal fluid cytology is possible and could help avoid a surgical procedure in high-risk situations.
Strongyloides Hyperinfection/Disseminated Disease: An Unexpected Cytologic Diagnosis With Autopsy Follow-up (Poster No. 24)

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Infection by Strongyloides stercoralis is common worldwide, but it is relatively rare in the United States. Most chronically infected patients are asymptomatic; however, severe clinical manifestations, including hyperinfection and disseminated disease (increase in worm burden without or with spread to organs beyond normal migration pattern, respectively) have been reported in up to 2.5% of infected patients, with high mortality rates. The most commonly reported risk factor for hyperinfection and disseminated disease is immunosuppression secondary to steroid use. We have been reported in up to 2.5% of infected patients, with high mortality with spread to organs beyond normal migration pattern, respectively.

Bile Duct Brush Cytology: Indeterminate Diagnosis Is Essential (Poster No. 26)

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Context: Bile duct brush cytology is often the primary diagnostic procedure for treatment decisions of biliary lesions. These samples are often difficult to interpret because of reactive changes. Indeterminate (atypical or suspicious) diagnoses are frequent, although not as useful as a malignant or benign diagnosis. We conducted this study to determine whether the indeterminate diagnoses can be reduced by refining diagnostic criteria.

Results: Twenty-eight cases, 25 atypical and 3 suspicious, were included. Of the 16 cases with malignant follow up, 9 (56%) were upgraded to malignant, and 1 was downgraded to benign by at least 3 of 5 pathologists. Two remained nondiagnostic. Of the 12 cases with benign follow up, 4 (33%) were downgraded to benign, 5 (42%) were upgraded to malignant, and 2 remained nondiagnostic by the majority. In the remaining cases, there was no majority agreement. In the 5 false-positive cases, 3 patients had stents, 1 had stones, and 1 had gallstones with cholangitis. Features that showed significant difference between benign and malignant lesions were single, atypical cells and irregular nuclear membranes (P < .05).

Conclusions: Indeterminate categories are necessary to avoid false-positive and false-negative diagnoses. Single, atypical cells and irregular nuclear membranes may be the most useful features in recognizing malignancy in difficult cases.

Angiosarcoma Mimickers on Fine-Needle Aspiration Cytology (Poster No. 27)

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The cytologic diagnosis of angiosarcoma is challenging because the morphology may simulate that of nonvascular malignant tumors. The incidence of this neoplasm is increasing in cases of breast-conserving therapy for breast carcinoma. Cytologic evaluation of patients with a pertinent clinical history requires careful on-site screening of slides for proper triaging of cellular material, allowing for allocation of material for immunocytochemistry, immediate additional sampling, and preparation of cell blocks for appropriate special studies. An 80-year-old woman with a history of prior surgeries for breast cancer presented with cervical lymphadenopathy. Fine-needle aspiration of the lymph node revealed a hypercellular specimen with dispersed, isolated malignant cells with prominent macronucleoli, raising the suspicion of a lymphoproliferative disorder. Rare “cell in cell” appearance was noted. On flow cytometry, the cells were positive for CD30 and CD34 and were negative for other hematopoietic markers. Review of slides from the breast lesion showed features of high-grade angiosarcoma with abundant mitoses and necrosis, strong, diffuse positivity for CD31 and CD34, and lacking expression of pan-cytokeratin (AE1/3). The fine-needle aspiration findings were cytomorphologically identical to the prior angiosarcoma. In patients with a pertinent clinical history, it is important to consider angiosarcoma in the differential diagnosis of lesions with epithelioid morphology. Recognizing the cytologic features during adequacy assessment would allow appropriate intervention.
Hematologic malignancies are rarely encountered in the female genital tract, either as a primary malignancy or as systemic dissemination. Without known clinical history, the cytologic diagnosis of these neoplasms may be very challenging. Here, we report a case with primary uterine diffuse large B-cell lymphoma, which was first detected by liquid-based cervicovaginal Papanicolaou (Pap) test. A 75-year-old, white woman underwent a Pap test for vaginal bleeding and endometrial thickening. On SurePath Pap test, numerous atypical mononuclear cells were present singly or admixed with groups of squamous cells and inflammatory cells. These atypical cells varied in size and had irregular hyperchromatic nuclei, coarse chromatin, and minimal cytoplasm. Some of the cells showed cytologic features that mimicked high-grade squamous intraepithelial lesions (HSIL) or admixed with groups of squamous cells and inflammatory cells. Some of the cells showed cytologic features that mimicked high-grade squamous intraepithelial lesions (HSIL) or admixed with groups of squamous cells and inflammatory cells. The histologic findings are listed in the Table.

Conclusions: The incidence of histologic CIN 2/3 was markedly higher in women with HSIL cytology than in women with LSIL cytology. No CIN 2/3 was noted in older women with LSIL cytology and negative hrHPV testing. hrHPV testing might be helpful for risk assessment for older women with LSIL cytology but not for older women with HSIL cytology.

Langerhans Cell Histiocytosis: E-Cadherin and Cyclin D1

Primary Uterine Diffuse Large B-Cell Lymphoma Detected in a Cervicovaginal Papanicolaou Test: A Case Report and Review of the Literature

Primary Uterine Diffuse Large B-Cell Lymphoma Detected in a Cervicovaginal Papanicolaou Test: A Case Report and Review of the Literature

*Jian-Feng Wang, MD, PhD (iwang2@bhs1.org); Xiangrong Zhao, MD, PhD; Teri Cooper, MD. Department of Pathology, Berkshire Medical Center, Pittsfield, Massachusetts.*

Epidermal Langerhans cells (LCs) account for 3% to 5% of all nucleated cells in the epidermis and constitutively express E-cadherin, which anchors LCs to keratinocytes. Langerhans cell histiocytosis (LCH) is a clonal proliferative disorder of LCs and often occurs in children as a cutaneous disease. The course of disease is characterized by either spontaneous regression or multisystemic dissemination with poor prognosis. The mechanisms of migration of LCs from epidermis to dermis, proliferation, and dissemination are unclear. We report one case of multisystemic LCH and Irvine-Winter syndrome caused by observing expressions of E-cadherin and Cyclin D1. A 15-month-old girl presented with multiple papules and splenomegaly for 1 week. Skin and bone biopsies revealed that the dermal and bone marrow lesions were positive for CD1a and S100. Furthermore, the lesion cells were negative or weakly positive for E-cadherin but demonstrated strong nuclear positivity for cyclin D1. E-cadherin is an important cell-adhesion molecule and is essential for the homing of LCs to epithelium. Decrease of E-cadherin expression has been related to either inflammatory lesions, squamous intraepithelial lesions, or other types of malignant tumors. Therefore, it is critical to keep these malignancies in the differential diagnosis and initiate further diagnostic workup when they are suspected.

Significance of hrHPV Testing in Women Age 50 Years or Older With Low-Grade Squamous Intraepithelial Lesion and High-Grade Squamous Intraepithelial Lesion Cytology

*Chengquan Zhao, MD (zhaoc@upmc.edu); Amer Heider, MD; R. Marshall Austin, MD, PhD. Department of Pathology, Magee Women’s Hospital, University of Pennsylvania Medical Center, Pittsburgh.*

Epidermal Langerhans cells (LCs) account for 3% to 5% of all nucleated cells in the epidermis and constitutively express E-cadherin, which anchors LCs to keratinocytes. Langerhans cell histiocytosis (LCH) is a clonal proliferative disorder of LCs and often occurs in children as a cutaneous disease. The course of disease is characterized by either spontaneous regression or multisystemic dissemination with poor prognosis. The mechanisms of migration of LCs from epidermis to dermis, proliferation, and dissemination are unclear. We report one case of multisystemic LCH and Irvine-Winter syndrome caused by observing expressions of E-cadherin and Cyclin D1. A 15-month-old girl presented with multiple papules and splenomegaly for 1 week. Skin and bone biopsies revealed that the dermal and bone marrow lesions were positive for CD1a and S100. Furthermore, the lesion cells were negative or weakly positive for E-cadherin but demonstrated strong nuclear positivity for cyclin D1. E-cadherin is an important cell-adhesion molecule and is essential for the homing of LCs to epithelium. Decrease of E-cadherin expression has been related to either inflammatory lesions, squamous intraepithelial lesions, or other types of malignant tumors. Therefore, it is critical to keep these malignancies in the differential diagnosis and initiate further diagnostic workup when they are suspected.

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Significance of hrHPV Testing in Women Age 50 Years or Older With Low-Grade Squamous Intraepithelial Lesion and High-Grade Squamous Intraepithelial Lesion Cytology

*Chengquan Zhao, MD (zhaoc@upmc.edu); Amer Heider, MD; R. Marshall Austin, MD, PhD. Department of Pathology, Magee Women’s Hospital, University of Pennsylvania Medical Center, Pittsburgh.*
LCH dissemination and poor prognosis. Cyclin D1 involves cells prolif-eration. The expression of cyclin D1 in LCH has never been reported. Down-regulation of E-cadherin may explain the migration of LCs and dissemination of LCH, and overexpression of cyclin D1 may explain the proliferation of LCs in LCH. The data demonstrated that decrease of -cad-herin and increase of cyclin D1 expression play important roles in the pathogenesis of LCH and might be markers for evaluating disease dis-semination and prognosis.

**Lymphomatoid Granulomatosis in a Patient With Granulomatous-Type Mycosis Fungoides**

(Poster No. 31)

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Lymphomatoid granulomatosis (LG) is a rare Epstein-Barr virus (EBV)-driven B-cell lymphoproliferative disorder that occurs in the lungs or oth-er extranodal sites in the setting of immunodeficiency. We report a case of LG that developed after chemotherapy for granulomatous mycosis fungo-ides (MF). A 35-year-old, white man with granulomatous MF was ini-tially treated with topical preparations but failed initial therapy and pro-gressed to extracutaneous disease (stage III). High-dose systemic chem-otherapy (cyclophosphamide and prednisone) was then administered during a 9-month period. The MF was in clinical remission 2 years after chemotherapy when he developed an omental mass. Excisional biopsy demonstrated polymorphous lymphoid infiltrate with angiostriction, focal necrosis, primarily B-cell phenotype, and EBV positivity, consistent with grade I LG. He was then treated with rituximab with complete re-sponse; however, 4 years later, the patient developed a 10-cm lung mass, which, on lobectomy, revealed EBV+ monomorphic large B cells consistent with grade III LG. Although EBV+ B-cell lymphoma has been reported in rare cases of MF, no reports have linked its occurrence to corresponding treatment. This case seems best to fit into the category of iatrogenic immuno-deficiency-associated lymphoproliferative disorder by the new 2008 World Health Organization criteria.

**Sebopapocrine Carcinoma: A Rare Histologic Variant of Sebaceous Carcinoma**

(Poster No. 32)

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Sebaceous carcinoma masquerades clinically and histologically as a vari-ety of lesions. Histology shows basoid and squamous differentiation that can be misdiagnosed as basal or squamous cell carcinoma. Apocrine differentiation in sebaceous carcinoma is rare. It consists of glands lined by cuboidal cells expressing epithelial membrane antigen (EMA) and oth-er apocrine markers. A 78-year-old man presented with an enlarging nod-ular lesion at the right upper eyelid. The lesion started as an itch and developed into an ulcer. He underwent wide excision of the eyelid with growth into a 2-cm nodule during 10 months. His renal and pancreatic function remained normal, and no additional lesions were identified radiographically. An excisional biopsy was performed. A hema-toxylin-eosin stained section shows a nodular aggregate of plasma cells in the dermis. Most plasma cells were well to moderately differentiated, whereas a few were multilobed or multinucleated giant cell forms (Figure 74). The plasma cells, including giant cell forms, were positive for CD138, CD56, and k light-chain isotype. In situ hybridization for EBV-encoded RNA was positive in plasma cells. The plasma cells were negative for λ light chain, CD30, CD20, CD3, SI0, and pancytokeratin. Ki-67 demonstrated a proliferation index of 30% in plasma cells. Giant cell plas-macytoma has been described in patients without history of organ trans-plant or being immunocompromised. In the setting of PTLD, plasmacy-toma-like lesions have been well-documented; however, primary cutane-ous plasmacytoma of giant cell type, in the setting of PTLD, has not been reported in the English literature. The clinical significance of this mor-phologic variant remains to be further studied.

**Desmoplastic Malignant Melanoma With Myofibroblastic Differentiation**

(Poster No. 34)

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Desmoplastic malignant melanoma (DMM) is an uncommon melano-cytic lesion. DMM has been reported, in some cases, to have an association with cells with smooth muscle differentiation, without being clear wheth-er this is due to melanoma cells with smooth muscle differentiation or to a proliferation of reactive myofibroblasts. A right breast lesion from a 68-year-old woman was excised and demonstrated a poorly circumscribed spindle cell neoplasm in the dermis. Overlying melanoma in situ was not identified. Immunohistochemistry studies were ordered: S100, smooth muscle actin (SMA), and calponin were positive; HMB-45, Melan-A, des-min, pankeratin, and CD1a were negative. A double-staining technique was performed for S100 and SMA. The largest part of spindle cells was ei-thers100+ or SMA+. An unequivocal double staining was demonstrated in few spindle cells. Literature review demonstrated various combinations of Schwannian, fibroblastic, and smooth muscle differentiation by electron microscopy in individual malignant cells of DMM. Melanoma cells in-duced fibroblasts to produce a 2-fold increase in the rate of collagen syn-
thesis, when fibroblasts and melanoma cells were in close proximity. Demonstration of double staining in some of the malignant cells with SiO and SMA with negativity for desmin is very suggestive of a true myofibroblastic differentiation in this neoplasm. These facts, along with a stimulus of normal fibroblastic cells to grow and produce collagen, by melanoma cells, suggests a double mechanism for the fibrosis and the positivity of SMA, which is a true myofibroblastic differentiation and a stimulus of myofibroblasts and fibroblasts to produce collagen.

**Facial and Extremity Spitz Nevi in Childhood: Architectural and Immunohistochemical Features, Similarities, and Differences**

(Poster No. 35)

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**Context:** Spitz nevus (SN) occur frequently in prepubertal children and at birth, with a predilection for the face and neck. SN may be junctional, compound, or intradermal. This is a review of 21 childhood SN.

**Design:** The clinical features and biopsies of 21 children with SN were reviewed. Twelve were from extremities, and 9 were from the face/neck. Patients with facial SN ranged from 7 weeks to 14 years with 6 males and 3 females. Patients with extremity SN ranged from 1 year to 15 years with 6 males and 6 females. Hematoxylin–eosin slides were reviewed. Melan-A, HMB-45, and Ki-67 slides were reviewed when available.

**Results:** All cases showed melanocytic lesions with confluent distribution of spindled and epithelioid nevus cell nests and Kamino bodies. Five of 9 facial SN (56%) were compound; 4 of 9 (44%) were junctional. All facial SN immunostained, showing Melan-A–lesional cells and coexpressing HMB-45. Ki-67 was restricted to keratinocytes. Four of 12 extremity SN (33%) showed epidermal hyperplasia and prominent lymphocytic infiltrates. Two of 12 (17%) were atypical (architectural disorder, cytologic atypia, fibrosis, and lymphocytic response). One of 12 (8%) was a variant of SN, desmoplastic nevus.

**Conclusions:** Spitz nevus occur on the face and extremities. Facial SN occur in earlier childhood and generally lack features of atypia. Extremity SN may show features of atypia, prominent epidermal hyperplasia, and lymphocytic host response. Extremity SN are more likely to include variants, or belong to a spectrum between pure spindle cell nevus of Reed and SN. Recurrent extremity SN show scarring and inflammation and may be difficult to differentiate from melanoma.

**Eccrine Porocarcinoma of the Vulvar**

(Poster No. 36)

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Eccrine porocarcinoma (EPC) is a rare skin adnexal tumor, with less than 200 cases reported in the English literature. Involvement of the vulva by EPC is even rarer, with only 5 previously reported cases. This case study was observed in a 48-year-old woman who presented with a 5-cm, verrucous, polypoid, pedunculated left vulvar mass, which she reported had been increasing in size during the preceding 6 months. The mass was excised and histopathologic examination of the lesion showed features diagnostic of malignant eccrine poroma (eccrine porocarcinoma) with an in situ component. Because of the rarity of EPC, coupled with its heterogeneous and nonspecific clinical and histologic features, this tumor often presents as a diagnostic challenge to clinicians and pathologists. Therefore, extensive clinical, radiologic, and histopathologic workups may be required to rule out metastatic tumor, especially in cases where the tumor cells are poorly differentiated. On the other hand, cases with extensive squamous differentiation may be misdiagnosed as squamous cell carcinoma. Considering the clinical behavior (prognosis) of EPC is worse than that of squamous cell carcinoma, there is the need for correct diagnosis of this rare entity to ensure appropriate therapy can be instituted in a timely manner. Key histopathologic diagnostic features and the immunohistochemical profile for making the correct diagnosis of EPC are highlighted.

**Immunohistochemical Staining Pattern of Malignant Melanoma With Coexisting Melanocytic Nevus**

(Poster No. 37)

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**Context:** Although malignant melanoma and melanocytic nevi often coexist, the relationship between them remains unclear. We investigated immunohistochemical staining patterns of 3 novel markers that have recently been reported in the literature: glypican 3 (GPC-3), p16, and insulin-like growth factor II mRNA binding protein 3 (IMP-3) to further evaluate this relationship.

**Design:** Twenty-four cases of malignant melanoma with coexisting melanocytic nevi were identified through a database search of May 2003 to February 2008 Barnes-Jewish Hospital files. Monoclonal antibodies to GPC-3, p16, and IMP-3 were used to evaluate differential staining patterns between nevus and melanoma cells. All slides were independently reviewed by 2 pathologists and graded according to intensity and proportion of staining.

**Results:** Discordant staining was noted between malignant melanoma and melanocytic nevus cells in 4 cases for GPC-3, 6 cases for p16, and 2 cases for IMP-3. In most discordant cases, GPC-3 and IMP-3 stained melanoma cells and not nevi. However, one case showed no GPC-3 staining in melanoma and focal, weak staining in nevus cells. Most discordant cases showed p16 staining in nevus cells and no staining in melanoma; however, one case showed weak p16 staining in melanoma and no staining in nevus cells.

**Conclusions:** Immunohistochemical staining for GPC-3, p16, and IMP-3 has limited value in evaluating the relationship between malignant melanoma and coexisting melanocytic nevi. In general, when a discordant staining pattern was observed, GPC-3 and IMP-3 were positive in melanoma cells more often than nevi, whereas p16 was positive in melanocytic nevi more often than melanomas.

**Predictive Immunohistochemical Staining Pattern in 2 New Cases of Malignant Eccrine Acrospiroma**

(Poster No. 38)

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**Context:** Malignant acrospiroma, also called malignant hiradenoma or hiradenocarcinoma, is a rare aggressive neoplasm of the eccrine sweat gland for which no consensus treatment strategy exists. Since first described in 1954, fewer than 100 cases have been reported. Previous immunohistochemical (IHC) studies have shown these lesions to be positive for Ki-67, p53, cytokertatin, estrogen receptor, and progesterone receptor while negative for carcinoembryonic antigen, epithelial membrane antigen, and S100. To our knowledge, the expression profile for the predictive IHC markers, epidermal growth factor receptor (EGFR), vascular endothelial growth factor, HER2/Neu, and CD117, has not been determined. We present 2 new cases of malignant acrospiroma and the IHC staining patterns for common therapeutic targets.

**Design:** Two new cases of malignant acrospiroma were diagnosed on the lower back of a 63-year-old man and the back of an 80-year-old man. IHC was performed on representative sections of the 2 tumors.

**Results:** IHC evaluation of both cases showed a concordant immunophenotype, with positive staining for pancytokeratins, focal positive staining for epithelial membrane antigen, and an increased Ki-67 proliferation index (19% and 75%, respectively) (Figure 75). Strong diffuse membranous staining for EGFR was present. Both tumors were negative for
CD117, estrogen receptor, progesterone receptor, HER2/neu, and vascular endothelial growth factor.

Conclusions: Expression of therapeutic targets in malignant acrosiroma is uncertain and consensus treatment strategies do not exist. Two previously unreported cases were studied by IHC and showed strong positivity for EGFR, suggesting a possible therapeutic role for anti-EGFR drugs, such as gefitinib, erlotinib, or cetuximab.

