Abstracts and Case Studies From the College of American Pathologists 2007 Annual Meeting (CAP '07)

Abstract and case study poster sessions will be conducted during the College of American Pathologists' Annual Meeting (CAP '07), which is scheduled for September 30 to October 3, 2007. The meeting will occur at the Sheraton Chicago Hotel & Towers, Chicago, Ill. The poster sessions will occur in the Connection Café and Exhibit Hall. Specific dates and times for each poster session are listed below. Also shown below each poster session listing are the subject areas that will be presented during each session.

POSTER SESSION 100: SUNDAY, SEPTEMBER 30, 2007, 10:00 AM–12:30 PM

Informatics; Hematopathology

Synoptic Reporting of Cancer Resection Specimens Using a Synoptic Tool: A 3-Year Experience With More Than 7500 Specimens
(Poster No. 1)

Anil V. Parwani, MD, PhD1 (parwaniav@upmc.edu); Ronald Angeles, MD2; Anthony Piccoli, BS3; Sharon Winters, MS2; Samuel Yousum, MD2; Michael Becich, MD, PhD3. Departments of 1Pathology and 2Cancer Registry, University of Pittsburgh Medical Center, Pittsburgh, Pa; 3Department of Biomedical Informatics, University of Pittsburgh, Pittsburgh, Pa.

Context: Cancer checklists comprising standardized data elements are valuable tools that clinicians use to guide them in managing patients. We describe our experience with the use of Synoptic Worksheet entry tool for multiple malignant resections and also describe the use of synoptics in providing reports in our clinical environment of multiple academic and community centers.

Design: We used a synoptic reporting tool as part of existing laboratory information system, CoPathPlus, from Cerner DHT Corp. We modified the College of American Pathologists checklists into worksheets for select organ systems and 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 7626 specimens in our network had synoptic report completed. Breast (1534), prostate (1373), colorectum and appendix (673), lung (606), and melanoma (533) were the most used templates in the system. Rarer malignancies including parathyroid and adrenal cortical carcinoma, penile tumor, and gallbladder tumors had fewer synoptic templates in the system (Table).

Conclusions: Use of the new synoptic report minimizes transcription errors, 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 malignant resection specimens.

This work is partially supported by College of American Pathologists Foundation Rippey Grant for Quality Assurance.

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Table:

<table>
<thead>
<tr>
<th>Organ System</th>
<th>Total Worksheets</th>
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<tbody>
<tr>
<td>Breast/Cyn</td>
<td>2455</td>
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<tr>
<td>Genitourinary</td>
<td>1866</td>
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<tr>
<td>Gastrointestinal</td>
<td>1021</td>
</tr>
<tr>
<td>Thoracic</td>
<td>606</td>
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<tr>
<td>Melanoma</td>
<td>513</td>
</tr>
<tr>
<td>ENT/endocrine</td>
<td>471</td>
</tr>
<tr>
<td>Hemopath</td>
<td>386</td>
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<tr>
<td>Neuropath</td>
<td>245</td>
</tr>
</tbody>
</table>

Analysis of a Standardized Colorectal Cancer Resection Reporting Process in a Subspecialized Academic Pathology Department
(Poster No. 2)

Chad R. Rund, DO (rundcr@upmc.edu); Sharon B. Winters, MS, RHIA, CTR; Anthony L. Piccoli, BS; Anil V. Parwani, MD, PhD. Department of Pathology, University of Pittsburgh School of Medicine, Pittsburgh, Pa.

Context: University of Pittsburgh Medical Center (UPMC) use (Cerner’s CoPathPlus) of reporting College of American Pathologists (CAP) colorectal resection synoptic defined clinical elements was studied. Specific aims included (1) does UPMC synoptic use reflect the CAP requirements, (2) are CAP checklists more accurate and complete than traditional reports, and (3) will pathologists routinely use the checklists.

Design: Fifty random colorectal synoptics were chosen and evaluated for accuracy with respect to the 15 CAP scientifically validated elements (2005). Synoptics were compared with final text diagnoses and comments and codes were assigned according to completeness and accuracy. Text-based and synoptic values were assessed for the same cases but not at the individual pathologist level.

Results: UPMC synoptic use exceeded CAP required recommendations by adding the 8 optional data elements. Absence of nearest surgical margin documentation (code 6), text based to synoptic final diagnosis discrepancy (code 0), and optimal TNM staging (code 1) was identified in 76%, 22%, and 100% of the cases, respectively. A 95% compliance rate was recorded.

Conclusions: Based on this limited study, UPMC synoptic use is effective at capturing CAP required elements and standardizing reports.
Multispectral Imaging of Urine Cytology: Comparison of 2 Available Tools
(Poster No. 3)

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Context: Multispectral imaging is an emerging tool that uses both spatial and spectral image information to classify benign versus malignant cells. Two such tools include GENIE, which is a hybrid genetic algorithm-based artificial intelligence system (AIS), and MIDAS, which is a neural network-based AIS. Both of these tools classify images using automatically learned spatial-spectral features. The aim of this study was to compare the ability of these 2 tools in differentiating benign versus malignant urothelial cells (UCs) in urine cytology, with the ultimate goal of reproducibly distinguishing low-grade urothelial carcinoma from benign and reactive changes.

Design: A random training set (4 negative, 5 positive) and a testing set (5 negative, 5 positive) of urine cytology were selected. GENIE was limited in number of pixels that could be trained. All cases in both sets had a follow-up biopsy to confirm the cytopathologic interpretation. Both tools were trained on random well-preserved cells (77 normal UCs and 77 malignant UCs) from the training set. Solution was developed from both tools and was tested on a testing set. The testing set was composed of 191 normal UCs from 5 negative cases and 223 malignant UCs from 5 malignant cases. Cells were categorized as positive or negative when more than 80% of the pixels delineating the cell were classified by the solution.

Results: Results generated by testing the solutions from GENIE and MIDAS on the testing set are summarized below (Tables 1 and 2).

Conclusions: Both tools showed similar sensitivity; however, MIDAS showed a statistically significant increase in specificity (75.39%) as compared with GENIE (60.2%) among the negative training set (P = .05). We aim to conduct further studies to optimize and develop MIDAS-based multispectral imaging to differentiate various equivocal urothelial lesions.

Table 1. Classification of Number of UCs by Solutions From Both Tools

<table>
<thead>
<tr>
<th>Classification</th>
<th>GENIE</th>
<th>MIDAS</th>
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<tbody>
<tr>
<td>True negative</td>
<td>115</td>
<td>144</td>
</tr>
<tr>
<td>False-positive</td>
<td>76</td>
<td>47</td>
</tr>
<tr>
<td>True positive</td>
<td>222</td>
<td>223</td>
</tr>
<tr>
<td>False-negative</td>
<td>1</td>
<td>0</td>
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Table 2. Summary of Sensitivity and Specificity From Solutions Created by Both Tools

<table>
<thead>
<tr>
<th>Statistics</th>
<th>GENIE, %</th>
<th>MIDAS, %</th>
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<tbody>
<tr>
<td>Sensitivity</td>
<td>99.5</td>
<td>100</td>
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<tr>
<td>Specificity</td>
<td>60.2</td>
<td>75.4</td>
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<tr>
<td>PPV</td>
<td>74.5</td>
<td>82.6</td>
</tr>
<tr>
<td>NPV</td>
<td>99.2</td>
<td>100</td>
</tr>
</tbody>
</table>

Anatomic Pathology Reporting System for the 21st Century
(Poster No. 4)

Stephen K. Lau, MD1 (slau@emory.edu); Theresa Gillespie, PhD2; Joseph Lipscomb, PhD; Kenneth Gerlach, MPH; Patricia Jamison, MPH; Vijay Varma, MD1. Departments of Pathology and Research and Development, Atlanta VA Medical Center and Emory University, Decatur, Ga; 1Department of Informatics, Centers for Disease Control and Prevention, Atlanta, Ga.

Context: Surgical pathology reports provide critical information for patient care. They are also the source of data for clinical and translational research. Increasing work load and the complexity of information required on each diagnostic report has made the traditional narrative reports difficult to produce and difficult to use. We report on an electronic system that we are developing, which produces reports that meet the College of American Pathologists (CAP) standards, facilitates SNOMED CT coding, and at the same time creates a searchable data repository.

Design: The custom software application consists of interactive forms driven by a relational database. Service Oriented Architecture was used to facilitate interoperability. The forms have drop-down menus with logical dependencies that prompt the user to include all the necessary data. Each menu field is populated with a dictionary of standardized terminology from the CAP checklists. Each of these terms is associated with appropriate SNOMED CT numerical code. Permissions enable stratified access for laboratory staff, residents, and attending physicians to enter data, edit, revise, and finalize reports.

Results: The electronic templates are user-friendly but with powerful interactive features. The reports have a clear and consistent format and include all the data elements, and the captured data can be easily searched with predefined or custom queries. Data sharing with tumor registry and billing departments improves efficiency and accuracy.

Conclusions: Anatomic pathology reporting application built on a database system and interactive electronic forms is a user-friendly system that enhances the quality of the diagnostic reports, creates a searchable database, and enables controlled access to this critical data.

Interactive Pathology Atlas
(Poster No. 5)

Vijay Varma, MD (vvarma@emory.edu); Stephen K. Lau, MD; Christine Norton, MD; Stephen B. Hunter, MD. Department of Pathology, Emory University, Atlanta, Ga.

Context: When faced with difficult cases, to arrive at a specific diagnosis, pathologists consult books on clinical and morphologic features of lesions and consider differential diagnoses. Books are now supplemented by CDs and Web sites. We report on a database-driven Web site that produces dynamic pages on demand that provide a rich interactive teaching and reference resource.

Design: The software application consists of a relational database back end and an HTML front end with PERL, java script, and AJAX in the middle layer. An authoring tool consisting of electronic forms and an image manager is integrated into the application. Permissions allow selective access to various functions of editors, authors, and users.

Results: Clicking on any of the titles and FigNo. in the table of contents launches the main page that provides clinical, radiologic, and pathologic features of that lesion in an outline format. Tables and detailed explanations are embedded in a deeper layer that can be accessed with a click. Links to search for up-to-date literature on each topic are provided. High-resolution images are linked to thumbnails on the outline page. The differential diagnosis of each lesion can be viewed on a page with side-by-side comparisons of images as well as key features. This page can be customized to add and remove images as well as lesions. The authoring tool provides a way to edit the text and tables online.

Conclusions: A database-supported Web site provides a powerful, rich, and up-to-date resource for teaching and consultation. Dr Varma has a financial interest in Contexta, Inc, and is also a consultant for Elsevier, Inc.

Quantitative Analysis of Flow Cytometry Immunophenotypic Data in the Diagnosis of Myelodysplastic Syndromes
(Poster No. 6)

Ha Nishino, MD1 (nishino@bcm.edu); April Ewton, MD; Youli Zu, MD, PhD; Audrey Ponce De Leon, MD; Chung-Cheng Chang, MD, PhD2; Department of Pathology, Baylor College of Medicine, Houston, Tex; 2Department of Pathology, The Methodist Hospital, Houston, Tex.

Context: Recent studies using qualitative analysis of flow cytometry data have demonstrated various immunophenotypic abnormalities associated with myelodysplastic syndromes (MDSs). However, there are limited reports assessing the ability of quantitative immunophenotypic analysis to discriminate MDS from other cytopenic conditions.

Design: Using flow cytometry, we studied 37 bone marrow specimens from 23 patients with MDS and 14 cytopenic patients with nonclonal hematologic disorders (age-matched with MDS patients). Samples were analyzed quantitatively for percentages of T cells, B cells, natural killer cells, granulocytes, monocytes, blasts, erythroid precursors, and plasma cells; CD4/CD8 ratio; percent CD56+ cells; and % erythroid precursor subsets.

Results: Quantitative analysis of immunophenotypic data in MDS patients compared with controls showed decreased total granulocytes (P = .04) and mature subsets of CD11b1+ CD1666+67 granulocytes (P = .005) and CD10+ granulocytes (P = .005). MDS patients also showed a trending increase in subset percentage of CD56+ monocytes (P = .06). Using receiver operating characteristic analysis, cut-off values for these parameters favoring a diagnosis of MDS were identified as follows: total granulocytes less than 60%, CD11b1+ CD1666+67 granulocytic subset less than 40%, CD10+ granulocytic subset less than 40%, and CD56+ monocyte subset more than 10%. Subsequently, a scoring system was proposed whereby a score of 1 was assigned for the presence of each quantitative abnormality. Using...
Flow Immunophenotypic Properties of the Hodgkin Lymphoma Inflammatory Infiltrate

(Every No. 10)

Eve M. Bentacourt, MD (evanson@uth.tmc.edu); Jyoti Patel, MT(ASCP); S. D. Hudnall, MD. Department of Pathology, University of Texas Medical Branch, Galveston.

Context: Hodgkin lymphoma (HL) is characterized by few malignant Reed-Sternberg cells admixed with numerous reactive T cells. We performed a detailed retrospective comparison of the flow immunophenotype of HL and reactive lymphoid hyperplasia (RLH) to identify HL-specific immunophenotypic features.

Design: Single-cell suspensions from 60 lymph nodes involved by HL (at initial diagnosis) and 38 lymph nodes involved by RLH were subjected to a battery of fluorochrome-conjugated monoclonal antibodies to lymphocyte subsets. Cells were analyzed on a FACSCalibur flow cytometer with CellQuest software (Becton Dickinson, San Jose, Calif).

Results: CD3+ T cells were increased, and CD19+B cells decreased, in HL versus RLH. In terms of HL subtypes, the CD3/CD20 ratio difference, when compared with RLH, was only significant in nodular sclerosis HL (NSHL). The CD4/CD8 ratio was increased in NSHL, while decreased in mixed-cellularity HL (MCHL), in comparison with RLH. Natural killer-like T cells were slightly increased in HL, especially in MCHL. No differences in CD8+ T-cell content were detected in any group. More CD7−T cells were detected in nodular lymphocyte-predominant HL and RLH than in NSHL and lymphocyte-depleted HL. CD4/CD25+T cells were significantly increased in HL. Although no significant difference was detected in Epstein-Barr virus-positive versus Epstein-Barr virus-negative NSHL, a trend toward increased CD3/CD20 ratio, increased natural killer cells, and decreased CD4/CD25+T cells in Epstein-Barr virus-positive HL was noted.

Conclusions: The cellular composition of the lymphocytic infiltrate in HL differs significantly from that seen in RLH. It is characterized by increased T cells (excluding MCHL), decreased B cells (excluding MCHL and lymphocyte-rich HL), increased CD4/CD8 ratio (NSHL only), and increased CD4/CD25+T regulatory cells.

Bone Marrow Talc Granulomatosis

(Poster No. 11)

Suzanne H. Martin, MD (smartin@usouthal.edu); Andrea G. Kahn, MD, J. Allan Tucker, MD; Zhuang Zuo, MD, PhD; Jacek M. Polski, MD. Department of Pathology and Laboratory Medicine, University of South Alabama, Mobile.

Context: Intravenous drug abuse sometimes involves injecting adulterated drugs with insoluble filler substances such as talc. Granulomatous reaction ensues as a result of these practices. Talc granulomata are usually located in lungs but can sometimes be disseminated as documented by a few case reports. We recently encountered a bone marrow aspiration with multiple small and poorly formed granulomata composed of foamy macrophages with refractile crystals. Scanning electron microscopy and energy dispersive x-ray microanalysis (EDXA) of clot sections revealed that the particles were composed of magnesium and silicon, consistent in ratio with talc. A retrospective study of bone marrow aspiration and biopsy was undertaken to study the frequency of talc granulomatosis in archival cases of bone marrow granulomata at our institution including study with EDXA.

Design: Thirty-nine additional cases of bone marrow granulomata of all etiologies were retrieved from our laboratory information system. The hematopoietin–eosin–stained and periodic acid–Schiff–stained sections were examined with polarizing light filters for refractile material. Cases with polarizable crystals were evaluated using EDXA.

Results: Of the 39 additional cases of bone marrow granulomata reviewed, 1 case showed polarizable crystals within the granulomata. The crystals were morphologically consistent with talc crystals. However, EDXA was unsuccessful because B5 precipitates preclude identification of the crystals.

Conclusions: This study documents that bone marrow talc granulomatosis is a rare condition (in our study, 5% of bone marrow granulomata). However, the possibility of talc granulomatosis should be considered in cases of bone marrow granulomata and can be evaluated with EDXA.

Role of Peripheral Blood Flow Cytometry in the Evaluation of Patients With Myelodysplasia

(Poster No. 12)

Hooman H. Rashidi, MD (hooman.rashidi@yale.edu); Nelofar Shafi, MD; Brian R. Smith, MD; Michal G. Rose, MD. "Department of Pathol-
ogy and Laboratory Medicine, Yale School of Medicine, New Haven, Conn; 2Department of Pathology and Laboratory Medicine, Yale School of Medicine/VA Connecticut Health Care System, New Haven/West Haven.

**Context:** Myelodysplastic syndromes (MDSs) comprise a heterogeneous group of hematopoietic disorders with a variable clinical course. Diagnosis is made by morphology of bone marrow specimens and cytogenetics. Flow cytometry (FC) of the bone marrow (BM) specimen is used to determine percent blasts and may suggest abnormal myeloid maturation. There are little data on the use of FC evaluation of peripheral blood myeloid cells in patients with MDS. Here, we evaluate the utility of peripheral blood FC immunophenotypic abnormalities in predicting MDS in patients with cytopenias.

**Design:** FC evaluation of patients with BM-proven high-risk (n = 14) and low-risk (n = 15) MDS (based on World Health Organization guidelines) was compared with 16 controls. The ratio of mean marker fluorescence to mean control autofluorescence was calculated.

**Results:** The mean granulocyte CD10-control fluorescence ratio (±SD) was 3.67 ± 0.65 for the control group (n = 16), 3.65 ± 0.9 for the low-grade MDS group (n = 15), and 2.2 ± 0.7 for the high-grade MDS group (n = 14), P < .001. The sensitivity and specificity of granulocyte CD10 expression ratio less than 3 in predicting BM involvement by high-risk MDS was 52% and 88%, respectively. Positive and negative predictive values of the CD10 expression ratio less than 3 were 88.2% and 87.5%, respectively.

**Conclusions:** Our preliminary data suggest that peripheral blood FC for granulocyte CD10 expression may help rule-out high-risk MDS in patients with cytopenias, without the need to perform an invasive BM evaluation. This approach may be particularly valuable in the majority of MDS patients who are elderly with multiple comorbidities.

**Marginal Zone Variant of Mantle Cell Lymphoma:**

**A CD5-Negative Cyclin D1–Positive Variant**

(Poster No. 13)

Natalia Golardi, MD; M. Tarek Elghetany, MD; 1Department of Pathology, University of Texas Medical Branch, Galveston; 2Department of Pathology, Cancer Care Specialists of Central Illinois, Decatur.

An 83-year-old white man presented with pneumonia, persistent cough, and 30-lb weight loss for the past 15 months. Blood count was significant for neutrophilia and mild anemia. Computed tomography scan showed extensive necrotic mediastinal, cervical, and retroperitoneal lymphadenopathy; a large right hilar mass encasing the right upper lobe bronchus; bilateral pleural effusions; and a soft tissue mass near the gastroesophageal junction. A right upper lobe lung biopsy and a right axillary lymph node showed involvement by predominantly small cleaved lymphocytes with a small proportion of large cells. No epithelial invasion was seen in the lung biopsy. On initial frozen sections, small cell lung carcinoma was considered. However, the cells were positive for CD20 and CD45 and negative for CD3, neuron-specific enolase, and chromogranin. A morphologic diagnosis of follicular lymphoma, grade 2 of 3, was rendered. Flow cytometry on the lymph node showed the B lymphocytes to be negative for CD5 and CD10. Morphologic reassessment showed the small lymphocytes to have monocytoid appearance and prominent cell borders surrounding naked germinal centers. Cyclin D1 unequivocally stained the nuclei of 40% to 50% of cells. Bone marrow examination revealed extensive involvement by cells with similar morphologic and immunophenotypic characteristics. Moreover, cytogenetic analysis on the marrow showed a clone with the following karyotype: "-3,-6,-11,t(11;14)(q13;g2) consistent with mantle cell lymphoma. Because of the aggressive clinical behavior, the patient received multigraft lymphoma chemotherapy. Marginal zone variant of mantle cell lymphoma is a challenging diagnosis that needs to be recognized because of its aggressive clinical behavior.

**Epstein-Barr Virus Is Exceptionally Rare in Nodular Lymphocyte-Predominant Hodgkin Lymphoma Cases From North America**

(Poster No. 14)

Miriam D. Post, MD (mdpost@partners.org); Lawrence R. Zuckerberg, MD; Robert P. Hassieran, MD. Department of Pathology, Massachusetts General Hospital, Boston.

**Context:** Both histologic features and clinical behavior distinguish nodular lymphocyte-predominant Hodgkin lymphoma (NLPHL) from classical Hodgkin lymphoma (cHL). Epstein-Barr virus (EBV) is strongly associated with cHL and is present in up to 90% of cases in developing countries. The relationship between EBV and NLPHL is less clear, as few cases have been studied in a limited geographic distribution.

**Design:** We searched one institution’s database to identify cases of NLPHL originating in North America and evaluated EBV early RNA expression by in situ hybridization. Cases were considered positive if any of the large neoplastic cells demonstrated staining. We compared our results to those reported for NLPHL globally.

**Results:** Only 1 of 29 North American NLPHL cases showed positive EBV staining by EBV early RNA expression in situ hybridization. This case was from the cervical lymph node of a 44-year-old man with stage IA disease. The large neoplastic cells stained positively for PAX5 and were variably positive for CD20; a subset weakly expressed CD30 but were negative for CD15. Overall, this case showed features intermediate between NLPHL and lymphocyte-rich cHL.

**Conclusions:** Compared with previous studies demonstrating EBV in NLPHL cases from Europe (5/26 cases; 19%) and developing countries (9/51 cases; 18%), we found EBV in only 1 (3%) of 29 North American NLPHL cases. Our findings demonstrate that EBV expression in NLPHL is exceptionally rare in North America and that this feature may help distinguish it from lymphocyte-rich cHL. Additionally, the geographic differences in EBV expression in NLPHL seem to parallel those observed in cHL.

**Lymphoma-Specific S-Phase Fractions in 2 Subtypes of Diffuse Large B-Cell Lymphomas**

(Poster No. 15)

David D. Grier, MD (grierdd@gmail.com); Samer Z. Al-Quran, MD; William Clapp, MD; Ying Li, MD, PhD; Raul C. Brayan, MD. Department of Pathology, Immunology and Laboratory Medicine, University of Florida, Gainesville.

**Context:** Recent studies of diffuse large B-cell lymphomas (DLBCL) using cDNA microarray techniques have shown that DLBCL can be divided into prognostically significant subgroups such as the germinal center B-cell-like (GC-DLBCL) and activated B-cell-like (ABC-DLBCL) types. The GC-DLBCL subgroup has a significantly better survival rate than the ABC-DLBCL subgroup. However, it is unknown if these 2 DLBCL subtypes have different cell cycle kinetic properties (ie, DNA S-phase fraction [SPF]).