**Syringocystadenocarcinoma Papilliferum: A Case Report With Review of the Literature**  
*(Poster No. 39)*

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Syringocystadenocarcinoma papilliferum (SCAP), the malignant counterpart of Syringocystadenoma papilliferum (SP), is a very rare, malignant neoplasm of the sweat glands. SCAP has many histologic similarities with SP but can be differentiated by architectural asymmetry, poor circumscision with extension into subcutis, and variable degrees of cytologic atypia with accompanying mitoses. To date, 11 cases of SCAP have been reported. We report a case of SCAP in an 80-year-old, otherwise healthy woman who presented with a long-standing, right infratemporal region mass. The specimen consisted of a 4.2 × 2.6 × 0.5-cm, oval fragment of skin bearing a tan-pink to red, exophytic, friable mass measuring 4.2 × 1.3 × 1.3 cm. The cut surface had focal cystic areas. Histologically, the tumor had solid and cystic patterns. The in situ carcinoma component consisted of cuboidal to columnar cells with cytologic atypia and decapitation secretion. Numerous plasma cells and lymphocytes were identified in the stroma. Immunohistochemical staining showed strong and diffuse expression of epithelial membrane antigen, cytokeratin 7, CAM 5.2, and high molecular weight kininogen (HMWK; 34BE12). Gross cystic disease fluid protein-15 (CDGFP-15), carcinoembryonic antigen (CEA), and MIB-1 expression varied among the tumor components: less CEA staining was observed in the micropapillae and cribriform areas, whereas less CDGFP-15 staining was observed in the coarse and tertiary papillae; MIB-1 expression was greater in micropapillae than in cribriform areas and in coarse and tertiary papillae. Based on these histopathologic findings, a diagnosis of SCAP was made. Our patient is on close follow-up for a year without any evidence of disease.

**Human Immunodeficiency Virus-Associated Myopathy: Novel Immunostains and Electron Microscopy Highlight Structural Disarray**  
*(Poster No. 40)*

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Human immunodeficiency virus (HIV)-associated myopathy has been described in 2 patterns: HIV-related polymyositis and a structural myopathy. Mitochondrial abnormalities, including enlargement, distortion of cristae, and the presence of vesicles, electron-dense deposits, and paracrystalline inclusions, have been reported. The routine histochemical and immunostains, including manganese superoxide dismutase (MnSOD) and antimitochondrial antibody (AMA), and electron microscopy were performed on a thigh muscle biopsy from a 58-year-old man with HIV and long-standing, severe myopathy. To our knowledge, the use of AML1693 and MnSOD immunostains in the evaluation of myopathies has not been previously reported. Light microscopy revealed extensive endomyosial fibrosis, scattered necrotic fibers, scattered mononuclear cells, atrophic fibers, and hypertrophic fibers with myofibrillar disarray, without the presence of cytoplasmic bodies or vacuolization. Staining for succinate dehydrogenase activity showed a central lack of activity and fibers with lobulations, indicating structural disarray. Immunostaining for mitochondria and MnSOD revealed a lack of uniform staining in the structurally altered fibers and uniform staining in the infarred areas. Electron microscopy showed large, pleomorphic mitochondria with disorganization of cristae, and the presence of vesicles, electron-dense deposits, and para-crystalline material, 2 mitochon-dria with “fuzzy” matrix granules. Extensive Z-disc streaming was present in myofibrils with structural disarray. Light and electron microscopic findings were consistent with a mitochondrial myopathy with structural disarray. Immunostains for AMA and MnSOD can be used on paraffin-embedded tissue to highlight structurally and functionally altered myofibers, respectively.

**Rapidly Progressive Fatal Dementia Secondary to Lymphomatosis Cerebri**  
*(Poster No. 41)*

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Lymphomatosis cerebri is a term indicating a diffusely infiltrating form of primary central nervous system lymphoma without evidence of a mass lesion. This is a rare entity, with only a few cases described in the literature. We report a unique, autopsy-diagnosed lymphomatosis cerebri case with widespread infiltration of the brain by rod-shaped, microribosomal appearing tumor cells. The patient was a 71-year-old immunocompetent, independently living woman who developed rapid-onset dementia. She had a complete intracranial workup. Magnetic resonance imaging showed a nonspecific, ill-defined signal in the white matter bilaterally. The case illustrates that lymphomatosis cerebri should be included in the differential diagnosis of rapidly progressive dementia, especially when there is no mass lesion, and that pathologists should be aware of the existence of atypical morphology of central nervous system lymphomas.

**Anaplastic Meningioma With Carcinomatous Differentiation**  
*(Poster No. 42)*

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A 77-year-old man presented with a 4-month history of visual impairment, memory problems, and headache. Magnetic resonance imaging of the head showed a 6.9 × 6.2 × 3.3-cm, heterogeneously enhancing, hypervascular, dural-based, right posterior falx mass, which invaded through the right pia-arachnoid calvarium into the scalp. The patient underwent right pia-arachnoid craniotomy with resection of the tumor and overlying skull. Histologically, the neoplasm showed 2 basic patterns, which merged with each other. Some areas had features of atypical meningiomas, whereas others had sheets of malignant cells with brisk mitotic activity and focal squamous differentiation. The differential diagnosis included anaplastic meningioma with carcinomatous features versus metastatic carcinoma to a meningioma. Immunohistochemical stains showed strong immunoreactivity for AE1/AE3 in about 50% of frankly malignant areas and in rare cells with meningothelial features. Both components were strongly, diffusely immunoreactive for vimentin and focally for CK7 and P63. CK5/6 was focally immunoreactive in the malignant areas and negative in meningothelial areas. Epithelial membrane antigen was strongly, diffusely immunoreactive in the malignant epithelial and in 10% to 40% of cells in meningothelial areas. MOC31 was immunoreactive in up to 40% of the malignant epithelial component and negative in meningothelial areas. About 12% of neoplastic cells were positive for PR, CK20, CEA, S100, ER, and TTF-1 were negative throughout. The above findings support the diagnosis of anaplastic meningioma with carcinomatous differentiation for which cytologic features are described in the most recent World Health Organization Tumors of the Central Nervous System.

**Asymptomatic Diffuse “Encephalitic” Cerebral Toxoplasmosis in a Patient With Chronic Lymphocytic Leukemia: Case Report and Review of the Literature**  
*(Poster No. 43)*

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Arch Pathol Lab Med—Vol 133, October 2009
Composite Tumors and Cortical Dysplasias in the Brain of a Patient With Chronic Epilepsy

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Tumors in patients with epilepsy are not uncommon. This case report describes a rather rare composite tumor of a ganglioglioma and dysembryoplastic neuroepithelial tumors (G-DNT tumors) with cortical dysplasia. A 21-year-old woman presented with a history of seizures. MRI described a large right temporal lobe mass with surrounding vasogenic edema. This lesion was operated on and diagnosed as ganglioglioma. The MRI described a right arachnoid cyst in the right middle fossa and small cystic lesions in the right basal ganglia with minimal if any change on the left side. The dominant right parietal cyst measured 3.2 cm in maximum diameter, with a surrounding vasogenic edema. This lesion was operated on and diagnosed as dysembryoplastic neuroepithelial tumor. Few cases have been described with such features. We will discuss the pathologic findings of these composite tumors and review the literature on the subject.
potential, and expression of some carcinogenic markers in adult medulloblastomas.

**Design:** We analyzed the immunohistochemical expression of survivin, c-Kit, BCL2, fascin, p53, and Ki-67 (all antibodies, Neomarkers, Fremont, California) in 18 adult (older than 16 years) patients with medulloblastomas.

**Results:** Study included 14 men and 4 women (mean age, 22.9 ± 2.8 years). Fourteen cases were classical, 2 desmoplastic/nodular, and 2 large cell medulloblastomas. Moderate to high Ki-67 index was observed with high percentages (55%–100%) in all medulloblastomas. However, BCL2 was mildly positive in only one case. Interestingly, mildly to moderate cytoplasmic c-Kit expression was demonstrated in 16 cases (89%) without membranous immunostaining. Fascin expression was observed in 13 medulloblastomas (72%) with moderate to high immunoreactivity in 9 tumors. Mild p53 expression was present in 4 cases (22%). Mean Ki-67 index was 20.6% (range, 8%–55%).

**Conclusions:** Frequent nuclear survivin expression indicates the predominance of antiapoptotic factors in carcinogenesis of adult medulloblastomas. It may also be a potential therapeutic target for adult medulloblastomas. Although BCL2 immunoreactivity was reported in approximately 30% of medulloblastomas, it was rarely expressed in the present series of adult medulloblastomas. This is the first study to demonstrate fascin expression in medulloblastomas. It may be related to the neuronal differentiation. Mild to moderate cytoplasmic c-Kit immunoreactivity without membranous staining in adult medulloblastomas may support the previous studies reporting low level of c-Kit protein expression with a lack of activating mutations in medulloblastomas. It seems p53 is rarely involved in the carcinogenesis of adult medulloblastomas.

**Supratentorial Primitive Neuroectodermal Tumor With an Unusual Translocation (t[14;19])**

**Poster No. 48**

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Suprasellar primitive neuroectodermal tumor (PNET) is an uncommon, malignant embryonal neoplasm of the cerebral hemispheres. It is composed of undifferentiated to poorly differentiated neuroepithelial cells showing divergent differentiation of variable degree along neuronal, glial, or, rarely, mesenchymal lines. We report a case of a supratentorial PNET with an unusual reciprocal translocation involving the long arms of chromosomes 14 and 19 ([t(14;19)(q32;q13.3)]). The patient is an 18-year-old man with a previous history of a primary B-cell central nervous system lymphoma, status postchemotherapy and radiation therapy at age 11. Seven years later, the patient presented with headaches, neck pain, and seizures, including headache and seizure and visual disturbances. Head computed tomography revealed a large mass in the left periventricular region with lateral extension into the left frontal convexity. Microscopic evaluation of the brain biopsy revealed a small, round blue cell tumor with finely granular chromatin and scant cytoplasm. Immunohistochemical staining revealed reactivity for synaptophysin and FLI1 with weak positivity for SMA and HHF35. A diagnosis of supratentorial, primitive neuroectodermal tumor was rendered. Chromosomal analysis of the specimen subsequently revealed a highly complex karyotype, including a t[14(19)] translocation. Relatively few cytogenetic studies of supratentorial PNETs have been reported. Currently, no characteristic chromosomal abnormalities have yet been identified. The t[14;19] translocation is a rare but recurrent translocation found in patients with B-cell malignancies. To our knowledge, this is the only report of a supratentorial, primitive neuroectodermal tumor with a t(14;19) translocation.

**Presacral, Immature Teratoma With Predominant Medulloepithelioma Component Accompanied by Sacrococcygeal Bone Defect and Intradural Extension**

**Poster No. 49**

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Presacral teratomatic tumors combined with sacral bone defects are uncommon. We report a rare case that contains medulloepithelioma component. An 11-month-old, female infant presented with several weeks' history of constipation and flaccid lower extremities. Magnetic resonance imaging of the lumbar spine revealed a large mass (5.5 × 4.8 × 4.5 cm) in the presacral space, accompanied by a defect of the fourth and fifth sacral and coccygeal bony spine. The mass extended posteriorly into the spinal canal, surrounded the cauda equina, and extended superiorly to the eighth thoracic spine. The patient underwent excision of the presacral and intradural portion of the tumor (25 of 26 blocks, entirely submitted) was composed largely of immature, neural parenchymal tissue at different stages of maturation, admixed with benign connective tissue, within which was a solitary area of pure medulloepithelioma-like component up to 2.5 cm on greatest dimension. A small area of the tumor (25 of approximately 30 blocks) contained mature skin with hair and respiratory mucous-secreting glands. These features are consistent with a diagnosis of immature teratoma with predominant medulloepithelioma component. This patient was treated with surgery only. At 5 years' follow-up, there was no evidence of recurrence. Thorough search is important in this case served for the tissue for confirming a teratomatous phenotype is small. As per our search in the English literature, the combination of teratoma with medulloepithelioma-like component with sacral bone defects has not been reported.

**Navajo Neurohepatopathy: First Description of Cardiac Mitochondrial Disease**

**Poster No. 50**

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Navajo neurohepatopathy is an autosomal recessive disease affecting 1 in 1600 live births in the Navajo population of the southwestern United States. The clinical features previously described include hepatopathy, corneal anesthesia, progressive sensorimotor neuropathy, failure to thrive, and cerebellar atrophy. We report a case of a 2-year-old boy, status postorthotopic liver transplantation for Navajo neurohepatopathy, who presented with a small patent ductus arteriosus and pulmonary hypertension. While vascular coiling of the ductus arteriosus was being performed, a right ventricular heart biopsy was taken to evaluate his cardiac muscle for mitochondrial disease, which may have led to left ventricular hypertrophy. The cardiac biopsy showed immature muscle fibers of varying sizes, many containing subsarcolemmal and intermyofibrillary aggregates (ragged red fibers). Nicotinamide adenine dinucleotide (NADH) histochemical staining illustrated an abnormal intermyofibrillar network. Electron microscopy revealed a significant increase in the number of mitochondria, which appear large and diffusely swollen, in addition to impressive amplification of cristae with focal condensations. This is the first reported description of mitochondrial disease within cardiac muscle in a patient with Navajo neurohepatopathy.

**A Mysterious Peripheral Nerve Sheath Tumor of the Cauda Equina Mimicking Myxopapillary Ependymoma: A Case Report With Emphasis on Differential Diagnosis**

**Poster No. 51**

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Myxoid peripheral nerve sheath tumors can be diagnostic dilemmas, especially when these tumors present in unusual locations. These tumors are usually subcutaneous and may have nonspecific gross and microscopic presentations. Immunohistochemistry and electron microscopy may be beneficial to render a precise diagnosis. An example of such a dilemma involves a 49-year-old woman who presented with back pain that had become severe during the course of a month. An L5 disk herniation and a spinal cord tumor at the level of L2 were found by magnetic resonance imaging. During surgery, an intraoperative frozen section was suggestive of myxopapillary ependymoma, which was also the clinical impression. The tumor was found to be encapsulated and to involve a single nerve root and was completely excised. Examination of hematoxylin-eosin–stained sections at low power demonstrated a lobular morphology. Higher magnification revealed delicate, spindle-shaped cells separated by a myxoid matrix. Foci of spindled cells without myxoid change were also observed. Palisading of tumor cells was not identified. Based on these findings, myxopapillary ependymoma was ruled out, and the diagnoses considered included neurothecoma, nerve sheath myxoma, and schwannoma. Immunohistochemical staining for S100 was strongly positive, glial fibrillary acidic protein showed weak, focal cell positivity, and epithelial membrane antigen was negative. Ultrastructural examination demonstrated long, interwoven collagen fibrils and processes lined by basal lamina and numerous Luse bodies, consistent with Schwannian differentiation.
Diffuse Leptomeningeal Oligodendrogliomatosis Diagnosed at Autopsy (Poster No. 52)

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Widely disseminated subarachnoid involvement by oligodendroglioma in the absence of a clinically apparent intraparenchymal focus is rare; only 12 cases have been reported in the English literature. We describe an autopsy case of a 37-year-old woman who presented with new onset of seizures and a 6-month history of headaches. Imaging demonstrated diffuse intracranial leptomeningeal thickening, as well as a mass lesion in the distal thoracic spinal cord and conus medullaris. She developed refractory intracranial hypertension and died 2 days after hospital admission. At autopsy, the lumbosacral leptomeninges and spinal cord were involved by a glistening, white mass, which extended throughout the length of the posterior spinal cord. Microscopic examination revealed a well-differentiated oligodendroglioma in the subarachnoid space surrounding the spinal cord, spinal nerve roots, parietal and temporal lobes, medulla, and optic chiasm. Tumor also infiltrated the lumbosacral spinal cord. Tumor cells were immunoreactive with glial fibrillary acidic protein and were negative for epithelial membrane antigen, NeuN, synaptophysin, and chromogranin. The MIB-1 labeling index was approximately 2%. Fluorescence in situ hybridization markers for 1p19q (1p36/1q25, 1p32/1qtel, 1q31/19p31) were intact. Another unusual finding in this case was a pleomorphic adenoma arising within the choroid of the left eye. To our knowledge, this represents the first case of diffuse leptomeningeal oligodendrogliomatosis in which fluorescence in situ hybridization analysis for 1p/19q deletion was performed. Analysis of additional cases may provide insight into the biologic characteristics of this rare presentation of oligodendroglioma.

Fatal Cerebral Infarction in a Young Man Secondary to Disseminated Giant Cell Arteritis (Poster No. 53)

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Giant cell arteritis is unusual in patients younger than age 50, and concurrent intracranial and visceral involvement in this disease is extremely rare. We report the case of a rapidly progressing, disseminated giant cell arteritis in a 24-year-old man who presented with a history of severe headache leading to collapse. Computed tomography studies showed filling defects involving both middle cerebral arteries and infaracts in multiple arterial territories. Results of routine blood work, cultures, serologies, and autoimmune and hypercoagulability workups were unremarkable. Attempts at recanilization failed, and the patient died of multiple cerebral infarctions. Postmortem examination showed arteritis composed of multinucleated giant cells, lymphocytes, and histiocytes causing thrombosis in segments of both middle and anterior cerebral arteries and one posterior cerebral artery. Both carotid sinuses and one renal artery segment were also involved. The arteritis was circumferential with many CD4+ and CD8+ lymphocytes in the adventitia and fragmentation of the internal elastic lamina by invading giant cells (Figure 78). The arteries affected ranged from 2.0 to 3.5 mm in diameter, and all lesions were the same age as the little fibrinoid necrosis. Special stains for fungi, bacteria, β-amyloid, and in situ hybridization for varicella-zoster virus were negative. These findings are consistent with giant cell arteritis and rule out a primary central nervous system vasculitis. To our knowledge, this is the first reported case in the literature of disseminated giant cell arteritis in an atypical age group with concurrent involvement of the anterior, middle, and posterior cerebral arteries and extracranial visceral arteries.

A Rare Neoplasm of the Extramedullary Intracranial Spinal Canal (Poster No. 54)

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The most common extramedullary intradural spinal tumors in adults include meningioma, schwannoma, metastasis, and secondary lymphoma/leukemia. A 30-year-old man presented after several months of progressive weakness and sensory deficit in his left lower extremity. Magnetic resonance imaging revealed an ovoid well-defined extramedullary intradural mass at the T11 to T12 level, which avidly enhanced following contrast administration. Following a complete staging workup that was negative for additional masses, the patient underwent surgical excision of the tumor. Intraoperative findings revealed a firm extramedullary tumor under the left-sided distal thoracic nerve roots. The tumor was diagnosed as a probable nerve sheath tumor (schwannoma vs neurofibroma) by intraoperative cytology. On submission of the mass in formalin for routine permanent sections, the tumor was grossly identified as an ovoid, well-circumscribed, firm, tan-white mass. Histologic study revealed a tumor with a patternless architecture, and numerous small to medium-sized, branching “stag-horn” blood vessels. Many spindle-shaped and uniform cells with little cytoplasm, indistinct borders, and vesicular bland nuclei were dispersed among abundant thick bands of hyalinized collagen (Figure 79). Immunohistochemistry revealed the spindle-shaped cells to be positive for CD34 and BCL2 and negative for S100 and epithelial membrane antigen. Morphologic and immunophenotypic features supported the diagnosis of solitary fibrous tumor. A solitary fibrous tumor of the spinal canal is a rare entity that should, nevertheless, be considered in the differential diagnosis of an extramedullary intradural spinal tumor.

Neuronal Intranuclear Inclusion Disease Diagnosed Incidentally at Autopsy (Poster No. 55)

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Neuronal intranuclear inclusion disease (NIID) is an exceedingly rare neurodegenerative disorder characterized by eosinophilic intranuclear inclusions in neurons and glia of the central nervous system and neurons of the peripheral nervous system. The clinical features of the disease are highly heterogeneous. In adult-onset cases, in which dementia may be a prominent feature, inclusions are seen more frequently in glial cells than...
neurons. Most cases are sporadic; however, familial cases have rarely been reported. NIID is suspected to be a trinucleotide repeat (CAG) disorder, but this has not been proven definitively. We present a case of NIID diagnosed incidentally at autopsy in a 71-year-old woman who died of sepsis. Gross examination of the brain revealed only mild frontal-para temporal cortical atrophy, commensurate with age. Microscopic examination revealed characteristic intranuclear inclusions in neurons and glial cells throughout the neuraxis. Inclusions were also identified in other central and peripheral nervous system cells, including myenteric plexus and cell Gallagher ganglion neurons. The inclusions were decorated by ubiquitin, but were negative for Gallyas and other markers, including 7, α-synuclein, and neurofilament protein. On electron microscopy, the inclusions demonstrated filamentous ultrastructure. Subsequent discussion with a family member revealed that the patient had 2 children with mental retardation of undetermined origin. Subsequently, 2 children in the family were diagnosed with Niemann-Pick disease type C1, demonstrating potential for a genetic link. This case demonstrates that NIID may be asymptomatic and present late in life. The more clinically apparent symptoms seen in this patient's children are suggestive of "anticipation," which is characteristic of trinucleotide repeat disorders.

**Metastatic Cranioopharyngioma (Poster No. 56)**

**Pushkar A. Phadke, MD, PhD** (pushkarphadke@yahoo.com); William Miele, MD; Carl Heilman, MD; Rolf Planl, MD. Departments of Neurology and Neurosurgery, Tufts Medical Center, Boston, Massachusetts.

A 51-year-old man was treated 2 years prior at another institution for a suprasellar cranioopharyngioma with subtotal resection and postoperative radiation therapy. One year following the initial resection, he underwent a second surgery at our institution for gross total resection of a suprasellar recurrence. Follow-up magnetic resonance imaging 1 year after this second surgery demonstrated an intracranial mass in the suprasellar region. The new tumor was distinct from the primary tumor bed or tract of prior surgical resection. The tumor was dissected free of the temporal cortex via a right temporal craniotomy. All tumor was removed, the field irrigated, and the crianiotomy closed. Histopathology confirmed cranioopharyngioma in the suprasellar space. Metastatic recurrence of cranioopharyngioma is a rare complication of tumor resection. Cranioopharyngioma tumor cells seeded to the cerebrospinal fluid intraoperatively have metastatic potential. Analysis of past reports shows these tumors recur at a median of 2 years following the most recent operation. Long-term neuroimaging follow-up is indicated.

**Early and Late Solvent-Related Neuropathology (Poster No. 57)**

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**Context:** The neuropathology of solvent inhalation (especially toluene) has characteristic features, consisting of patchy myelin loss with white matter macr ostructures that contain granular inclusions.

**Design:** A retrospective study from 1985 to 2008 including 73 autopsy cases with documented history of solvent abuse. Among these are 6 fe tus and infants with history of maternal exposure; 15 children, age 12–17 years; and 52 adults, age 18–66 years. Circumstances of death included 22 acute intoxications, 15 hangings, 7 traumas, 7 sepsis/aspirations, 4 fire/burns, and 3 hypothermias. Paraffin blocks from 61 cases were recut and stained with solochrome cyanin to demonstrate myelin and periodic acid-Schiff (PAS) to highlight the characteristic inclusions. All slides were examined in a blinded manner by the senior author. Patchy loss of myelin and the prevalence of inclusions were documented semiquantitatively.

**Results:** Eleven patients (age, 23–49 years; median, 40 years) had well-established leukoencephalopathy with multilocular perivascular myelin loss and inclusion-containing macrophages. Five patients (age, 15–53 years; median, 22 years) had early cortical changes consisting of patchy myelin loss with no obvious myelin change. All parts of brain, but not spinal cord, were involved. The clinical history, per- inoperative evaluation of the specimen showed a prolifera tion of small, round lymphocytes with admixed plasma cells. Permanent sections displayed dura infiltrated by small lymphocytes, macrophages, and transformed B cells. Proliferating cells were immunopositive for CD20 and S100. Occasional lymphocytes on leukocyte common antigen were positive. Glial fibrillary acidic protein was negative. Based on the clinical history, permanent histologic findings, and the immunohistochemical profile, the final diagnosis had 2 children with mental retardation of undetermined etiology. The patient had previously functioned well as a nurse. This case demonstrates that NIID may be asymptomatic and present late in life. The more clinically apparent symptoms seen in this patient's children are suggestive of "anticipation," which is characteristic of trinucleotide repeat disorders.

**SOX2 Is a Glioma-Specific Marker and Potential Target for Therapy (Poster No. 59)**

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**Context:** It is becoming increasingly apparent that biologic pathways active during tumorigenesis often parallel developmental pathways. SOX2 is a homeodomain transcription factor expressed during the neural plate stage of human central nervous system (CNS) development during neural tube closure. SOX2 is essential for normal neural development and is a transcription factor expressed in astrocytic gliomas but not in neuronal tumors. We hypothesized that SOX2 expression is lost during neural development but maintained during gliogenesis. We hypothesized that SOX2 expression is lost during neural development but maintained during gliogenesis. We hypothesized that SOX2 expression is lost during neural development but maintained during gliogenesis.

**Design:** One hundred twenty-eight gliomas and 47 nonglial primary CNS tumors were evaluated by immunohistochemistry for SOX2 expression. Published gene expression microarray data were analyzed for SOX2 in grade II to grade IV astrocytomas, grade II and III oligodendrogliomas, and medulloblastomas. We further evaluated the effects of SOX2 expression in glioma cell lines.

**Results:** SOX2 protein was expressed in 95% (122 of 128) of gliomas, including astrocytomas (World Health Organization [WHO] grades I–IV), oligodendrogliomas (WHO grade II, III), ependymomas (WHO grades I–III), and oligoastrocytomas (WHO grade II). Of the 47 nonglial primary CNS tumors, 83% (39 of 47) were nonreactive for SOX2 protein, including 81% (29 of 36) of tumors with neural features. RNA expression microarrays indicated strong SOX2 expression in astrocytomas and oligodendrogliomas and less in medulloblastomas, consistent with immunohistochemistry. We found a significant decrease in cell number (up to 50%) in all 5 cell lines.

**Conclusions:** Our results suggest that inhibition of SOX2 or one of its upstream or downstream factors may be a good target for glioma therapeutics. SOX2 may also serve as a diagnostic target for gliomas in the diagnostic setting.

**MALT Lymphoma of the Dura Mater (Poster No. 60)**

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We present the case of a 61-year-old woman who sought medical attention for vertebral headaches and vertigo lasting a few months in duration. Magnetic resonance imaging (MRI) showed a diffuse dural-based isointense, contrast-enhancing, extra-axial lesion in the right posterior fossa along the right lateral wall, thought to be an en-plaque meningioma. During a 6-week preoperative interval, the patient was maintained on steroids, and a repeat MRI on day of surgery showed significant shrinkage of the mass. Intraoperative evaluation of the specimen showed a proliferation of small, round lymphocytes with admixed plasma cells. Peri toneal sections displayed dura infiltrated by small lymphocytes, marginal zone B cells, plasmacytoid cells, plasma cells, and transformed B cells. Proliferating cells were immunopositive for CD20 and CD79a and immunonegative for CD5, CD10, CD43, and CD23. Many of...
these B cells were MUM1+ and showed a light-chain restriction. Epstein-Barr virus LMP-1 immunostain was negative. These features were consistent with a diagnosis of extranodal marginal-zone B-cell lymphoma of the mucosa-associated lymphoid tissue (MALT) type. Polymerase chain reaction (PCR) for immunoglobulin heavy-chain gene rearrangements showed a polyclonal rearrangement pattern. However, PCR has an approximately 20% false-negative rate in detecting clonal immunoglobulin H gene rearrangement. Primary lymphomas of the dura are rare, with most cases falling within the spectrum of MALT lymphoma. Overlap with plasmacytoma may exist, although it is not a factor in our case. With correct diagnosis and treatment, dural extranodal marginal zone lymphomas of MALT-type have a very favorable prognosis. This entity deserves wider recognition among pathologists responsible for diagnosis of neurosurgical material.

**Neuropathologic Causes of Medically Intractable Epilepsy in Magnetic Resonance Imaging—Negative, Anterior Mesial Temporal Lobe Resections Other Than Hippocampal Scarring**

(Poster No. 61)

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**Context:** Among a pool of 388 anterior mesial lobe neurosurgical resection specimens from 1997 to 2008, 86 were designated as patients with magnetic resonance imaging (MRI)-negative, medically intractable seizures. Thirty-eight cases were neuropathologically classified as hippocampal scarring (HPC-S). Twenty-five were negative for HPC-S. Five patients had MRI-negative, neuropathologic causes of intractable epilepsy other than HPC-S.

**Design:** Histologic sections were reviewed with 2 observers rating 12 neuropathologic criteria and scoring 1 to 5 (mild-moderate-severe). Observers were blinded, except to MRI-negative status. Neuropathology criteria scored were presence of gliosis or pyramidal cell neuronal loss in CA4; outer rim of CA4/layer 3 dentate cortex; CA3; proximal CA1; Sommer sector; distal CA1, with sparing of CA2; presence of cortical dysplasia/migration defect; lesions of dentate gyrus/entorhinal cortex; amygdala; and vascular hyalinization/endothelial hyperplasia. MRIs were reviewed separately by 2 neuroradiologists, the neurosurgeon, and epilepsy team.

**Results:** Five patients had neuropathologic causes of temporal lobe-localized epilepsy, other than primary HPC-S. Patients had (1) adult polyclonal body (Lafora) disease; (2) cortical dysplasia; (3) glial-neuronal migration defect; (4) viral encephalitis; and (5) cavernous hemangiom (Table).

**Conclusions:** The patients with Lafora disease and viral encephalitis had HPC-S pattern disease suggesting the possibility of secondary HPC-S developing in association with viral infections and neurodegenerative diseases, whereas developmental (cortical dysplasia/migration defect) and vascular lesions did not produce a HPC-S pattern. Neuropsychological intervention was effective, resulting in patients who were seizure-free (n = 3) and nearly seizure-free (n = 2). Inflammatory, vascular lesions, polyclonal bodies with calcifications may be MRI-negative causes of temporal lobe epilepsy; other localizing modalities may be needed before surgical intervention.

**Clinical and Neuropathologic Data of the 5 MRI-Negative Medically Intractable Epilepsy Patients**

<table>
<thead>
<tr>
<th>Patient</th>
<th>Engel Classification</th>
<th>PET/SPET</th>
<th>Main Pathology</th>
<th>Finding</th>
<th>HPC-S</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>II</td>
<td>Normal</td>
<td>Lofara disease</td>
<td>Moderate</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>II</td>
<td>Normal</td>
<td>Cavernous hemangioma</td>
<td>Negative</td>
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<tr>
<td>3</td>
<td>II</td>
<td>Normal</td>
<td>Migration defect</td>
<td>Negative</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>I</td>
<td>Normal</td>
<td>Viral encephalitis</td>
<td>Mild</td>
<td>moderate</td>
</tr>
<tr>
<td>5</td>
<td>I</td>
<td>Positive</td>
<td>Cortical dysplasia</td>
<td>Negative</td>
<td></td>
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</table>

**Immunohistochemical Analysis of Interleukin-27 (WSX-1/TCCR) Receptor Expression in Human Neuronal Cell Bodies**

(Poster No. 62)

John H. Irlam, DO (john.irlam@utoledo.edu). Department of Pathology, The University of Toledo Medical Center, Toledo, Ohio.

**Context:** Interleukin-27 is a newly identified interleukin-12 related cytokine that has demonstrated the ability to induce proliferation and differentiation of naïve CD4+ T cells into a Th1 population as well as attenuating and suppressing cytokine production. In addition, interleukin-27 has demonstrated potent antitumor effects as well as playing a role in the regulation of hematopoietic stem cell differentiation. To date, there has been limited reporting on interleukin-27 receptor (WSX-1/TCCR) expression in the human central nervous system. Through immunohistochemical analysis of brain tissue using an antibody to the interleukin-27 receptor (WSX-1/TCCR), we hope to further elucidate and qualify interleukin-27 receptor expression in the human brain.

**Design:** Grossly and microscopically unremarkable cerebral cortex tissue was collected from autopsy specimens. A rabbit polyclonal antibody to the human interleukin-27 receptor (WSX-1/TCCR; Abcam, Cambridge, Massachusetts) was applied to paraffin-embedded tissues after antigen retrieval. Immunohistochemical analysis of interleukin-27 receptor expression was qualified by light microscopy and compared with splenic T lymphocytes with known receptor expression.

**Results:** Examination of normal tissue demonstrated strong cytoplasmic staining in neuronal cell bodies without significant staining in neuronal axons or other cells of the brain, including astrocytes, microglial cells, or oligodendrocytes.

**Conclusions:** Preliminary results demonstrate a strong positive staining pattern in neuronal cytoplasm for interleukin-27 receptor (WSX-1/TCCR) expression in the human brain without significant expression in astrocytes, microglial cells, or oligodendrocytes. To our knowledge, this has not been previously reported in human neurons. We submit that the expression of this expression has yet to be determined and that further evaluation is needed.

**Concurrent Oligodendroglioma and Hemangioblastoma in the Brain of a 49-Year-Old Man**

(Poster No. 63)

Jonathan L. Klein, MD (kleinnmd@gmail.com); Steven Drexler, MD. Department of Pathology, Winthrop University Hospital, Mineola, New York.

We report a case of a 49-year-old man who presented with generalized tonic-clonic seizure. The patient was found to have enhancing right cerebellar and nonenhancing right parietal masses on magnetic resonance imaging. The right cerebellar mass was resected, and the histology showed 2 distinct cell populations; one population consisted of interstitial cells with intracytoplasmic fat vacuoles, and a second population consisted of endothelial cells forming vascular channels. A Giemsa stain showed scattered mast cells. The findings were consistent with a World Health Organization (WHO) grade I hemangioblastoma. Eighteen days later, the patient returned for a biopsy of the parietal nonenhancing mass. The histologic sections at this time showed a tumor composed of a homogeneous cell population of intermediate-sized cells with prominent chromatin, occasional small nucleoli, and perinuclear clearings. There was no vascular endothelial hyperplasia, necrosis, or observable mitoses. Fluorescence in situ hybridization studies revealed the tumor to have deletions of 1p and 19q. The findings were consistent with a WHO grade II oligodendroglioma. The occurrence of 2 concomitant primary brain neoplasms is extremely rare and may represent a genetic syndrome. Hemangioblastomas are associated with Von Hippel-Lindau syndrome; however, there is no literature showing an association of oligodendrogliomas with this syndrome. To our knowledge, the patient has not yet received genetic testing for an altered Von-Hippel Lindau gene as he was lost to follow-up.

**Pending Case Reports: Tools for Reducing Turnaround Time and for Practice Improvement**

(Poster No. 64)

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**Context:** Turnaround time (TAT) is an important quality measure. Laboratory information systems can provide TAT and pending case reports (PCRs).

**Design:** We sought to use PCRs to evaluate practice performance, identify areas for improvement, allocate resources, and evaluate impact of these measures. We reviewed weekly PCRs during 21 weeks to identify sources contributing to overdue/pending cases. Weekly overdue charges were reviewed.

**Results:** Four contributing sources were identified. (1) Equipment failure (electron microscope [EM]). An alternate EM was identified within the institute, cases were completed, and a mechanism was established for
ongoing use. Pending EM cases went from 27 to 0. (2) We process 250+ placentas each month. A backlog of cases was successfully cleared (from 138 to 2 cases) with changes made to histology work distribution and to a backup service plan. (3) A slow decalcification process replaced with a rapid technique that simultaneously detects multiple viruses in 24 hours or less. (4) Thyroid fine-needle aspiration (FNA) cases were traditionally signed out in a longer timeframe than other cytology cases. Instead of submitting all thyroid FNAs to one cytopathologist on a given day, cases were distributed with direct notification to all practicing cytopathologists. This has reduced TAT from 4.5 to 2.4 days. The overall pending list was significantly reduced (from a maximum of 154 cases in a week to 2 cases in a week). Overdue charges significantly decreased (from $70.5 K to $1K).

Conclusions: VRS are a valuable tool for practice assessment. Using them enabled our service to achieve and even exceed TAT benchmarks.

Voice Recognition Software Use Enhances Surgical Pathology Work Flow
(Poster No. 65)

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Context: Based on experience with voice recognition software (VRS) for gross descriptions, we initiated a pilot study to determine its efficacy in surgical pathology sign-out.

Design: Dragon Naturally Speaking software (Version 10) enhanced by a pathology VRS (VoiceOver from VoiceBrook) was used. After 1 hour of training, pathologists used VRS for surgical pathology reports. A second group of similar cases was submitted in the routine manner for typing (RMT). The time it took to sign-out different types of cases by both methods was tracked.

Results: A significant time benefit was obtained with VRS use versus RMT (mean, 1.6 vs 747 minutes; median, 2 vs 495 minutes for a total of 62 cases). The VRS reports became available in the hospital information system within minutes of viewing the slides. VRS misinterpretations were uncommon and were corrected in real-time before electronic release of reports. Errors related to handwriting with the RMT were avoided. A seamless flow from looking at the slides under the microscope, dictating the case, and signing it out, before moving on to the next case was obtained. Memory recall was not necessary. Cases could be completed independent of transcriptionists at a time and pace that suited the pathologist. This enabled our service to achieve and even exceed TAT benchmarks.

Conclusions: VRS is a valuable tool for practice assessment. Using them enabled our service to achieve and even exceed TAT benchmarks.

Multiplex Polymerase Chain Reaction Diagnosis of Viral Respiratory Infections: Projected Cost Savings and Effect on Patient Admission Length
(Poster No. 66)

Ian M. Bovim, MD (bovim@pathology.ufl.edu); Howard Rampersaud, BS, MT; Kenneth Rand, MD. Department of Pathology, University of Florida, Gainesville.

Context: Viral respiratory infections (VRI) account for numerous hospitalizations. Viral culture is hampered by prolonged turnaround time and suboptimal sensitivity, potentially resulting in extended length of stay (LOS). Multiplex polymerase chain reaction (PCR) is a sensitive, rapid technique that simultaneously detects multiple viruses in 24 hours or less. As molecular technology approaches the market, expenses must be justified by demonstrating the ability to economically improve patient care. We sought to project cost savings and LOS impact by implementing multiplex viral PCR.

Design: We analyzed LOS for inpatients tested for influenza or RSV by direct antigen testing (DAT) or culture from June 2003 to June 2008. To exclude significant comorbidities, we included only patients younger than 16 years with LOS of 10 or fewer days. LOS was divided into 4 subgroups depending on result (positive or negative) and type (rapid or nonrapid) of test. Number and relative percentages of patients discharged on days 0 through 10 for positive/rapid, positive/nonrapid, negative/rapid, and negative/nonrapid were calculated. The assumption is LOS by DAT can serve as a surrogate indicator for LOS by other rapid (ie, multiplex PCR) diagnostic modalities.

Results: LOS in admission days per 100 patients was as follows (Figure 80): positive/rapid (301.7), positive/nonrapid (360.8), negative/rapid (339.8), negative/nonrapid (431.5). For positive groups, χ² was 0.31; however, rapid versus nonrapid influenza was 0.0038. For negative groups, χ² was 3.35 × 10⁻². With multiplex PCR implementation, it is assumed (regarding LOS) that nonrapid groups shift to rapid groups, resulting in $276 000 annual variable admission cost savings.

Conclusions: VRI multiplex PCR has potential for cost savings and improved patient care.

Time-Out Procedure for Collection of Type and Screen Blood Bank Transfusion Samples: An Easy Solution to a Serious Problem
(Poster No. 67)

Saeed Bajestani, MD (saeed.bajestani@jax.ufl.edu); David Wolfson, MD. Department of Pathology, University of Florida, College of Medicine, Jacksonville.

Context: The first step in the correct pretransfusion technique is accurate patient identification. Many institutions employ a buddy system to ensure correct collection of a sample. Even the tandem specimen collection does not always achieve 100% accuracy in patient identification. This may lead to a wrong blood in test tube (WBIT), essentially a disaster in the making. To combat this situation, our transfusion services adopted a time-out procedure that the Joint Commission on Accreditation of Healthcare Organizations advocates for invasive procedures. This was implemented in 2004 and reinforced to a time-out procedure in 2007. We assessed the effect of this policy.

Design: Blood bank specimen rejections from 2005 to 2008 were reviewed, and the average number of specimen rejections per month for each year determined. We then compared these averages before and after implementation of the time-out policy. We also reviewed the data on WBITs from 1999 to 2008, documented WBIT numbers for each year, and compared the number of WBITs before and after implementation of the time-out policy.

Results: After implementing this policy in 2004, the number of WBITs reduced from 6 to 1 per year. The average number of rejections was reduced from 80 to 19 per month after reinforcement of the policy in 2007 with increasing the bar to a formal time-out procedure.

Conclusions: Annually, we transfuse more than 4000 patients in our institution. Potentially, 1 in every 969 patients were transfused the wrong blood before adopting this policy. Implementing this policy is a successful method to improve patient safety and avoid unnecessary expenses and lawsuits.