**Design:** DLBCL cases with SPF data were identified. SPF was measured using DRAQ5 (a dye that binds supravitally to DNA in intact cells), with simultaneous labeling of 2 B-cell surface antigens. This approach allowed the SPF to be measured specifically in the lymphoma cells. The cases of DLBCL were classified based on the results of immunohistochemistry using 3 antibodies (CD10, Bcl-6, and MUM1). Two pathologists reviewed the immunohistochemistry and staining greater than 30% of the lymphoma cells was considered positive.

**Results:** Fourteen DLBCL were identified (8 GC-DLBCL and 6 ABC-DLBCL). SPF ranged from 5% to 22% (mean, 11.1%) in GC-DLBCL and 6% to 20% (mean, 12%) in ABC-DLBCL. There was no statistical difference in SPF between the 2 DLBCL subtypes.

**Conclusions:** In this preliminary study, we observed ample variability and no significant differences in lymphoma-specific SPF between GC-DLBCL and ABC-DLBCL. If confirmed by a larger number of samples, these data do not support the notion that the differences in prognosis observed between patients with GC-DLBCL and ABC-DLBCL are related to differences in tumor growth kinetics.

**Development of an In Vitro Human Erythroid Cell Expansion Model Correlating the Morphology With the Immunophenotypic Markers**

(Poster No. 16)

Archana M. Agarwal, MD (archana.agarwal@hsc.utah.edu); Donghoon Yoon, PhD; Hana Bruchova, PhD; Josef T. Prchal, MD; Jaroslav F. Prchal, MD. 1Department of Pathology and 2Division of Hematology, University of Utah School of Medicine, Salt Lake City; 3Department of Oncology, McGill University, Montreal, Quebec, Canada.

**Context:** In vitro erythroid expansion model (using cytokine support) is used widely to study red cells at their different stages of development. In these models, specific erythroid stage is currently estimated by using differential expression of CD71 (transferrin receptor) and CD235a (glycoprotein A). However, the expression of these immunophenotypic markers has never been correlated with morphology in expanded human erythroid progenitor cells.
(Poster No. 17)

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1Department of Pathology, Boston Medical Center, Boston, Mass; 2Department of Epidemiology, Boston University School of Public Health, Boston, Mass.

**Context:** Acute chorioamnionitis (ACA) is associated with neonatal sepsis. Unlike in adults, white blood cell parameters are less reliable in neonates for an infection workup. Our objective was to determine if cord blood (CB) can be used for a complete blood count with differential in correlation with pathologically confirmed ACA in comparison with peripheral blood (PB).

**Design:** CB was retrieved from consecutively submitted placentas. The complete blood count with differential parameters for CB and clinician-drawn PB includes the white blood cell count, absolute neutrophil count, mononuclear cell count, band count, percent, immature neutrophil percent, mean neutrophil volume, neutrophil distribution width, hemoglobin, and hematocrit. Statistical analysis was run using Statistical Analysis System software.

**Results:** Of the 64 cases, 14 had ACA. The absolute neutrophil count was a significant CB predictor for ACA (Table). CB white blood cell count and neutrophil percent were borderline predictors for ACA. From the smaller PB subset (29 cases), band percent and immature neutrophil percent were significant predictors for ACA (Table). When comparing CB and PB hematologic parameters, hemoglobin, hematocrit, and white blood cell count were strongly correlated. Absolute neutrophil count had moderate correlation. Neutrophil percent, band percent, and immature neutrophil percent had weak correlation. Lastly, increasing gestational age correlated with increasing neutrophil distribution width (t test: P = .008).

**Conclusions:** The absolute neutrophil count in CB was a significant predictor of ACA. CB has advantages in that it is faster, easier, and safer to obtain than PB. CB may be an alternative to PB as a source for complete blood count with differential in the early neonatal sepsis workup.

| Significant Cord and Peripheral Blood Parameters in Predicting Acute Chorioamnionitis |
|---------------------------------|-----------------|-----------------|-----------------|
|                                  | t test          | ROC c            | ROC P            |
| CB blood absolute neutrophil count | .02             | 0.7              | .02             |
| Peripheral blood band %          | <.001           | 0.82             | .01             |
| Peripheral blood immature neutrophil % | .001           | 0.81             | .01             |

**The Transcription Factor Yin Yang 1 Is Widely Expressed in Lymphoma Tissue**  
(Poster No. 18)

Rodney R. Miles, MD, PhD (rodneym@umich.edu); Sheryl R. Tripp, MT(ASCP); George Z. Rassidakis, MD, PhD; L. J. Medeiros, MD; Megan S. Lim, MD, PhD; Kojo S. Elenitoba-Johnson, MD.  
1Department of Pathology, University of Michigan, Ann Arbor; 2Institute for Research and Development, ARUP Laboratories, Salt Lake City, Utah; 3Department of Hematopathology, The University of Texas M. D. Anderson Cancer Center, Houston.

**Context:** We identified the transcription factor yin yang 1 (YY1) in a mass spectrometry–based screen of follicular lymphoma (FL)–derived cells. YY1 can inhibit apoptosis in lymphoma cells, and increased YY1 mRNA has recently been associated with worse outcome in FL and diffuse large B-cell lymphoma (DLBCL) patients.

**Design:** We performed an immunohistochemical study of YY1 expression in arrays of reactive lymphoid tissue, 37 hematopoietic cell lines, and Hodgkin lymphoma (HL) and non-Hodgkin lymphoma (NHL) tissues. We also evaluated YY1 expression in 11 hematopoietic cell lines using Western blotting.

**Results:** YY1 expression in tonsillar tissue was strongest in the small lymphocytes of mantle and marginal zones and was weak in centrocytes and centroblasts of the germinal centers. Strong YY1 expression was seen in 27 of 37 human myeloid, B-cell, and T-cell lines. YY1 was expressed in all DLBCLs (42/42); FLs (10/10); and small lymphocytic (2/2), splenic marginal zone (2/2), and mantle cell lymphomas (1/1). Most DLBCLs (79%) and FLs (70%) showed weak expression as did 8 of 8 HLs. Twenty-four of 27 anaplastic large cell lymphomas expressed YY1. The expression was found in 13 cases and did not correlate with anaplastic lymphoma kinase expression. By Western blotting, YY1 was expressed in 4 of 5 B-cell and 5 of 6 T-cell NHL cell lines.

**Conclusions:** YY1 was expressed in nearly all reactive lymphoid tissues, hematopoietic cell lines, and HL and NHL tissue samples tested. Weak staining was noted in DLBCL, FL, HL, and anaplastic large cell lymphoma. Further studies are warranted to determine the basis of weak to absent expression of YY1 in a subset of lymphomas.

**Utility of Ki-67 Proliferation Index Marker in Assessing Clinical Aggressiveness of Follicular Lymphoma: Retrospective Study and Clinicopathologic Correlation**  
(Poster No. 19)

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Department of Pathology, University of Illinois, Chicago.

**Context:** Although follicular lymphoma (FL) is usually an indolent disease, some patients experience a more aggressive clinical course. The proliferation index (PI) of FL generally correlates with histologic grade. However, in cases of discordance (low-grade and high PI or high-grade and low PI), histologic grade or PI may not correlate with clinical aggressiveness. In this study, we evaluate the utility of Ki-67 proliferation index marker in assessing the clinical aggressiveness of FL.

**Design:** Formalin-fixed, paraffin-embedded tissues from 23 FL cases at the time of initial diagnosis were analyzed. PI was determined via Ki-67 immunostaining and automated image analysis and recorded as an average percentage of proliferating cells within 10 randomly selected microscopic high-power fields (low PI < 20%, high PI ≥ 20%). The correlation of PI with histologic grade and clinical aggressiveness (transformation to diffuse large B-cell lymphoma) were evaluated.

**Results:** The correlations of PI with histologic grade (r = .34, P = .11) and clinical aggressiveness (r = .09, P = .97) were weak and not statistically significant. Discordance between histologic grade and PI was present in 4 cases (3 grade 1 with high PI, 1 grade 3 with low PI). There was no clinical follow-up in 3 discordant cases; the other case (grade 1 with high PI) had persistent disease without transformation.

**Conclusions:** Our study did not provide evidence that Ki-67 immunostaining is a better predictor of the clinical aggressiveness of FL than simple and less expensive histologic grading. The low number of discordant cases with clinical follow-up prevented an assessment of the predictive value of Ki-67 immunostaining.

**Cytogenetic Abnormality Correlation With Megakaryocyte Dysplasia in Myelodysplastic Syndromes**  
(Poster No. 20)

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**Context:** We identified the correlation factor yin yang 1 (YY1) in a mass spectrometry–based screen of follicular lymphoma (FL)–derived cells. YY1 can inhibit apoptosis in lymphoma cells, and increased YY1 mRNA has recently been associated with worse outcome in FL and diffuse large B-cell lymphoma (DLBCL) patients.

**Design:** We performed an immunohistochemical study of YY1 expression in arrays of reactive lymphoid tissue, 37 hematopoietic cell lines, and Hodgkin lymphoma (HL) and non-Hodgkin lymphoma (NHL) tissues. We also evaluated YY1 expression in 11 hematopoietic cell lines using Western blotting.

**Results:** YY1 expression in tonsillar tissue was strongest in the small lymphocytes of mantle and marginal zones and was weak in centrocytes and centroblasts of the germinal centers. Strong YY1 expression was seen in 27 of 37 human myeloid, B-cell, and T-cell lines. YY1 was expressed in all DLBCLs (42/42); FLs (10/10); and small lymphocytic (2/2), splenic marginal zone (2/2), and mantle cell lymphomas (1/1). Most DLBCLs (79%) and FLs (70%) showed weak expression as did 8 of 8 HLs. Twenty-four of 27 anaplastic large cell lymphomas expressed YY1. The expression was found in 13 cases and did not correlate with anaplastic lymphoma kinase expression. By Western blotting, YY1 was expressed in 4 of 5 B-cell and 5 of 6 T-cell NHL cell lines.

**Conclusions:** YY1 was expressed in nearly all reactive lymphoid tissues, hematopoietic cell lines, and HL and NHL tissue samples tested. Weak staining was noted in DLBCL, FL, HL, and anaplastic large cell lymphoma. Further studies are warranted to determine the basis of weak to absent expression of YY1 in a subset of lymphomas.
of MDS.

Addition, megakaryocytic dysplasia was observed in 83% (10/12) of pa-
vients with chromosome 7, 79% (11/14) with chromosome 5, 78% (7/9) with
chromosome 17, 60% (3/5) with chromosome 8 abnormalities, and all 5 cases with chromosome 20 abnormalities. Although megakaryocytic dysplasia was commonly observed, severe megakaryocyte dysplasia was
significantly more common in abnormalities of chromosome 5, chromosome
7, or both (P = .01) compared with other cytogenetic findings. Chromo-
osomal 5 and 7 structural defects accounted for 48% of the cases with
dysplastic megakaryocytes.

Conclusions: Abnormalities of chromosomes 5 and 7 are associated
with dysplastic megakaryocytes. However, these cytogenetic abnormali-
ties cannot explain the significant megakaryocyte dysplasia in many cases of
MDS.

**Posttransplant Lymphoproliferative Disorder Hodgkin Lymphoma**
(Poster No. 21)

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Hodgkin lymphoma disease (HD) posttransplantation is rare. Posttrans-
plant lymphoproliferative disorders (PTLs) comprise a spectrum, ranging
from early Epstein-Barr virus (EBV)-driven polyclonal proliferations resembling infectious mononucleosis to EBV-positive or EBV-negative lymphomas of predominantly B-cell or less often T-cell type. Even though non-Hodgkin lymphoma in brain has been reported, to our knowledge ours is the first case of HD in the brain. A 46-year-old man presented with an onset of right focal upper extremity seizure. His medical and surgical history was significant for vision problems because of diabetes following kidney transplant 15 years ago and cadaveric pancreatic transplant 5 years ago. He was on immunosuppressive therapy for the past 15 years. We received 2 frozen fragments of grey-brown tissue measuring 1.1 and 2.5 cm in greatest dimension. Microscopy revealed brain paren-
chyma with large areas of chronic and granulomatous inflammation in a
slightly nodular pattern. The inflammatory infiltrate included lympho-
cytes, histiocytes, plasma cells, and rare eosinophils. Scattered throughout this background were large atypical cells with large nuclei and prominent nucleoli. The atypical cells were positive for CD30, and rare cells showed
CD15 positivity (Figure 1). The frequency of HD after transplantation

**When Should a Differential Count Be Done on Cerebrospinal Fluid?**
(Poster No. 22)

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Context: Historically, the Lourdes Hospital Laboratory has attempted a
differential count on any diagnostic cerebrospinal fluid (D-CSF) speci-
men when the total cell count was 1 or more white blood cells (WBCs)
per microliter. We were interested in determining whether the policy in
respect to D-CSF was necessary. Also we felt the data would help to
define review criteria when new instrumentation automating body fluid
cell counting was acquired.

Design: We reviewed results on 566 CSF cell counts performed during
a 2-year period. Of these, 308 were myelogram-derived CSFs. The 0 to
97.5 percentiles of the latter group defined the reference interval for WBC
count (0–8/µL).

Results: Of the 258 D-CSFs, 115 specimens from 104 patients had 1 or
more WBCs per microliter. The electronic medical records with regard to
these 115 specimens were reviewed. Sixty specimens (51 patients) had
more than 8 WBCs/µL. Of these, 27 (53%) patients had a discharge di-
agnosis of meningitis (all types), encephalitis, or cerebral abscess. The
median count among these 27 patients was 171 WBCs/µL (range, 28–
5000). Of the 55 specimens (53 patients) with 8 or fewer WBCs per mi-
croliter, 53 specimens had 2 or fewer polymorphonuclear leukocytes per
microliter and only 1 patient (human immunodeficiency virus–positive)
had a discharge diagnosis of ‘likely aseptic meningitis’ with a cell count of
5 WBCs/µL.

Conclusions: On the basis of this data, a reference interval for CSF cell
count was defined as 0 to 8 WBCs/µL, and differential counts on speci-
mens with total cell counts within the reference interval were discontin-
ued unless specifically requested by the attending clinician.

**Blastic Transformation of Follicular Lymphoma**
(Poster No. 23)

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Context: Follicular lymphomas (FLs) can undergo transformation to
high-grade lymphomas/leukemias with blastic morphology. There is little
literature available on this entity.

Design: We evaluated the clinical and pathologic features of 2 cases of
FL with blastic morphology.

Results: Case 1: A 72-year-old woman, with prior history of stage IV
low-grade FL 5 years ago, presented with cervical lymphadenopathy.
Peripheral blood and bone marrow showed a large population of mono-
clonal lymphoblasts that were evaluated by flow cytometry to be positive
for CD10, CD19, CD22, and partial CD20 without TdT. Karyotyping re-
vealed multiple cytogenetic abnormalities. A diagnosis of blastic trans-
formation of FL was made. She had short-lasting partial response to sal-
vage chemotherapy and died 4 months after presentation because of re-
fractory disease. Case 2: A 71-year-old man presented with abdominal
lymphadenopathy. Lymph node biopsy revealed complete effacement of
nodal architecture by a dense atypical lymphoid infiltrate with blastic
morphology and expressed monoclonal light chains, Bcl-6, Bcl-2, and
CD10 but not Bcl-1, CD5, or TdT. Karyotyping revealed multiple cyto-
egenic abnormalities. A diagnosis of blastic transformation of FL was
made. She had short-lasting partial response to salvage chemotherapy
and died 4 months after presentation because of refractory disease.

Conclusions: The present study highlights the importance of recognizing
these cases for their aggressive nature and treatment challenges.

**DRAQ5 Cell Cycle Analysis and CD71 Expression Differences in Diffuse Large B-Cell Lymphoma and Low-Grade B-Cell Non-Hodgkin Lymphoma**
(Poster No. 24)

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Clinical Experience of Capillary Zone Electrophoresis to Traditional (Non–High-Performance Liquid Chromatography) Methods for the Evaluation of Hemoglobinopathies
(Poster No. 26)

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Context: Traditional methods have been reliably used to evaluate hemoglobinopathies but are labor intensive and time consuming. Capillary zone electrophoresis for automated quantitation and elucidation of hemoglobin (Hb) variants has the potential for improving hemoglobinopathy diagnosis.

Design: Parallel studies were performed using traditional methods and Hb program on the CAPILLARYS 2 (Sebia, France). Traditional methods included Hb electrophoresis and densitometry (Paragon kit, Beckman Instruments, Brea, Calif), isoelectric focusing (Resolve Hb kit, Perkin Elmer, Wallac, Akron, Ohio), HbA, quantitation performed by Sickle-Thai Quick Column method (Helena Laboratories, Beaumont, Tex), and Hb and quantitation by alkali denaturation method. Interpretive patient studies, precision, and timing studies were performed.

Results: CAPILLARYS intra-assay precision demonstrated coefficients of variation (CVs) ranging from 0.1% to 3.4% depending on Hb variant and percentage. Inter assay CVs using frozen and thawed controls (n = 7–10, 2-month period) ranged from 0.07% to 5.04%. Stability studies during 20 to 30 minutes, whereas manual methods required batching and took up to 1 week. Interpretive studies showed excellent correlation between CAPILLARYS and traditional methods.

Conclusions: Automated capillary zone electrophoresis provides an alternative, rapid method of hemoglobinopathy determination in comparison with traditional (non–high-performance liquid chromatography) methods.

Peripheral T-Cell Lymphoma Associated With Anti–Tumor Necrosis Factor α Antibody Therapy for Ulcerative Colitis
(Poster No. 27)

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The risk of development of lymphoproliferative disorders in patients with inflammatory bowel disease has been attributed to immunosuppressive and immunomodulatory therapies. Infliximab is a chimeric monoclonal IgG1 antibody directed against tumor necrosis factor (TNF-α) that was approved by the US Food and Drug Administration (FDA) in 1998 as an effective agent against inflammatory bowel disease. We analyzed the histologic, immunophenotypic, and molecular features of a T-cell lymphoproliferative disorder involving the axillary lymph node of a 33-year-old man following treatment with infliximab. The lymph node was effaced by a proliferation of small to intermediate-sized atypical T lymphocytes that expressed CD2, CD3, CD5, CD4, CD8, and CD30 but not TIA-1 or CD56. In situ hybridization studies were negative for Epstein-Barr virus RNA (EBER-1). Although the effacement of architectural and cytologic atypia were suspicious for a peripheral T-cell lymphoma, molecular studies for T-cell receptor gene rearrangement demonstrated a polyclonal T-cell population. Lymphomas of both B- and T-cell lineage have been reported in patients treated with TNF-α blockade. To date 6 cases of T-cell lymphoproliferative disorders associated with infliximab have been reported to the FDA’s Adverse Event Reporting System, all of which have been subclassified as hepatosplenic T-cell lymphomas with aggressive clinical outcomes. These lymphomas, along with the peripheral T-cell lymphoma described in this case report, have been negative for Epstein-Barr virus RNA suggesting that lymphoproliferative disorders following infliximab treatment for inflammatory bowel disease may involve Epstein-Barr virus–independent immune dysregulation. The spectrum of lymphoproliferative disorders associated with infliximab and the potential mechanisms by which they occur are discussed.

Langerhans Cell Histiocytosis With Coexisting Classical Hodgkin Lymphoma
(Poster No. 28)

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Proliferation of Langerhans cells in one or multiple organ systems defines Langerhans cell histiocytosis (LCH). A number of cases have been
Hodgkin lymphoma. The nature of this association is uncertain. Some patients died at the time of diagnosis. These cases illustrate association of LCH with Reed-Sternberg cells rather than neoplastic and potentially aggressive disease. Studies suggest that it may represent a reactive proliferation of Langerhans cells, eosinophils, and necrosis. Reed-Sternberg cells and Hodgkin cells were positive for CD15 and CD30. The Langerhans cells were positive for S100 and CD1a. There was no clinical evidence of systemic LCH disease. The patients were a 52-year-old man and a 38-year-old woman presenting with cervical and inguinal lymphadenopathy, respectively. Exci- sional biopsy of the cervical lymph nodes in the first case revealed exten- sive involvement by lymphohistiocytic infiltrate containing scattered Reed-Sternberg cells and Hodgkin cell variants. In addition, both cases contained focal, sinusoidal aggregates of Langer- hans cells, eosinophils, and necrosis. Reed-Sternberg cells and Hodgkin cells were positive for CD15 and CD30. The Langerhans cells were pos- itive for S100 and CD1a. There was no clinical evidence of systemic LCH disease at the time of diagnosis. These cases illustrate association of LCH with Hodgkin lymphoma. The nature of this association is uncertain. Some studies suggest that it may represent a reactive proliferation of Langer- hans cells rather than neoplastic and potentially aggressive disease.

Characterization of Immature Reticulocytes Fraction and Absolute Neutrophil Count Following Engraftment in a Tandem Cord Blood Transplant Patient

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Context: Donor engraftment following hematopoietic stem cell trans- plantation is conventionally determined by measuring absolute neutrophil count (ANC) with engraftment defined as the first of 3 consecutive days when ANC exceeds 500/µL in peripheral blood.

Design: In this study, we monitored peripheral blood ANC, immature reticulocyte fraction (IRF), and other parameters readily measurable by the Sysmex XE-2100 weekly in a chronic myelocytic leukemia patient re- covering from tandem cord blood transplants directly into the bone mar- row. We compared the trends of ANC, IRF, and other parameters to variable number of tandem repeats data from the bone marrow.

Results: IRF increased simultaneously as the cord blood engrafted and decreased as the engraftment was lost, as compared with the pattern of variable number of tandem repeats. ANC had a delayed but otherwise similar pattern response following engraftment. IRF was superior to ANC in that it not only simultaneously reflected engraftment (several days be- fore the ANC) but also remained low with relapse of the chronic myelo- cytic leukemia, whereas the ANC increased with relapse.

Conclusions: IRF appears to predict engraftment earlier as compared with ANC. ANC also was slightly later to decline with loss of engraftment and increased with relapse of chronic myelocytic leukemia, whereas IRF declined up to 1 week sooner with engraftment loss and remained low during relapse.

Hodgkin Lymphoma Presenting as Paraneoplastic Encephalitis

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Hodgkin lymphoma is a common hematologic malignancy, generally presenting as lymphadenopathy, with or without systemic “B” symptoms. We report a case of Hodgkin lymphoma with an unusual presentation, mimicking encephalitis. A 23-year-old man with fever, headache, and neck stiffness for 1 month developed progressive vision and hearing loss, dys- phagia, slurred speech, and unsteady gait. No lymphadenopathy was ev- ident on physical examination. A presumptive diagnosis of viral menin- gitis was made. His symptoms initially improved but then worsened again; at which time, neurologic evaluation demonstrated depressed mood, normal pupillary reaction, bilateral positive Babinski sign, a weak gag reflex, and a wide-based unstable gait. A complete blood count and metabolic panel were normal. Spinal fluid showed a mild to moderately elevated cell count with high protein content and a negative bacterial culture. Computed tomography scan of the head was normal, but mag- netic resonance imaging showed changes suggestive of autoimmune en- cephalitis. A chest radiograph revealed a widened superior mediastinum, which computed tomography scan demonstrated to be the result of ex- tensional lymphadenopathy. A mediastinal lymph node biopsy showed classical Hodgkin lymphoma, nodular sclerosing type. Following chemo- therapy, the patient had a full neurologic recovery. Paraneoplastic syn- dromes are an uncommon presentation of Hodgkin lymphoma and, in the absence of clinical lymphadenopathy, may result in misdiagnosis as a neurologic condition. After excluding infection, Hodgkin lymphoma should be considered among the causes of neurologic paraneoplastic syn- dromes (Figure 2: Reed-Sternberg cell).