Cardiac Epithelioid Angiosarcoma With Pulmonary Metastases Presenting as Primary Pulmonary Epithelioid Hemangioendothelioma
(Poster No. 68)

Mark Podberezn, MD (markp@uic.edu); Thitiwat Sriprasart, MD; Eugene DeGuzman, MD; Sangeeta Mehendale, MD; Carey August, MD. Department of Pathology, University of Illinois, Chicago; Departments of 'Internal Medicine and 'Pathology, Advocate Illinois Masonic Medical Center, Chicago.
We report a case of a cardiac epithelioid angiosarcoma with pseudoaneurysmal communication with right atrium and bilateral lung metastases, presenting as primary pulmonary epithelioid hemangioendothelioma. To the best of our knowledge, this is the first case of this kind of cardiac tumor with pseudoaneurysmal communication with the right atrium. The patient was a 43-year-old, previously healthy man, who presented with a 6 month history of progressive dyspnea on exertion, hemoptysis, and severe right-sided chest pain. Computed tomography of the chest showed multiple subcentimeter pulmonary nodules, and open lung biopsy confirmed the presence of circumscribed, but ill-defined, nodules, comprising cells with a mixed epithelioid and spindle morphology and numerous extravasated erythrocytes frequently in a myxoid or hyalinized background. Mitotic activity was not prominent, but the nuclei were moderately atypical, with vesicular chromatin and occasional prominent nucleoli. Within the myxomatous and hyalinized areas, cells often contained intracytoplasmic vacuoles. The lesional cells were immunoreactive with vascular markers CD31, CD34, and factor VIII. The morphologic findings were thus most consistent with a primary epithelioid hemangioendothelioma. Cardiac magnetic resonance imaging revealed a 4-cm, right atrial mass with pseudoaneurysmal cavity. Considering the presence of a solitary cardiac mass accompanied by multiple pulmonary nodules with focus of cytologic atypia, the final diagnosis was primary cardiac epithelioid angiosarcoma with multifocal pulmonary metastases. This case illustrates the morphologic overlap between epithelioid hemangioendothelioma and epithelioid angiosarcoma and emphasizes the importance of correlating pathologic findings with clinical data and imaging studies.

**Poster Session 600: Tuesday, October 13, 2009, 11:00 AM–1:30 PM**

**Endocrine Pathology; Head, Neck and Oral Pathology; Informatics; Microbiology; Ophthalmic Pathology; Molecular Pathology; Pathology Education; Quality Assurance**

**Morphoproteomic Confirmation of an Activated Nuclear Factor–κBp65 Pathway in Follicular Thyroid Carcinoma**

(Disclaimer No. 1)

Jing Liu, MD, PhD (jing.liu@uth.tmc.edu); Robert E. Brown, MD. Department of Pathology and Laboratory Medicine, University of Texas Health Science Center, Houston, TX; Houston Methodist Hospital, Houston, TX.

Context: Follicular thyroid carcinoma is the second most common malignant thyroid neoplasm. The role of the nuclear factor–κBp65 pathway in the pathogenesis of follicular thyroid carcinoma has not been fully investigated.

Design: We retrieved 10 cases of follicular thyroid carcinoma from our files. Tissue microarrays were constructed using 2.0-mm cores from formalin-fixed, paraffin-embedded tissue blocks. Tissue microarray sections were immunohistochemically stained for p-nuclear factor–κBp65, interleukin 8 (IL-8), and glutathione S-transferase–pi. Staining intensity (0 to 3+), extensiveness (0%–100%), and subcellular compartmentalization were evaluated. The positive staining intensity was graded as weak (1+), moderate (2+), or strong (3+).

Results: Both nuclear and cytoplasmic immunoreactivities with p-nuclear factor–κBp65 (Ser 536) were observed in all 10 cases, including moderate to strong nuclear staining intensity with a range of extensiveness from 20% to 100% of tumor cells. Moderate or strong cytoplasmic expression of IL-8 was present in 50% to 100% of tumor cells in all cases. Glutathione S-transferase–pi diffusely (70%–100%) and moderately or strongly stained the tumor cytoplasm in all cases except in one case with insufficient tissue. Three of these cases also demonstrated nuclear positivity.

Conclusions: Morphoproteomic analysis revealed the constitutive activation of the nuclear factor–κBp65 pathway in follicular thyroid carcinomas (phosphorylation at Ser 536 with nuclear translocation and with correlative expression of transcriptionally activated gene products, IL-8, and glutathione S-transferase–pi). These results provide some insight into the biology of follicular thyroid carcinoma and a potential therapeutic target.

**Incidental Papillary Thyroid Microcarcinoma With Lung Metastasis, an Autopsy Case Study: Should We Adopt the Term Papillary Micro-Tumor of the Thyroid Instead of Microcarcinoma?**

(Disclaimer No. 2)

Oleksandr N. Kryvenko, MD (okryven1@hfhs.org); Osama Alassi, MD. Department of Pathology, Henry Ford Hospital, Detroit, MI.

Papillary thyroid microcarcinoma (PTMC) is defined by the World Health Organization as a tumor measuring less than 10 mm and demonstrating cytologic features of conventional papillary thyroid carcinoma. Most tumors in this group are indolent and are found incidentally. Occasionally, they may present as cervical lymph node metastasis. Some suggest using the term papillary micro-tumor instead of PTMC for intra-thyroid tumors with favorable prognosis. We discuss the case of a 58-year-old woman who presented with loss of consciousness secondary to bilateral cerebellar infarcts. Suboccipital craniotomy was performed in an effort to decompress the posterior fossa. However, the patient died shortly thereafter. Routine gross examination of the internal organs and microscopic slides with immunohistochemical stains were performed. The cause of death was bilateral cerebellar and frontotemporal infarcts. The thyroid was symmetric and nonenlarged, with an 8-mm solid nodule in the right lobe. Microscopic examination of the thyroid revealed PTMC with no extrathyroid extension and no vascular or lymphatic invasion. The lung sections revealed microscopic foci of thyroid papillary carcinoma in 2 lobes, which were confirmed by positive thyroglobulin immunostain (Figure 81).

Although the primary focus of this PTMC did not demonstrate high-risk histologic features, such as vascular invasion and extrathyroid metastases were seen. It is unlikely that these metastases contributed to the patient’s death; however, this case demonstrates the potential for widespread dissemination of PTMC and possible adverse outcome.
Expression of Matrix Metalloproteinase 7 and Fibronectin in Papillary Thyroid Cancer: Gene Expression Profiling Using Real-Time Polymerase Chain Reaction

(Postal No. 4)

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Context: Papillary thyroid cancer (PTC) is usually indolent with a high frequency of lymph node metastasis. Rarely, PTC behaves in a more aggressive fashion; however, the mechanisms of invasion and metastasis in thyroid cancer remain poorly understood. We recently encountered a case of aggressive PTC with metastasis to the spine that prompted us to study molecular profiles of PTC with aggressive behavior.

Design: We studied 5 cases of PTC for which fresh-frozen tissue was available. In 3 cases, there was a distant metastasis to the lung and bone; the other 2 cases had only local disease. We used the human tumor metastasis RT2 Profiler PCR Array (SA Bioscience, Frederick, Maryland) and a high-performance SYBR green LightCycler real-time PCR (Roche, Indianapolis, Indiana). The array represents 84 genes known to be involved in metastasis. Statistical analysis was performed using the PCR Array Data Analysis Web Portal.

Results: Analysis of the 2 PTCs without hematogenous metastasis showed down-regulation of matrix metalloproteinases and fibronectin. Significant over-expression of metalloproteinases, especially MMP7, and fibronectin were found in 3 PTCs with hematogenous metastasis (group 1; Figure 83). Compared with normal control and PTC without hematogenous metastasis, the ratios of fibronectin and MMP7 expression were 1066.5 and 700.3, respectively.

Conclusions: Metalloproteinases, particularly MMP7, and fibronectin were over-expressed in PTC with hematogenous metastasis. Metalloproteinases are a family of proteolytic enzymes that degrade protein components of extracellular matrix; thus, these enzymes are believed to play an important role in tumor progression, invasion and metastasis.

Anaplastic Carcinoma of the Thyroid With Osteoclast-Like Giant Cells

(Postal No. 5)

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We report a case of a 44-year-old woman with anaplastic carcinoma of the thyroid occurring in association with 2 distinct, differentiated thyroid carcinomas. The patient presented with a neck mass causing trachea deviation and internal jugular vein narrowing. The histology showed anaplastic undifferentiated carcinoma that was composed of spindle and epithelioid cells with osteoclast-like giant cells. Additionally, we identified 2 areas of differentiated tumor. The first area had papillary architecture with ground-glass chromatin and nuclear grooves that were consistent with papillary carcinoma (Figure 84). The second area exhibited a nested growth pattern with finely granular oncocytic cytoplasm and round nuclei, which was consistent with Hurthle cell carcinoma. The Hurthle cell carcinoma was metastatic to one lymph node. The anaplastic carcinoma was not present in any lymph nodes but exhibited high mitotic activity, extracapsular extension, and lymphovascular invasion with tumor emboli. Immunohistochemical stains for cytokeratins were positive in the Hurthle and papillary components and focally positive in the anaplastic component. Thyroid transcription factor-1 and thyroglobulin were positive in the Hurthle and papillary components and negative in the anaplastic component. The osteoclast-like giant cells were positive for CD68 but not for cytokeratin. Ancedotal case report data in the literature suggest that some thyroid papillary carcinomas can progress to Hurthle cell carcinoma. However, this is the first case report of anaplastic thyroid carcinoma with osteoclast-like giant cells and 2 separate well-differentiated components. This observation raises the possibility of a progression from a well-differentiated papillary carcinoma to Hurthle cell and then to anaplastic carcinoma.
Papillary Thyroid Carcinomas in the Pediatric Age Group and the Significance of Pathologic Parameters (Poster No. 7)

Abha Goyal, MBBS (abogyal@yahoo.com); Jaya Mahajan, MBBS, MHA; Tarush Kohli, MD; Tawfiquil Bhuyia, MD. Department of Pathology, Long Island Jewish Medical Center, New Hyde Park, New York.

Context: Pediatric thyroid carcinomas are relatively rare, and most are papillary carcinomas with an excellent prognosis. Our study aimed to identify those pathologic parameters that could influence the prognosis of papillary thyroid carcinomas in children.

Design: Twenty-four cases of papillary thyroid carcinomas in the 0- to 18-year-old age group were retrieved from the databases (1989 to 2007) of Long Island Jewish Medical Center and North Shore University Hospital. Hematoxylin-eosin slides were reviewed. The documented clinicopathologic features included age at diagnosis, sex, radiation exposure, treatment, relapse, follow-up duration, clinicopathologic subtype, tumor size, tumor foci, vascular invasion, extrathyroidal extension, margin status, additional pathologic findings, nodal metastases, extranodal extension, distant metastases, and pTNM staging. Statistical analysis was performed using the Fisher exact test. The overall survival rate was derived from a Kaplan-Meier plot.

Results: The most common histologic subtypes were as follows: 16 cases (66.7%) of papillary carcinoma, not otherwise specified, 7 cases (29.2%) of follicular variant, and 1 case (4.2%) of diffuse sclerosing variant. Nineteen cases (79.2%) had nodal metastases at diagnosis. Four patients (16.7%) relapsed with regional lymph node recurrence. A comparison of pathologic parameters between cases with and without recurrence is depicted in Table. The mean follow-up duration was 8 years. The overall 5-year survival rate was 100%.

Conclusions: Our study confirms the excellent prognosis in cases of pediatric papillary thyroid carcinomas. Positive surgical margins were the only statistically significant pathologic parameter associated with relapse. This finding indicates a need for more frequent follow-up.

| Comparison of Pathologic Parameters Between Cases With and Without Recurrence |
|---------------------------------|-----------------|-----------------|-----------------|
| Parameter                       | With Recurrence | Without Recurrence | P Value |
| Histologic subtype of papillary carcinoma, not otherwise specified | 4               | 12              | .26            |
| Vascular invasion               | 2               | 64              | .25            |
| Extrathyroidal extension        | 3               | 4               | .06            |
| Extranodal extension            | 2               | 1†             | .10            |
| Positive surgical margins       | 3               | 0               | .002           |

* P < .05 was considered statistically significant.
† Extranodal extension in the group without recurrence was from 1 of 15 cases.

Demographics and Long-term Follow-up of Ductal and Endocrine Carcinomas of the Pancreas (Poster No. 8)

Jorge Albores-Saavedra, MD1 (alboresjorge@yahoo.com); Kristen Batch, BA; Arnold M. Schwartz, MD, PhD; Donald E. Henson, MD.1 Department of Pathology, Instituto Nacional de Ciencias Medicas y Nutricion, Mexico City, Mexico; Departments of Cancer Prevention and Control and Pathology, George Washington University Medical Center, Washington, DC.

Context: Of all human malignant neoplasms, ductal carcinoma (DC) of the pancreas is one of the most lethal, whereas endocrine pancreatic carcinomas are considered to be low-grade malignant tumors. Few studies have described the demographics and long-term survival rates in cases of DC and EC of the pancreas. Logarithmic transformation plots of age-adjusted incidence rates were analyzed.

Results: We identified 114761 cases of pancreatic DC. Of these, 49% were men; 51% were women. We identified 2864 cases of EC. Of these, 54% were men; 46% were women. The mean age of diagnosis was 70.3 years for DC and 58.8 years for EC. Gastrinoma (40.7%), insulinoma (29.6%), glucagonoma (19.6%), and vipoma (10.1%) were the most common functioning ECs. The 10-year relative survival rates for pancreatic DC and EC were 27.6% and 2.5%, respectively. For distant stage at time of diagnosis, 59.6% of cases were EC; 49.6% of cases were DC. Logarithmic transformation plots revealed pancreatic EC and DC as having separate carcinogenic pathways.

Conclusions: DCs of the pancreas were slightly more common in women. ECs were much more common in men and presented at younger ages. Gastrinoma, insulinoma, and glucagonoma were the most common functioning ECs. Although pancreatic EC is considered to be of low-grade histology, it does not have a favorable long-term survival rate. Pancreatic EC and DC arise from different cells and have separate carcinogenic pathways.

The Use of Human Papillomavirus Polymerase Chain Reaction in the Histopathologic Diagnosis of Florid Oral Papillomatosis Associated With Malignant Acanthosis Nigricans Versus Multifocal Epithelial Hyperplasia or Heck Disease (Poster No. 9)

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Multifocal epithelial hyperplasia or Heck disease and oral papillomatosis have similar clinical presentations, including multiple small papules or nodules in the oral mucosa and histologic features of parakeratinized, stratified squamous epithelium with marked acanthosis. Although multifocal epithelial hyperplasia is associated with human papillomavirus and may show koilocytic changes, florid oral papillomatosis is associated with malignant acanthosis nigricans. We present 2 patients, a 24-year-old and a 47-year-old, who sought dental treatment for lesions covering the oral mucosa. In addition to the oral lesions, clinical examination revealed skin lesions that were consistent with acanthosis nigricans. The biopsies for both patients revealed papillomatosis with mild hyperkeratosis, marked acanthosis, and focal koilocytes. Human papillomavirus DNA polymerase chain reaction analysis (Maxim Biotech, Inc., Rockville, Maryland) was negative in both biopsies. Both patients underwent gastric and colonic biopsies. The first patient, age 24, was diagnosed with colonic and gastric polyposis with more than 100 polyps, including some with dysplasia. This patient was not aware of intestinal problems before the biopsies. The second patient, age 47, had a history of untreated vomiting and weight loss during a 6-month period. Following a gastric biopsy, she was diagnosed with advanced gastric adenocarcinoma. In conclusion, human papillomavirus DNA polymerase chain reaction analysis is useful in the histopathologic differential diagnosis of florid oral papillomatosis associated with acanthosis nigricans and multifocal epithelial hyperplasia or Heck disease.

Malignant Pindborg Tumor (Poster No. 10)

Ranjana Gottipati, MD1 (ranjana-gottipati@ouhsc.edu); Glen Houston, DDS2; Jesus E. Medina, MD3; Anthony M. Alleman, MD3; Kar-Ming Fung, MD, PhD1. Departments of Pathology,1 Otorhinolaryngology, and Radiology, The University of Oklahoma Health Sciences Center, Oklahoma City.

Calculating epithelial odontogenic tumors account for less than 1% of all odontogenic tumors. Malignant calcifying epithelial odontogenic tumor, also known as malignant Pindborg tumor, is an even rarer entity. We describe the case of a 40-year-old man who self-extracted his right mobile third maxillary molar tooth and sought consultation for a nonhealing extraction site. Imaging studies revealed a destructive mass involving the floor and lateral wall of the right maxillary sinus with extension into the pterygoid plate and soft tissue. An incisional biopsy was performed, and histologic review identified a malignant epithelial neoplasm. Squamous cell carcinoma and malignant Pindborg tumor were top considerations in the differential diagnosis. The patient subsequently underwent a right partial maxillectomy, and gross examination revealed a 2.0 × 1.5 × 1.3-cm, tan-white, fleshy, lobulated tumor involving the floor and lateral wall of the maxillary sinus. The tumor also grossly invaded the alveolar bone and associated molar tooth. Microscopically, the tumor had an infiltrative pattern and was composed of sheets, islands, and strands of polygonal...
epithelial cells. The cells had abundant eosinophilic cytoplasm, large pleomorphic nuclei with scattered atypical mitotic figures, and vascular tumor emboli. There were foci of calcified deposits along with Liesegang ring calcification. The tumor also invaded the mucosa of the hard palate. Malignant Pindborg tumor is an exceedingly rare tumor, and a definitive diagnosis can only be rendered when there is evidence of infiltrative growth, metastases, and vascular or perineural invasion. Differentiation from squamous cell carcinoma is not always possible on small biopsies.

**A Rare Case of Malignant Mesothelioma With Metastasis to the Tonsil**

(Poster No. 11)

Stephen Samuel, MD (ssamuel@swmail.sw.org); Lisa Lopez, MD. Department of Pathology, Scott and White Memorial Hospital–Texas A&M Health Science Center College of Medicine, Temple.

Malignant mesothelioma is a rare tumor that most commonly arises from the mesothelial lining of the pleural space. It has also been reported to develop from uncommon sites, such as the peritoneal surface, pericardium, and tunica vaginalis. Patients often present with local aggressive disease, and if metastasis is present, it typically involves the regional lymph nodes. Although rare, clinically evident distant hematogenous spread has been documented. Typical sites include brain, lung, bone, and soft tissue. Metastases to unusual sites, such as tongue, eye, and skin, have also been reported. We report a case of a patient who presented with a tonsillar metastasis 9 months after being diagnosed with malignant pleural mesothelioma. To our knowledge, this is the second reported case of metastatic malignant mesothelioma to the tonsil.

**The Significance of Intranuclear Pseudoinclusions in Fine-Needle Aspiration of Papillary Carcinoma of the Thyroid: Can We Count on Them?**

(Poster No. 12)

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**Context:** Our objective was to identify the significance of intranuclear inclusions and other cytologic features on fine-needle aspiration biopsy that were signed out as “suspicious” for papillary carcinoma of the thyroid.

**Design:** We conducted a retrospective slide review of fine-needle aspiration biopsies that were signed out as “suspicious for papillary carcinoma of the thyroid” during a 2-year period at Danbury Hospital. We also reviewed 20 random cases. The following cytologic features were graded from 1 to 3: nuclear grooves, overall cellularity, and cell overlap. We counted the total number of intranuclear pseudoinclusions.

**Results:** A total of 58 fine-needle aspiration biopsy cases were identified. Diagnoses for papillary carcinoma of the thyroid included the following: “suspicious” (n = 52), “worrisome” (n = 2), “possibility of” (n = 2), “cannot rule out” (n = 1), and “indeterminate” (n = 1). Twenty-four cases had no surgical follow-up at our institution and were excluded from the study. The age of the patients ranged from 37 to 80 years. There were 27 women and 7 men. The 34 cases with surgical follow-up included 20 papillary carcinoma of the thyroid (59%), 6 multinodular hyperplasia (18%), 5 nodular hyperplasia (15%), 2 follicular adenoma (6%), and 1 hyalinizing trabecular tumor (3%). Statistically significant features included intranuclear pseudoinclusions, nuclear grooves, and overall cellularity. Cell overlap was not statistically significant.

**Conclusions:** Our study used a semiquantitative system to assess the likelihood of papillary carcinoma. Although no single cytologic characteristic is diagnostic of papillary carcinoma, the presence of intranuclear pseudoinclusions, nuclear grooves, and overall cellularity help in making this diagnosis with a high level of certainty.

**Nuclear Protein in Tissue-Associated Carcinoma in the Salivary Gland of a Pediatric Patient**

(Poster No. 13)

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Nuclear protein in tissue (NUT) midline carcinomas (NMCs) are a rare and recently described class of poorly differentiated tumors that exhibit highly aggressive clinicopathologic behavior. Although NMCs carry a thymogenic BRD4-NUT fusion gene, they frequently go unrecognized because of their rarity and lack of distinguishing histologic features. Such tumors rarely affect pediatric patients and have never been reported in the salivary glands. We report the first case of NMC involving the salivary gland in an adolescent. A previously healthy, 15-year-old, adolescent boy presented with a left submandibular mass of 3-month duration. He reported waxing and waning pain and episodes of swelling and regression of the mass. Ultrasound showed no evidence of cystic degeneration, hemorrhage, or invasion. He underwent submandibular sialadenectomy with histopathologic evaluation and subsequent left neck dissection. Grossly, the tumor was circumscribed and white and firm, mimicking a pleomorphic adenoma. On histology, tumor cells were predominantly undifferentiated with high mitotic activity, atypical mitoses, and nondescript immunoprofile. Perineural and perivascular invasion were noted. Tumor cells were positive for NUT translocation by fluorescence in situ hybridization. Left neck dissection revealed that 1 of 33 lymph nodes was positive for metastatic tumor. This case identifies salivary gland NMC as a diagnostic consideration in poorly differentiated salivary gland carcinomas affecting pediatric patients. Because poorly differentiated tumors lack distinguishing histologic or immunohistochemical features, molecular diagnosis is essential for accurate categorization and treatment. Any such midline or head and neck tumors that do not exhibit lineage-specific differentiation markers should be considered for NUT rearrangement testing.

**Differential Expression of Cytokeratins, p63, and Epidermal Growth Factor Receptor in Spindle-Cell (Sarcomatoid) Squamous Cell Carcinoma of the Head and Neck**

(Poster No. 14)

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**Context:** Spindle-cell squamous cell carcinoma (sSCC) of head and neck frequently lacks expression of typical immunohistochemical markers of conventional squamous cell carcinoma (sCC), making it difficult to diagnose, especially in the absence of sCC component and/or in limited biopsy specimens. We aimed to characterize the immunohistochemical profile of sSCC.

**Design:** We identified 20 cases of sSCC and 17 cases of sCC from our files. The microscopic features were reviewed. Tissue microarray blocks were constructed from formalin-fixed, paraffin-embedded tumor blocks containing 0.6-mm cores of each tumor. Immunohistochemistry was performed for high- and low-weight molecular cytokeratins (CKs), including AE1/AE3, CAM 5.2, CK-super cocktail (CAM 5.2, AE1/AE3, CK903, and MAK6), CK5/6, and CK903, and for p53, p63 and epidermal growth factor receptor. Intensity of staining for CKs was recorded as high or low and was scored semiquantitatively on a 0 to 5 scale: 0%, less than 10% 10% to 25%, 26% to 50%, 51% to 75%, and 76% to 100%. Epidermal growth factor receptor immunostain was scored (0 to 3+) based on membranous staining pattern, and 2+ or 3+ was recorded as positive. Greater than 20% nuclear staining for p53 and p63 was considered positive.

**Results:** We excluded 2 cases of sCC because of tissue loss (Table).

**Conclusions:** Our study highlights the differential expression of CKs between sSCC and sCC. Lack of immunostaining for keratin super-cocktail and p63 in many of the cases of sCC emphasizes the need to use a CK-panel approach to diagnosis. Underexpression of p63 and epidermal growth factor receptor in sSCC indicates different a biology compared with sCC and thus different potential therapeutic targets.

**Immunostain Results**

<table>
<thead>
<tr>
<th>Stain</th>
<th>sCC, No. (%)</th>
<th>sSCC, No. (%)</th>
</tr>
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<tbody>
<tr>
<td>AE1/AE3</td>
<td>15/17 (88)</td>
<td>5/17 (29)</td>
</tr>
<tr>
<td>CK5/6</td>
<td>13/16 (81)</td>
<td>7/18 (39)</td>
</tr>
<tr>
<td>CK903</td>
<td>15/17 (88)</td>
<td>7/18 (39)</td>
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<tr>
<td>CK-super cocktail</td>
<td>15/17 (88)</td>
<td>6/18 (33)</td>
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<tr>
<td>p53</td>
<td>5/16 (31)</td>
<td>5/18 (28)</td>
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<tr>
<td>p63</td>
<td>13/16 (81)</td>
<td>6/18 (33)</td>
</tr>
<tr>
<td>Epidermal growth factor receptor</td>
<td>6/17 (35)</td>
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Arch Pathol Lab Med—Vol 133, October 2009

**Abstracts**
Chernobyl-Related Thyroid Carcinoma
(Poster No. 15)

Keith D. Bohman, MD (kbohman14@aol.com); Robert L. Booth Jr, MD. Department of Pathology, University of Toledo, Ohio.

On April 26, 1986, the Chernobyl nuclear accident exposed millions of people to significant radiation in Belarus, Russia, and the Ukraine. The environment quickly became contaminated with radioactive isotopes, leading to an increase in the incidence of papillary thyroid carcinomas in these nations. Papillary thyroid carcinomas in Chernobyl victims were first reported 3 to 4 years after the accident, and these tumors have tended to be of the solid histologic subtype. It has been proposed that the occurrence of the solid-type of papillary thyroid carcinoma in these cases may be, in part, due to the amount of iodine in the Russian diet, a characteristic iodine-poorest diet. A 48-year-old Caucasian woman of Eastern-European descent, who lived approximately 100 miles from Chernobyl during the 1986 nuclear reactor accident, presented with an enlarging neck mass in 2006 (Figure 85). Histologic examination of the tumor showed a very distinct and well-formed, solid-type papillary carcinoma, which merged almost imperceptibly with anaplastic areas. There appears to be a variable period between the time of radiation exposure and the onset of papillary thyroid carcinoma in Chernobyl victims, and a significant number of cases are occurring in individuals who were children at the time of exposure. With the increase in world travel, Chernobyl victims may be encountered in a variety of nations outside the former Soviet Union. Therefore, when presented with a papillary thyroid carcinoma, one must take a thorough history, including nation of origin, to investigate a possible association with the Chernobyl accident.

Evaluation of Microsatellite Instability in Mucoepidermoid Carcinoma
(Poster No. 17)

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Context: Microsatellite instability (MSI) is a replication/repair genetic error resulting from aberrations in the following mismatch repair genes: MLH1, MSH2, MSH6, and PMS2. The most commonly involved genes are MLH1 and MSH2. MSI has been detected in both hereditary and sporadic tumors, including colorectal, pancreatic, gastric, and endometrial adenocarcinomas. Studies addressing the role of MSI in mucoepidermoid carcinogenesis (MEC) are limited. We aimed to determine whether MSI contributed to the pathogenesis of MEC.

Design: Subjects consisted of 12 patients who underwent surgical resection for primary MEC of the parotid gland. Hematoxylin-eosin–stained slides were reviewed for confirmation of diagnosis. A section containing malignant and nonneoplastic salivary gland tissue was selected from each case. Three 5-μm, unstained sections were obtained from the corresponding formalin-fixed, paraffin-embedded tissue blocks. DNA was extracted from microdissected tumor and normal tissue. Five mononucleotide loci (BAT26, NR21, NR24, BAT25, NR22) were amplified in 2 multiplex polymerase chain reactions using fluorescently labeled primers. Products from polymerase chain reaction were subjected to capillary electrophoresis on an ABI Prism 3100 Genetic Analyzer (Applied Biosystems Inc., Foster City, California) followed by fragment analysis using Genotyper 4.0 software (Applied Biosystems, Inc.). Tumor and matched normal tissue were compared at each locus to determine instability.

Results: MSI was not present in 12 of 12 primary MECs of the parotid gland.

Conclusions: This preliminary study suggests that replication error is an unlikely mechanism in the pathogenesis of MEC. A larger cohort study using additional methods to determine MSI will be necessary to determine its potential involvement in MEC.

Improved Frozen-Section Diagnosis of Mucormycosis
(Poster No. 18)

Harvey E. Sasken, MD1 (hsasken@gmail.com); Rita Roure, MD2; Ronaldo Zamuco, MD; Amy Paul, MD3. Departments of Pathology and Otolaryngology, Lincoln Medical Center, Bronx, New York.

Context: Acute fulminant fungal rhinosinustis caused by Mucor is a not-uncommon, life-threatening infection that is associated with poorly controlled diabetes, ketoacidosis, or immunosuppression. Characteristically, it invades blood vessels and rapidly spreads along nerves and across tissue planes to involve the orbit or the brain. The reported mortality rate is approximately 50%. Immediate diagnosis by frozen section has been suggested as an aid in rapidly instituting appropriate therapy. Frozen sections cut at 5 to 10 micra reveal only small fragments of fungal organisms. If the organisms fragments are identified, the diagnosis is established; however, because they may be difficult to identify, there is a strong potential for a false-negative diagnosis. The addition of a rapid Wright stain (Poly Scientific, Bay Shore, New York) or metachromatic stain on a touch preparation reduces this danger.

Design: Four cases of suspected mucormycosis were submitted for diagnosis using hematoxylin-eosin–stained frozen sections that were cut at 5 micra. The specimens consisted of a debridement of necrotic tissue. They were examined by routine frozen sections that were hematoxylin-eosin–stained and cut at 5 micra and by touch preparations stained with either a metachromatic or rapid Wright stain.

Results: The touch preparations revealed easily identifiable, large, unbroken masses of fungal elements. The routine frozen sections showed fragments of fungus with their association with the blood vessels and native tissues preserved.

Conclusions: The use of routine frozen section (hematoxylin-eosin) and touch preparations (rapid Wright or metachromatic stain) provides the necessary criteria for the diagnosis of mucormycosis and reduces the danger of a false-negative diagnosis.
Calciﬁng Epithelial Odontogenic Tumor: A Case Report and Review of Literature (Poster No. 19)

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Pindborg tumor is a rare, benign lesion that represents fewer than 1% of all odontogenic tumors. It presents in adults ranging in age from 30 to 50 years. Most tumors are located in the posterior mandible often with an impacted molar tooth. These lesions are locally aggressive with a tendency to recur. We describe a 53-year-old man who presented with complaints of an intraoral mass growing for 4 months. Clinical examination showed a 3 × 4-cm, tender, nonulcerated mass in the right upper quadrant of the mouth between the third and fourth teeth. The overlying mucosa was extensively erythematous. The i-CAT imaging (Imaging Sciences International, Hatﬁeld, Pennsylvania) revealed it to be of mixed radiolucent and radiopaque density. The patient underwent biopsy and subsequently surgical resection of the mass. Gross examination revealed a 2.5 × 2.3 × 1.1-cm, tan mass with a homogenous, calcified, tan cut surface. Microscopic examination (Figure 86) showed strands of polyhedral epithelial cells with distinct cell borders within a ﬁbrous stroma. Liesegang ring calcifications were present throughout the diffuse areas of amyloid-like material that were fused, forming large masses. Congo-red stain revealed these to be pools of amyloid-exhibiting, apple-green birefringence when viewed under a polarized light. The histopathology, cytologic, and radiologic features are discussed. As much as this is a benign tumor, some have been documented as having invasive features, and one has been reported to have metastasized to a lymph node. These possibilities warrant attention to histologic detail.

Merkel Cell Carcinoma of the Oral Cavity: An Entity Distinct From Mucosal High-Grade Neuroendocrine Carcinoma? (Poster No. 20)

Paul Klonowski, MD (pklonowski@path.wustl.edu); Eric Duncavage, MD; J. S. Lewis Jr, MD. Department of Pathology and Immunology, Washington University School of Medicine, St. Louis, Missouri.

Context: Merkel cell carcinoma (MCC) and high-grade neuroendocrine carcinoma (HGNEC) are rare tumors with similar morphology, arising in sun-exposed skin or upper aerodigestive tract, respectively. Several publications report cases of oral cavity MCC (excluding the lips), whereas others describe oral cavity HGNEC. No one has attempted to distinguish these 2 entities.

Results: From our files, we identiﬁed 12 primary head and neck MCC and 15 mucosal HGNEC cases. We reviewed hematoxylin-eosin morphology and performed immunohistochemistry for cytokeratin 20 (CK20), thyroid transcription factor 1, p63, neuroﬁlament, and achaete-scute complexlike 1.

Results: With hematoxylin-eosin staining, 87% HGNEC cases showed angulated nuclei with molding and crush artifact, whereas only 13% showed round, regular nuclei with ﬁne chromatin. MCC cases were split, with 50% showing angulated nuclei, and the other 50% showing round, regular nuclei. See Table for immunohistochemistry results. One case, previously diagnosed as tongue HGNEC, was CK20– and negative for thyroid transcription factor 1. It showed the classic “dotlike,” perinuclear CK20 staining that is associated with MCC. Its nuclei were round with ﬁne chromatin, which is also seen more commonly in MCC. It was negative for neuroﬁlament and thyroid transcription factor 1.

Conclusions: Based on these ﬁndings, this tongue tumor likely represents a true MCC of the oral cavity, which may be a distinct primary oral cavity malignancy that must be considered in the differential diagnosis of HGNEC. Nuclear features, CK20, neuroﬁlament, and thyroid transcription factor 1 immunostains may be helpful in making this distinction. Despite previous reports, we found achaete-scute complexlike 1 not to be discriminatory.

<table>
<thead>
<tr>
<th>Immunohistochemistry Staining Results</th>
<th>MCC, No. (%)</th>
<th>HGNEC, No. (%)</th>
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<tbody>
<tr>
<td>Thyroid transcription factor 1</td>
<td>0 (0)</td>
<td>5 (33)</td>
</tr>
<tr>
<td>Cytokeratin 20</td>
<td>11 (92)</td>
<td>3 (20)</td>
</tr>
<tr>
<td>Neuroﬁlament</td>
<td>8 (67)</td>
<td>2 (13)</td>
</tr>
<tr>
<td>Achaete-Scute complexlike 1</td>
<td>11 (92)</td>
<td>12 (80)</td>
</tr>
<tr>
<td>p63</td>
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<td>12 (80)</td>
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</table>

Clinicopathologic Correlation and Microvascular Density Counts in Sinonasal Melanomas (Poster No. 21)

Elizabeth Kerr, MD (ehanson@uab.edu); Omar Hameed, MD; Alfred Bartolucci, PhD; Dezhi Wang, MD; Nasser Said-Al-Naief, DDS, MS. Departments of Pathology and Biostatistics, University of Alabama, Birmingham.

Context: Microvascular density (MVD) in cutaneous malignant melanomas has a signiﬁcant negative correlation with survival; however, this has not been well-studied in mucosal melanomas. This study evaluated MVD in relation to the clinicopathologic features and survival in sinonasal melanomas.

Design: The clinicopathologic features of 7 cases of primary sinonasal melanoma were reviewed. MVD was evaluated in each case by immunostaining with CD31 antibody (Dako, Glostrup, Denmark) and by using Bioquant Image Analysis software (R&M Biometrics, Nashville, Tennessee). We examined the relationship between the MVD and various clinicopathologic features.

Results: We have evaluated 7 cases to date, including 5 men and 2 women, ranging in age from 52 to 81 years (mean, 66 years; median, 70 years). Nasal obstruction was the most common presenting symptom (83%). The most common histologic patterns were spindle and epithelioid. One patient died in the immediate postoperative period. After a median follow-up period of 36.5 months (range, 6 to 93 months), all remaining patients developed recurrences and/or distal metastasis, and except in the case of one patient, they died of disease. The MVD of the tumors ranged from 31.2 to 732 vessels/mm² (mean, 207.7 vessels/mm²). There was no signiﬁcant correlation between the MVD and various clinicopathologic features seen within the tumors, including histologic pattern, mitotic counts, extent of necrosis, and vascular invasion. Neither MVD nor any of these features could predict a particular outcome.

Conclusions: Although the ﬁndings conﬁrm the aggressive nature of sinonasal melanoma, predictive factors remain to be determined. Accrual of additional cases and further evaluation is ongoing.

Fine-Needle Aspiration Diagnosis in a Case of Follicular Dendritic Cell Sarcoma (Poster No. 22)

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Follicular dendritic cell (FDC) sarcoma is a rare, neoplastic proliferation of follicular dendritic cells. Although the histopathology and immunophenotype have been fairly well characterized, FDC sarcoma remains underrecognized, and one-third of extranodal cases are initially misdiagnosed. Cytology features of FDC sarcoma have been reported in only 4 cases. A 24-year-old woman presented with a painless neck mass of a few weeks’ duration. Physical examination revealed a deeply located, firm, 3.0-cm mass in the right posterior neck. Diff-Quik–stained slides showed many large, oval- to spindle-shaped neoplastic cells singly or in loosely

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and has not been previously reported in a setting of CLL/SLL treated biopsy showed monomorphic, large plasmacytoid cells with frequent apoptosis and focal necrosis. These large cells expressed dim CD45, CD138, and EBV–EBNA-2 and were negative for CD20, CD79a, Pax-5, and T-cell antigen markers. Proliferation index was 90%. Although EBV–LMP-1 and MUM-1 and were negative for CD20, CD79a, Pax-5, and T-cell antigen markers, we saw no atypia, mitoses, necrosis, or osteoid formation. This tumor was classified as chondroblastoma-like chordoma of soft tissue. During the 3-month follow-up period, the patient had no recurrence. Pathologists should be aware that chondroblastoma-like chordoma may occur in the base of the skull and that this lesion should be differentiated from other benign or malignant tumors arising in this area.

Experience With Voice Recognition in Surgical Pathology at a Large, Academic, Multi-Institutional Center (Poster No. 25)

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Context: There are few reports of institutional use of voice recognition technology in clinical practice. We have used voice recognition-integrated synoptic-like dictation, associating templates with key spoken phrases, in gross examination of common specimens and as a major component of our workflow since 2001.

Design: The sites include 5 hospitals and the dental school. The primary application is VoiceOver Enterprise (Voicebrook, Inc., Lake Success, New York), which uses Dragon NaturallySpeaking Medical Edition as its speech engine. Hardware requirements are reasonable, and orientation is simple. Dictation can be performed naturally at speeds of 160 words per minute. The dictionary exceeds 260,000 words and has more than 60,000 medical terms and phrases. The Voicebrook module integrates with the Anatomic Pathology Laboratory Information System (AFLIS) and other applications, such as Microsoft Office.

Results: Eighty users (48 pathology assistants, 12 residents, and 20 attending doctors) have access to the Voicebrook module. Of these, 15 to 25 use it at any one time. The largest user group, pathologists assistants, mainly dictate biopsies, using templates for dermatology; transplant; dental; gastrointestinal; ears, nose, and throat; gynecology; and nongynecology. Since 2001, this includes approximately 210,000 specimens.

Conclusions: Despite the start-up cost, we have had a good return on investment, including improvements in turnaround time, results standardization, and cost savings. The most helpful features of the software have been templating, which incorporates departmental reporting standards and reduces editing and correction of reports, the seamless integration with the AFLIS, and the voice command creation tools. Voice recognition technology has been useful in our anatomic pathology workflow.

Enhancing Pathology Research: Expanding the Search for Specimens With a Common Biorepository Model (Poster No. 26)

Jan M. Fore, DPhil; Anna T. Fernandez, PhD (fernandez.anna@bhab.com); Juergen A. Klenk, PhD; Andrew W. Brochak, BA; Elizabeth K. Prince, BS. 1Center for Bioinformatics and Information Technology, National Cancer Institute, Rockville, Maryland; Departments of 2Civil Health...
and Modeling, Simulation, Wargaming, and Analysis, Booz Allen Hamilton, Rockville; Sapient Corporation, Arlington, Virginia.

**Context:** Pathology researchers often use locally obtained specimens because there is no easy way to search for and locate specimens outside a laboratory or institution. The ability to aggregate similar specimens from various sites would expand the validation of pathology research findings and more quickly affect patient care. The Common Biorepository Model (CBM) is an information model that interfaces with systems by sharing key specimen information, enabling a single search across multiple biobanks. The goal is to reduce the time and effort required by researchers to locate a biobank that has needed specimens. This model is part of the National Cancer Institute's cancer Bioinformatics Grid initiative to develop methods and models to support and fast-track research.

**Design:** With a CBM, data fit a standardized, simple domain model to promote sharing. CBMs can define infrastructure and enable a dynamic and continuously updated repository that serves its users. As data are exchanged using a CBM, the documentation and quality of biomaterials improve.

**Results:** Representatives of biobanking software vendors and the National Cancer Institute stakeholders convened to develop CBM 1.0. Currently, CBM 1.0 is an evolving, searchable catalog of basic specimen information that is simple, mutually understood, and community supported. By establishing a new system-independent model, the team seeks to gain the widest possible adoption through consensus.

**Conclusions:** CBM provides an information model that has been developed with researcher and vendor input to enable high-level sharing of specimen information that could speed up research efforts; CBM is also an example of interoperability efforts in the community.