Primary Bone Marrow Lymphoma With Unusual Presentation

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Primary extranodal involvement occurs as an initial presentation of diffuse large B-cell lymphoma in up to 40% of cases, with the gastrointestinal tract, testis, soft tissue, and salivary glands being common sites of involve- ment. The bone marrow and peripheral blood are among the rarest sites of initial presentation. We report a case of primary bone marrow lymphoma. A 27-year-old man presented complaining of intermittent fever, fatigue, and bone pain during a 3-week period. He also had renal failure. He was noted to have hypercalcemia, decreased parathyroid hormone, and normal parathyroid-related peptide. Computed tomography scan for renal stones showed multiple lytic bone lesions. Lymphadenopathy was not present. A monoclonal band was detected neither on serum nor on urine protein electrophoresis. Bone marrow biopsy and fine-needle aspira- tion of the lytic lesions showed a population of medium- to large-sized cells with basophilic cytoplasm and cytoplasmic vacuolization. Flow cyto- metric identified a B-cell population with surface κ restriction positive for CD45, CD19, CD20, CD10, CD22, CD23, and HLA-DR. Immunohis- tochemistry showed Bcl-6 negativity, Bcl-2 positivity, and a Ki-67 prolif- eration index of 70% to 90%, consistent with a high-grade diffuse large B-cell lymphoma. The patient received 1 cycle of hyper-CVAD chemo- therapy during hospitalization and was discharged to go home. This case illustrates a rare process of primary bone marrow diffuse large B-cell lymphoma with an unusual presentation of multiple lytic bone lesions. The Ki-67 proliferation index, along with the presentation, is instrumental in deciding the appropriate therapy.

Cytogenetic Findings in Primary Cutaneous Anaplastic Large Cell Lymphoma

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Primary cutaneous anaplastic large cell lymphoma (CALCL) is a T-cell lymphoproliferative disorder clinically and morphologically distinct from systemic anaplastic large cell lymphoma. Rearrangements of anaplastic large cell lymphoma kinase are characteristic of anaplastic large cell lymphoma but not of CALCL. In fact, few reports characterizing the chromosomal abnormalities in CALCL have been published. We report the case of a 24-year-old woman with a history of multiple ulcerated skin lesions on her arms and legs that had increased in size compared with the previous year; the lesions measured up to 13.0 cm. Multiple skin biopsies revealed a dense dermal infiltrate of variably sized lymphoid cells. Large cells were CD3 and CD30 positive but epithelial membrane antigen and anaplastic large cell lymphoma kinase negative. The clonal T-cell population was positive for CD2, CD3, CD4, and CD5 but negative for CD7. Cytogenetic study of 3 chromosomally abnormal cells indicated that all were near tetraploid, with 87 to 94 chromosomes, and contained structural abnormalities of chromosomes 1, 2, 6, 8, 9, and 14. No anaplastic large cell lymphoma kinase rearrangements were identified. Although current literature on chromosomal abnormalities in CALCL is limited, previous reports have detected multiple complex chromosomal imbalances, some at recurring loci. Our case, although limited, confirms these abnormal results. No additional follow-up is available. Large granular lymphocytes were identified in both PBs (Figure 3). Case 2 also showed ab-

normal lymphocytes. FC revealed 68% (case 1) and 46% (case 2) of PB lymphocytes were CD2\(^+\), CD3\(^+\), CD5\(^-\), CD7\(^-\), CD8\(^+\), CD4\(^-\), CD16\(^-\), and CD56\(^-\) without monoclonal B cells. TCR \(V_{\beta}\) testing (case 2) revealed \(V_{\beta}\)3 and \(V_{\beta}\)5,1 expansions within the CD8 compartment (Figure 4). Our cases highlight the utility of FC in evaluating post-autologous BMT lymphocytes. Etiology of the T-LGLL in these post-autologous BMTs is unclear. Of interest, 1 of 2 cases also revealed T-LGLL in the pheresis product.

**Nodular Lymphocyte–Predominant Hodgkin Lymphoma Presenting With Bone Marrow Involvement by Diffuse Large B-Cell Lymphoma** (Poster No. 33)

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Nodular lymphocyte–predominant Hodgkin lymphoma (NLPHL) is a distinctive and uncommon type of Hodgkin lymphoma. Patients with NLPHL primarily present with low-stage disease and have excellent long-term survival. Bone marrow involvement is rare in NLPHL. Another rare but documented event in NLPHL is a transformation to diffuse large B-cell lymphoma (DLBCL). This case report describes our experience with NLPHL associated with bone marrow involvement by DLBCL. A 16-year-old boy presented with a history of weight loss, headache, and sweating. He had cervical lymphadenopathy with a large, painful left neck mass. Imaging revealed hepatosplenomegaly with mass lesions. The patient underwent lymph node and bone marrow biopsies. The lymph node biopsy revealed a nodular proliferation of scattered large neoplastic cells in a background of small lymphocytes and histiocytes. Immunoperoxidase stains documented expression of CD20 and CD45 by the neoplastic cells. The bone marrow biopsy revealed extensive involvement by sheets of neoplastic B cells consistent with DLBCL. The patient underwent 5 cycles of therapy with doxorubicin, bleomycin, vincristine, etoposide, prednisone, and cyclophosphamide followed by radiotherapy. The patient responded clinically to the therapy and is currently in clinical remission. Follow-up bone marrow biopsies were negative for disease. This case documents NLPHL presenting with bone marrow involvement. Furthermore, the bone marrow involvement was discordant with morphologic features of DLBCL. This is a very unusual presentation of NLPHL. This case should be considered a gray zone between NLPHL and DLBCL and documents an overlap between these 2 lymphomas.

**Two Cases of T-Cell Large Granular Lymphocytic Leukemia Following Autologous Transplantation for Mantle Cell Lymphoma** (Poster No. 34)

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T-cell large granular lymphocytic leukemia (T-LGLL) rarely occurs post-allogeneic bone marrow transplantation (BMT) for hematolymphoid malignancies. To our knowledge, T-LGLL post-autologous transplantation has not previously been reported. Case 1: A 71-year-old man with previous colorectal cancer presented with leukemic blastoid mantle cell lymphoma. He received multiagent chemotherapy (MAC) and 18 months later developed gastrointestinal and brain involvement. He then received additional MAC and autologous peripheral blood cell transplantation (PBSC). Six weeks post-autologous PBSC, flow cytometry (FC) of a peripheral blood (PB) lymphocytosis (13 400000/\(\mu\)L) showed a T-cell large granular lymphocyte (T-LGL). T-cell \(\gamma\) gene rearrangement (TCR-\(\gamma\)) detected a major T-cell clone. FC of the autologous stem cellpheresis product also showed T-LGLL. He is currently doing well without T-LGLL treatment. Case 2: A 66-year-old man presented with persistent chest pain. Studies showed widespread lymphadenopathy, diagnosed as mantle cell lymphoma, with bone marrow involvement. He received MAC and autologous BMT. Six weeks post-autologous BMT, a 2-cm left axillary lymph node was associated with a PB lymphocytosis (8100000/\(\mu\)L with abnormal lymphocytes). PB FC showed a T-LGL, FC T-cell receptor (TCR) \(V_{\beta}\)4, and TCR-\(\gamma\) analysis revealed abnormal results. No additional follow-up is available. Large granular lymphocytes were identified in both PBs (Figure 3). Case 2 also showed ab-

**Primary Monocytic Sarcoma of the Testis With Progression to Leukemia** (Poster No. 35)

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Acute myeloid leukemia can occasionally involve the testis secondarily, but only rare cases have been reported with primary presentation in the testis. We describe a patient with testicular monocytic sarcoma with rapid evolution to acute monocytic leukemia (FAB M5b). A 58-year-old man presented with a 3.3-cm right testicular solid mass. Examination of the orchietomy specimen revealed an intertubular infiltrate of large cells...
with moderate amounts of cytoplasm and large oval, occasionally folded nuclei with prominent nucleoli, interpreted as seminoma. Four weeks following orchectomy, the patient presented with fatigue and pancytopenia. A bone marrow biopsy revealed sheets of large cells with irregular, folded nuclei and abundant pink cytoplasm. On the bone marrow aspirate, these cells had prominently vacuolated basophilic cytoplasm. Immunohistochemistry showed positive staining for CD68 and lysozyme and no staining for CD45, CD30, CD34, myeloperoxidase, and ALK-1. A diagnosis of acute monocytic leukemia (FAB M5b) was made. Reevaluation of the testicular tumor revealed a similar immunophenotype, consistent with monocytic sarcoma. Cytogenetic analysis of the marrow revealed 2 abnormal clones, 1 diploid and 1 tetraploid, with extra copies of chromosome 8; fluorescence in situ hybridization analysis of the testis also revealed aneuploidy of chromosome 8. Primary testicular presentation of acute myeloid leukemia is rare and often leads to diagnostic confusion with more common testicular tumors. This case was unusual in that the marrow leukemia showed more pleomorphic morphology than the testicular tumor and a distinct tetraploid clone, suggesting rapid disease evolution.

Primary Anaplastic Large Cell Lymphoma of Bone
(Poster No. 36)

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Primary bone lymphoma is an uncommon disease with poor clinical outcome. Non-Hodgkin lymphoma of bone comprises approximately 7% of malignant bone tumors and 5% of extranodal lymphomas. A majority of the cases are diffuse large B-cell non-Hodgkin lymphomas. We report a patient with primary anaplastic large cell lymphoma of bone. The patient was a 74-year-old man with multiple medical conditions who presented with right hip pain. Bone scan revealed intertrochanteric fracture of the right femur and multiple sclerotic bony lesions involving most of the skeleton. A bone marrow biopsy with flow cytometry showed mild reactive plasmocytosis. Subsequently computed tomography-guided biopsy of the right hip fracture site was performed. The microscopy showed a malignant neoplasm with highly pleomorphic cells, irregular nuclear outlines, finely dispersed chromatin, one to multiple nucleoli, and abundant pink cytoplasm. On the bone marrow aspirate, these cells had prominently vacuolated basophilic cytoplasm. Immunohistochemistry showed positive staining for CD68 and lysozyme and no staining for CD45, CD30, CD34, myeloperoxidase, and ALK-1. A diagnosis of acute monocytic leukemia (FAB M5b) was made. Reevaluation of the testicular tumor revealed a similar immunophenotype, consistent with monocytic sarcoma. Cytogenetic analysis of the marrow revealed 2 abnormal clones, 1 diploid and 1 tetraploid, with extra copies of chromosome 8; fluorescence in situ hybridization analysis of the testis also revealed aneuploidy of chromosome 8. Primary testicular presentation of acute myeloid leukemia is rare and often leads to diagnostic confusion with more common testicular tumors. This case was unusual in that the marrow leukemia showed more pleomorphic morphology than the testicular tumor and a distinct tetraploid clone, suggesting rapid disease evolution.

Mast Cell Sarcoma of the Spinal Cord: Morphologic and Immunophenotypic Profile
(Poster No. 37)

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Mast cell (MC) sarcoma is an extremely rare variant of systemic mastocytosis with only a few cases described in the literature. It is characterized by uncontrolled proliferation of MCs into a malignant solid tumor. We present the morphologic and immunophenotypic profiles of spinal cord MC sarcoma evolving into leukemic phase, discuss diagnostic challenges, and review reported cases in the literature. A 22-year-old woman presented with back pain and lower extremity weakness. Spinal magnetic resonance imaging revealed an extradural mass, which was subsequently resected. Initial pathologic evaluation revealed diffuse proliferation of large, discohesive cells with pleomorphic nuclei and giant multinucleated forms. The immunohistochemical profile of the tumor cells was inconclusive (Table). The preliminary diagnosis was undifferentiated malignant neoplasm. Additional staining found the tumor cells to express tryptase (Figure 5), CD45, and CD68, suggestive of MC neoplasm. Subsequent bone marrow (BM) biopsy revealed extensive infiltration by malignant MCs. Aspirate smears contained numerous mature, immature, and dyspoietic MCs, including binucleated, giant, and variably granulated, specific esterase–positive and toluidine blue-metachromatic forms. Immunophenotypic profile is presented in the Table. Overall findings were fully consistent with BM involvement by MC sarcoma, “mast cell sarcoma, leukemic phase.” Diagnostic challenges encountered in the present case included morphologic variance, as malignant MCs were heavily granulated in Giemsa-stained BM aspirate, whereas granular cytoplasm was not readily appreciated in the hematoxylin-eosin–stained biopsies. Also worthwhile is the inconsistent immunohistochemical staining profile of the tumor cells, which may be explained by different processing techniques. Finally, tryptase stain was essential in confirming the diagnosis.

### Immunophenotypic Profile of Malignant Mast Cells

<table>
<thead>
<tr>
<th>Immune Marker</th>
<th>Spinal Cord Mass</th>
<th>Bone Marrow*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Initial†</td>
<td>Additional/ Repeat</td>
</tr>
<tr>
<td>Tryptase</td>
<td>NA†</td>
<td>Positive</td>
</tr>
<tr>
<td>c-Kit (CD117)</td>
<td>Positive</td>
<td>NA</td>
</tr>
<tr>
<td>LCA (CD45)</td>
<td>Negative</td>
<td>Positive</td>
</tr>
<tr>
<td>KPI (CD68)</td>
<td>Negative</td>
<td>Positive</td>
</tr>
<tr>
<td>CD34</td>
<td>Negative</td>
<td>Positive</td>
</tr>
</tbody>
</table>

* Malignant mast cells brightly expressed CD15, CD33, and c-Kit in flow cytometric immunofluorescence on the bone marrow aspirate. Other negative immune markers performed on bone marrow aspirate and biopsy include CD2, CD5, CD7, CD10, CD11b, CD13, CD14, CD19, CD56, CD61, CD235a, and myeloperoxidase.
† Other negative immune markers performed initially on spinal cord mass include CD3, CD20, CD30, cytokeratin, desmin, factor VIII, human chorionic gonadotrophin (HCG), HMB-45, myoD1, myogenin, placental alkaline phosphatase (PLAP), and S100. Positive stains included HHF-35 and vimentin.
‡ NA indicates not performed.

### Concomitant Chronic Lymphocytic Leukemia and Acute Lymphoblastic Leukemia
(Poster No. 38)

Chandrani GhoshDasgupta, MD (chandrani.7@hotmail.com); Humayun K. Islam, MD, PhD; Myron R. Melamed, MD. Department of Pathology, Westchester Medical College & New York Medical College, Valhalla.

Acute lymphoblastic leukemia (ALL) and chronic lymphocytic leukemia (CLL) are common hematologic malignancies as separate entities; however, concurrent primary presentation of ALL with CLL is extremely rare. Here, we report such a unique case of composite precursor B-ALL and B-CLL. A 63-year-old man presented with vague symptoms of weakness and lethargy. There was no organomegaly or lymphadenopathy. He had no previous history of hematologic disease. Peripheral blood revealed cytopenia, relative lymphocytosis (61%), and increased lymphoblasts (18%). Flow cytometry of peripheral blood revealed 2 populations of cells: im-
mature B cells and λ clonal mature B cells, each comprising 21% of cellularity. The former expressed CD19, CD20, CD22, CD10, and TdT, whereas the latter expressed CD19, CD20, CD22, CD25, and CD5. Bone marrow biopsy was hypercellular with involvement by precursor B-ALL and without any involvement by CLL. There was no CD5/CD20 lymphoid population in the biopsy specimen. Cytogenetics and molecular studies were negative for any abnormalities, including cyclin D1 gene translocation. These immunophenotypic findings confirmed the rare diagnosis of precursor B-ALL and B-CLL occurring simultaneously at initial presentation. Composite hematologic malignancy is not a rare event in clinical practice. CLL has been reported with other mature B-cell neoplasms, with Hodgkin lymphoma, and rarely with acute myeloid leukemia. Thus far, no case has been reported in the English literature describing concurrent CLL and ALL. To our knowledge, this is the first reported case with a unique combination of precursor and mature B-cell leukemia occurring simultaneously at presentation.

Burkitt Lymphoma Lacking B-Cell–Associated Antigen Expression
(Poster No. 39)
Karimireddy J. Reddy, MD (karimireddy.reddy@ucdmc.ucdavis.edu); Cecilia Yeung, MD; Koushan Siami-Namini, MD; Kim Janatpour, MD; Denis M. Dwyre, MD. Department of Pathology, University of California Davis Medical Center, Sacramento.

Burkitt lymphoma (BL), a highly aggressive B-cell lymphoma, is characterized by a high proliferation index; c-myc translocations, t(8;14), t(2;8), or (t;8;22); and B-cell gene rearrangements. The malignant cells are uniform, in medium-sized, and express B-cell antigens (CD19, CD20, CD22), CD10, and Bcl-2. Lack of B-cell–associated antigen expression by immunoperoxidase staining has not been reported in untreated BL. We report an unusual case of BL lacking B-cell–associated antigen expression. A 35-year-old man presented with a left maxillary/orbital mass and was subsequently identified to be human immunodeficiency virus (HIV) positive. A biopsy of the mass demonstrated a monotonous population of CD45– lymphocytes with a high mitotic rate and a classic BL morphology. The cells were negative for B-cell–associated antigens (CD20, CD79a, CD22) and lacked T-cell antigen expression. Immunoglobulin heavy chain gene rearrangement was demonstrated by polymerase chain reaction. Fluorescence in situ hybridization studies revealed the characteristic translocation, t(8;14), confirming BL. To our knowledge, this is the first reported case of B-cell-associated antigen–negative BL. Other hematologic malignancies such as diffuse large B-cell lymphoma and mantle cell lymphoma can also feature c-myc translocations and should be considered in the differential diagnosis. However, in addition to the c-myc translocation and immunoglobulin H gene rearrangements, the high proliferation index and morphologic evidence favor BL. HIV infection has been associated with unusual lymphoid tumors and may contribute to this unusual phenotype lacking general B-cell markers. This case also emphasizes the importance of molecular studies as a powerful diagnostic tool in the routine workup of hematologic malignancies.

Mature T-Cell Leukemia/Lymphoma With CD4 CD8 Double-Positive Sézary Cells and Extensive Cutaneous Involvement
(Poster No. 40)
Silvia Skripenova, MD (Silvia.Skripenova@hsc.utah.edu); Mohamed Salama, MD. Department of Pathology, University of Utah, Salt Lake City.

Mature T-cell leukemia/lymphomas include T-cell prolymphocytic leukemia, adult T-cell leukemia/lymphoma, and Sézary syndrome. Aberrant CD4 CD8 coexpression is reported in approximately a third of T-cell prolymphocytic leukemias and in very rare cases of adult T-cell leukemia/lymphoma. The patient is a 45-year-old man who presented with multiple erythematous skin lesions; elevated white count (39.3 × 10^9/L); and axillary, abdominal, and inguinal adenopathy. Skin biopsy showed T-cell lymphoma with aberrant CD4 CD8 coexpression. Bone marrow biopsy revealed only rare atypical T cells. Peripheral blood contained atypical T cells with prominent cerebriform nuclear morphology and CD4 CD8 coexpression. Other T-cell antigen markers, CD2, CD3, CD5, and CD7, were normally expressed. Atypical cells did not express TdT, CD10, CD54, or CD25. T-cell receptor rearrangement studies were positive by polymerase chain reaction on peripheral blood and skin biopsy. Cytogenetic studies showed multiple numerical and structural abnormalities. Inguinal lymph node biopsy showed involvement by atypical T lymphocytes with CD4 CD8 coexpression. Studies for human T-cell leukemia/lymphoma virus types 1 and 2 were negative by immunoblot and serology. The lesion was classified as cutaneous lymphoma with Sézary syndrome. The patient demonstrated a relatively good initial clinical response to treatment; however, a few months later he presented with new skin lesions. We report an unusual case of Sézary syndrome with CD4 CD8 coexpression. Inclusion of Sézary syndrome in the differential diagnosis of CD4 CD8 double-positive mature T-cell leukemias/lymphomas will assist in proper classification and treatment of these patients.

Precursor B-Cell Acute Lymphoblastic Leukemia/ Lymphoma Presenting as Acute Renal Failure
(Poster No. 41)
Renuka Agrawal, MD (reagrawal@llu.edu); Craig Zuppan, MD; Jun Wang, MD. Department of Pathology, Loma Linda University Medical Center, Loma Linda, Calif.

Precursor B-cell acute lymphoblastic leukemia/lymphoma (ALL) is a common pediatric hematologic malignancy. Although renal failure resulting from tumor lysis is a recognized complication of its treatment, initial presentation with renal failure is distinctly uncommon. We report here a 19-year-old Hispanic man with ALL who presented with acute renal failure because of parenchymal infiltration. About 6 months prior to diagnosis, he had noted increased urine volume and frequency. When he eventually sought medical attention, he was found to be hypertensive with renal insufficiency (serum creatinine of 7.1 mg/dL). Pancytopenia was also noted, without circulating blasts on peripheral blood smear review. Further evaluation demonstrated bilateral renal enlargement with lymphadenopathy in the neck and retroperitoneum. Needle biopsy of the left kidney showed a diffuse infiltrate of monotonous blastoid cells obliterating the normal renal architecture (Figure 6). Immunophenotyping by flow cytometry and immunohistochemistry showed the tumor cells to coexpress CD19, CD20, CD10, CD34, CD38, CD79a, HLA-DR, and TdT. Subsequent bone marrow biopsy showed a similar blast population replacing more than 80% of the marrow, and a diagnosis of precursor B-cell ALL was made. ALL must be considered among the causes of acute renal failure when the kidneys are enlarged. A combined analysis, including careful morphologic study and immunophenotyping by flow cytometry or immunohistochemistry, is helpful in arriving at the correct diagnosis and in avoiding confusion with other small "blue cell" tumors that may involve the kidney, such as Wilms tumor, small cell carcinoma, or primitive neuroectodermal tumor.

CD20-Negative CD5-Positive Small Mature B-Cell Non-Hodgkin Lymphoma in a Patient Without Prior Rituximab Therapy: An Exceptional Case Report and Therapeutic Implications
(Poster No. 42)
Pranil Chandra, DO (pranilchandra4@yahoo.com); Alec Goldenberg, MD; Cynthia Liu, MD, PhD; Sherif Ibrahim, MD, PhD.1 Departments of 1Hematopathology and 2Hematology, New York University, New York.

We describe an exceptional case of a CD20-negative CD5-positive small mature B-cell non-Hodgkin lymphoma with unusual clinical, morphologic, and immunophenotypic features in a 67-year-old man without prior history of rituximab therapy who presented with abdominal fullness. A computed tomography scan demonstrated a 19 × 18 × 18-cm retrospi-
toneal mass. Core biopsies revealed lymphoid tissue with completely ef-
faced architecture by a diffuse predominantly lymphocytic infiltrate con-
posed of a monotonous population of small to intermediate lymphocytes with scant cytoplasm, round nuclei, and clumped chromatin and occa-
sional large lymphocytes with prominent nuclei admixed with abun-
dant scattered histiocytes. Focally, the lymphocytes showed a monocytoid appearance. Immunohistochemical staining showed that the majority of the cells were positive for CD5, Bcl-2, and CD79a and negative for CD20, CD10, CD23, cyclin D1, CD38, and Bcl-2/6, highlighted the histiocytes. Ki-67 was positive in the large cells and in some histiocytes. Im-
munophenotypic analysis by flow cytometry revealed a λ-restricted B-cell population expressing CD19 and CD5 and lacking CD10, CD20, and CD23. Molecular analysis was unable to demonstrate t(11;14). Cytogenetic analysis of the bone marrow aspirate was normal. A diagnosis of CD5-
B-cell non-Hodgkin lymphoma was rendered. Because of the lack of CD20, this patient was not treated with anti-CD20 monoclonal antibody, rituximab. Furthermore, this case could not be classified by current World Health Organization standards and suggests the need for large-scale mo-
lecular studies to more profoundly evaluate molecular biology and clin-
ical behavior in such neoplasms and to offer useful data for optimal clin-
ic management.