**Media-Enhanced Reporting**

(Poster No. 27)

Daniel J. Cowden, MD (Daniel.Cowden@yahoo.com); Dave Romer, BSEE; Peter C. Kolbeck, MD. Department of Pathology, Path Logic, Carmichael, California.

**Context:** Information enthusiasts continue to profit the benefits of virtual microscopy and whole-slide imaging; however, in practice, this type of virtual microscopy has not come to full fruition. Perhaps video streaming, a simple technology for viewing digitized slides, is more feasible. To date, no study has compared these 2 technologies and how they can be effectively used in pathology reporting systems. In this study, the use of these technologies in pathology reporting systems was designated media-enhanced reporting.

**Design:** Using data extracted from Aperio ScanScope (Aperio Technologies, Inc., Vista, California) and CamStudio, we compared whole-slide imaging and audio/video streaming by marginal-cost curve analysis, production times for AVI media files (Aperio ScanScope and CamStudio) and XML annotation (Aperio), and number of hits generated for each URL-hyperlink. Finally, a user opinion poll was collected.

**Results:** Video streaming had significantly lower start-up costs than whole-slide imaging; however, both had similar hardware and storage requirements. Neither technology had a sustainable business model; however, video streaming was the preferred media based on opinion polls (90%). Video streaming was preferred for 3 reasons: (1) 85% of clinicians preferred an audio-guided video review of the diagnosis versus annotations, (2) 100% of clinicians considered video streaming a more familiar technology, and (3) 70% of clinicians preferred that all diagnostic information be presented to them on the same report (media-enhanced reporting).

**Conclusions:** Neither form of digital imaging has a sustainable business model; however, video streaming may be a better solution for digital imagery than whole-slide imaging.

**Use of Telepathology Technology in Computed Tomography–Guided Biopsy Specimen Evaluation**

(Poster No. 28)

Mark W. Nelson, DO (nelsonma@summa-health.org); Cherie R. Hart-Spicer, MD; Amy H. Derken, MD. Department of Pathology, Summa Health System Akron City Hospital, Akron, Ohio.

**Context:** The use of telepathology systems has been evaluated in routine practice and in intraoperative consultation for histology specimens. We assessed the utility of real-time telepathology in determining the adequacy of cytology fine-needle aspiration biopsy specimens.

**Design:** Residents prepared and evaluated slides for microscopic adequacy. We used the Olympus America, Inc. (Center Valley, Pennsylvania) telepathology system. A pathologist accessed live images of the microscopic images as seen by the resident. The pathologist recorded adequacy and diagnostic impressions based on the live digital images and light microscopy. After routine processing, a final diagnosis was rendered. The efficacy of the telepathology system was analyzed using 3 categories: Adequate vs Not Adequate for Diagnosis, Benign vs Malignant, and Change in Diagnostic Category.

**Results:** We made 61 touch preparations and 156 smears using aspirated materials and core biopsies from 150 cases. The Adequate vs Not Adequate category had 170 determinations, with 165 (97%) showing no change. The remainder changed from Not Adequate to Adequate. We analyzed 91 cases in the Benign vs Malignant category; 77 (85%) of these showed no change from the initial telepathology images to the final diagnosis. We analyzed 91 cases for Change in Diagnostic Category; 68 (75%) of these showed no change from the preliminary telepathology images to the final diagnosis.

**Conclusions:** The telepathology system demonstrated high concordance between digital images and light microscopy in adequacy determination, confirming that the system is useful for remote adequacy determinations. However, the diagnostic capabilities were suboptimal, possibly because of image quality or the inherent limitations of cytology.

This research was supported by a College of American Pathologists Telepathology Grant, which was purchased with the Olympus of America (Center Valley, Pennsylvania) equipment.

**Genetics Café: A Web-Site Consortium for Genetic Information**

(Poster No. 29)

Elizabeth Howe, MPH (bhowe@access-genetics.com); Ronald McGlennen, MD. Department of Research, Access Genetics, Minneapolis, Minnesota.

**Context:** Molecular diagnostic testing is a growing field that lacks standard methodologies; consequently, test results may vary between different laboratories and test platforms, and no central database exists to compare results of population-level analyses. Access Genetics provides expertise in molecular diagnostic operations and test interpretation through an integrated Web portal, which includes tools for abstracting and correlating analytic results from distinct laboratories and testing technologies. Genetics Café is a Web database designed to facilitate comparisons of real-time genetic data on a population level.

**Design:** Access Genetics has developed an interactive Web site using web-based widgets; abstractions of analytic results can be used to compare one laboratory’s findings to the cumulative group results. The Web site, Genetics Café, presents real-time displays of these data, including features for uploading adjunctive demographic and anatomic test results to create a consortium of genetic information.

**Results:** The Web site is designed as a series of laboratory widgets that are compiled from results obtained from more than 75 laboratories and one million tests. One featured widget set compares the analytic performance of 3 human papillomavirus (HPV) test platforms, including findings from more than 50 clinical laboratories using genotype-specific HPV detection, a geographic HPV-type heat-map (Figure 88), and a normalized HPV use rate based on common clinical HPV testing patterns.

**Conclusions:** Genetics Café is a unique way to compare genetic-testing information and to improve the quality of clinical test results. Advantages include interlaboratory, interplatform, morphologic, and molecular correlations. This Web site adds value for researchers and the industry.
Laboratory Information System-Based Synoptic Reporting Tool for Genitourinary Cancer Resection Specimens: A 6-Year Experience With More Than 3700 Specimens (Poster No. 30)

Shveta Hooda, MD (drshveta@gmail.com); Anthony Piccoli, BS; Anil V. Parwani, MD, PhD. Department of Pathology, University of Pittsburgh Medical Center, University of Pittsburgh, Pennsylvania.

Context: Cancer checklists comprising standardized data elements are valuable tools that clinicians can use for guidance in managing patients. We describe our experience with the use of the Synoptic Worksheet entry tool for genitourinary cancer resections and also describe the use of synoptics in providing reports in our clinical environment of multiple academic and community-based oncology programs.

Design: We used a synoptic reporting tool as part of our existing laboratory information system, CoPathPlus, from Cerner DHT Corp. We modified the College of American Pathologists’ checklists into worksheets for select genitourinary organ system malignancies. The synoptics have been in use for 40 months in our laboratory information system. The data were present as discrete data elements. A data element, that is, tumor type, is in the value dictionary under the value of tumor type, allowing users to search for cases that have that value point populated.

Results: A total of 3736 genitourinary resection specimens in our network had a synoptic report completed. Prostate (n = 2811), kidney (n = 833), urinary bladder (n = 281), kidney pelvis (n = 110), testsis (n = 86), ureter (n = 34), and penis (n = 11) were the most used templates in the system. See Table.

Conclusions: Use of the new synoptic report enables quicker access to information and improves communication for cancer management. Such uniformity lends itself to ease of data viewing and extraction, as demonstrated by rapid production of standardized, high-quality data from these genitourinary cancer resection specimens.

<table>
<thead>
<tr>
<th>Organ</th>
<th>Total Worksheets, No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prostate</td>
<td>2381</td>
</tr>
<tr>
<td>Kidney</td>
<td>833</td>
</tr>
<tr>
<td>Urinary bladder</td>
<td>281</td>
</tr>
<tr>
<td>Kidney pelvis</td>
<td>110</td>
</tr>
<tr>
<td>Testsis</td>
<td>86</td>
</tr>
<tr>
<td>Ureter</td>
<td>34</td>
</tr>
<tr>
<td>Penis</td>
<td>11</td>
</tr>
</tbody>
</table>

Mycobacterium Vertebral Osteomyelitis in a Patient With a History of Bacillus Calmette-Guérin Intravesical Therapy (Poster No. 31)

Hannah H. Wong, MD (thwong@llu.edu); Anwar Raza, MD. Department of Pathology and Laboratory Medicine, Loma Linda University Medical Center, Loma Linda, California.

Bacillus Calmette-Guérin (BCG) intravesical immunotherapy using Mycobacterium bovis has been used in the treatment of low-grade bladder tumors since the 1970s. Complications are generally limited to cystitis, fever, hematuria, and prostatitis. Cases of Mycobacterium bovis vertebral osteomyelitis following BCG therapy are rare, with fewer than 10 cases reported in the literature. A 79-year-old man presented with vertebral osteomyelitis 14 years after a diagnosis of bladder cancer and BCG therapy. He had received a 1-month course of dexamethasone for idiopathic thrombocytopenia a month prior, and he subsequently developed leukocytosis. Magnetic resonance imaging revealed multiple paraspinal abscesses and a 5.2 x 0.9-cm abscess in the T11 to T12 disk space. He rapidly developed paraplegia requiring decompression laminectomy. Microscopic examination revealed an acute and chronic necrotizing granulomatous inflammation with acid-fast-positive bacillary forms. Cultures revealed acid-fast bacilli, which were identified as Mycobacterium tuberculosis complex organisms using the Gen-Probe (San Diego, California) Amplified Mycobacterium Tuberculosis Direct test. The organisms identified by this method are Mycobacterium tuberculosis, Mycobacterium bovis, Mycobacterium bovis BCG, Mycobacterium africanum, Mycobacterium microti, and Mycobacterium canetti. Standard mycobacterium therapy was initiated, and further speculation was not pursued. Despite therapy, the patient remains a paraplegic and in critical condition. Careful review of his clinical history revealed no other Mycobacterium exposures, favoring the possibility of Mycobacterium bovis osteomyelitis secondary to BCG therapy. Vertebral osteomyelitis due to acid-fast bacilli is a rare entity and should be considered in patients with a history of intravesical BCG therapy because early therapy may significantly reduce complications.

Chronic, Recurrent Epiglottitis in a Young Adult With Actinomyces israelii Infection (Poster No. 32)

Anna Castiglione Richmond, MD (neuron7777@yahoo.com); Michael G. Swaby, MD; Audrey Wangen, PhD; Marylee M. Kott, MD. Department of Pathology, University of Texas, Houston.

Actinomyces israelii is a common inhabitant of the oral cavity. This gram-positive microorganism is normally nonpathogenic, but there have been reported cases in which an infection ensued at the site of injury following a traumatic insult to the oral mucosa. Rarely, this microorganism can cause a chronic infection to a nontraumatized part of the oral cavity. These rare occurrences have been described in immunocompetent patients who are older than 60 years but not in young adults. We present a case of a 34-year-old, immunocompetent woman with good dental hygiene who presented twice at our institution within a 2-month period. She had shortness of breath, a sore throat, and dysphagia related to both solids and liquids. Her symptoms had progressively worsened during several weeks. During both hospitalizations, the patient was admitted to the intensive care unit and required intubation because of severe epiglottitis swelling and airway compromise. A biopsy from the base of the tongue was obtained during the second hospitalization. Actinomyces was seen on the hematoxylin–eosin–stained slide and was further confirmed by Grohomi methemamine–silver stain. The patient was treated with intravenous penicillin. The infection resolved, and the patient continues to remain asymptomatic. Nontraumatic, chronic epiglottitis due to an Actinomyces infection is a rare occurrence in young women. To the best of our knowledge, such a presentation in a young woman has not been previously described. We conclude that physicians should be aware of, and have a high degree of suspicion regarding, this atypical presentation of Actinomyces.

Is the QuantiferON TB Gold In-Tube Method a Good Replacement for the Tuberculin Skin Test in Tuberculosis Screening: A Pilot Study at Berkshire Medical Center (Poster No. 33)

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Context: QuantiferON TB Gold In-Tube method (QFT-GIT, Cellestis, Inc., Valencia, California) is an interferon-γ release assay that was recently approved by the US Food and Drug Administration to detect tuberculosis infection, which has been screened for using a tuberculin skin test (TST) for nearly a century. We report a pilot study comparing the QFT-GIT and TST results in screening health care workers at Berkshire Medical Center, the second hospital in Massachusetts to employ QFT-GIT.

Design: We screened 40 health care workers at Berkshire Medical Center using the QFT-GIT test. Of the 40 workers, 20 had TST-positive results, and 20 had TST-negative results.

Results: All 20 subjects with TST-negative results also had QFT-GIT-negative results, whereas only 10 of 20 subjects with TST-positive results also had QFT-GIT-positive results. The overall agreement between the QFT-GIT and TST results was 75% (κ value = 0.5; 95% confidence interval, 0.268–0.732).

Conclusions: The suboptimal agreement was partially due to a higher specificity of QFT-GIT. Confounding factors (eg, bacillus Calmette-Guérin vaccination status and birthplace) are discussed, and literature regarding interferon-γ release assays in comparison to TST is reviewed in detail.

Human Pythiosis in a Bone Marrow Transplant Recipient (Poster No. 34)

Anjali S. Godambe, DO1 (agodambe@lumc.edu); Brian Nickoloff, MD, PhD; J. P. O’Keefe, MD2; Sherril Yong, MD.1 Departments of Medicine and 2Infectious Diseases, Loyola University Medical Center, Maywood, Illinois.

Pythium insidiosum is an aquatic pseudofungus belonging to the class Oomycetes. Pythium rarely causes human infection but has been reported in animals. We describe a case of human pythiosis in an immunocompromised patient. A 52-year-old man with acute lymphocytic leukemia had undergone allogeneic hematopoietic stem cell transplantation 6 months before admission. He presented with a complicated soft tissue infection of the right lower extremity after having sustained trauma from...
striking his leg on the edge of a chlorinated swimming pool. The wound appeared as multiple indurated nodules. After surgical debridement, the infected tissue was sent for culture and pathology. The surgical pathology revealed extensive epidermal erosion with superficial and deep perivascular inflammation, necrosis, and hemorrhage. In tissue sections, the organisms appeared as hyaline, pauci-septate hyphae (6–7 μm wide). There were some branching forms; these, however, were infrequent. The organism stained strongly with Gomori methenamine-silver and was also positive with periodic acid–Schiff (Figure 89). The hyphal forms were scattered throughout the mid and deep dermis, as well as in deep dermal blood vessels. Tissue cultures grew a septate hyphal organism that failed to sporulate on traditional media. Fluorescent anti–Pythium insidiosum staining positively identified the organism. Western blot analysis on the patient’s serum sample positively detected all Pythium insidiosum antigens.

We describe the first case of cutaneous human protothcois occurring in a patient with acute lymphocytic leukemia 6 months after allogeneic hematopoietic stem cell transplantation.

Human Protothecosis: Lethal, Disseminated Infection by 
Prototheca zopfii in a Pediatric Patient With Leukemia
(Poster No. 35)

Adelina T. Luong-Player, MD 1 (tluong@uci.edu); Stephen G. Romansky, MD 1; Departments of Pathology, University of California, Irvine, Orange; 2Department of Pathology, Long Beach Memorial Medical Center, Long Beach, California.

Prototheca species, or achlorophyllic algae of the genus Prototheca, have rarely been identified as causative agents in lethal human infections. Of the few reported cases of disseminated protothecosis, only 2 were due to Prototheca zopfii, and both were in adult posttransplant patients. We report a case of a lethal, disseminated infection by Prototheca zopfii, causing multisystem organ failure in a 9-year-old boy with no transplant history, as a complication of treatment for acute T-cell lymphoblastic leukemia. A full autopsy was performed. Tissues from lung abscesses were submitted for culture, and organs were studied by light and electron microscopy and by histologic and immunohistochemical staining methods. Experienced pathologists reviewed slides, stains, cultures, and electron microscopy. Prototheca zopfii was speciated from blood, and its identity was further confirmed by a national reference laboratory. Tissue cultures also grew Prototheca. Microscopically, these organisms consisted of sporangia-containing endospores, some arranging into morula formations, admixed with nonendosporulating cells (Figure 90). The cells of Prototheca were positive for standard histologic stains commonly used for fungal organisms. Electron microscopy revealed dense granules and needle-shaped structures, which are typically found in Prototheca. Cytomegalovirus and Aspergillus were also identified. In conclusion, disseminated protothecosis is an uncommon but deadly infection in humans that is caused by a group of algae of the genus Prototheca. Immunocompromised individuals are most susceptible to systemic protothecosis and are more likely to be infected with other organisms. In this case, the extensive damage to multiple organs speaks to the potential lethality of infection by Prototheca zopfii.

Increased Prevalence of Antimicrobial-Resistant Organisms in Urinary Tract Infections in Patients at Long-term Care Facilities
(Poster No. 36)

Rita H. Khoury, MD (rkhoury@aculabs.com); Shakira Gibbs, BS; B. P. Salmon, MS; Asha Gandhi, BS; Peter Gudaitis, BS; Dauna Gudaitis, BS. Aculabs, Inc., East Brunswick, New Jersey.

Context: Urinary tract infection is the most common bacterial infection in the elderly. The emerging thread of the antimicrobial-resistant organism is making it a major health problem, especially in long-term care facilities where it is associated with higher mortality rates and longer hospital stays.

Design: We collected 2805 specimens (1184 from 2007 and 1621 from 2008) for urine cultures from residents in long-term care facilities. The cultures were done using MicroScan Walkaway96 conventional panels. No growth or fewer than 10000 colony-forming unit (CFU)/mL were considered negative. Cultures with more than 50000 CFU/mL were considered positive. If a specimen was collected from a catheter, any growth was considered positive. The positive cultures were segregated further by the isolated organisms.

Results: More than 70% of the patients were women (72.3% in 2007 and 73.9% in 2008). Of the total number of cultures, 46.5% and 55.0% were positive in 2007 and 2008, respectively; the large increase was mostly among male patients. Of the positive cultures, 13.27% in 2007 and 15.7% in 2008 were drug resistant. No changes were observed in the methicillin-resistant Staphylococcus aureus during the test period (Table).

Conclusions: Urinary tract infection occurs at a high rate in the elderly; the prevalence of antimicrobial-resistant organisms is increasing among residents in long-term care facilities. Although many believe that methicillin-resistant Staphylococcus aureus and vancomycin-resistant enterococci are more common, we found that cases of extended-spectrum β-lactamase account for more than 60% of multidrug resistance. This finding indicates that nursing homes or acute care settings are a reservoir for cases of extended-spectrum β-lactamase.

<table>
<thead>
<tr>
<th>Urine Culture Results</th>
<th>Women, 2007, %</th>
<th>Women, 2008, %</th>
<th>Men, 2007, %</th>
<th>Men, 2008, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total positive</td>
<td>49.07</td>
<td>56.84</td>
<td>39.63</td>
<td>49.88</td>
</tr>
<tr>
<td>Total drug resistant</td>
<td>12.62</td>
<td>14.39</td>
<td>15.35</td>
<td>19.91</td>
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<tr>
<td>Extended-spectrum β-lactamase, %</td>
<td>6.90</td>
<td>8.22</td>
<td>11.54</td>
<td>12.80</td>
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<tr>
<td>Methicillin-resistant Staphylococcus aureus, %</td>
<td>1.90</td>
<td>1.76</td>
<td>1.54</td>
<td>1.42</td>
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<tr>
<td>Multidrug resistance, %</td>
<td>2.38</td>
<td>1.76</td>
<td>1.54</td>
<td>3.79</td>
</tr>
<tr>
<td>Vancomycin-resistant enterococci, %</td>
<td>1.43</td>
<td>2.64</td>
<td>0.77</td>
<td>1.90</td>
</tr>
</tbody>
</table>
Blood Culture Contamination in Long-term Care Facilities
(POSTER NO. 37)
Rita K. Khoury, MD (rkhoury@aculabs.com); Shakira S. Gibbs, BS; Asha Gandhi, BS; B. P. Salmon, MS; Peter Gudaitis, BS; Dauna Gudaitis, BS. Aculabs, Inc., East Brunswick, New Jersey.

Context: Blood cultures are among the most important tests performed in the laboratory for the diagnosis of serious infection; and because clinicians rely on culture results to diagnose and monitor their patients, contaminated blood cultures are as important as positive cultures. They are, however, very costly and, at times, confusing for physicians.

Design: We received 438 sets of blood cultures from residents in long-term care facilities during February 2009. Every set included 2 vials (aerobic and anaerobic). Cultures were analyzed using Microscan WalkAway 96. Positive blood cultures were considered contaminated when one or more of the following organisms were identified in at least one of a series of blood culture specimens: coagulase-negative Staphylococcus species, Propionibacterium acnes, Micrococcus species, viridans streptococci, Corynebacterium species, or Bacillus species.

Results: Twenty-eight of the cultures (6.4%) were positive. The contamination rate was 2.35%; the contaminants represented 35.7% of the positive cultures. Coagulase-negative Staphylococcus species accounted for 80% of the contamination, and Staphylococcus epidermidis was responsible for 60% of the cases. Seventy percent of contaminated cases occurred with patients who were older than 70 years.

Conclusions: The contamination rate for blood cultures was lower than most of the reported rates, which may be due to the extensive training and strict aseptic technique used by our phlebotomists when taking blood specimens. Clinicians should pay attention to the number of blood culture sets that are positive. When more than one culture is positive with the same organism, even if contaminated, it may represent a real disease.

Increased Incidence of Multidrug-Resistant Acinetobacter baumannii Complex in a Midwestern, US, University Hospital
(POSTER NO. 38)
Jeffrey S. Hudson, MD (jeffrey.hudson@utoledo.edu); Victor S. Flauta, MD, Department of Pathology, University of Toledo Medical Center, Toledo, Ohio.

Context: The emergence of multidrug-resistant Acinetobacter baumannii (MDRAB) has recently plagued health care institutions locally and globally. This has greatly challenged current strategies for successfully controlling the spread of this organism.

Design: To improve our understanding of the growth characteristics and extent of MDRAB infection at our institution, a retrospective study of MDRAB-associated wound infections was performed for the period of October 2007 to February 2009. Sixteen patients were identified with MDRAB wound infections. Their growth characteristics and susceptibility profiles were recorded and were compared with data from a year prior.

Results: The susceptibility percentages for MDRAB from the study period versus the year prior were as follows: ampicillin/sulbactam, 12.5% versus 62%; cefepime, 0% versus 25%; ciprofloxacin, 0% versus 33%; gentamicin, 12.5% versus 39%; piperacillin/tazobactam, 0% versus 54%; tobramycin, 31.2% versus 54%; imipenem, 7.1% versus 60%; levofloxacin, 0% versus 34%; and trimethoprim/sulfamethoxazole, 0% versus 33%. Additionally, tigecycline showed 10% susceptibility, 80% intermediate resistance, and 10% full resistance. Colistin showed 75% susceptibility, 8.3% intermediate resistance, and 16.7% full resistance. The mortality rate was 3 of 16 (19%). Many patients (58%) were diabetic or had increased glucose levels at the time of collection. Most isolates (75%) revealed polymicrobial infections, with the most frequent organisms being Enterobacteriaceae (31%), Enterococcus species, and Pseudomonas aeruginosa (19%).

Conclusions: Our data demonstrate a dramatic increase in the incidence of MDRAB. The medical community must facilitate changes in antimicrobial stewardship strategies and implement new control measures to prevent the emergence of pan-resistant Acinetobacter baumannii.

An Unusual Presentation of Focal Myositis With Bilateral Eyelid Swellings
(POSTER NO. 39)
Sonali P. Ayar, MD (sayar@usouthal.edu); Sree Ravula, MD; Jeffrey Sosnowski, MD, PhD; Jack Polski, MD. Department of Pathology, University of South Alabama, Mobile.

Focal myositis is a rare, self-limiting inflammation of skeletal muscle. Fever, fatigue, and arthralgia are the most common symptoms. Most cases are located in the limbs. We report a unique case of myositis involving bilateral eyelid musculature and eyelid swellings. A 31-year-old woman presented with bilateral eyelid swellings and a medical history of fibromyalgia. Clinically, she was diagnosed with dermatomyositis and a bilateral upper eyelid mass. A fine needle aspiration revealed inflammatory cells and T cells. Immunohistochemistry showed a clonal population of T cells with a rearranged TCR alpha/beta chain. The patient’s T-cell population in myositis should not be confused with lymphoma. To our knowledge, this is the second case of focal myositis presenting with bilateral eyelid swellings.

S100-Negative Metastatic Choroidal Melanoma
(POSTER NO. 40)
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The immunohistochemical stain S100 is highly sensitive for metastatic melanoma and is positive in approximately 99% of these tumors. Although very few melanomas are negative for S100, a dispersed, low-grade population of these neoplasms may be undetected. We report a case of S100-negative, metastatic melanoma to the peritoneum in a patient with a history of choroidal melanoma.

Mutations in Exons 12 to 16 of the Janus Kinase 2 Gene Are Rare in JAK2V617F-Negative Chronic Myeloproliferative Neoplasms
(POSTER NO. 41)
Rashmi Kanagal Shamanna, MD (rshaman1@hfhs.org); Lisa Whiteley, BA; Milena Cankovic, PhD; Dhananjay Chitale, MD; Kedar Inamdar, MD, M. D. Anderson Cancer Center, Houston, TX; The University of Texas, MD Anderson Cancer Center, Houston, TX; The University of Texas, MD Anderson Cancer Center, Houston, TX.
PhD. Department of Pathology and Laboratory Medicine, Henry Ford Hospital, Detroit, Michigan.

**Context:** Constitutive activation of tyrosine kinases due to JAK2V617F mutation (exon 14) is central to the pathogenesis of chronic myeloproliferative neoplasms (CMPN). It occurs in 95% of polycythemia vera cases and in other CMPN cases less frequently. Pathogenesis of JAK2V617F-negative polycythemia vera is unclear. Recent studies have identified recurrent somatic mutations in exon 12 of the JAK2 gene. Similar mutations in other exons may contribute to kinase activation. We sought to identify them in patients at our hospital with JAK2V617F-negative polycythemia vera.

**Design:** We analyzed peripheral blood DNA from 46 cases of suspected polycythemia vera by bidirectional direct sequencing of exons 12 to 16 of the JAK2 gene (tyrosine kinase domain). Patients had tested negative for JAK2V617F mutation by polymerase chain reaction. Sequences for each of the exons 12 to 16 were manually analyzed.

**Results:** Sequencing reaction was successful in 36 cases. In one case, we identified a novel exon 13 mutation causing substitution of glycine, a nonpolar amino acid to serine, which is a polar amino acid at position 571 (G571S). Known exon 15 single nucleotide polymorphism (ID rs2290728) between thymine and cytosine were identified in 2 cases. No mutations were identified in exons 12 (novel or previously reported), 14, and 16.

**Conclusions:** We report a previously undescibed exon 13 mutation in a case of JAK2V617F-negative CMPN. Although functional significance remains to be elucidated, this finding may contribute to disease phenotype in similar cases. The low prevalence of the mutations outside JAK2V617F does not warrant routine clinical testing but may be targeted in clinically suspicious JAK2V617F-negative CMPN.

**Microarray-Based Determination of Estrogen Receptor, Progesterone Receptor, and HER2 Expression: TargetPrint**

(Poster No. 42)

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**Context:** A number of interlaboratory comparison studies of hormonal receptor status and HER2 assessment have shown discrepant results. In this study, we assessed the association between mRNA expression, as measured by microarray and immunohistochemistry for estrogen receptor (ER), progesterone receptor, and human epidermal growth factor receptor 2 (HER2) in various hospitals and a reference laboratory certified under the Clinical Laboratory Improvement Amendments, and developed a microarray-based test called TargetPrint.

**Design:** Microarray expression data for ER, progesterone receptor, and HER2 were obtained by hybridizing mRNA isolated from 652 breast carcinomas on custom-made arrays. Tumor HER2 immunohistochemical status was scored as 0, 1+, 2+, or 3+; a tumor was considered HER2+ for status 0 and 1+ and HER2- for status 3+. For 2+ samples, fluorescence in situ hybridization was performed to assess final HER2 gene amplification status.

**Results:** Optimal microarray thresholds for ER, progesterone receptor, and HER2 were determined based on 100 training samples. Readout of ER, progesterone receptor, and HER2 was validated on about 610 independent samples and resulted in accuracies of 94%, 84%, and 96% compared with immunohistochemical scoring with q scores of 0.81 (95% confidence interval [CI], 0.75–0.86) for ER, 0.66 (95% CI, 0.59–0.71) for PR, and 0.85 (95% CI, 0.79–0.90) for HER2.

**Conclusions:** TargetPrint microarray readout of hormone and HER2 receptor status showed strong correlation with immunohistochemistry assessment, especially for ER and HER2. These results indicate the potential for a more objective and quantitative readout of breast tumor hormonal receptor and HER2 receptor status using microarrays.

**Optimum Tissue Type for Cytogenetic Analysis of Products of Conception**

(Poster No. 43)

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**Context:** Chromosomal studies of products of conception (POC) are an important tool in determining cause of pregnancy loss. We explore selecting the appropriate POC tissue types for cytogenetic evaluation. Appropriate selection of tissue will streamline the process of specimen submission, reduce processing time, and reduce reagent/supply costs without compromising patient care.

**Design:** We retrospectively reviewed 100 cases of cytogenetically abnormal POC. Data included tissue type submitted for analysis and final karyotype. Saline expense and reagent/supply costs were also analyzed.

**Results:** We found 8 of 100 cases to have mosaic karyotypes. Of these, one proved to be true confined placental mosaicism with abnormal placenta and normal fetal karyotype. Another case showed mosaicism among the placental tissues. A normal chromosome complement was seen in the cells studied from cultured villi, whereas an individually cultured villi and chorion each showed a low level of mosaicism. In 92 cases, we saw nonmosaic chromosomal abnormalities in all tissue types studied.

**Conclusions:** Because of its viability, villi are the overall preferred tissue for chromosome analysis of POC. Skin is the second choice because unlike amnion, it is from the fetus proper. American College of Medical Genetics, College of American Pathologists, and New York State do not dictate which tissue type is the optimal source from POC for cytogenetic analysis. We currently study all tissue types from placentia, as well as skin, when available. By using villi, we can save a minimum of $81 in salary expense and reagent/supply costs per case without compromising the quality of patient care.

**Microarray Evaluation of Single Nucleotide Polymorphisms Associated With 5-Fluorouracil Toxicity**

(Poster No. 44)

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**Context:** 5-Fluorouracil (5-FU)/capecitabine (its oral prodrug) is considered first-line treatment for colon cancer and is also used as chemotherapy for breast and head/neck carcinomas. Approximately 30% of patients who take 5-FU/capecitabine develop a significant toxic response, which has been associated with single nucleotide polymorphisms (SNPs) in the dihydropyrimidine dehydrogenase gene (DPYD). Other genes, including thymidylate synthase (TYMS) and methylenetetrahydrofolate reductase (MTHFR) may also influence 5-FU/capecitabine response. Pharmacogenetic studies at our institution have demonstrated variations in SNPs of targeted genes, UGT1a1 and VKORC1/CYP2C9, that affect response to irinotecan and warfarin, respectively. We hypothesize that the presence of similar polymorphisms in the DPYD, TYMS, and MTHFR genes can be evaluated using microarrays and may reliably identify patients susceptible to 5-FU/capecitabine toxicity.

**Design:** Using a multiplex microarray detection platform (Infinium 5-FU, AutoGenomics, Inc., Carlsbad, California), we analyzed DNA samples from 25 colorectal cancer patients for specific genetic polymorphisms in DPYD (85T>C, 1590T>C, 1679T>G, and 2846A>T), MTHFR (677C>T and 1298A>C), and TYMS (ins/del TTAAAC in the 3′-untranslated region).

**Results:** SNP genotyping using this microarray technology successfully identified mutations in DPYD, TYMS, and MTHFR of the selected patients. Most patients tested were heterozygous carriers. However, homozygous mutations of TYMS (TS1494A/ins), DPYD (85T>C), and MTHFR (677C>T) were identified in several patients.

**Conclusions:** SNPs in TYMS, DPYD, and MTHFR can be reliably and efficiently detected using microarrays. Pretherapeutic SNP analysis may help design a panel of mutations that is useful in screening 5-FU/capecitabine candidates to minimize severe toxicity, patient morbidity, and cost ineffectiveness.

**Mucolipidosis II With Skeletal or Pacman Dysplasia**

(Poster No. 45)

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Mucolipidosis II or inclusion cell disease is a rare, autosomal-recessive lysosomal trafficking disorder with a high mortality rate before 10 years. The molecular aberrations identified in this condition include mutations in the GNPTAB gene. As a result of the mutation, the lysosomes have a deficiency of multiple hydrolases. If bone abnormalities are also identified, Pacman dysplasia should be considered. We present a case of mucolipi-
dosis II/Pacman dysplasia in a 4-month-old male infant who was born at 30-weeks gestation and who was noted to have dysmorphic facial features, including prominent hypertropic gums. The upper extremities had contractures of the fingers. Radiographic studies showed severe demineralization of the calvarium, long bones, and ribs; brachycephaly; pelvic bone hypoplasia; fractures of the ribs, humeri, femora, and fibulae; and punctate calcifications of calcanei and orbital bones. Gene-sequencing studies showed 2 pathogenic mutations in the GNP1AB gene, both of which were expected to result in a premature stop codon and subsequently in a truncated protein. Autopsy findings showed cardiomegaly with thickened valve leaflets and microcephaly. Collections of positive periodic acid-Schiff, foamy, vacuolated cells were seen in the placenta, liver, and lungs. Positive oil-red-O staining, representing mild lipid deposition, was seen in the liver. Electron microscopy showed membrane-bound lysosomes with osmiophilic dense bodies and fat globules in skeletal muscle, liver, and heart. This case showed an excellent correlation among morphology, immunohistochemistry, electron microscopy, and molecular techniques, such as gene sequencing, in making a conclusive diagnosis of this rare, usually lethal, disorder.

**Homzygous Deletion and Mutation of Exons 5 and 8 of the Fragile Histidine Triad Gene in Differentiated Thyroid Carcinoma**

(Poster No. 46)

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**Context:** Fragile histidine triad (FHIT) gene, which has been isolated in positional cloning, encompasses the most common human fragile site FRAXB at 3p14.2, a region involved in homozygous deletions in a variety of human tumors. It is considered a tumor-suppressor gene that is frequently inactivated in different types of cancer.

**Design:** To investigate the potential role of FHIT gene in thyroid tumorigenesis, we detected homozygous deletion and mutation of exons 5 and 8 of the FHIT gene in 65 cases of differentiated thyroid carcinoma and their matched, noncancerous epithelium by using exon-specific polymerase chain reaction amplification technique and polymerase chain reaction single-stranded conformation polymorphism technique.

**Results:** In differentiated thyroid carcinoma, the rate of homozygous deletion of exon 5 was 20 of 65 (30.8%), and it was related to tumor lymph node metastasis (P < .05). The rate of homozygous deletion of exon 8 was 19 of 65 (29.2%), and it was related to tumor pathologic grade, TNM stage, and lymph node metastasis (P < .05). There was a distinct correlation between homozygous deletion of exons 5 and 8 (P < .01). No point mutation was observed in exon 5 or exon 8.

**Conclusions:** Our results suggest that exons 5 and 8 might be important target regions of deletion in the FHIT gene, and homozygous deletion of exons 5 and 8 might be good biomarkers in evaluating the biologic behavior of differentiated thyroid carcinoma. Point mutation appears not to be an important factor in inactivation of the FHIT gene in differentiated thyroid carcinoma.

**Validation of RNA Stability in Room Temperature–Stored Paraffin Blocks**

(Poster No. 47)

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**Context:** Standard, routinely processed, formalin-fixed, paraffin-embedded tissues are generally unsuitable for recovery of RNA and investigation of gene expression. Alternative fixatives and processing methods have been demonstrated to preserve macromolecules in paraffin-block sections. The stability of the RNA in paraffin blocks stored at room temperature has not been previously documented.

**Design:** Human melanoma cells were inoculated onto a chicken chorioamniotic membrane. After 10 days, the chicken chorioamniotic membrane containing tumor cells was removed, fixed in a molecular-friendly fixative of 80% and 70% ethanol, and processed on a Tissue-Tek Xpress ×120 (Sakura Finetek USA, Inc, Torrance, California), and embedded into paraffin blocks. Four-micron sections were cut for hematoxylin-eosin stains and for the laser-capture microdissection procedure. Unstained tissue sections were used for laser-capture microdissection, followed by total RNA extraction and quantitative real-time reverse transcription-polymerase chain reaction analyses. After a 24-month interval, all steps were repeated on the same tissue blocks, which had been stored at room temperature.

**Results:** Routinely stained sections retained their morphology. Qualitative real-time reverse-transcription–polymerase chain reaction for the housekeeping gene GAPDH showed good-quality RNA. Quantitative real-time reverse-transcription–polymerase chain reaction for the LMA4, ITGB1, ITGB3, MMP2, and RSPA genes demonstrated RNA of good quality that was suitable for gene expression quantification from the initial and 24-month interval experiments.

**Conclusions:** These results demonstrate that good-quality RNA can be extracted from formalin-fixed, microwave-processed tissue sections made from paraffin blocks stored at room temperature for at least 24 months after tissue processing and that this RNA remains suitable for gene expression profiling.

The research for this abstract was supported in part by a grant from Sakura Finetek USA Inc., Torrance, California.

**Copresence of Epstein-Barr Virus and Human Papillomavirus Type 16 in Lymphoepithelioma-Like Carcinoma of the Uterine Cervix**

(Poster No. 48)

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Epstein-Barr virus (EBV) has been reported to play a role in the etiology of lymphoepithelioma-like carcinoma (LELC) of the uterine cervix in Asian women. LELC is rare in the Western world, where it is reported not to be associated with EBV. Human papillomavirus (HPV), however, has been detected in some cases in Western countries. We postulated that EBV varies geographically in the pathogenesis of LELC and that LELC in Western countries may have a different etiology. We studied a case of LELC by molecular method. A 37-year-old African American woman had a hysterectomy because of LELC. Histologically, the tumor was poorly differentiated with a syncytial-like growth pattern and intense lymphocytic background, which is typical of LELC. A paraffin-embedded tumor-tissue block was deparaffinized, and DNA was extracted. Polymerase chain reaction amplifications were performed on the extracted DNA using by using EBV-positive-specific and HPV-negative-specific primers. HPV genotype was further determined by DNA sequencing. EBV and HPV type 16 genomes were detected by polymerase chain reaction. By contrast, in situ hybridization failed to detect EBV or HPV in the tumor block. This negative finding implies that in situ hybridization is either less sensitive than polymerase chain reaction and/or that there is no active viral replication in tumor cells. This is the first reported case of LELC in the Western world in which both EBV and HPV were present. Whether EBV plays a role in the etiology of LELC in Western countries, as it does in the Orient, merits further investigation.

**A Microarray-Based Gene Expression Test for Tumors With Uncertain Origins Using Formalin-Fixed, Paraffin-Embedded Specimens**

(Poster No. 49)

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**Context:** Tumors with uncertain origins represent 5% to 10% of new cancer cases. The Pathwork Tissue of Origin Test is a gene expression test that aids in the diagnosis of tumors with uncertain origins using frozen specimens. It is the first test of its kind to be cleared by the US Food and Drug Administration. We validate a version of the test that works with formalin-fixed, paraffin-embedded (FFPE) specimens.

**Design:** Poorly differentiated and metastatic FFPE human tumor specimens with available diagnoses representing the 15 tissue-of-origin sites on the Origin-FFPE panel were blinded and processed at 2 independent laboratories to generate microarray data files. A prespecified classification model using more than 1500 genes was applied to each data file to yield similarity scores corresponding to the 15 tissues on the test panel. Results were blinded and compared with the available diagnoses.

**Results:** Of specimens processed, 352 of 405 (87%) yielded qualified data files. Based on the top similarity score, the overall agreement with available diagnoses was 89%. Metastatic and poorly differentiated primary specimens showed similar performance. Additionally, an average of 12 of 15 correct calls for each specimen could be ruled out with greater than 99% probability.

**Conclusions:** The large size of this study allows for an accurate estimate...
mate of the confidence of test results for ruling in and ruling out tissues as likely sites of origin. The Origin-FFPE test makes the potential benefits of microarray-based gene expression tests for tumors with uncertain origins available for use with the most common type of histology specimen, FFPE.

An Investigational Prostate Cancer Methylation Assay Shows Predictive Value While Other Clinical Risk Factors Do Not
(Poster No. 50)

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Context: The ProCaM assay detects aberrant methylation in postdigital rectum examination urine of men with prostate-specific antigen values between 2.0 and 10.0 ng/mL. We compared the assay’s predictive performance to that of other clinical risk factors and determined its ability to detect aggressive cancer.

Design: The assay contains 3 methylation markers, GSTP1, RAR\delta2, and APC, and an endogenous control, \beta-actin, in a multiplexed format. This assay was evaluated on postdigital rectum examination urine samples prospectively collected from 185 (74 cancer, 111 noncancer) consenting subjects at 11 clinical sites. We obtained Institutional Review Board approvals. Assay results were not used for patient management.

Results: With univariate and multivariate analyses, the assay was the only significant independent predictor of positive biopsy (Table). The assay’s area under the curve (AUC) value for predicting subjects with positive versus negative biopsy results was 0.73, which was higher than the AUCs for the Prostate Cancer Prevention Trial risk calculator (AUC = 0.55, \( P = 0.01 \)) and for a biomarker consisting of prostate-specific antigen, digital rectum examination result, and age (AUC = 0.60, \( P = 0.02 \)). The assay’s sensitivity was higher (\( P = 0.003 \)) when more than 30% of cores were histologically positive (76%) versus when fewer than 30% were positive (41%). It was also higher (\( P = 0.01 \)) when at least one core was normal with more than 50% tumor (76%) versus no cores with more than 50% tumor (48%).