Chediak-Higashi Syndrome: Report of an Unusual Presentation in an African American Boy
(Poster No. 43)
Barry White, MD (bawhite@mcc.edu); Trevor Maurer, BS; Elizabeth Manaloor, MBBS. Department of Pathology, Medical College of Georgia, Augusta.

The patient was an 11-year-old African American boy who was referred to our institution for evaluation of anemia of uncertain origin, severe peri-
odental disease, and easy bleeding of the gingiva. One year previous, the patient was admitted to an outside hospital for a syncopal episode and was found to be anemic, with a hemoglobin count of 10 mg/dL. Hema-
tologic evaluation, including hemoglobin electrophoresis and iron studies, was normal at that time. He had no significant medical history except for recurrent gingivitis. There was no family history of hematologic problems. During the current evaluation, a peripheral blood smear was reviewed in the hematology laboratory. Multiple large granules were identified in neutro-
philis, monocytes, and rarely, lymphocytes. A provisional diagnosis of Chediak-Higashi syndrome (CHS) was made and peripheral blood smear was sent for electron microscopy. Electron microscopy confirmed the diag-
nosis of CHS by identification of large, electron-dense granules in neutro-
philis, eosinophilis, and to a lesser extent in monocytes. Our patient was African American and did not have the prototypical oculocutaneous al-
binism. His late presentation, absence of severe infections, and normal neurologic development contributed to a low clinical suspicion and late diagnosis of CHS. CHS in persons of African descent is not well docu-
mented, and it is possible that such patients may present more frequently with an unusual presentation of symptoms and physical findings. This case illustrates the importance of a peripheral blood smear review in pa-
tients with hematologic abnormalities.

An Atypical Presentation and Immunophenotype of Acute Promyelocytic Leukemia, Microgranular Variant
(Poster No. 44)
Marisa Mammappallil, MD (Marisa.Mammappallil@ttuhsc.edu); Safaa Labib, MD. Department of Pathology, Texas Tech University Health Sciences Center, Lubbock.

We present a case of acute promyelocytic leukemia (APL), microgran-
ular variant, arising in a pancytopenic individual. The leukocyte count should be very high. Phenotypically, both forms of APL are CD34 nega-
tive. Our case revealed CD34 positivity in approximately 20% of leukemic cells. This is a rare presentation and an atypical immunophenotype of this uncommon APL subtype, which is hypogranular and may lend itself to missed or delayed diagnosis. The patient is a 41-year-old woman who presented with a 2-month history of generalized weakness. Physical ex-
amination revealed pallor and several ecchymoses. Laboratory values re-
vealed pancytopenia: WBC 3.7 × 10^3/μL (4.1–11.2 × 10^3/μL), hemoglobin 4.9 g/dL (11.5–15.5 g/dL), hematocrit 13.8% (35.0%–46.1%), platelets 23 × 10^3/μL (140–400 × 10^3/μL). She was admitted to the hospital, and a bone marrow biopsy was performed. Evaluation of bone marrow biopsy and aspirate revealed a large population of mononuclear cells with hypogranular cytoplasm and convoluted nuclear contours. Rare Auer rods were seen. The core biopsy was 100% cellular. Immunohistochemistry showed expression of CD3, CD43, CD56, CD117, TdT, and CD9, in 20% of the cells in both the core and aspirate. Flow cytometric analysis revealed CD34 positivity in approximately 20% of leukemic cells and their originating tumors including plasmablastic myeloma. Although CD34 is consistent, it is nonspecific for plasma cells being ex-
mated, and it is possible that such patients may present more frequently with an unusual presentation of symptoms and physical findings. This case illustrates the importance of a peripheral blood smear review in patients with hematologic abnormalities.

Hemoglobin Oleander and Hemoglobin S: A Previously Unreported Combination
(Poster No. 45)
David D. Grier, MD (grierdd@gmail.com); Richard Lottenberg, MD; Diana M. Cardona, MD; David A. Ostrov, PhD; David H. Chui, MD; Neil S. Harris, MB, ChB, MD. Departments of Pathology, Immunology and Laboratory Medicine and Hematology and Oncology, University of Florida, Gainesville; Departments of Medicine and Pathology and Labora-
tory Medicine, Boston University, Boston, Mass.

Hemoglobin Oleander, a α16(GH4) Glu→Gln, is a rarely described α-
chain hemoglobin variant with normal functional properties and no re-
ported clinical abnormalities. We describe a case of a 39-year-old African American man with known sickle cell trait and a nonspecific history of persistent fatigue and atypical pain associated with physical activity. His complete blood count was unremarkable with no evidence of anemia, hemolysis, or sickling. There was no evidence of splenic infarction on imaging studies and no clinical evidence of sickling. Hemoglobin analysis by cation-exchange high-performance liquid chromatography showed 46% hemoglobin A, 29.1% hemoglobin S, and 2 hemoglobin variants at 8.6% and 14.8%. Hemoglobin A2 was normal. At 22%, α2-globin mutation. Further studies are required to determine the nature of the glo-
bin chain interactions.

CD138 Expressions in Merkel Cell Carcinoma: A Potential Diagnostic Pitfall With CD138-Positive Hematologic Malignancies
(Poster No. 46)
Prashant A. Jani, MD (dr.prashant.jani@gmail.com); Dina El Demel-
lawy, MD. Department of Pathology, Thunder Bay Regional Health Sci-
cence Centre, Thunder Bay, Ontario, Canada.

Context: Merkel cell carcinoma is a neuroendocrine carcinoma of the skin that overlaps morphologically with hematologic malignancies having blastic morphology. The consistent expression of CD56 has been docu-
mented in Merkel cell carcinoma. A recent report has found CD138 expres-
sion in a subset of cases. The current study assesses Merkel cell carcinoma expression for CD138.

Design: Ten cases with the diagnosis of Merkel cell carcinoma were retrieved retrospectively from the Thunder Bay Regional Health Science Centre archives, from the period of 2000 to 2007. For all cases, review of the clinical and pathologic data was performed. In addition, immunohis-
tochemical staining using antibodies against CD138, cytokeratin (CK) 20, CK7, epithelial membrane antigen, TdT, Bcl-2, CD45, CD20, synaptophysin, and CD56 was assessed.

Results: CD138 has been consistently expressed in all cases of Merkel cell carcinoma (Table).

<table>
<thead>
<tr>
<th>Marker Expression</th>
<th>Interpretation</th>
<th>% of Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>CD138 Membranous</td>
<td>Positive</td>
<td>90</td>
</tr>
<tr>
<td>TdT, CK7, CD45, CD20</td>
<td>None</td>
<td>0</td>
</tr>
<tr>
<td>CD56, Bcl-2, epithelial membrane antigen</td>
<td>Cytoplasmic</td>
<td>100</td>
</tr>
<tr>
<td>CK20 Cytoplasmic</td>
<td>Positive</td>
<td>100</td>
</tr>
<tr>
<td>Synaptophysin Cytoplasmic</td>
<td>Positive</td>
<td>80</td>
</tr>
</tbody>
</table>

Conclusions: CD138 is documented as a consistent marker of plasma cells and their originating tumors including plasmablastic myeloma. Although CD138 is consistent, it is nonspecific for plasma cells being ex-
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Abstracts
pressed in most Merkel cell carcinomas. Other markers, such as CD56, epithelial membrane antigen, and Bcl-2, are expressed in a subset of melanoma and in almost all Merkel cell carcinoma. Plasmablastic lymphomas are also CD138 positive. In dealing with CD138-positive tumors that show a blastoid morphology, a panel of immunohistochemical markers, including hematologic, neuroendocrine markers, and CK20, is recommended to differentiate blastoid hematologic malignancies from Merkel cell carcinomas. To the best of our knowledge, this is the first study to report CD138 expression in Merkel cell carcinoma, and it highlights the potential diagnostic pitfall.

Loss of the Y Chromosome: An Age-Related or Clonal Phenomenon in Acute Myelogenous Leukemia and Myelodysplastic Syndrome?

Anna Wong, MD (anna.wong@cshs.org); Belle Fang, MD, MS; Xiuping Guo, PhD; Ling, Zhang, MD; Stephen Lee, MD; Rhona Schreck, PhD. Department of Pathology and Laboratory Medicine and Medical Genetics Institute, Cedars Sinai Medical Center, Los Angeles, Calif.

Context: Various publications report that loss of the Y (−Y) chromosome is an age-related phenomenon. It is also known that the incidence of acute myelogenous leukemia (AML) and myelodysplastic syndrome (MDS) increases with age. The clinical association between −Y chromosome and AML and MDS disorders has been difficult to delineate because they are both related to aging. One comprehensive report suggests that −Y chromosome in more than 75% of cells may indicate a clonal phenomenon that could be a marker for AML and MDS. This study attempts to evaluate this relationship.

Design: A retrospective review of cytogenetic reports of male patients from 1996 to 2007 was performed. Karyotypes with −Y chromosome were stratified based on the percentage of cells missing the Y. Age and bone marrow biopsy diagnosis was collected. Association between AML and MDS and −Y chromosome was evaluated by logistic regression analysis, with and without adjusting for age effect.

Results: One hundred forty-four patients showed −Y chromosome. An increased incidence (P < .05) of AML and MDS were seen only in patients with −Y chromosome in 100% of cells (Table).

Conclusions: Loss of the Y chromosome, in most cases, appears to be primarily an age-related phenomenon, with the percent of cells missing the Y chromosome increasing with age. However, in individuals in whom all cells in the bone marrow show −Y chromosome, there is a statistically significant increase in AML and MDS compared with patients with some or all 46,XY cells, even after adjusting for age, suggesting that the absence of any normal cells may be more indicative of AML and MDS.

Plasmablastic Lymphoma With c-myc Rearrangement in Human Immunodeficiency Virus–Positive Patients

Hung S. Luu, MD (luuh@cshs.org); Ling Zhang, MD; Randa Alsabeh, MD. Department of Pathology, Cedars-Sinai Medical Center, Los Angeles, Calif.

Plasmablastic lymphoma (PBL) is an uncommon, aggressive lymphoma characterized morphologically by the plasmacytoid and blastoid appearance of cells and immunophenotypically by loss of pan-B markers and positive CD138 reactivity. PBL is considered a variant of diffuse large B-cell lymphoma. Translocation associated with c-myc gene (8q24) is a hallmark of Burkitt lymphoma and is also associated with 10% to 15% of diffuse large B-cell lymphoma as well as multiple myeloma and other solid tumors. c-Myc positivity may portend more advanced stage or aggressive clinical behavior.

Pathologic Features and Clinical Outcomes in 2 Cases of Plasmablastic Lymphoma

<table>
<thead>
<tr>
<th>Age, y/SEX/HIV Status</th>
<th>Biopsy Site</th>
<th>Key Immunohistochemical Stains</th>
<th>c-myc FISH*</th>
<th>Outcomes: Follow-up at 4 Mo</th>
</tr>
</thead>
<tbody>
<tr>
<td>39/M+ Right thigh</td>
<td>CD138  +  BOB-1  +  OCT-2  +  p53  +  Ki-67 &gt; 95%  EBER  +  HHV-8  +  Deceased</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>42/M+ Rectum</td>
<td>CD138  +  BOB-1  +  OCT-2  +  p53  +  Ki-67 &gt; 95%  EBER  +  HHV-8  +  Undergoing radiation treatment</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* FISH indicates fluorescence in situ hybridization.

Homozygous Versus Heterozygous JAK2 Gene Mutations in Chronic Myeloproliferative Disorders

Mohamed El-Fakharany, MD (m72m@hotmail.com); Xiuling Meng, MT; Domnita Crisan, MD, PhD. Department of Clinical Pathology, William Beaumont Hospital, Royal Oak, Mich.

Context: An activating JAK2 mutation (JAK2 V617F) has been reported in almost all patients with polycythemia vera and in approximately one half of patients with essential thrombocythemia and idiopathic myelofibrosis. Our goal is to identify the distribution of homozygous and heterozygous JAK2 mutations in these disorders and to evaluate for correlation with clinical presentation.
Design: Patients were identified retrospectively by myeloproliferative disorder diagnosis based on morphology and JAK2 mutation analysis between February 2006 and November 2006. DNA samples extracted from bone marrow and peripheral blood specimens were used for real-time polymerase chain reaction–based quantitative detection to determine percentage of mutant allele and hence determination of zygosity.

Results: Twelve patients have tested positive for homozygous JAK2 mutations, and 47 were identified as heterozygous. Polycythemia vera was the clinical diagnosis in 10 (83%) of homozygous cases and 9 (19%) of heterozygous cases; idiopathic myelofibrosis was the clinical diagnosis in 1 (8%) of homozygous cases and 3 (6%) of heterozygous cases. Seven peripheral blood samples were heterozygous for JAK2, but no myeloproliferative disorder diagnosis was established at the time of testing (see Table for results).

Conclusions: Homozygous JAK2 mutations are mostly associated with polycythemia vera ($P < .05$), whereas heterozygous mutations are more frequent in patients with essential thrombocythemia ($P < .05$). This finding may have prognostic implications, the evaluation of which requires a prospective study of a larger patient population to investigate the relationship between JAK2 V617F gene dose and clinical evolution.

<table>
<thead>
<tr>
<th>Summary of Results</th>
<th>Homozygous/Heterozygous</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>Polycthyemia Vera</td>
</tr>
<tr>
<td>Patients, No.</td>
<td>12/47</td>
</tr>
<tr>
<td>Mean age, y</td>
<td>74.9/67.5</td>
</tr>
<tr>
<td>Male-female</td>
<td>5.7/20:27</td>
</tr>
<tr>
<td>Mean white blood cell count, bil/L</td>
<td>27.9/15.5</td>
</tr>
<tr>
<td>Mean hemoglobin, g/dL</td>
<td>15.0/14.2</td>
</tr>
<tr>
<td>Mean platelet count, bil/L</td>
<td>851.3/784.8</td>
</tr>
</tbody>
</table>

**POSTER SESSION 200: SUNDAY, SEPTEMBER 30, 2007, 1:30 PM–4:00 PM**

**Microbiology; Molecular Pathology; Neuropathology; Pathology Education; Pulmonary and Mediastinal Pathology; Quality Assurance**

**Characterization of the Enterotoxigenic *Escherichia coli* Tia Protein and Its Interactions With Intestinal Cells**

*Poster No. 1*

Joseph Mammarappallil, PhD (joseph.mammarappallil@ttuhsc.edu); Michael San Francisco, PhD. Department of Biological Sciences, Texas Tech University, Lubbock.

**Context:** Enterotoxigenic *Escherichia coli* (ETEC) is a major worldwide health concern. Annually, ETEC accounts for 600 million cases of diarrhea and 1.2 million deaths. The organism colonizes the proximal small bowel via its colonization factor antigens. After adherence, ETEC delivers its enterotoxins leading to diarrhea. It is believed that colonization factor antigens and enterotoxins are the only virulence factors that ETEC strains possess; however, human volunteers challenged with nontoxigenic ETEC strains still develop disease, suggesting uncharacterized virulence determinants.

**Design:** ETEC adherence and invasion was determined by bacterial cell plating. For actin studies, Tia-stimulated cells were treated with rhodamine-phalloidin and visualized at 550 nm. Animal studies were performed with known amounts of bacteria added to surgically ligated bowel loops.

**Results:** Using an ileocecal cell line, we tested ETEC’s ability to adhere to and invade the distal small bowel. An F-actin stain of the invaded ileocecal cells determined that ETEC invasion caused increases in host F-actin. An ETEC chromosomal screening method identified a specific outer membrane protein (Tia) that mediates the distal small intestinal effects. In vivo effects of Tia on ETEC pathogenesis were seen in rabbit ileal loop assays performed with Tia-deleted ETEC mutants. The deletion of Tia from ETEC significantly reduced the amount of fluid collected in the rabbit intestinal lumen.

**Conclusions:** We have identified a novel area of attachment for the microorganism, and invasion represents a novel mechanism of pathogenesis for ETEC. Tia may play a significant role in this process. Continued study may provide new targets to reduce ETEC pathogenesis.

**Recommendations for Repeat Testing for Clostridium difficile Toxins**

*Poster No. 2*

Diana M. Cardona, MD (cardod@pathology.ufl.edu); Linda Pugh, BSMT; Kenneth H. Rand, MD. Department of Pathology, University of Florida, Gainesville.

**Context:** *Clostridium difficile* is the leading cause of antibiotic-associated diarrhea and pseudomembranous colitis, which have significant morbidity and mortality. Accurate and timely diagnosis is critical. Current recommendations suggest repeating enzyme immunoassays for *C difficile* toxin in 2 or more stool samples because of less than 100% sensitivity.

**Design:** All *C difficile* tests between January 1, 2006 to December 31, 2006 were retrospectively analyzed for results and testing patterns. The Wampole *C difficile* TOX A/B II ElA kit (sensitivity 92% and specificity 100%) was used. Patient encounters were defined as 10 days from initial testing; further tests within the subsequent 3 months were excluded.

**Results:** There were a total of 6058 tests from 3112 patients; 2789 (46%) were repeat tests. Of the 1337 initially negative tests, 56 (4.2%) became positive on repeat testing within 10 days. Of tests repeated on the same day as the first (day 0), 1.2% (4/335) were repeat tests. Of those repeat tests, 1.5% (12/480) on day 2, 1.9% (5/262) on day 3, 3.8% (15/403) on days 4 to 6, and 3.8% (10/265) on days 7 to 10. Of initially positive patients, 93.1% were positive on repeat on day 0, 69.8% on day 1, 73.2% on day 2, 22.7% on day 3, 16.7% on days 4 to 10, and 17.8% on days 7 to 10.

**Conclusions:** Depending on the clinical setting, these data support not repeating *C difficile* tests within 2 days of a negative result and limiting repeat testing to 1 week or more of a positive result. This practice can help reduce overutilization.

**Phaeohyphomycosis: 2 Unusual Cases**

*Poster No. 3*

Jyotinder N. Punia, MD (jnpunia@hotmail.com); Chad H. Stone, MD. Department of Pathology and Laboratory Medicine, Henry Ford Hospital, Detroit, Mich.

Phaeohyphomycosis is primarily a fungal infection of the subcutaneous tissues caused by dematiaceous fungi. Phaeohyphomycosis rarely can be responsible for life-threatening infections in both immunocompromised and immunocompetent individuals. We present 2 cases of phaeohyphomycosis with unusual presentations. In case 1, a 66-year-old woman with a history of systemic lupus, breast carcinoma, and lung adenocarcinoma, following chemoradiation, presented 2 years later with a swollen, darkly discolored knee. Imaging revealed a multicellular prepatellar cyst; fine-needle aspiration contained cloudy brown fluid, which was sent for cytology and fungal cultures. Cytology showed brown-pigmented septate hyphae and yeastlike forms amid neutrophils. Fungal culture was positive for the same species. Subsequent follow-up bronchoscopic examination showed a dark “eschar” at the prior resection site. The eschar was excised and the tissue sent for histologic examination. The biopsy contained necrotic tissue with pigmented septate hyphae and yeastlike forms, compatible with phaeohyphomycosis. Based on this diagnosis, the patient underwent repeat bronchoscopy; no residual lesion was visualized and bronchial washings were negative for fungus. Subsequent follow-up bronchoscopy has remained negative for dematiaceous fungus. The latter case highlights that (1) fungal infection may not be clinically suspected, (2)
**Bordetella hinzii Septicemia in Association With Epstein-Barr Virus Viremia and an Epstein-Barr Virus–Associated Diffuse Large B-Cell Lymphoma**

(Poster No. 4)

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**Context:** Bordetella hinzii has been recognized as a rare but emerging cause of opportunistic infections in humans. To date, B hinzii bacteremia has only been reported in 2 patients and was successfully treated in 1 patient. B hinzii has not been previously associated with Epstein-Barr virus (EBV) erythrophagocytosis or EBV-associated lymphomas.

**Design:** We present a case of B hinzii infection in the setting of immunosuppression induced by EBV viremia and lymphoma.

**Results:** A previously healthy 36-year-old woman developed fever to 104°F, full-body livedo reticularis, and fatigue. Despite rheumatologic and infectious diseases investigations, no etiology was identified and the patient's symptoms slowly progressed. Nine months following her initial presentation, the patient's sputum cultures grew B hinzii. One month later, the patient was noted to have EBV viremia and subsequent diagnosis of an EBV-associated diffuse large B-cell lymphoma with erythrophagocytosis. Shortly following this diagnosis, blood and sputum cultures revealed B hinzii and the patient died in the setting of sepsis and multiple organ failure. Definitive identification of B hinzii necessitated analysis of cellular fatty acids by gas-liquid chromatography and 16s rRNA gene sequencing in addition to phenotypic methods.

**Conclusions:** Although B hinzii was previously only known as an occasional pathogen in poultry, it is a rising cause of human infections, particularly in the immunosuppressed. Laboratory diagnosis is challenging and may require multiple diagnostic modalities. Further, resistance to many antimicrobial agents limits treatment of B hinzii. B hinzii may contribute to mortality in the immunosuppressed, yet diagnosis and treatment may be challenging.

**Molecular Characterization Assay for Enriched Circulating Tumor Cells**

(Poster No. 5)

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**Context:** The number of circulating tumor cells (CTCs) before treatment is an independent predictor of progression-free survival and overall survival in patients with metastatic breast cancer.

**Design:** Through the use of the CellSearch System (Veridex, LLC), we designed and evaluated methods for CTC enrichment, in vitro culturing, and downstream nucleic acid isolation for the identification of candidate biomarkers for the early detection of epithelial cells in the peripheral blood. We have developed a quantitative reverse transcription polymerase chain reaction molecular characterization assay to study the biomarker performance using specimens from patients with nonmetastatic prostate disease. The CTCs captured from patients were monitored using both the CellTracks Auto Analyzer System and molecular characterization assay (Veridex, LLC).

**Results:** The CellTracks Auto Analyzer detected CTCs in 36% of patient samples with nonmetastatic prostate disease. However, when the CellTracks Auto Analyzer was complemented by the molecular characterization assay, CTCs were detected in 49% of patient samples. These results have demonstrated it to be an effective companion for the CellTracks Auto Analyzer System for enumeration of CTCs in cases in which a small number of intact cells or partially intact cells exist.

**Conclusions:** The implications for such an assay in clinical settings could have a profound effect in complementing the algorithm used by the CellTracks Auto Analyzer System for enumeration of CTCs. Importantly, the molecular companion assay results could provide additional clinical information when combined with the enumeration of circulating epithelial cells to aid in the therapeutic management of patients. All of the authors own stock in Johnson & Johnson. Veridex, LLC, is a Johnson & Johnson company.