Conclusions: This assay shows high sensitivity for aggressive prostate cancers. Preliminary data suggest that the ProCaM assay may improve prostate cancer screening algorithms to more efficiently identify men with significant prostate cancer.

Independent Biopsy Predictors

<table>
<thead>
<tr>
<th>Source</th>
<th>Multivariate P Value</th>
<th>Univariate P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
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<td>.63</td>
</tr>
<tr>
<td>Race</td>
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<td>.59</td>
</tr>
<tr>
<td>Digital rectal examination</td>
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<td>.06</td>
</tr>
<tr>
<td>Prostate-specific antigen</td>
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<td>.08</td>
</tr>
<tr>
<td>Previous biopsy</td>
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<td>.07</td>
</tr>
<tr>
<td>Family history</td>
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<td>.28</td>
</tr>
<tr>
<td>Procam</td>
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</tbody>
</table>

Mutational Surrogate for Acidification of Capsaicin Receptor, Transient Receptor Potential Vanilloid 1: Analysis of Influence on Ligand Recognition
(Poster No. 51)

Daniela Mihova, MD (damihova@yahoo.com); Alexandra Czap, BS; Noemi Kedey, MD; Peter M. Blumberg, PhD. Department of Molecular Mechanisms of Tumor Promotion, National Cancer Institute, Bethesda, Maryland.

Context: The transient receptor potential vanilloid 1 (TRPV1) is a non-selective cation channel that is predominantly expressed by peripheral sensory neurons and is known to play a key role in the detection of noxious and painful stimuli. TRPV1 receptors are activated by capsaicin, heat, low pH levels, and endogenous ligands. Previously, it has been reported that VR1 could be strongly activated by acidification of the extracellular milieu. To optimize drug selectivity for TRPV1, we wished to understand how a modeled acidic environment would affect ligand recognition and receptor response.

Design: To model the activity of TRPV1 in a chronic low pH setting, we generated an E600Q-TRPV1 mutant, substituting glutamic acid with glutamine. We created a noninducible system by transient transfection using HEK293 cells. We performed 45Ca2+ uptake functional assays 24 hours after the transfection, comparing the function of wild-type TRPV1 and mutated E600Q toward various full agonists (capsaicin, olvanil) and full antagonists (BCTC, AMG9810).

Results: The results from the 45Ca2+ uptake functional assays for wild-type versus mutated were as follows: capsaicin, partition coefficient (Kd) = 514 ± 77 versus Kd = 123 ± 24; olvanil, Kd = 49.9 ± 9 versus Kd = 136 ± 19; BCTC, inhibition coefficient (Ki) = 1.37 ± 0.28 versus Ki = 2.99 ± 0.1; AMG9810, Ki = 61.4 ± 9.9 versus Ki = 209 ± 20. \( P < .01 \) for all.

Conclusions: In contrast to what has been previously reported, we found that E600Q mutant receptors are less sensitive toward various agonists and antagonists. The explanation is that the receptors become desensitized over time in conditions of low pH stimulation because of either the effect of the environment or leakiness through the receptor.

The research for this abstract was supported in part by the Intramural Research Program of the National Institutes of Health, Center for Cancer Research, National Cancer Institute.

Recurrence of Breast Cancer in Women of Northwestern Mexico
(Poster No. 52)

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Context: We compared recurrence of breast cancer with the expression of estrogen receptor, progesterone receptor, and HER2 in women of northwest Mexico.

Design: This cross-sectional study included 397 cases of breast cancer. Correlation between clinical and pathologic factors, including estrogen receptor, progesterone receptor, and HER2 expression in the primary tumor, and the recurrence of disease were evaluated. Immunohistochemistry for estrogen receptor, progesterone receptor, and HER2 was interpreted; results were considered positive with 10% or higher expression in tumor cells. Variables with differences reaching statistical significance were incorporated into logistic regression analysis to predict the biomarker’s effect in disease recurrence. A value of .05 was considered statistically significant.

Results: The average age was 52 ± 12 years. Recurrence of disease occurred in 23% of patients (95% CI, 19–27; \( P = .001 \)), including 152 of 397 stage II (38%; 95% CI, 33–43; \( P = .035 \)), 201 of 397 estrogen-positive (51%; 95% CI, 46–56; \( P = .007 \)), 170 of 397 progesterone-positive (43%; 95% CI, 38–48; \( P = .076 \)), and 129 of 397 HER2+ (32%; 95% CI, 28–37; \( P = .08 \)) cases (Table). Death due to disease occurred in 15 of 397 cases (3%; 95% CI, 2–21; \( P = .001 \)). Univariate analysis, 9% of recurrences were associated with the expression of estrogen receptors (\( R = 0.09 \); \( P = .03 \)).

Conclusions: Recurrence in our study is similar to that reported in other series. Estrogen receptor is an excellent marker in the prognosis of breast cancer; progesterone receptor and HER2 do not add information to prognosis and risk of recurrence in breast cancer cases.

<table>
<thead>
<tr>
<th>Source</th>
<th>Recurrence/Count (%)</th>
<th>95 CI (%)</th>
<th>OR (95 CI %)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ER (+)</td>
<td>38/201 (19)</td>
<td>14 to 24</td>
<td>0.64 (0.40 to 1.03)</td>
</tr>
<tr>
<td>PR (+)</td>
<td>34/170 (20)</td>
<td>14 to 26</td>
<td>0.76 (0.47 to 1.23)</td>
</tr>
<tr>
<td>HER2 (+)</td>
<td>36/129 (28)</td>
<td>20 to 36</td>
<td>1.53 (0.94 to 2.49)</td>
</tr>
</tbody>
</table>

Abbreviations: 95% CI, 95% confidence interval; ER, estrogen receptors; HER2, c-erbB-2/neu; OR, odds ratio; P, calculated with \( \chi^2 \); PR, progesterone receptors.

Pathology Coursework for Honors High School Students Considering Health Care Careers
(Poster No. 53)

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Context: Reports from the US Institute of Medicine encourage the de-
Implementing Digital Slides at Resident “Unknown” Conferences
(Poster No. 54)

Brad E. Chaser, MD (brad-chaser@ouhsc.edu); Lewis A. Hassell, MD, Department of Pathology, University of Oklahoma, Oklahoma City.

Context: The use of digital slides appears imminent for routine diagnostic pathology workflow and research. They have already claimed a niche in medical school teaching and postgraduate education. However, the role of digital slides in residency training remains unexplored.

Design: Teaching conferences offered residents unknown slides in either a glass (centralized location only) or digital format (Imagescope/Webviewer) with online remote access. Following each conference, residents completed a questionnaire examining these 7 questions: (1) time reviewing cases as a whole, (2) time per case, (3) slide availability, (4) quality of images, (5) ease of use of equipment, (6) value of conference to education, and (7) likelihood of postconference review.

Results: Survey results are presented in the Table below. Also, educational value ranked 7.8 for digital and 9.0 for glass. Likelihood of review scored 6.9 for digital and 6.5 for glass. Results are based on a 10-point scale ranging from poor to excellent.

Conclusions: Digital slides face several significant barriers before they can replace traditional microscopy for resident teaching. In general, residents spent approximately one-third more time per case when using digital slides. Follow-up surveys revealed that the digital media initially presented several problems with software access. However, after resolving the technical problems, residents continued to favor glass rather than digital for image quality. Further improvements in digital slide interfaces and depth of field are necessary to encourage wider adoption in resident education.

<table>
<thead>
<tr>
<th>Survey Results</th>
<th>Mean Time/Case (h)</th>
<th>Availability*</th>
<th>Quality</th>
<th>Ease of Use*</th>
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<tbody>
<tr>
<td>Digital</td>
<td>0.6</td>
<td>4.6</td>
<td>6.5</td>
<td>4.8</td>
</tr>
<tr>
<td>Glass</td>
<td>0.4</td>
<td>8.5</td>
<td>9.4</td>
<td>9.3</td>
</tr>
</tbody>
</table>

* Ten-point scale, ranging from poor to excellent.

Anatomic Pathology and Its Role in the Development of the Health Care System in the Lao People’s Democratic Republic
(Poster No. 55)

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Context: Anatomic pathology services are lacking in many developing countries. This deficiency negatively affects patient care and planning for the development of health care systems because of the absence of accurate statistics about the burdens of disease. Laos is a developing country with an urgent need for improvements in its health care system. Although it has modernized many of its hospitals, the country lags behind in providing pathology services, even at its biggest institutions.

Design: A team of pathologists and a laboratory technologist from Canada and Thailand visited Laos to assess the state of anatomic pathology in its hospitals and to determine potential areas for development. During a 4-week period, the team traveled between academic/urban centers and rural hospitals. They provided cytopathology diagnostic services and were involved in the development of a histopathology laboratory. They interacted with patients, pathologists, clinicians, technologists, students, and administrators. They provided practical training in cytopathology and laboratory technology.

Results: The main causes of poor pathology services in Laos are the insufficient number of well-trained pathologists and technologists, inadequate equipment maintenance, and unavailability of reagents. Training of pathologists is hampered by limited access to educational material because of linguistic barriers and the absence of a pathology-training curriculum.

Conclusions: Sustained, structured collaboration between pathologists from developed countries and institutions in Laos is essential for development of that country’s medical education programs and health care system. Our data show that significant impact can be made using simple techniques. Customized training programs can make a significant impact on morbidity and mortality in this setting.

Transformative Resident Training: A Proposed Model for Pathology Resident Education in Coagulation
(Poster No. 56)

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Context: Clinical pathology resident education requires an understanding of laboratory testing within the clinical context of the patient. Different

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<th>Redesigned Curriculum</th>
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<td>Information integration (clinical and laboratory)</td>
<td>(1) Participation in clinical conferences and in pediatric hematology clinics with direct patient contact</td>
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1 Didactic lectures
2 Written quizzes and final examination, including esoteric topics/cases that the resident may not have observed during rotation
forces in the health care environment may change the practice of medicine. These changes will require a transformation in how clinical pathology is practiced. We describe a novel approach to teaching pathology residents coagulation testing that could serve as a model for training future pathologists.

**Design:** During 2004 to 2005, the clinical pathology residency curriculum at our institution was restructured to dedicate 1 month to resident education in coagulation. The curriculum concept for this rotation was to educate pathology residents in the following: (1) integration of clinical context with laboratory testing, (2) laboratory coagulation testing, management and accreditation, and (3) linkage between concepts, scientific literature, practical experience, and test taking.

**Results:** The objective of the redesign was achieved (Table). The rotation teaching staff grew from 2 pathologists and 1 medical technologist in 2004 to 2005 to the current staff consisting of 2 pathologists, 3 pediatric hemato logists, 2 hemophilia nurses, and 6 medical technicians. The 21 pathology residents who have completed this rotation have successfully passed the written evaluations; 33% required a make-up quiz on esoteric topics.

**Conclusions:** Clinical pathology resident training in coagulation provides an excellent opportunity to educate residents in the benefits of providing to clinicians value-added interpretation of laboratory results. Transforming pathology resident education to be more clinically comprehensive and integrative is an effective model to prepare pathology residents for future practice.

**Digital Cytology Images: A Multiplex Role With Potential as a Learning Tool for Pathology Residents**  
(Poster No. 57)

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**Context:** In our cytology laboratory, digital images of outgoing consultation material are collected and archived. We assessed the utility of digital images in resident education. We hypothesized that they could serve as a valuable tool in education and assessment.

**Design:** The images were reviewed, and a pilot set from 20 consecutive cases that included various organ sites were selected for teaching and assessing residents from all postgraduate years (n = 11). The residents were provided with a clinical history and had to assign a category (non-diagnostic, negative, benign, atypical, malignant) and a specific diagnosis, if feasible. The results were reviewed confidentially, correlated with postgraduate year, and shared with the residents.

**Results:** We had an average of 4 images per case. Negative and malignant cases were included. Image quality was excellent in 80% and acceptable in 20% of cases. A total of 215 diagnoses (97.7%) were rendered; there were 5 abstruse diagnoses. The 2-step discrepancy rate was 19 of 215 (8.8%). No discrepancies were identified between consultant review and the original diagnosis. Diagnostic difficulty was noted for small cell carcinoma and lymphoma, irrespective of organ site. We had a diagnosis accuracy goal of 75%. Five of 11 residents (45.4%) from the first 3 postgraduate years showed room for improvement in their cytology knowledge.

**Conclusions:** Digital images can have a multiplex role in cytology. We have found them to be useful for archiving outgoing consultation material. The same database can serve as a resource for cytology education and self-study and as a tool for prerotation and postrotation assessments.

**Virtual Slide Telepathology in a Breast Pathology Quality Assurance Program**  
(Poster No. 58)

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**Context:** Virtual slide telepathology represents a potential tool in providing quality assurance review of surgical pathology cases for a second hospital.

**Design:** The University of Arizona implemented a quality assurance program between 2 university hospitals. University Medical Center handles approximately 10 times the number of surgical pathology cases (about 20,000) than a smaller, affiliated hospital, University Physicians Healthcare Hospital (UPHH). UPHH is staffed by a rotating, part-time pathologist from University Medical Center. To provide same-day-quality assurance review of breast surgical pathology cases, we installed a DMetrix DX-40 ultrarapid virtual slide scanner (DMetrix, Inc., Tucson, Arizona) at UPHH. Glass slides of breast cases are scanned on the same day as they are produced at the UPHH histology laboratory. The pathologist at UPHH generates a printed slide report based on light microscopy. At 3 pm each day, virtual slides of breast cases from UPHH are rereviewed at University Medical Center by staff pathologists and residents on a 50-inch plasma monitor, using virtual slide viewer software.

**Results:** We analyzed 154 breast pathology cases. There was complete concurrence with the primary diagnosis in 139 cases (90.3%). There were 4 major discrepancies (2.6%), which would have resulted in different therapy, and 3 minor discrepancies (1.9%). Three cases (1.9%) were deferred for immunohistochemistry. Two cases (1.3%) were deferred for examination of glass slides. Discrepant cases incorporated the virtual slide diagnosis.

**Conclusions:** The quality assurance program found a small number of significant diagnostic discrepancies, promoted group decision making in a university subspecialty pathology practice, and increased job satisfaction for the pathologists.

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**Context:** Critical values are routinely confirmed by a repeat run before being communicated to the patient's caregiver. This study was designed to answer a question frequently asked by clinicians and laboratory professionals: Is confirmation necessary even in this era of new and improved automated technology?

**Design:** We selected 5 tests performed in the hematology laboratory: hemoglobin, white blood cell count, platelet count, prothrombin time, and activated partial thromboplastin time. Using institutionally established critical value limits, a minimum of 500 consecutive critical values were collected retrospectively for each test category. The absolute and percentage differences between the duplicate runs of each critical value were calculated and averaged for each category. Duplicate runs of individual critical values with absolute differences outside the mean range of plus/minus 3 standard deviations were tallied to determine the percentage of outliers in each category.

**Results:** The means obtained for the absolute and percentage differences between duplicate runs were as follows: 0.08 (1.4%) for hemoglobin, 0.05 (10.2%) for white blood cell count, 1.5 (9.9%) for platelets, 0.7 (1.4%) for prothrombin time, and 5.1 (4.4%) for activated partial thromboplastin time. The percentage of specimens with absolute differences outside 3 standard deviations (ie, outliers) ranged from 0.2 to 2.2 among the test categories (Table). The means of differences for each test category and the differences noted for individual outliers were not considered clinically significant from the standpoint of patient management.

**Conclusions:** Our findings indicate that repeat analysis of these tests is not necessary.
Review of Surgical Pathology Cases Before Sign-Out: A Q-Probes Study of 45 Laboratories by the College of American Pathologists

Poster No. 61

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Context: To help prevent errors, many surgical pathology departments have instituted a practice of reviewing a case by a second pathologist before it is signed out. The purpose of this study was to determine the extent and characteristics of this practice.

Design: Forty-five laboratories participated in the study. Participants retrospectively examined a maximum of 400 cases to identify a maximum of 30 cases that were reviewed by at least one additional pathologist before the case was signed out. For these cases, participants documented the organ system, primary disease type, number of additional pathologists consulted, and reason for case review.

Results: We examined 18032 surgical pathology cases, with an aggregate of 1183 cases (6.6%) having documented reviews before sign-out. The median laboratory reviewed 8.2% of cases. The top 4 organ systems reviewed were gastrointestinal (20.5%), breast (16.0%), skin (12.7%), and female genital tract (10.0%). Malignant neoplasms (45.3%) far exceeded any other category of disease. The malignant cases were reviewed by one additional pathologist 78% of the time. The most common reasons for review were “difficult diagnosis” (46.2%) and “required audit per departmental policy” (43.0%). Seventy-one percent of laboratories had departmental policies regarding review of cases. They reviewed cases at a significantly higher rate than laboratories without policies (9.6% vs 6.5%).

Conclusions: Surgical pathology review of cases before sign-out appears to be a widely accepted practice, with 71% of study participants reporting the existence of a policy. Cases were reviewed before sign-out at an aggregate rate of 6.6% and a median rate of 8.2%.

Using Amended Report Rates to Monitor Preanalytic and Postanalytic Errors in an Anatomic Pathology Laboratory

Poster No. 62

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Context: There is currently national impetus to improve the quality of health care services. Logistic complexities exist in managing specimen receipt, preparation, and reporting. Monitoring amended pathology reports provides a mechanism for assessing process improvement effects on error reduction.

Design: Report amendment data from 2007 and 2008 were collected. Department quality improvement minutes were reviewed. Classifications for preanalytic errors were as follows: missing clinical history, missing patient information, labeling error, or accessioning error. Postanalytic data were gathered from amended reports. Classifications for postanalytic errors were as follows: major diagnostic errors, diagnostic clarification, proofreading, missing or damaged specimens, and incorrect result assignment. Interventions identified sources of error; process improvement techniques were applied. Faculty, residents, and support staff participated in this exercise.

Results: The department issued an average of 24000 surgical reports per year. Rates of corrected reports because of a lack of error correction history were reduced from 0.27% in 2007 to 0.11% in 2008. Significant typographic error rates were reduced from 0.21% to 0.04%, and incorrect patient assignment to a case decreased from 0.05% to 0.02%. The “diagnosis clarification” category increased from 0.07% to 0.14%. A “pathology timeout” on the specimen requisition helped to reduce patient labeling errors from 6 to 0 in the endoscopy suite.

Conclusions: Using the principles of manufacturing quality management, which involves systematically identifying and eliminating errors, we reduced the overall report amendment rate. An increase in diagnostic clarification was attributed to more involved participation in quality assurance sessions by faculty. These findings translate into improved delivery of quality health care.

The Effects of Formalin Fixation on the Immunolocalization of MLH1 and MSH2 Proteins

Poster No. 63

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Context: Preanalytic factors, such as length of formalin fixation, can affect the quality of immunohistochemical staining. This study evaluated the effect of formalin fixation time on the immunohistochemical localization of mismatch repair protein MutL Homolog 1 Protein (MLH1), and MutS Homolog 2 Protein (MSH2). Microsatellite instability is a genetic manifestation of defective MMR proteins. Loss of MMR function in individuals with microsatellite instability can lead to hereditary, nonpolyposis colorectal cancer. Monoclonal antibodies to MLH1 and MSH2 and MLH1 were evaluated on benign tonsil tissues fixed in formalin from 1 to 120 hours to determine the effects of fixation on the immunolocalization of the MMR proteins in routinely processed tissue specimens.

Design: Mouse monoclonal anti-human MLH1 (clones ES05 and G168-15) and anti-human MSH2 (clones FE11 and G219-1129) were evaluated in immunohistochemistry on formalin-fixed, paraffin-embedded tonsil tissue fixed for 1, 4, 24, 48, and 120 hours. All tissue was pretreated with Tris/EDTA target-retrieval solution, and bound antibody was visualized with the Dako FLEX detection system.

Results: The highest staining intensity and most discrete nuclear localization were observed for MLH1 and MSH2 on tissue fixed in formalin for 4 and for 24 hours. Moderate to strong cytoplasmic staining was observed with antibodies to MLH1 and MSH2 in tissues fixed longer than 24 hours.

Conclusions: This study demonstrates that formalin fixation time is important for obtaining optimal immunohistochemical staining of the MMR proteins, MLH1 and MSH2. Standardization of preanalytic processing of tissue can help eliminate observed variations in the immunostaining intensity and cellular localization of proteins.