**Ehrlichia ewingii Detection by Real-Time Polymerase Chain Reaction Testing on the Roche LightCycler: A 3-Year Retrospective Study**

(Poster No. 6)

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**Context:** This is a home-brew assay for the qualitative detection of Ehrlichia ewingii (one of the agents responsible for human granulocytic ehrlichiosis) by polymerase chain reaction (PCR) made in response to clinicians suggesting that other species of Ehrlichia may be present locally, based on 1 or more cases of classical ehrlichiosis symptoms that tested negative for the Ehrlichia smear, PCR, and antibodies. Design: A total of 288 specimens from 2004 to 2006 were screened using the genebank sequence U72628 that concurrently tested for E. ewingii, Ehrlichia chaffensis, and Anaplasma phagocytophila in a multiplex LightCycler assay. We requested and received positive control material from various institutions (E. ewingii from Mayo Clinic and the Children's Hospital of St Louis, Mo, E. chaffensis and A. phagocytophila from New York State Department of Health) as well as our own stocks based on our own Ehrlichia-modified Taqman PCR performed at Danbury Hospital. This method record the difference in patients and clinicians for earlier treatment and better correlation with clinical diagnoses. In our tested population of 288 samples, no E. ewingii was detected.

**Morphologically Normal Bone Marrows With Increased Levels of Cytopagnostically Abnormal Cells May Represent Early Embryonic Stem Cells**

(Poster No. 7)

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**Context:** Histologic evidence of bone marrow infiltration in lymphoma is associated with cytogentic findings. However, cases of lymphoma patients without such histologic evidence of infiltration, yet revealing a low percentage of marrow cells with cytogentic abnormalities, are reported. It is hypothesized that cells with cytogentic abnormalities are derived from the primary neoplasm, but because of low-level expression, morphologic evidence in the marrow is not identified. Also, cancer cytogentic abnormalities are seen in a low percentage in normal individuals without evidence of malignancy.

**Design:** We report 3 patients with non-Hodgkin lymphoma with no histologic evidence of disease, yet showing a large number of cells with cytogentic abnormalities in the marrow. Our results challenge the hypothesis that a low-level expression of cytogentic abnormalities might not lead to morphologic transformation of the marrow.

**Results:** Patients 1, 2, and 3 were diagnosed with small lymphocytic lymphoma (Richter transformation), diffuse large B-cell lymphoma, and plasmoblastic lymphoma, respectively. Bone marrow cytogentic evaluation revealed inv(2)[15/20], del(7q)[8/20], and t(8;14) and +12[10/20] in patients 1, 2, and 3, respectively.

**Conclusions:** We propose that these abnormalities are acquired within early embryonic stem cells and, although are seen in large numbers, by themselves are not sufficient to induce morphologic transformation of the marrow. These early stem cells, with clonal cytogentic abnormalities, remain quiescent until a second mutagenic event, similar to the 2-hit hypothesis, occurs in these cells to transform them into tumor cells. Recent reports of BCR-ABL, TEL-AML1, and PML-RARA transcripts in healthy individuals further support our hypothesis.

**Mismatch Repair Proteins and Clinicopathologic Factors in Colorectal Cancer**

(Poster No. 8)

Mahsa Molaee, MD1 (molaemahsa@yahoo.com); Babak Noorinayer, MD2; Ali Ghanbari-atomlahg, MD; Reza Mashayekhi, MD; Somayeh Ghia
Semi-quantitative Analysis of the Janus Kinase 2 V617F Mutation
(Poster No. 9)

Christopher N. Thompson, MD1; Kimberley Hocker, MT(ASCP)2; Arundhati Rao, MD, PhD1.1 Department of Pathology, Scott and White Hospital, Texas A&M University Health Science System JAK2 Quantitative Detection) from Eragen Biosciences (Madison, Tex.

Design: A total of 20 patients with myeloproliferative disorders was evaluated. One discrepant result was observed with the Eragen assay giving a positive result and the InvivoScribe method giving a negative result. This positive JAK2 V617F mutation was confirmed by an alternate external test to be a true positive result. Analysis showed rising semi-quantitative values to correlate with increasing white blood cell count and increased morbidity. The lowest semi-quantitative values were seen in essential thrombocytosis.

Conclusions: The semi-quantitative assay from Eragen Biosciences is robust and detects the JAK2 V617F mutation in as little as less than 1% of the cell sample. However, the lowest values were observed in essential thrombocytosis. Rising the possibility that testing enriched lymphocyte samples may not be as efficacious as using whole blood.

Quantitation of HER-2 Protein Expression and HER-2 Homodimerization in Formalin-Fixed, Paraffin-Embedded Breast Cancer Tissues Using a Novel Proximity-Based Assay
(Poster No. 10)

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Context: The best method to assess HER-2 status remains controversial. Here we characterize a novel assay format that quantifies HER-2 protein (H2T) and homodimerization (H22D) and that can be applied to predictive testing for targeted HER-2 therapies in breast cancer.

Design: H2T and H22D are detected through the release of fluorescent tags (eTags) conjugated to HER-2 antibodies, requiring proximity to a second HER-2 "scissors" antibody. Signal quantified by capillary electrophoresis is normalized to tumor area. Assay verification compared eTag signals with (1) standard HER-2 immunohistochemical (IHC) test categories, (2) HER-2 gene amplification in cell lines, and 174 formalin-fixed, paraffin-embedded breast cancers; and (2) HER-2 gene amplification by fluorescence in situ hybridization (FISH) in 19 breast cancers.

Results: Measured H2T and H22D levels were proportional to known expression levels in cell lines. H2T levels in 174 breast cancers demonstrated a continuum over a wide dynamic range (>2 log), in contrast to conventional IHC categories. The correlation between H2T and IHC categories was significant (P<.001). The eTag assay signal correlates well with IHC Histoscore at lower H2T levels; however, at high H2T levels, eTag provides extended dynamic range. HER-2 gene amplification measured by FISH (HER2/CEP17; gene copy #) correlates loosely with IHC categories and H2T values. Correlation exists between H22D and H2T (r² = 0.7, P < .001).

Conclusions: The results demonstrate that the eTag assay reliably measures H2T and H22D in formalin-fixed, paraffin-embedded tissues. The continuum of H2T over a wider dynamic range compared with conventional IHC and FISH HER-2 tests, along with the novel H22D measure, may provide better predictive tests for targeted HER-2 therapy.

Clinicopathologic Study of Human Immunodeficiency Virus–Positive Lymphoid Neoplasms in India
(Poster No. 11)

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Context: Patients with acquired immunodeficiency syndrome (AIDS) with low CD4 counts have an increased risk of developing non-Hodgkin lymphomas. Although the background positivity is less than 2%, India has the largest number of human immunodeficiency virus (HIV)–positive individuals in the world. However, data from AIDS-related malignancies and T-cell lymphomas are not widely available.

Design: We investigated the association of lymphoid neoplasms and the Epstein-Barr virus (EBV) association and CD4 and CD8 counts in 35 HIV-positive patients from India. The biopsy samples were studied for histology and for expression of CD20, CD3, CD15, CD30, light chains, CD138, Bcl-2, and EBV. In situ hybridization was performed with EBV-encoded nuclear RNA-1 probe. Polymerase chain reaction was performed on DNA extracted from paraffin sections for EBV-subtype analysis.

Results: The CD4 count was less than 200 mm3 in most of the cases. The 35 cases included 14 cases of diffuse large B-cell lymphoma (DLBL), 4 cases of high-grade B-cell lymphoma (unspecified), 3 cases of Burkitt lymphoma (BL), 7 cases of Hodgkin disease, 4 cases of plasmacytoma, and the rest were other subtypes. EBV association was noted in all cases of Hodgkin disease, 2 of 3 BL, and 3 of 14 DLBL. Polymerase chain reaction analysis of the EBNA-3C gene revealed amplifiers corresponding to EBV DNA.

Conclusions: In contrast to the earlier studies in the world, we found (1) that there was a preponderance of DLBLs and (2) that BL was less common in our study population. The incidence of DLBL and BL correlated with a low CD4 count.

Genome-Wide Oligonucleotide Microarray Analysis of Recurrent Malignant Melanoma
(Poster No. 12)

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sion profiling from formalin-fixed, paraffin-embedded patient tissue samples to discriminate metastatic melanoma from primary lesions.

**Design:** Specimens from 3 patients (2 pairs of primary lesion and nodal metastasis as well as 1 pair of 2 apparently distinct primary lesions from a third patient) were run on the Arcturus Paradise system and the GeneChip X3P array. Microarray data was background corrected and normalized using log scale robust multiarray analysis and then analyzed with unsupervised and supervised clustering methods, using centered correlation as the similarity measure and analysis proceed as expressed in primary and metastatic melanoma samples. We also compared our data to an independent data set corresponding to fixed breast carcinoma tissue.

**Results:** We obtained expression profiles for 14,432 probe sets above background. Unsupervised analyses showed that expression profiles were distinct from controls and known cancers clustered as predicted. Surprisingly, when applying a limited gene list that discriminates metastatic melanoma from primary lesions, the 2 samples of indeterminate origin from 1 patient cluster together and have a gene signature more like metastases than primary tumors.

**Conclusions:** Our study shows that total RNA could be extracted from formalin-fixed, paraffin-embedded melanoma tissue for gene expression microarray analyses. The analyses performed here suggest that tumors of unknown origin could have arisen from an unknown common primary tumor or that the proband has a novel germline mutation.

**Genetic Background of Korean Patients With Marfan Syndrome** (Poster No. 13)

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**Context:** Marfan syndrome (MFS) is an autosomal dominant disorder caused by mutations in the fibrillin-1 gene (FBN1), and the clinical spectrum of MFS is highly variable. Therefore, identification of FBN1 mutation is important to confirm the diagnosis.

**Design:** From May 2003 to December 2006, a total of 65 patients were referred for FBN1 analysis. Among them, 28 patients fulfilled or possibly met the Ghent criteria (group I), but 10 patients did not (group II). The remaining 27 patients could not be evaluated because of lack of information (group III). All patients’ genomic DNA was extracted, amplified, and sequenced for whole exons and their flanking intronic regions of the FBN1.

**Results:** In group I, 23 (82%) of 28 patients had the FBN1 mutations, but none in group II and 11 (41%) of 27 in group III had the mutation. We detected 34 different FBN1 mutations, 26 (77%) of which were novel. There were 12 missense (53%), 15 nonsense or frameshift (44%), and 1 splice site mutations (3%). Twenty-three mutations (68%) occurred in cDNA-like exons and 11 (18%) in 5-cysteine modules.

**Conclusions:** Classical and suspected mutations showed higher probability of carrying FBN1 mutation, but none had the mutation who did not fulfill the Ghent criteria. Therefore, careful evaluation of any patient with suspected FMS is important for predicting positive result on FBN1 testing and the mutation analysis of FBN1 is very useful for confirmatory diagnosis for MFS.

**Utilization of Fluorescence In Situ Hybridization to Distinguish a Transient Increase in Blasts Following Treatment With Granulocyte Colony-Stimulating Factor From Relapsed Acute Leukemia** (Poster No. 14)

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Granulocyte colony-stimulating factor (G-CSF) stimulates granulocyteopoiesis following intensive chemotherapy for acute leukemia, alleviating infectious risk from neutropenia. G-CSF has been associated with a transient increase in blasts in the periphery in immunomimicking relapsed acute leukemia, but molecular correlation has largely been absent. This case report demonstrates the utility of molecular techniques to avoid the misdiagnosis of relapsed acute leukemia following G-CSF. A 16-year-old adolescent boy presented with a 1-month history of fatigue, arthralgia, myalgia, and fever. The peripheral blood cell count was a slightly elevated leukocyte count with no circulating blasts; however, the corresponding bone marrow revealed a hypercellular marrow with 70% B-precursor lymphoblasts expressing CD19, CD20, CD10, and CD34. Further testing demonstrated a t(9;22)(q34.1;q11.2) BCR-ABL translocation and the p210 BCR-ABL variant tyrosine kinase. The patient was started on the AALL-0031 intensive chemotherapy protocol for high-risk pediatric acute lymphoblastic leukemia, and 30 days postinduction was in clinical remission with 1% marrow blasts. During consolidation chemotherapy 3-months postdiagnosis and after the third dose of G-CSF, a peripheral blood smear demonstrated 20% blasts. Although the blasts were myeloid by flow cytometry and had a switch with relapse of BCR-ABL leukemia could not be excluded until fluorescence in situ hybridization demonstrated the absence BCR-ABL. G-CSF was halted with prompt disappearance of the blasts from the peripheral blood. Molecular techniques such as fluorescence in situ hybridization are useful to distinguish a transient increase in blasts following G-CSF and to avoid overtreatment of acute leukemia.

**Cancer-Associated Fibroblasts in Schwannian Stroma—Poor But Not in Schwannian Stroma—Rich Neuroblastoma Regions and Tumors** (Poster No. 15)

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**Context:** Cancer-associated fibroblasts (CAFs) promote tumor angiogenesis and are associated with aggressive clinical behavior in prostate, lung, colon, and breast carcinoma and are identified in gastric carcinomas. CAFs represent a population of stromal ‘‘activated fibroblasts’’/myofibroblasts that are routinely identified by a-smooth muscle actin (aSMA) expression and distinguished from mature pericytes by lack of expression of heavy MW-Caldesmon (h-CD). Neuroblastomas are pediatric neoplasms that exhibit 7 histologic subtypes classified as either Schwannian stroma (SS)-poor or SS-rich/dominant.

**Design:** To investigate whether CAFs also play a role in mediating angiogenesis in neuroblastoma, we histologically examined 28 tumors diagnosed at Children’s Memorial Hospital in Chicago. Adjacent paraffin-embedded sections were stained with hematoxylin-eosin and Masson tri-chrome, and immunohistochemistry was performed for aSMA, h-CD, and CD31. Microvascular proliferation was defined as vessels with hypertrophic CD31+ endothelial cells and additional layers of vascular mural cells including aSMA+ cells.

**Results:** Light microscopic examination revealed the presence of a population of stromal cells that were strongly positive for aSMA and were negative for CD31 and h-CD consistent with CAFs. CAFs were abundant within extensive reactive stromal bands in SS-poor undifferentiated (n = 2), poorly differentiated (n = 5), and differentiating (n = 13) neuroblastomas. CAFs were associated with microvascular proliferation. By contrast, CAFs were less widely distributed in ganglioneuroblastomas and were rare in SS-rich regions (intermixed, n = 5; nodular, n = 1). In SS-dominant ganglioneuroblastos (n = 4) CAFs were rare. Pericytes in normal vessels were aSMA− and h-CD+.

**Conclusions:** CAFs were identified in neuroblastoma and were associated with SS-poor regions and microvascular proliferation. Our data indicate that CAFs promote angiogenesis in SS-poor neuroblastomas.

**Akt/Glycogen Synthase Kinase-3B Expression in Gliomas** (Poster No. 16)

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**Context:** The Akt/glycogen synthase kinase-3b (GSK-3b) pathway has a vital role in the cell death and survival pathway after a variety of cell death stimuli. The protein on activation can phosphorylate other important nuclear proteins such as c-Jun, p53, and cyclin among other molecules. GSK-3b phosphorylates and regulates the activity of Bax, a pro-apoptotic Bcl-2 family member that activates the cell death (apoptosis) pathway by causing the cytochrome c release from mitochondria. Enzastaurin treatment has been found to suppress the phosphorylation of GSK-3b and suppress the growth of human glioblastoma xenografts. Our aim was to examine the topographical localisation GSK-3b in gliomas to understand its function.

**Design:** We used 10 normal brains (autopsy cases) and 29 cases of gliomas (tissue microarray slides) of different World Health Organization (WHO) grades and examined the GSK-3b expression qualitatively and semiquantitatively using immunohistochemistry.
Results: We found 1 case of WHO grade I glioma, with 1+ staining intensity. In 7 cases of WHO grade II gliomas we found 4 cases stained greater than 2+ . In 12 cases, we found 5 cases of WHO grade III gliomas staining for greater than 2+ intensity; and in 9 cases of high-grade IV gliomas, 6 cases showed staining for greater than 2+ intensity. The cells pseudopalsading (undergoing apoptosis) at the edge of the necrosis showed intense positive staining. There was focal weak staining in the neurons and astrocytes. No oligodendroglial, microglial, or endothelial cell stained.

Conclusions: This study suggests that the Akt/GSK-3β pathway might be involved in apoptosis in gliomas.

High-Grade Gliomas Contain Mitochondrial DNA Mutations and Show Impaired Mitochondrial Function
(Poster No. 19)

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Context: Anaerobic metabolism is a hallmark of many tumors. Mutations in mitochondrial DNA (which code for critical electron transport proteins such as cytochrome oxidase) cause cells to shift to anaerobic metabolism. High-grade gliomas have not been extensively investigated for the presence of mitochondrial DNA mutations and impaired mitochondrial metabolism. If such defects were present, they could be exploited therapeutically.

Design: Flash-frozen tumor samples from 4 different high-grade gliomas (glioblastoma multiforme, astrocytoma grade 4) resections and 2 glioma cell culture lines (U-87 and U-251) were tested for mitochondrial electron transport activity using the cytochrome oxidase enzyme histochemical assay. Immediately to these samples were tested for mitochondrial DNA mutations (substitutions and large-scale deletions) by polymerase chain reaction amplification and sequencing. The 2 cell lines were also exposed to 5μM Adaphostin (NSC 680410), a tyrphostin-class chemotherapeutic agent that localizes to mitochondria, for 24 hours and evaluated for toxicity.

Results: Each glioma surgical and cell culture specimen demonstrated decreased to absent cytochrome oxidase activity in a heterogeneous pattern. Multiple mitochondrial DNA deletions, but not substitution mutations, were detected in each specimen and confirmed and characterized by sequence analysis. U-251 glioma cells were highly sensitive to Adaphostin treatment; U-87 cells were resistant.

Conclusions: Mitochondrial deletion mutations and electron transport chain failure are present in each sample studied. Adaphostin treatment is variably effective against the glioma cell lines, suggesting that mitochondrial genetics and metabolism may be a useful chemotherapeutic target in gliomas. Studies are ongoing to determine whether the degree of mitochondrial impairment in the glioma cell lines correlates with Adaphostin sensitivity.

Facial and Cranial Zygomycosis in a 24-Week-Old Premature Girl
(Poster No. 20)

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Zygomycosis is usually fatal in immunocompromised patients. The most common presentation is rhinofacial, cranial, and pulmonary. Facial and cranial presentations in premature babies are very rare. A baby girl was born prematurely at 24 weeks’ gestation, weighing 648 g with Apgar scores of 5/8/8. The mother was a 23-year-old, para 0 woman who had prenatal care and a medical history of chronic and pregnancy-induced hypertension, preeclampsia, and pneumonia. She presented with nonreassuring fetal heart tracings. An emergency cesarean delivery was performed. The baby developed respiratory distress was intubated and placed on antibiotics. On day 7, a periortal rash was noted, and biopsy of the lesion showed zygomycosis involving the skin and deep adipose tissue. The baby continued to be critically ill with thrombocytopenia, neutropenia, and sepsis. She died 13 days after birth. An autopsy was performed and the findings showed facial skin and subcutaneous tissue necrosis, involving the left hemisphere, periportal, periorbital, and right malar area. The brain had focal areas of hemorrhage in the right frontal lobe. Microscopic findings showed fungal meningoencephalitis with vasculitis and fungal hyphae invading the blood vessel walls. Infrequently, septate thin walled hyphae with focal bulbous dilations and irregular branching typical of Zygomycetes were seen. This is a rare presentation of facial zygomycosis involving brain in a 24-week-old premature infant. Surgical

Context:

In the past century, 4 human diseases characterized by early, rapid dementia with spongiform change in the brain have been described and classified as transmissible spongiform encephalopathies. Until recently, these diseases were considered to be very rare with an incidence of approximately 1 case per million in the world. The discovery in 1986 of a bovine spongiform encephalopathy epidemic among cattle in the United Kingdom led almost immediately to theories that the disease could be transmitted to humans. The rising number of Creutzfeldt-Jacob disease cases reported in the United Kingdom and other countries since then has fueled fears of a human epidemic that could potentially reach the hundreds of thousands.

Design: Current literature on variant Creutzfeldt-Jacob disease addressing genetic predispositions, epidemiology of current outbreaks, histopathology, and infectivity is examined.

Results: Currently, the only method for definitive diagnosis of any form of spongiform encephalopathy is by pathology. The infective route for humans is unknown but is suspected to be the ingestion of bovine spongiform encephalopathy–infected cattle. This identifies the population at risk but does not answer why some people develop the disease but others do not. There is some indication that homozygosity for methionine at codon 129 is a risk factor.

Conclusions: There is no treatment or cure for this inexorable, degenerative disease. The establishment of surveillance units in several countries has helped to delineate variant Creutzfeldt-Jacob disease from other transmissible spongiform encephalopathies. Further investigation into this disease will hopefully provide insight into the progression of and possible treatments for transmissible spongiform encephalopathies.
treatment could not be performed because of facial and cerebral involvement. The prognosis of this clinical presentation is dismal (Figure 7).

Intraoperative Evaluation of Brain Tumors: A Community Hospital Experience
(Poster No. 21)

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Context: Requests for intraoperative consultations (ICs) for brain tumors at community-based practices where expertise in neuropathology is not readily available are increasing in frequency. The current study was undertaken to evaluate the diagnostic accuracy of ICs for brain tumors rendered primarily by surgical pathologists in a tertiary community hospital.

Design: A retrospective review of all ICs for brain tumors done at our institution between January 2003 and December 2006 yielded 100 cases, all primary open biopsies. The initial intraoperative diagnosis was compared with the final diagnosis, to identify diagnostic inaccuracies and to ascertain possible causes including technical imperfection, sampling, and interpretational error.

Results: ICs concurred with the final diagnosis in 87% of the cases. Of the remaining 13% there was 1 false-positive case, 3 false-negative cases, and 3 incorrectly classified cases. The diagnosis was deferred in 6 cases. Interpretational errors were most common (10 cases), followed by sampling errors in 3 cases and technical imperfections in 2 cases. Frozen section procedure was used most often with concurrent use of touch and squash preparation in only 5 cases. Expert neuropathologic opinion was needed in 25% of the cases to confirm the final diagnosis.

Conclusions: ICs in our setting have a 10% interpretational error predominantly involving differentiating gliosis from glial tumors (6 cases) and diagnosis of intracerebral lymphomas (2 cases). The concurrent use of touch or squash preparation as well as correlation with location and radiologic data may increase diagnostic accuracy in this setting.

Suprasellar Spindle Cell Lipoma
(Poster No. 22)

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Central nervous system lipomas are uncommon, often incidental lesions. They presumably arise from adipocytes that surround the pituitary stalk. They are viewed by some to represent a congenital brain malformation, resulting from an abnormal differentiation of the primitive mениnx rather than a true neoplasm or hamartoma. To our knowledge, spindle cell lipoma of the suprasellar region has not been reported in the literature. We report a case of a 4-year-old boy with a suprasellar spindle cell lipoma. The patient presented with headaches and visual disturbances. He was found to have low growth hormone levels and a brain magnetic resonance imaging study revealed a 4- to 5-mm suprasellar mass, which was initially thought to be a lipoma or dermoid cyst. The patient was followed clinically and radiographically for 5 months. He was scheduled for surgical resection after subsequent imaging demonstrated ring enhancement of the mass suggestive of craniopharyngioma, hamartoma, or hypothalamic glioma. Pathology from the partial resection showed a circumscribed lesion consisting of mature adipose tissue with intermixed uniform spindled cells associated with a mucoid matrix, morphologically consistent with a spindle cell lipoma. The spindle cells and vasculature demonstrated focal positivity with CD34 antibody. There was no evidence of lipoblasts, mitoses, necrosis, or osseous tissue. Lipomatous neoplasms arising in the sellar or suprasellar region are unusual. Most cases represent ordinary lipomas; rarely is a spindle cell lipoma pattern observed.

Intrasellar Chordoma: Report of a Case and Review of the Literature
(Poster No. 23)

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Intracranial chordomas are uncommon primary brain tumors and usually arise from the cranial base, particularly the clivus. With no clinical and radiologic suspicion, it can be a diagnostic challenge when they arise in an atypical location. We report a case of intrasellar chordoma that presented with clinical and imaging features of a pituitary macroadrenoma. A 51-year-old man complained of headaches, diplopia, and ptosis for more than a year. Axial T2 and postaxial T1-weighted magnetic resonance imaging showed a 2.5 × 2.4 × 3.0-cm, heterogeneously enhancing, mixed signal mass within the sella. His serum chemistry and endocrine studies were within normal limits. Transsphenoidal resection was performed under the impression of nonfunctioning pituitary macroadrenoma. Histologic studies demonstrated a neoplasm with clusters and cords of pleomorphic cells with amphophilic cytoplasm in a myxoid background. Tumor cells with vacuolated cytoplasm (physaliphorous cells) and bone invasion was also present (Figure 8). Immunohistochemistry was positive for epi-

Primary Central Nervous System T-Cell Lymphoblastic Lymphoma: A Neuropathologist's Odyssey
(Poster No. 24)

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Primary central nervous system lymphoma (PCNSL) constitutes approximately 5% of all primary brain tumors in adults. In the pediatric population, PCNSL is less common constituting approximately 1% of all...
PCNSL patients and occurring more often in immunocompetent children. Here we report an even rarer example of a primary central nervous system T-cell lymphoma in a 5-year-old child. The patient was a previously healthy 5-year-old boy who presented with lower extremity weakness and facial droop for 3 weeks. On admission, imaging of the brain showed a large enhancing mass involving the left parietal lobe. A stereotactic biopsy was performed. Microscopic examination revealed a malignant neoplasm with a mixed population of large cells with minimal cytopenia and smaller cells with abundant cytopenia. A wide differential was considered. Immunohistochemical stains included glial, neuronal, muscular, histiocytic, epithelial, and lymphocytic markers. The larger cells were positive for CD45, CD3, and TdT. The smaller cells were positive for glial fibrillary acidic protein. The tumor cells were negative for all other markers. The diagnosis of a precursor T-cell lymphoblastic lymphoma was rendered. No systemic involvement was demonstrable. The diagnosis of PCNSL in a child is rare; however, the diagnosis of precursor T-cell lymphoblastic lymphoma as a PCNSL is even more uncommon (only 2 known reported cases). Obtaining accurate diagnosis in children may be complicated by the lack of appropriate studies because PCNSL is rarely a differential diagnosis for primary childhood brain tumors. We suggest that PCNSL should be considered in all pediatric brain tumors.

Photograph of a sarcomatous area of a meningioma.

Shelly-Ann P. Williams (shellyannw@gmail.com); David Dunaway, BSc; Nalin Ranasinghe, BA; Renuka Kulkarni, MD; Emelie Ongcapin, MD. Department of Pathology, St Barnabas Medical Center, Livingston, NJ.

A 67-year-old right-handed man with a history of recurrent glioblastoma multiforme in the left temporal lobe had undergone 3 craniotomies with tumor debulking for recurrent glioblastoma multiforme in the left temporal lobe. On presentation, a 3 cm mass was noted extending superiorly to the previous temporal lobe surgical site. Computed tomography of the head and facial region showed new prominent areas of soft tissue swelling on the left side of the face. Subsequent magnetic resonance imaging studies showed marked enlargement and inflammation of left-sided tissues around the parotid gland; furthermore, this swelling extended superiorly to the previous temporal lobe surgical approach. The patient was diagnosed with a parotid abscess and started on antibiotics. Six days later, the patient underwent left parotid incision, drainage, and biopsy. Microbiology culture of the drained specimen failed to show any growth after 5 days' incubation. Pathology of the biopsy revealed necrotic tissue with medium-sized tumor cells containing prominent nucleoli with extensive crush artifact in a desmoplastic stroma; however, salivary acini were not identified. Immunohistochemical stains were positive for glial fibrillary acidic protein and negative for CD45 and vimentin (Figure 9). Focal areas revealed a sarcomatous component. Comparision with the tumor excised from the patient's last craniotomy revealed similar morphology, and the mass was discerned to be a contiguous tumor from the intracranial origin to the left parotid region.

Extracranial Spread of Glioblastoma Multiforme Presenting as a Parotid Abscess

(Poster No. 25)

Photograph of a meningioma.

Monesh Kapadia, MD

Intravascular Lymphoma Presents as Rapid Onset, Potentially Confusing Variant of Meningioma

(Poster No. 27)

Monesh Kapadia, MD (monesh78@yahoo.com); M. Katayoon Rezaei, MD; Robert V. Jones, MD. Department of Pathology, The George Washington University, Washington, DC.

Meningiomas account for approximately 30% of all primary brain tumors and generally have a favorable prognosis. However, one of the rare variants, the papillary type, has been recognized to have an aggressive clinical behavior with a high rate of local recurrence and distant metastases. Because architectural and cytologic features of papillary meningioma overlap those of papillary carcinomas, intraoperative diagnosis of a papillary dural-based tumor may be challenging. An 82-year-old woman with a history of renal cell carcinoma was found to have a large dural-based tumor with features of meningioma and aggressive behavior. Histologically, the tumor was composed of malignant appearing meningothelial cells arranged radially around blood vessels and central connective tissue stroma. Immunohistochemistry showed loss of the reticulin network. Our case has 3 unusual features that, although individually described in literature, are nonetheless unusual in pituitary adenomas. These are (1) multinucleation and pleomorphism, (2) the presence of many cells expressing nonphosphorylated neuriteophylated protein lamina, and (3) the apparent coexpression of prolactin and follicle-stimulating hormone. Although the presence of neural elements in pituitary adenomas has already been reported, the case described here is pathogenetically different as described previously.

Papillary Meningioma: A Rare but Malignant and Potentially Confusing Variant of Meningioma

(Poster No. 27)

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Intravascular Lymphoma Presents as Rapid Onset, Rapidly Progressive Dementia

(Poster No. 28)

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Intravascular lymphoma (IVL) has recently been classified by the World Health Organization as a subtype of B-cell lymphoma, characterized by prominent arteriolar proliferation with small lymphocytic aggregates within the vessels, associated with systemic symptoms. The clinical and histopathologic features of IVL may be difficult to distinguish from other lymphomas, particularly those involving the central nervous system (CNS). In this report, we describe a case of IVL presenting as rapidly progressive dementia in a healthy 5-year-old boy who presented with lower extremity weakness and facial droop for 3 weeks. On admission, imaging of the brain showed a large enhancing mass involving the left parietal lobe. A stereotactic biopsy was performed. Microscopic examination revealed a malignant neoplasm with a mixed population of large cells with minimal cytopenia and smaller cells with abundant cytopenia. A wide differential was considered. Immunohistochemical stains included glial, neuronal, muscular, histiocytic, epithelial, and lymphocytic markers. The larger cells were positive for CD45, CD3, and TdT. The smaller cells were positive for glial fibrillary acidic protein. The tumor cells were negative for all other markers. The diagnosis of a precursor T-cell lymphoblastic lymphoma was rendered. No systemic involvement was demonstrable. The diagnosis of PCNSL in a child is rare; however, the diagnosis of precursor T-cell lymphoblastic lymphoma as a PCNSL is even more uncommon (only 2 known reported cases). Obtaining accurate diagnosis in children may be complicated by the lack of appropriate studies because PCNSL is rarely a differential diagnosis for primary childhood brain tumors. We suggest that PCNSL should be considered in all pediatric brain tumors.

Extracranial Spread of Glioblastoma Multiforme Presenting as a Parotid Abscess

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neoplastic lymphocytes within the lumina of small and medium-sized vessels. Symptoms result from obstruction of vessels by tumor lymphocytes and subsequent organ ischemia. Neurologic symptoms are extremely heterogeneous, the most dramatic being a precipitous decline in performance status. We present the case of a 50-year-old physician with a medical history of asymptomatic human immunodeficiency virus infection (CD4 > 200) of 23 years. The patient presented with new onset of headaches, low-grade fevers, and transient confusion. Neuropsychiatric testing was inconclusive and inconsistent with acquired immunodeficiency syndrome dementia. The patient’s condition worsened until he required a full-time caretaker to assist with daily living. The patient became progressively more obtunded and died 4 months after his first symptoms. Postmortem microscopy revealed vessels packed with neoplastic CD20+ lymphocytes (Figure 10) and diffuse ischemia in multiple organs.

Dandy-Walker Malformation and Down Syndrome
(Poster No. 29)

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Dandy-Walker malformation is a congenital defect of the fourth ventricle that develops during the sixth week of gestation. It consists of a cystic dilatation of the fourth ventricle with dysgenesis of the cerebellar vermis. It has been associated with genetic disorders and environmental exposures and has occurred sporadically. To our knowledge, Dandy-Walker malformation has only been reported once in the literature in association with Down syndrome. We report an autopsy of a 4-month-old infant with Down syndrome and a Dandy-Walker malformation. The patient was a 4-month-old white girl who remained hospitalized from birth. She was a twin, born 6 weeks premature to a 36-year-old, gravida 1, para 2, mother. Karyotyping, done secondary to Down features, revealed a 47,XX,+21 monosomy twin. A head ultrasound demonstrated the Dandy-Walker malformation. Her clinical course was marked by pericardial effusions treated by pericardioventiculostomy, complicated by right ventricular perforations. She had persistent respiratory distress and required ventilatory support and tracheostomy. At autopsy, there was foreshortening of the frontal lobes, atrophy of the superior temporal gyrus, and Dandy-Walker malformation. Additionally, she had focal acute neuronal necrosis of the hippocampi and focal cortical dystrophic calcification in the parieto-occipital region. Other anomalies at autopsy included the following: bicuspid aortic valve with atrial septal defect, esophageal atresia and a repaired right mainstem bronchopulmonary fistula, topographic lungs, and right pelvic kidney with hydrenephrosis. Although many congenital anomalies are known to occur in Down syndrome, the coexistence of a Dandy-Walker malformation is unusual. The precise relationship between the 2 entities is unknown.

Pituitary Adenoma in Association With Beckwith-Wiedemann Syndrome
(Poster No. 30)

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Beckwith-Wiedemann syndrome (exomphalos-macroglossia-gigantism syndrome) occurs with an estimated incidence of 1:13700 and is known to be associated with genetic changes in chromosome band 11q15. An increased risk of pediatric neoplasia in Beckwith-Wiedemann patients is well established. The most frequently reported tumors in Beckwith-Wiedemann syndrome are Wilms tumor, hepatoblastoma, embryonal rhabdomyosarcoma, and adrenocortical carcinoma. We present a case of silent corticotroph pituitary adenoma in a 15-year-old male patient in the context of genetically confirmed Beckwith-Wiedemann syndrome. To the best of our knowledge, the occurrence of pituitary adenoma in Beckwith-Wiedemann syndrome patients has not been previously reported. It is uncertain if this occurrence is sporadic or represents a previously unreported syndrome-associated phenomenon.

Malignant Glioneuronal Tumor, an Emerging Neoplasm: Clinical, Radiologic, and Immunohistochemical Characterization
(Poster No. 31)

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Certain brain tumors that have been traditionally classified as malignant gliomas are now being divided into newer subgroups with varying biologic profiles. Current World Health Organization classification of glial tumors is largely based on morphology. However, with rapidly evolving techniques in immunohistochemistry, neuroimaging, and molecular genetics, growing data suggest that conventional histologic patterns only partially reflect biologic behavior and outcomes. One of the emerging variants of malignant gliomas is the malignant glioneuronal tumor (MGNT) subtype that is still widely underrecognized. MGNTs present clinically and radiologically like glioblastomas (GBMs), or other high-grade gliomas, and can express abortive neuronal differentiation (at least immunoreactivity for neurofilament proteins). Certain MGNTs demonstrate a more favorable prognosis after gross total resection, and others do not. We present a 50-year-old man with a brain tumor whose radiographic appearance had characteristics of a GBM. The tumor was more superficially located and adherent to the meninges. It had a faintly “rhabdoid” profile. However, it did not express muscle antigens, and it retained the INI1-gene product. Further pathologic analysis with neuronal markers (synaptophysin, NFP, and Neu-N) confirmed the diagnosis of MGNT. Despite initial gross total resection, this patient presented with a recurrence in 3 months, with metastasis to the scalp and to a remote site. After resection the patient returned to preoperative neurologic status but died from progressive disease 6 months later. Further studies are clearly warranted to identify these unique neoplasms and to systematically assess their prevalence and their clinical, radiologic, and biologic characteristics.

Primary Myxoma of the Central Nervous System
(Poster No. 32)

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A 29-year-old man presented with blurred vision, headaches, and seizures. A magnetic resonance image revealed a left posterior parafalcine tumor measuring 2.5 x 2.0 x 1.0 cm. Cranietomy was performed and the tumor was resected. Grossly, the tumor was a discrete, nonencapsulated, tan-pink mass with a translucent, mucoid cut surface. Microscopically, the nonencapsulated mass was entirely composed of multiple closely spaced
lobules with myxomatous stroma. Lobules were separated by fibrovascular septae containing a small number of plasma cells and lymphocytes (Figure 11). Individual tumor cells were small, discohesive, spindle-shaped cells floating in a mucinous matrix. The tumor was entirely uniform throughout and lacked any areas with meningothelial, endothelio-matous, or fibromatous histology. The diagnosis of primary myxoma of the central nervous system was made. The differential diagnosis included myxomatous or chordoid meningioma, epithelioid hemangiendothelio-ma, and metastatic myxoma. Negative immunostaining for epithelial membrane antigen and cytokeratin and the absence of meningothelial fibroblastic areas excluded myxomatous meningioma, and epithelioid or mungioendothelio-ma should exhibit plump atypical endothelial cells, which were not present in this case. Metastatic myxoid tumors are typically accompanied by systemic symptoms and positive findings with imaging because of the primary tumor. In addition, metastatic myxoid tumors are usually vascular rather than dural based. Three previous cases of primary myxoma of the central nervous system involved the posterior fossa, pituitary fossa, and the dura of the right frontoparietal convexity. This rare tumor arises from cells of primitive mesenchymal origin and we have not identified any prior reports of this parafalcine location.

Acute Hemorrhagic Leukoencephalopathy Associated With Influenza Vaccination
(Poster No. 33)

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Influenza vaccination infrequently results in adverse neurologic complications, such as Guillain-Barré syndrome. We report a case of fatal acute hemorrhagic leukoencephalopathy, a rare, fulminant demyelinating disorder, temporally associated with influenza vaccination. A 47-year-old man with a history of hypertension and hepatitis C infection experienced abrupt onset of chest pain and loss of consciousness. Despite immediate hospitalization with aggressive respiratory support, pressor management, and dialysis, he remained comatose and died within 36 hours of presentation. A full autopsy was requested for possible elucidation of his sudden illness. General autopsy findings confirmed hepatic cirrhosis, cardiomegaly, and diffuse alveolar damage. The neuropathologic findings revealed diffuse cerebral edema with subfalcine and tonsillar herniation. Microscopically, there were white matter petechial hemorrhages and necrotic blood vessels surrounded by decreased, disrupted myelin. Acute hypoxic-ischemic neuronal injury was present throughout the brain. The neuropathologic changes were typical of acute hemorrhagic leukoencephalopathy; however, relatively little inflammation was noted. Because a similar disorder, acute disseminated encephalomyelitis, has been previously linked to influenza vaccination, apparently unique in the medical literature. The disorder was not suspected clinically, validating the importance of postmortem investigation.

Review of Death Certificates at Long Island Jewish Medical Center
(Poster No. 34)

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Context: Cause-of-death data have significant impact in the design of public health and medical interventions. In our experience, the cause-of-death statement in death certificates of patients dying in this hospital is often filed inaccurately. We attribute errors to house staff inexperience, fatigue, time constraints, and unfamiliarity with the hospital course of the deceased.

Design: We examined the accuracy of cause-of-death statements in 2 groups of decedents. The first group consisted of 65 random patients who died at our institution between January 2004 and January 2006, and the second group consisted of 35 patients who died at this institution during the same period and underwent autopsy.

Results: Ninety-five percent of death certificates recorded had errors; the most common errors involved the immediate cause of death. Forty percent of errors involved omitted and incomplete information that could have significant impact on vital statistics. Thirty-five percent of death certificates had minor errors. There was a 37% major error rate between premortem and postmortem cause of death based on autopsy results in the second group of patients.

Conclusions: The rate of major death certification errors at this hospital is high and this may lead to significant miscalculation of disease mortality rates for this population. House staff education in filing cause-of-death statements is recommended.

Monitoring Clinical Pathology Calls to Residents: More Than an Educational Tool
(Poster No. 35)

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Context: On-call responsibility is an important part of residency training in clinical pathology. This task provides important consultative services for the hospital and serves as a valuable learning experience for the resident. The purpose of this study was to identify the types of calls received by residents at a large teaching hospital and to assess how and why these calls have changed over time.

Results: Calls concerning medical–surgical consults (43.0% vs 9.0%), and requests for consultation for anemia (12.8%) and the blood bank (32.0% vs 47.9%) increased. Meanwhile, calls concerning panic values (2.9% vs 4.2%). These types of calls have been decreasing. The overall percentage of calls concerning laboratory services for the hospital affect the clinical laboratory and those who rely on it. These effects can be seen in the changing demands on clinical pathology residents on call. Thus, calls to clinical pathology residents not only serve as an educational tool but also reflect the ever-changing role of the clinical pathologist within the hospital system.

Cytokeratin 7 Immunostaining Does Not Help in Distinguishing Pulmonary From Cervical Squamous Cell Carcinoma
(Poster No. 36)

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**Context:** Squamous cell carcinomas of uncertain origin present a diagnostic problem for surgical pathologists and oncologists. The distinction between pulmonary and cervical squamous cell carcinoma has significant therapeutic implications, yet they appear similar on hematoxylin–eosin-stained sections. There is a recent report in the research literature suggesting that cytokeratin 7 (CK7) is expressed in cervical, but not pulmonary, squamous cell carcinoma. Furthermore, the distinction between various squamous cell carcinomas has been identified in the literature as an area in which immunohistochemical data are needed.

**Design:** To determine the utility of immunostaining for CK7 in the separation of pulmonary from cervical metastatic squamous cell carcinoma, we studied routinely processed, formalin-fixed archival tissue from 62 of these tumors, both primary and metastatic, using the commercially available OV-TL12/30 clone of the monoclonal antibody to CK7 (Dako Corp, Glostrup, Denmark) and an avidin-biotin immunohistochemical technique.

**Results:** Pulmonary primary and metastases were CK7 positive in 50% and 60% of samples, respectively. Cervical primary and metastases were CK7 positive in 44% and 67% of samples, respectively. Figure 12 illustrates CK7 expression in pulmonary primary squamous cell carcinoma.

**Conclusions:** CK7 immunostaining does not reliably separate pulmonary from cervical squamous cell carcinoma.

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**What Is the Etiology of Granulomatous Inflammation in Surgical Biopsies? A Comparison of Ziehl-Neelsen, Auramine-Rhodamine, and Gomori Methenamine Silver Stains and Cultures**

**Poster No. 37**

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**Context:** The etiology of granulomatous inflammation remains frequently unknown. The utility of auramine-rhodamine (AR) in biopsies remains controversial.

**Design:** Biopsies with granulomatous inflammation, cultured for fungi and mycobacteria and stained with Ziehl-Neelsen (ZN), AR, and Gomori methenamine silver, were studied. The sensitivity and specificity of each diagnostic procedure was assessed in 376 cases from open lung, lymph node, soft tissue, and bone biopsies.

**Results:** An infectious agent was detected by any of the 4 methods in only 141 biopsies (37%). Fungal cultures were positive in 34 biopsies; 33 of them were positive with Gomori methenamine silver stain. Mycobacterial cultures were positive in 81 (21.5%) biopsies. AR was positive in 55 (14.6%) cases, including 19 that were negative for mycobacterial cultures and 15 by ZN. ZN was positive in 52 (13.8%) cases, including 14 cases that were negative for mycobacterial cultures. Cultures were negative in 24 “positive” cases by AR and ZN, resulting in 77% sensitivity.

**Conclusions:** The etiology was apparently noninfectious in 63% of cases. If a positive mycobacterial culture is used as the standard, the specificities of AR and ZN were only 57.8% and 67.4%, respectively. The need for more accurate methods for the diagnosis of granulomatous disease is discussed.

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**Intrathoracic Frozen Sections in Patients With a History of Breast Cancer: A Review of “Best Evidence” With Assessment of Pretest Odds**

**Poster No. 38**

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**Context:** Pulmonary nodules in patients with a history of breast cancer are generally thought to be metastatic, although lung cancer and other conditions are common. Having an awareness of the pretest odds may be useful to thoracic surgeons and pathologists at the time of intrathoracic frozen section.

**Design:** A systematic review of the literature from 1970 to 2007 was conducted to query for “best evidence” regarding this question. One hundred twenty-nine cases of intrathoracic frozen sections in patients with a history of breast cancer performed at Cedars-Sinai Medical Center from 1989 to 2006 were reviewed. Data were analyzed with meta-analysis.

**Results:** Three hundred thirty-four cases were reported in the English literature; the odds for metastatic carcinoma were 0.662 (0.190–9), for primary lung cancer were 0.590 (0.098–2.33), and for benign conditions were 0.285 (0.3–3). The odds for metastatic carcinoma in our patients were 0.408, for primary lung were 0.923, and for benign conditions were 0.149. One of our patients underwent an unnecessary lobectomy for metastatic breast cancer. Seven other patients with primary lung cancer were misidentified at the time of frozen section and required a second thoracotomy.

**Conclusions:** In most institutions, the odds of a metastatic carcinoma are similar to those of a lung cancer in patients undergoing frozen section for a single lung nodule. At our institution, the odds ratio is 2.3 for primary lung to metastatic carcinoma. The posttest odds after histologic examination are discussed.

**Concomitant Pulmonary Sarcoïdosis and Usual Interstitial Pneumonia**

**Poster No. 39**

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A 71-year-old man with a 28-year history of sarcoidosis improved with long-term oral prednisone until 2003 when he developed progressive dyspnea on exertion. Auscultation in May 2006 revealed mid–lung crackles, a finding associated with usual interstitial pneumonia (UIP). High-resolution computed tomography scan showed enlarged hilar nodes consistent with sarcoidosis and lower lung subpleural fibrosis and honeycombing suggestive of UIP. Thoracoscopic lung biopsy in June 2006 showed granulomatous disease with fibrosis, as well as patchy paucicellular fibrosis not clearly related to granulomas and having numerous fibroblast foci. Fungal and acid-fast stains were negative. The patient worsened despite steroid, methotrexate, and infliximab therapy and died in December 2006. Autopsy findings included extensive pulmonary interstitial fibrosis with honeycombing and nodular hyalinization with rare residual noncaseating granulomas. Hilar lymph nodes were enlarged and showed complete hyalinization. This case demonstrates clinical, radiologic, and pathologic evidence that a patient with unequivocal sarcoidosis developed UIP. Traditionally, when a fibrotic lung condition occurs and sarcoidosis is present, UIP and other nongranulomatous conditions are not given much consideration. Any fibrosis present was attributed to sarcoidosis itself. Interestingly, when sarcoidosis involves the skin, the granulomas have a predilection for scars of surgical or other origin. The same phenomenon might be expected to occur in the lung, where the sarcoidal granulomas may have a predilection for areas of fibrosis caused by idioopathic disorders such as UIP. Therefore, fibrosis may not always be caused by sarcoidosis, and concomitant UIP and sarcoidosis may be more common than currently thought.

**Localized Versus Diffuse Malignant Mesothelioma: Diagnostic Challenges and Clinical Outcome**

**Poster No. 40**

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Localized malignant mesothelioma (LMM) is a rare entity and defined as a solitary, circumscribed tumor that is histologically identical to diffuse malignant mesothelioma (DMM). LMM is reportedly associated with a better outcome in comparison with DMM. We present 2 cases illustrating the importance of distinguishing LMM with a dominant localized mass and microscopic evidence of serosal spread from DMM. Patient 1 is a 60-year-old man with a dominant circumcised 10-cm gastric wall mass that was eventually diagnosed as mesothelioma. A liver biopsy performed at the time of surgery showed a malignant mesotheliomatous proliferation on the hepatic capsule. Twelve months later, the patient presented with diffuse peritoneal disease. Patient 2 was an 82-year-old man who presented with a circumcised 4-cm left pulmonary mass invading the chest wall and diagnosed as mesothelioma. The patient developed localized recurrence 6 months after resection and died 5 months later. An autopsy revealed chest wall and extrapericardial masses with metastases to mediastinal and hilar lymph nodes. These 2 cases demonstrate the diagnostic pitfalls and prognostic difficulties in distinguishing LMM from DMM. Both patients presented with solitary masses, implying a diagnosis of LMM; however, microscopic hepatic surface involvement away from the tumor in case 1 would suggest DMM with a dominant mass. The clinical course is also consistent with a diffuse, serosal spreading malignancy. In case 2, the localized mass and recurrence are consistent with LMM; however, the rapid clinical deterioration emphasizes the underreported aggressive clinical behavior of some LMM, similar to that of DMM.

Pulmonary Capillary Hemangiomatosis: A Case Associated With Dilated Cardiomyopathy

(Poster No. 41)

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Pulmonary capillary hemangiomatosis (PCH) is potentially fatal and currently considered a pulmonary angio-proliferative disease of unknown etiology. It is a rare disease, presenting symptoms of severe pulmonary hypertension in most cases. The mechanism in the development PCH remains unclear. It seems that PCH is a result of uncontrolled angiogenesis and the theories of causation are only speculative. We report a case of PCH in a patient with dilated cardiomyopathy. Postmortem findings in our case suggest that the severe pulmonary passive congestion may possibly be one of the causes for pulmonary capillary hemangiomatosis. Our conclusion concurs with Xuefeng Jing et al, who reported a case of PCH in a patient with hypertrophic cardiomyopathy.

Pulmonary Hypertension Reversed by Antibiotics in a Patient With Whipple Disease

(Poster No. 42)

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Whipple disease is a rare multisystemic disorder of infectious etiology caused by the organism Tropheryma whipplei. The disease is generally regarded as gastrointestinal, but involvement of all major organ systems has been described. Pulmonary involvement is a frequent finding, but pulmonary hypertension is rare. The underlying pathophysiologic mechanism of pulmonary hypertension has not been established but has reasonably been assumed to be induced by vascular involvement by T whipplei. The current case provides histologic evidence in support of this. Our patient was a 54-year-old white man with a 1-year history of progressively worsening respiratory and gastrointestinal symptoms leading to significant weight loss during 6 to 10 months. Imaging studies revealed generalized abdominal and thoracic adenopathy, pleural effusions, and ascites. An echocardiogram demonstrated moderate-to-severe pulmonary hypertension. Multiple biopsies were submitted. Duodenal biopsies were diagnostic of Whipple disease by both light and electron microscopy. Retrospective review of the pulmonary specimens showed macrophages and fibrinoid debris tethered to the endothelium of some of the pulmonary arterioles leading to partial luminal obliteration. These arteriolar intima and media cells demonstrated periodic acid-Schiff-positive cytoplasmic and basophilic cytoplasm and were positive for CD68 by immunohistochemistry, confirming their identity as macrophages. To our knowledge, this is the first histologic evidence demonstrating the pathogenetic mechanism of Whipple-associated pulmonary hypertension. Of further importance, this is only the third reported case of antibiotic-induced resolution of pulmonary hypertension. The World Health Organization does not currently list Whipple disease as a cause of pulmonary hypertension, the awareness of which is very important given its potential reversibility with antibiotic therapy.

Granulomatous Pneumocystis jiroveci (carinii) Pneumonia in a Patient With Large B-Cell Lymphoma

(Poster No. 43)

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Pneumocystis jiroveci (carinii) pneumonia (PCP) occurs frequently in patients with immunodeficiency syndromes, especially acquired immunodeficiency syndrome (AIDS). PCP presents classically as a diffuse intra-alveolar eosinophilic frothy exudate. Uncommonly, PCP can be granulomatous and can produce lung masses mimicking malignant tumor. Only a few cases of granulomatous PCP in non-AIDS patients have been reported. These patients often presented with nodules or masses on x-ray and with negative findings on bronchoscopy and bronchoalveolar lavage. The correct diagnosis was made on open lung biopsies. We report a case of granulomatous PCP in an 85-year-old man who had a diffuse large B-cell lymphoma in the testes and who had been treated with bilateral orchectomy and chemotherapy in 2005. The patient was admitted in 2006 with complaints of dyspnea, productive cough, and low-grade fever. A computed tomography scan showed pleural effusion and conglomerate masses in bilateral lungs, which were interpreted as metastatic tumor. The patient developed severe respiratory distress and died. At autopsy, multinodular firm white masses occupied 50% and 30% of the left and right lung upper lobes, respectively. Large B-cell lymphoma involving the lung, fungal infection, and tuberculosis were considered in the initial differential diagnosis. Microscopic examination showed only extensive necrotizing granulomas. Acid-fast bacilli stain was negative for mycobacteria. Granulomatous PCP was diagnosed after finding P jiroveci (carinii) within granulomas on Gomori methenamine silver stain. Granulomatous PCP has an atypical clinical, radiologic, and gross pathologic presentation. Our case illustrates the importance of recognizing this entity to prevent misdiagnosing it as malignant tumor.

Diagnostic Accuracy of Quality Assurance Surgical Pathology Specimens Using Virtual Microscopy

(Poster No. 44)

Jeffrey T. Henderson, MD1; Jeffrey T. Henderson, MD1 (jhenders@u.arizona.edu); Katherine M. Scott, MD; Lynne Richter, MT(ASCP); John B. Carpenter, MD2; Sarah Chang, BS3; Achyut K. Bhattacharyya, MD; Ronald S. Weinstein, MD1.
inappropriate cases for single slide review, requiring more sections to be submitted before a consensus diagnosis was rendered. The 1 diagnostic error occurred in a vulgar biopsy in which a subtle invasive component of squamous cell carcinoma was identified during glass slide rereview.

Conclusions: Diagnostic concordance between virtual and conventional microscopy in this series was similar or better than other studies that have addressed QA, using other telepathology technologies. Virtual microscopy is useful in practice settings that use consensus QA diagnoses between members of a group working at different hospital locations.

Dr. Weinstein is a member of the Board of Directors of DMetrix, Inc, and owns stock in this company. Ms. Richter has exercised stock options in DMetrix, Inc. All other authors have no relevant financial interest in the products or companies described in this abstract.

The Histology of Hot Dogs: What We Are Really Eating
(Poster No. 45)

Richard A. Prayson, MD (prayson@ccf.org); James T. McMahon, PhD; Brigid E. Prayson. Department of Anatomic Pathology, Cleveland Clinic Foundation, Cleveland, Ohio.

Context: Americans consume 20 billion hot dogs a year, accounting for more than $1.5 billion in retail sales. We sought to assess the meat and water content of several hot dog brands to determine if the package labels are accurate.

Design: Eight brands of hot dogs were evaluated for water content by microscopic cross-section analysis to determine the meat and water content of several hot dog brands to determine if the package labels are accurate.

Results: Package labels indicated the top listed ingredient in all 8 brands was meat; the second listed ingredient was water (n = 6) or another type of meat (n = 2). Water comprised 44% to 69% (median, 57%) of the total weight. Meat content (determined by microscopic cross-section analysis) ranged from 2.9% to 21.2% (median, 5.7%). The cost per hot dog (range, $.12 to $.42) was $0.21 per hot dog. Meat content (determined by microscopic cross-section analysis) ranged from 2.9% to 21.2% (median, 5.7%). The cost per hot dog (range, $.12 to $.42).

Conclusion: Hot dog ingredient labels are misleading; most brands were more than 50% water by weight. The amount of meat (skeletal muscle) in most brands comprised less than 10% of the cross-sectional surface area. More expensive hot dogs generally had more meat. All hot dogs contained other tissue types not related to skeletal muscle, most notably bone and cartilage; brain tissue was not present.

Evaluation of 2 Antibody–Dual Chromogen Immunohistochemical Stains for the Diagnosis of Mesothelioma Versus Adenocarcinoma (Poster No. 46)

Dennis O’Malley, MD (domalley@uslabs.net); Matthew Endlich, BA; Donald R. Chase, MD. 1Department of Pathology, US LABS, Irvine, Calif; 2Department of Pathology, California Tumor Tissue Registry, Loma Linda.

Context: Historically, the distinction between mesothelioma and adenocarcinoma has been difficult. The goal of this study was to test different combinations of 2 antibody–dual chromogen immunohistochemical stains to aid in this distinction. The antibodies selected for identification of adenocarcinomas were MOC-31 and BerEp4, and the antibodies for identification of mesothelioma were calretinin and D2-40. Performance characteristics as well as specificity and sensitivity were compared.

Design: Twenty-two cases with either a diagnosis of lung adenocarcinoma or mesothelioma were retrieved from the California Tumor Tissue Registry for evaluation. Eleven cases of adenocarcinoma and 11 cases originally diagnosed as mesothelioma were evaluated. After further review, 1 of the cases originally diagnosed as mesothelioma was reclassified as adenocarcinoma. Hematoxylin-eosin-stained slides were reviewed and on each case, double immunohistochemical stains were performed with the following combinations of antibodies: calretinin and MOC-31, calretinin and BerEp4, and D2-40 and BerEp4.

Results: Values for the sensitivity and specificity of the individual antibodies are illustrated in the Table. Three cases did not yield any immunohistochemical results with dual antibody stains; 2 originally identified as adenocarcinoma and 1 identified as mesothelioma.

Conclusions: Based on our results, dual antibody–dual chromogen staining is a robust and useful method for the distinction of mesothelioma from adenocarcinoma. The distinction of mesothelioma from adenocarcinoma was made easier in many cases by a simple distinction of one chromosome versus the other (eg, red vs brown). The combination of D2-40 and BerEp4 had the best specificity for the diagnosis of mesothelioma. Moreover, the staining of D2-40 was more robust than that seen for calretinin.

Specificity and Sensitivity of Stains

<table>
<thead>
<tr>
<th>Antibody Combination</th>
<th>Sensitivity, %</th>
<th>Specificity, %</th>
<th>Sensitivity, %</th>
<th>Specificity, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calretinin–MOC-31</td>
<td>67</td>
<td>80</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>Calretinin–BerEp4</td>
<td>67</td>
<td>73</td>
<td>80</td>
<td>82</td>
</tr>
<tr>
<td>D2-40–BerEp4</td>
<td>67</td>
<td>100</td>
<td>90</td>
<td>100</td>
</tr>
</tbody>
</table>

This research was funded by US LABS.

Assessing the Utility of Additional Histology Levels in Endoscopically Suspected Barrett Esophagus
(Poster No. 47)

Miles B. Levin, MD (mlevin@montefiore.org); Kathryn Tanaka, MD. Department of Pathology, Montefiore Medical Center, Bronx, NY.

Context: For gastrointestinal biopsies, our current practice is to examine 1 level. We often receive esophageal biopsies with the clinical history “rule out Barrett esophagus (BE), history of BE, suspicious for BE.” The diagnosis of BE incorporates endoscopic findings and the presence of intestinal metaplasia, specifically goblet cells (GCs); however, GCs can be sparse. This study is to assess the value of examining multiple levels to detect GCs in endoscopically suspected BE, including correlation with clinical history and histologic findings on level 1.

Design: We identified 32 consecutive esophageal biopsies taken for suspected BE and diagnosed with gastric-type epithelium (without GCs). Five additional hematoxylin-eosin levels were examined. The following were recorded: clinical history, specific findings (inflammation, multilayered epithelium, pancreatic acinar metaplasia) on level 1, and the level on which the GCs were found.

Results: The histologic findings are that on level 1, all cases showed inflammation of glandular mucosa and 3 showed pancreatic acinar meta-
plasia. Definitive multilayered epithelium was absent. On additional levels, 4 (8%) showed Gcs (Table). In 1 case, levels showed pancreatic acinar metaplasia.

Conclusions: This study suggests that, although there was no consistent histologic indication identified on level 1, the examination of additional levels may be helpful if the clinical history is ‘suspicious for BE’ or ‘history of BE.’ Three of those 4 cases had Gcs identified on subsequent levels (ie, BE). The difficult question is how many levels should be examined? In our study, examination of 4 additional levels would have detected 3 of 4 new cases.

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**Quality Improvement in Colorectal Carcinoma Reporting (Poster No. 48)**

**Eric A. Himmelfarb, MD (eric.himmelfarb@vanderbilt.edu); Kay Washington, MD PhD. Department of Pathology, Vanderbilt University Medical Center, Nashville, Tenn.**

**Context:** Standardization of surgical pathology reporting in academic settings is challenging because of the large number of pathologists involved and frequent turnover of house staff. In addition, inadequate retrieval of lymph nodes in colorectal carcinoma specimens is a recognized shortcoming that may lead to inaccurate staging. This study assesses whether a combination of synoptic reporting and staff education resulted in improvement in compliance with College of American Pathologists (CAP) checklists and lymph node retrieval per specimen.

**Design:** All primary colorectal carcinoma resection reports from 2004 to 2006 were stratified by patient history into no pretreatment and neoadjuvant therapy groups. The number of lymph nodes identified per resection was recorded, and reports were examined for inclusion of a statement regarding lymphovascular invasion (LVI).

**Results:** Audit results for 2004 cases were presented to surgical pathology faculty in early 2005, with each pathologist and resident receiving a report detailing compliance with CAP checklist and number of lymph nodes retrieved. Synoptic reporting was instituted in 2005. The average number of lymph nodes per resection for the non–pretreated group increased from 13.8 in 2004 to 20.6 in 2006. The average number of lymph nodes identified per resection for the neoadjuvant therapy group increased from 6.2 in 2004 to 13.4 in 2006 (Table). Inclusion of LVI improved from 77% of reports in 2004 to 97% in 2006.

**Conclusions:** Significant improvements in lymph node identification and reporting of LVI coincided with the addition of CAP checklist synopses and to the establishment of a program of auditing reports and providing feedback to attendings and residents.

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**POSTER SESSION 300: MONDAY, OCTOBER 1, 2007, 10:00 AM–12:30 PM**

**Gastrointestinal and Liver Pathology; Kidney and Genitourinary Pathology**

**Lymphatics in Colonic Lamina Propria: New Ideas in Neoplasia and Inflammation (Poster No. 1)**

**Barton Kenney, MD (barton.kenney@yale.edu); Dhanpat Jain, MD. Department of Pathology, Yale University School of Medicine, New Haven, Conn.**

**Context:** The American Joint Committee on Cancer staging for colon cancer recognizes no distinction between in situ and intramucosal carcinoma, based in part on the concept that there are no lymphatic vessels within the colonic mucosa, as suggested by early studies using light and electron microscopy. However, lymph node metastases are occasionally encountered in cases of intramucosal carcinoma. Few studies have used lymphatic-specific markers to assess for lymphatic vessels in the colon.

**Design:** Our institution’s surgical pathology database was searched for normal colon, inflammatory bowel disease, inflammatory polyps, adenomatous polyps, and intramucosal adenocarcinomas from 2005 to 2006. Representative sections from selected cases were stained for the lymphatic-specific antibody D2-40 and the endothelial marker CD34 and systematically examined for the presence of mucosal vessels. Extent of inflammation and ulceration were also evaluated.

**Results:** Examination of normal colon (n = 4) revealed no lymphatics above the muscularis mucosae (0%). Samples of inflamed colon (n = 4) demonstrated lymphatics within the lamina propria in all (100%) cases. Among adenomatous polyps (n = 12), inflammatory polyps (n = 5), and intramucosal carcinomas (n = 6), lymphatics were identified in the lamina propria in 9 (75%), 4 (80%), and 3 (50%) cases, respectively. CD34 high-lighted blood vessels within the lamina propria in all specimens (100%). Lymphatic vessel density correlated with the presence of inflammation.

**Conclusions:** Although lymphatics are absent in the lamina propria of normal colonic mucosa, they are identified in inflamed colon, inflammatory polyps, adenomatous polyps, and intramucosal carcinomas. Our findings also suggest that lymphatic development in the mucosa may be an inflammation-driven process, rather than one linked to neoplasia.

**Enterochromaffin-like Cells in Pediatric Gastric Biopsies: Relationship to Proton Pump Inhibitor Therapy and Chronic Gastritis (Poster No. 2)**

**Dan Phan, MD (phandanc@uams.edu); Matthew Quick, MD; Scott Scrape, MD; Susan Kemp, MD; Troy Gibbons, MD; Vinay Prasad, MD. Departments of Pathology and Gastroenterology, Arkansas Children's Hospital, Little Rock.**

**Context:** Studies on the relationship between chronic gastritis, proton pump inhibitor (PPI) therapy, and enterochromaffin-like (ECL) cells in children are lacking. We studied 25 children on chronic gastritis and 25 children on PPI therapy.

**Design:** Twenty-five pediatric chronically inflamed gastric biopsies were reviewed. The patients were 2 to 17 years old; there were 12 boys and 13 girls. In cases with increased ECL cells, chromogranin was used for confirmation. Additionally, the histories of gastric and esophageal biopsies of 25 patients with reflux esophagitis on PPI therapy were examined. PPI therapy ranged from 4 weeks (1/25) to 3 years (1/25), with most patients being on PPI therapy for 1 to 6 months (23/25). The patients ranged from 3 months to 17 years old, including 11 boys and 14 girls.

**Results:** In the first group, activity was noted in 11 cases, and Crohn disease was present in 6 cases. Of the 25 showed increased ECL cells. These biopsies showed chronic active gastritis and 4 to 12 ECL cells per gland (compared with 0 to 3 per gland seen normally). Hyperplastic ECL lesions were absent. The second group did not show increased ECL cells.

**Conclusions:** We identified an increase in ECL cells in 3 of 25 chronically inflamed gastric biopsies. We found no endocrine cell hyperplasia or parietal cell change in 25 children on PPI therapy. Larger, long-term detailed studies are required to understand ECL cell biology in response to chronic gastritis and PPI therapy. High gastrin levels, chronic gastritis, and *Helicobacter pylori* infection may act in concert to promote ECL cell growth.

**Number of Lymph Nodes Examined and Associated Clinicopathologic Factors in Resected Colorectal Cancer (Poster No. 3)**

**Bisong Haupt, MD (bhaup@tmh.tmc.edu); Mary R. Schwartz, MD; Jae Y. Ro, MD, PhD; Jijiang Zhu, MD; Steven S. Shen, MD, PhD.**

**Correlation of Clinical History With Identified Goblet Cells**

<table>
<thead>
<tr>
<th>Clinical History*</th>
<th>No. of Cases with Goblet Cells Seen on Additional Levels</th>
<th>Level Goblet Cells Appeared</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rule out BE</td>
<td>45</td>
<td>1</td>
</tr>
<tr>
<td>Probable BE</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>History of BE</td>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td>Suspicous for BE</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Total</td>
<td>52</td>
<td>4 (8%)</td>
</tr>
</tbody>
</table>

* BE indicates Barrett esophagus.
partment of Pathology, The Methodist Hospital, Houston, Tex; Department of Gastrointestinal Oncology and Digestive Diseases, The University of Texas M. D. Anderson Cancer Center, Houston.

Context: Lymph node metastasis is one of the most important prognostic factors in localized colorectal carcinoma. It is recommended that a minimum of 12 lymph nodes be examined for accurate staging. In this study, we assessed the clinicopathologic factors that are associated with the number of lymph nodes harvested from resections of colorectal cancer.

Design: We reviewed 317 consecutive cases of colorectal cancer, which were resected at a single tertiary hospital from 2002 to 2005. Multiple clinicopathologic factors were analyzed and correlated with the number of lymph nodes harvested. Multivariable logistic regression analysis was performed to determine the clinicopathologic factors that are associated with adequate number (≥12) of lymph nodes harvested.

Results: Of the 317 patients, 182 were men and 135 were women with a mean age of 67 years. Average length of bowel resected and number of lymph nodes harvested categorized by tumor locations are tabulated in Table 1. The regression analysis of number of lymph nodes obtained with clinicopathologic factors is summarized in Table 2. Patient age, tumor location, and bowel length were significantly associated with number of lymph nodes harvested. All other analyzed factors were not independent predictors of number of lymph nodes harvested.

Conclusions: Patient age, location of tumor, and length of the bowel resected are related to the number of lymph nodes obtained in colorectal cancer. These factors need to be taken into account if absolute minimum number of lymph nodes is used, not only to ensure accuracy of staging but as a quality indicator.

Table 1. Length of Resected Bowel and Number of Lymph Nodes by Locations

<table>
<thead>
<tr>
<th>Location (No. of Cases)</th>
<th>Resected Bowel Length, Mean ± SD, cm</th>
<th>Lymph Nodes, Total No. ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cecum (18)</td>
<td>19.5 ± 7.6</td>
<td>13.1 ± 5.4</td>
</tr>
<tr>
<td>Ascending (95)</td>
<td>24.4 ± 11.4</td>
<td>19.4 ± 14.3</td>
</tr>
<tr>
<td>Transverse/left (24)</td>
<td>28.3 ± 16.3</td>
<td>15.2 ± 10.3</td>
</tr>
<tr>
<td>Sigmoid (128)</td>
<td>20.4 ± 8.7</td>
<td>11.6 ± 6.6</td>
</tr>
<tr>
<td>Rectum (35)</td>
<td>25.7 ± 5.3</td>
<td>9.3 ± 4.5</td>
</tr>
<tr>
<td>Unspecified (17)</td>
<td>21.8 ± 15.0</td>
<td>13.9 ± 5.5</td>
</tr>
<tr>
<td>Total (317)</td>
<td>22.8 ± 10.7</td>
<td>14.2 ± 10.3</td>
</tr>
</tbody>
</table>

Table 2. Correlation of Lymph Nodes Obtained With Clinicopathologic Factors

<table>
<thead>
<tr>
<th>Parameter</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age and gender</td>
<td>.03* and .73</td>
</tr>
<tr>
<td>Tumor size</td>
<td>.13</td>
</tr>
<tr>
<td>Tumor location</td>
<td>&lt;.001*</td>
</tr>
<tr>
<td>Tumor stage</td>
<td>.70</td>
</tr>
<tr>
<td>Histologic type</td>
<td>.91</td>
</tr>
<tr>
<td>Histologic grade</td>
<td>.87</td>
</tr>
<tr>
<td>Bowel length</td>
<td>.02*</td>
</tr>
<tr>
<td>Association with adenoma</td>
<td>.81</td>
</tr>
<tr>
<td>Surgeon</td>
<td>.19</td>
</tr>
</tbody>
</table>

* indicates statistically significant.

Correlation of Epidermal Growth Factor Receptor With Size and Vascular and Villous Features of Colorectal Advanced Adenomas: A Case Series

(Poster No. 4)

Xiaoying Liu, MD (xliu@kumc.edu); Douglas H. McGregor, MD; Srinivas Puli, MD; Elena Sidorenko, MD; Ajay Bansal, MD. 3Department of Pathology and Laboratory Medicine, University of Kansas Medical Center, Kansas City; Departments of Pathology and Laboratory Medicine and *Gastroenterology, Kansas & Veterans Affairs Medical Center, Kansas City, Mo.

Context: Mutations of APC gene have been associated with increased activity of epidermal growth factor receptor (EGFR). Although EGFR has been shown to be overexpressed in colon adenomas, it has not been correlated with morphologic features of adenomas. We studied size, villous component, and vascularity of adenomas in relation to EGFR expression.

Design: Thirteen polyps (sizes, 3 mm to 5.5 cm) from a 63-year-old patient were initially stained for EGFR expression and examined for vascularity and villous component. Subsequently, a validation group of 30 polyps from 8 randomly selected patients who underwent average-risk colonoscopy were examined by 2 pathologists. EGFR staining, vascularity, and villous component were graded semiquantitatively.

Results: In the index case, the large 5.5-cm tubulovillous adenoma with marked submucosal arteriovenous telangiectasias had EGFR positivity in all of its neoplastic cells. Another 2-cm tubular adenoma with focal villous features and with some arteriovenous telangiectasia had 30% EGFR positivity. All other polyps and normal colon mucosa were negative for EGFR. Immunostaining of the 8 patients showed a significant correlation between EGFR positivity with adenoma size larger than 1 cm, villous component, and vascularity (all P < .01). Presence of villous features strongly correlated with presence of abnormal vascularity with 100% of adenomas with villous component having abnormal vascularity as opposed to only 11% of tubular adenomas (P < .01).

Conclusions: These findings suggest a role of EGFR in the development of prominent arteriovenous telangiectasia and advanced colonic adenomas. Advanced features in colonic adenomas could serve as surrogate biomarkers to allow targeted chemoprevention with EGFR antagonists.

A “Second Look” Improves the Yield of Lymph Nodes in Colorectal Cancer Resection Specimens

(Poster No. 5)

Thomas J. Bollinger, MD, MPH (tbom.bollinger@yahoo.com); Robert M. Lenington, MD; Jason G. Savell, MD; Shuan C. Li, MD. Departments of *Pathology and Surgery, Orlando Regional Healthcare System, Orlando, Fla.

Context: Colorectal cancer patients enjoy improved prognosis as the number of lymph nodes evaluated in their resection specimens increases. Elaborate fat clearing techniques have been devised to improve lymph node yield; however, they are not suitable for routine use in a busy pathologic practice. We studied the efficacy of a simple “second look” at colorectal cancer resection specimens with regard to increasing lymph node yield.

Design: Eighteen specimens resected for colorectal cancer were evaluated. Diagnosis was held for 1 day while additional nodes were recovered. A single reviewer removed the pericolonic fat from the specimen and manually palpated for lymph nodes by flattening the fat between an index finger and a corkboard. The number, size, and tumor status of nodes were determined histologically.

Results: Additional nodes were found in all cases (total, 285; mean, 16; range, 2–49). The average additional time required per case was 44 minutes. The percentage of cases yielding greater than 12 nodes improved from 57% to 94% (P = .01). One case was upstaged from N0 to N2. In cases in which 1 in 6 nodes found initially were 2 mm or less in diameter, subsequent examination did not affect patient prognosis (P < .001).

Conclusions: A “second look” for lymph nodes in colorectal carcinoma specimens, as described here, is an efficient and effective method for increasing lymph node yield. We propose that the proportion of nodes 2 mm or less is an indicator of quality of gross pathologic lymph node evaluation and should be reported.

Primary Adenocarcinoma of the Duodenum: Clinicopathologic and Immunohistochemical Study

(Poster No. 6)

Carrie M. Bradford, MD (cb Bradford@kumc.edu); Margo Shoup, MD; Michael Hurtuk, MD; Earle Holmes, PhD; Sherri Yong, MD; Kiyoko Oshima, MD. Departments of *Pathology and Surgery, Loyola University Medical Center, Maywood, Ill.

Primary duodenal adenocarcinomas are rare, and thus, the clinicopathologic features and biologic behavior are not well known. Twenty-six cases of primary duodenal adenocarcinoma were retrieved from our archives between 1991 and 2006. Sections were selected to include normal mucosa, adenocarcinoma, and, as applicable, adenomatous areas. Immunohistochemical stains (cytokeratins [CKs] 7 and 20, Ventana, Tucson, Ariz) were performed. Clinicopathologic features were correlated with clinical outcome. Patients ranged from 34 to 85 years (median, 68 years), with a slight male predominance (14/26). Seventeen cases (65.4%) arose from the second portion of the duodenum. Tumor sizes ranged from 1.5 to 13.5 cm. Tumors measuring less than 3.5 cm were significantly associated with higher incidence of node-negative disease (P = .004), an increase in frequency of direct extension into adjacent organs (P = .003), and decreased 1-, 3-, and 5-year survival rates (P < .001). Adenomas were identified in 13 cases, and their presence correlated with a significantly lower incidence of both node-positive disease (P = .047) and direct extension into adjacent organs (P = .02). Immunohistochemical analysis showed a significant trend toward loss of CK20 (P < .001), with a simultaneous trend toward gain of CK7 (P < .001), as cells progress from normal mucosa to adenocarcinoma.
carcinoma. Loss of CK20 and gain of CK7 immunoreactivity did not correlate with age, gender, tumor size, gross morphology, location, or stage. The presence of an adenoma and large tumor size (>3.5 cm) are indicators of better prognosis in duodenal carcinoma. Therefore, tumor size and the presence or absence of an adenoma should be included in the report for primary duodenal adenocarcinoma.

**Microscopic Collitis: A Closer Look**  
(Poster No. 7)

Kausal J. Jabbar, MD (kausaljabbar@stjohn.org); Chady Meroueh, MD; Haiitham Nasser, MD; Paul Mazzara, MD. Department of Pathology and Laboratory Medicine, St John Hospital and Medical Center, Detroit, Mich.

**Context:** We propose to evaluate and to further refine diagnostic criteria of microscopic collitis by comparing morphologic features of collagenous colitis (CC) and lymphocytic colitis (LC).

**Design:** We reviewed 46 colonic biopsies diagnosed as either LC (25) or CC (21) from January to August 2006 for the following morphologic features: (1) subepithelial collagen (SEC) thickness by hematoxylin-eosin and trichrome, (2) pattern of the SEC deposits, (3) percentage of surface epithelial sloughing, (4) intraepithelial lymphocytes (IELs) and eosinophils per 100 epithelial cells, (5) presence of expansion of the lamina propria by inflammatory cells, and (6) presence of neutrophilic cryptitis.

**Results:** In 8 (32%) of 25 cases diagnosed as LC, we found focally thickened, irregular, wispy SEC (7.5–15 μm) and increased IELs. The same irregular wispy finding was also focally observed in 9 cases of CC, having frank SEC thickening. The degree of collagen thickening and epithelial sloughing was statistically different between LC and CC as well as the overlap group (cases originally diagnosed as LC, but with abnormal SEC) (P < .001). The degree of collagen thickening and epithelial sloughing in the overlap group was similar to that observed in CC.

**Conclusions:** We found subtle changes in SEC in 1 of 3 of our cases diagnosed as LC. These cases have other features similar to CC. The histologic distinction between LC and CC may not be as sharp as previously thought. The fact that these cases have histologic features as well as patient demographics between LC and CC, but similar to CC, may suggest a possible progression from LC to CC.

**High-Grade Goblet Cell Carcinoid Is An Aggressive Neoplasm Often Associated With Abdominal Carcinomatosis and Ovarian Metastasis: A Clinicopathologic Analysis of 22 Cases**  
(Poster No. 8)

Olca Basturk, MD1 (olcabasturk@hotmail.com); Jeanette Cheng, MD; Basil El-Rayes, MD; Philip Philip, MD; Duangpen Thirabanjasak, MD; N. Volkman Adsay, MD2. 1Department of Pathology, New York University, New York; 2Department of Pathology and Oncology, Wayne State University and Karmanos Cancer Institute, Detroit, Mich.

**Context:** Although appendiceal goblet cell carcinoids (GCCs) are well-characterized low-grade indolent neoplasia, the definition and clinicopathologic features of their high-grade counterpart (mixed carcinoid-adeno carcinoma) are not well documented.

**Design:** Pathology material and clinical data on 22 examples of high-grade GCCs were analyzed.

**Results:** Clinical findings: Female-male ratio was 19:3. Mean age was 53.5 years. Nineteen had disseminated tumor in the abdomen (12 with gynecologic tract involvement). Ten were initially diagnosed as ovarian cancer. Three had high-grade GCC confined to the appendix. Pathology: All cases had some foci of conventional GCC pattern but also displayed 1 or more of the following: (1) goblet-type cells in cords or as individual cells, or microglandular pattern without goblet cells (n = 21); (2) diffuse infiltrative areas (n = 17)—cordlike and individual nonmucinous cells; (3) mixed component—intestinal pattern (n = 6) or extracellular mucin (n = 9); (4) marked nuclear atypia (n = 9). Immunohistochemistry: Chromogranin showed scattered positivity in 6, focal in 9, and abundant in 1. The tumors were cytokeratin (CK) 20++, CK7−, MUC2++, MUC1−, β-catenin++, Ki-67++. Clinical course: Nineteen patients had abdominal carcinomatosis, but only 1 (with intestinal component) had hepatic and pulmonary metastases. Follow-up: Ten died of tumor (median, 14 months), 3 are alive with disease (5, 10, and 23 months), and 1 is alive without disease (7 months).

**Conclusions:** The high-grade version of GCC is an aggressive neoplasm, which primarily affects females, often presents with carcinomatosis, and mimics ovarian cancer. Microglanular and goblet cell patterns are characteristic and helpful diagnostic features in extra-appendiceal sites. The prognosis is significantly worse than that of an ordinary carcinoid.

**Glycian 3: A Novel Diagnostic Marker for Hepatoblastoma**  
(Poster No. 9)

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**Context:** Glycian 3 (GPC3) is a proteoglycan bound to the cell surface that is theorized to participate in signaling, embryonic growth, and differentiation. GPC3 is mutated in Simpson-Golabi-Behemel syndrome, features of which include increased risk for hepatoblastoma. GPC3 has been detected in hepatic stem cells and was identified as the most overexpressed gene in hepatoblastoma by microarray. Our objective was to analyze the expression of GPC3 in a large series of hepatoblastoma using immunohistochemistry.

**Design:** Immunohistochemical staining using a monoclonal antibody specific to GPC3 was performed on 65 cases of hepatoblastoma (21 biopsies, 39 resections, 5 lung metastases). Immunoreactivity for each case and histologic pattern were semiquantitatively evaluated: 0 (<5% cells stained), 1+ (5%–10%), 2+ (11%–50%), or 3+ (>50%). Staining intensity was scored from 0 to 3. Benign liver and lung and 3 cases of fetal liver were also assessed.

**Results:** All hepatoblastomas demonstrated cytoplasmic GPC3 immunoreactivity with strong intensity (Table). Most fetal, embryonal, and small cell patterns had 2+ or 3+ staining, whereas mesenchymal and teratoid patterns were almost completely negative. Adjacent benign liver and lung were negative. Fetal hepatocytes had diffuse, strong staining.

**Conclusions:** We observed strong expression of GPC3 in primary hepatoblastoma, before and after chemotherapy, and in metastatic lesions. Thus, GPC3 is a valuable novel diagnostic marker for hepatoblastoma. GPC3 may play a role in tumor development, as GPC3 is expressed in hepatic progenitor cells, hepatoblastoma, and fetal liver, whereas benign pediatric and adult hepatocytes are negative.

**Expression of Osteopontin in Primary Small Intestinal Adenocarcinoma**  
(Poster No. 10)

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**Context:** Recent studies have identified osteopontin, a secreted integral membrane phosphoglycoprotein involved in diverse physiologic and pathologic processes including cell adhesion, motility, survival, and angiogenesis, as a potentially useful prognostic marker for a number of tumors including colon cancer, where it portends a poor prognosis. The aim of this study was to examine osteopontin expression in primary small intestinal adenocarcinoma (SIA), a rare malignancy that is morphologically similar to colorectal adenocarcinoma and that has not been previously investigated.
Design: Formalin-fixed, paraffin-embedded tissue sections from 40 nonapillary SIAs (5 from duodenum, 22 jejunum, 8 ileum, and 5 unspecified) were immunohistochemically stained for osteopontin using a polyclonal antibody (K-20, Santa Cruz Biotechnology). The stains were scored by 2 observers as negative (<5% of the cells stained), 1+ (5%–25%), 2+ (26%–50%), and 3+ (>50%), as well as being weak or strong for staining intensity. The staining characteristics of normal-appearing small intestinal mucosa in the same sections were evaluated for comparison. Ten additional small bowel specimens resected for nonneoplastic pathologies were also included in this study for comparison.

Results: Negative staining was observed in nonneoplastic small intestinal mucosa. Cytoplasmic staining was detected in 24 SIAs (60%), of which 18 cases (75%) showed 2+ or 3+ immunoreactivity, and 6 cases (25%) exhibited a strong staining pattern (Table).

Conclusions: Osteopontin is overexpressed in a large proportion of SIAs. These observations suggest that osteopontin may serve an important role in tumor progression during small intestinal tumorigenesis, a feature shared with colorectal adenocarcinoma.

**Summary of Immunohistochemical Results for Osteopontin Expression**

<table>
<thead>
<tr>
<th>Expression</th>
<th>Positive</th>
<th>Weak/Strong</th>
</tr>
</thead>
<tbody>
<tr>
<td>Negative</td>
<td>16</td>
<td>5 (5/1)</td>
</tr>
<tr>
<td>Small intestinal adenocarcinoma (N = 40)</td>
<td>6</td>
<td>6 (5/1)</td>
</tr>
<tr>
<td>3+</td>
<td>12</td>
<td>8 (8/4)</td>
</tr>
</tbody>
</table>

**Activation of the Serine/Threonine Protein Kinase AKT During the Progression of Colonic Neoplasia**

(Poster No. 11)

Ozlem Saglam, MD; Christopher R. R. Garrett, MD; David Boulware, MS; David Shibata, MD; Mokene Malafa, MD; Timothy Yeatman, MD; Jin Q. Cheng, PhD; Said Sebti, PhD; Domenico Coppola, MD; Zena Sayegh, PA; Departments of Anatomic Pathology, Gastrointestinal Oncology, Biostatistics and Drug Discovery, Interdepartmental Oncology, and Anatomic Pathology and Gastrointestinal Oncology, Moffitt Cancer Center, University of South Florida, Tampa, Florida.

Context: AKT has been identified as a major regulator of cell proliferation, tumorigenesis, and regulator of apoptosis. In this study, we evaluated activity of AKT during colon cancer progression.

Design: We used stage-oriented human colon cancer tissue microarrays, including 99 invasive carcinomas (CAs), 28 tubular adenomas, and 18 samples of normal colonic mucosa. The tissue microarrays were stained for pAKT using a polyclonal rabbit anti-phospho-AKT antibody and the avidin-biotin–complex method.

Results: Activation of AKT was detected mostly in the invasive CAs. Sixty-three percent of CAs demonstrated strong to moderate AKT activity. Seven percent of CAs showed AKT negative (0%) or 30% (3/9) were weakly positive for pAKT. Conversely, 76% of normal colonic mucosa were pAKT negative, and only 4 samples stained weakly for pAKT. Eighty-two percent of tubular adenomas were weakly positive for pAKT, 1 was pAKT negative, and none exhibited strong or moderate pAKT stain. At a significance level of .05, the distribution of pAKT stain scores for cancer is shifted to the right of both adenoma (P < .001) and normal (P < .001), and the distribution of pAKT stain for adenoma is shifted to the right of normal (P < .001).

Conclusions: We report increasing activation of AKT during the progression from normal colonic mucosa to adenoma and to carcinoma. This finding implicates pAKT in colon carcinogenesis and provides a rationale for using pAKT inhibitors such as API-2/triciribine for the treatment of CA.

**Histopathology of 4-Month Protocol Liver Biopsy Can Predict Fibrosis Progression Among Patients Undergoing Liver Transplantation for Hepatitis C**

(Poster No. 12)

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Context: Hepatitis C recurs in virtually all patients after liver transplantation, but the disease progression varies. Previous studies have had mixed results in determining the progression to liver cirrhosis using the hepatitis C activity index developed by Knodell. The objective of this study was to examine the value of counting the number of hepatocytes undergoing apoptosis in 4-month protocol biopsies for predicting the development of fibrosis.

Design: Fifty-five cases of patients with liver transplant for hepatitis C were obtained. Counts of apoptotic hepatocytes were determined from the 4-month protocol biopsy in 5 high-power fields (×400 magnification) in the area of hepatic lobules. These counts were compared with the fibrosis stage of the patient’s subsequent protocol biopsies at year 2 post-transplantation.

Results: Counts of apoptosis on protocol biopsies at 4 months after transplantation have a strong positive correlation with the stage of fibrosis at 2 years posttransplantation, Pearson correlation coefficient, r (53) = 0.41, P < .01. Patients with fewer than 10 apoptotic hepatocytes (n = 32) had a significantly lower stage at 2 years (average of 1.75) compared with those with 10 apoptotic hepatocytes or greater (n = 23, average stage of 3.65), P = .001.

Conclusions: On protocol liver biopsies performed as early as 4 months after transplantation, counts of apoptotic hepatocytes predicts the progression of liver fibrosis. Early identification of patients at increased risk for fibrosis may enable clinicians to better target those individuals for antiviral therapy.

**Ablerrant Expression of γ-Catenin in Small Intestinal Adenocarcinoma: Lack of Correlation With ApoC and c-Myc Protein Expression**

(Poster No. 13)

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Context: The β-catenin homologue γ-catenin has been shown to be regulated by the adenomatous polyposis coli (APC) tumor suppressor that leads to c-Myc overexpression in colorectal tumorigenesis. This pathway has not been investigated in small intestinal tumorigenesis.

Design: Thirty-three surgically resected sporadic, nonapillary small intestinal adenocarcinomas were studied. Formalin-fixed tissue sections were immunohistochemically stained for the expression of γ-catenin, APC, and c-Myc proteins. The staining patterns (membranous, cytoplasmic, or nuclear) and intensity in tumor cells were compared with non-neoplastic small intestinal mucosa in the same sections.

Results: A weak membranous and cytoplasmic staining pattern for γ-catenin was universally present in nonneoplastic small intestinal epithelium. In contrast, strong predominantly cytoplasmic, but not nuclear, immunoreactivity was evident in 32 (97%) small intestinal adenocarcinomas. One tumor showed a staining pattern comparable to nonneoplastic epithelium. Immunostaining for the carboxyl terminus of the APC protein showed a complete lack of immunoreactivity in tumor cells presumably resulting from mutations of the APC gene in 11 cases (33.3%). The adjacent normal mucosa stained positive. In the remaining cases, positive APC staining was detected in both normal and neoplastic tissues. There was no significant difference in the nuclear expression of c-Myc protein in tumor cells and the adjacent nonneoplastic intestinal epithelium.

Conclusions: Although the expression pattern of γ-catenin protein is altered in small intestinal adenocarcinoma, the lack of c-Myc overexpression argues against a regulatory role of γ-catenin in c-Myc expression. These observations suggest that deregulation of γ-catenin involves molecular mechanisms independent of APC and c-Myc in small intestinal tumorigenesis.

**Arterial and Capillary Neovascularization of Hepatic Lesions: The Utility of Smooth Muscle Actin, CD31, and CD34 for Their Differential Diagnosis**

(Poster No. 14)

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Context: Neangiogenesis is associated with emergence of hepatocellular malignancy. We therefore aim to analyze angiogenic immunophenotype of hepatocellular adenoma (HA), hepatocellular carcinoma (HCC), focal nodular hyperplasia (FNH), and regenerative nodule (RN) and evaluate its possible diagnostic relevance.

Design: Twelve HAs, 7 FNHs, 19 HCCs, and 8 cirrhotic nodules were selected. Immunostain for endothelial cells (CD31, CD34) and smooth muscle actin for unpaired arteries was performed. CD31 and CD34 staining was graded semiquantitatively. The number of unpaired arteries was counted in 5 random fields (×10). Statistical analyses, Kruskal-Wallis, and Sign test of significance for k-independent samples were performed using SAS version 9.1 (SAS Institute, Cary, NC).
Results: The mean difference of CD34 expression between HCC and HA (0.95; 95% confidence interval, 0.01-1.89) and HCC and RN (1.87; 95% confidence interval, 0.79-2.94) was significantly higher in HCC (P = .05). The level of CD34 expression in the well-differentiated HCC (3.44 ± 0.89) was significantly higher than in HA (2.41 ± 0.99) (P = .02). Between HCC and FNH, CD34 did not show significant difference. No significant difference was detected at P = .05 for the level of CD31 expression. Mean value of smooth muscle actin for unpaired arteries for both HA and HCC was 6.6. Both FNH and RN did not have any unpaired arteries.

Conclusions: CD34 stain is better than CD31 to differentiate HCC from the other 3 entities. However, positive staining of CD34 does not confirm a diagnosis of HCC because a significant number of HA also stained positive. The number of unpaired arteries was not useful in distinguishing HA from HCC; however, their presence excludes FNH and RN.

Diagnostic Utility of Glypican-3 Immunoreactivity in Distinguishing Hepatocellular Carcinoma From Benign Hepatocellular Masses and Metastatic Lesions to the Liver
(Poster No. 15)

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Context: Distinction between hepatocellular carcinoma (HCC) and benign hepatocellular lesions may be difficult. We analyzed the diagnostic value of Glypican-3 (GPC3) immunoreactivity in differentiating between HCC and other hepatic and nonhepatic lesions.

Design: Immunohistochemical staining using a monoclonal antibody specific for GPC3 (clone IG12; Biossicais, Burlington, VT) was performed on 59 liver tissue specimens. These included 20 HCCs, 13 hepatocellular adenomas, 6 focal nodular hyperplasias, 1 benign liver, 5 submassive hepatic necrosis, 2 hepatitis C virus infections, 2 cirrhosis, 1 macrovesicular steatosis, 1 macroregenerative nodule, and 8 metastatic tumors. Immunoreactivity was graded as 1+ (weak), 2+ (moderate), or 3+ (strong).

Results: GPC3 immunoreactivity was detected in 15 (75%) of 20 HCCs, whereas 33% of non-HCC or metastatic tumors (total of 39 cases) expressed GPC3 immunoreactivity. In HCCs, GPC3 expression tended to be seen more frequently in moderately and poorly differentiated tumors (60%), whereas 33% of cases expressed only focal positivity. GPC3 in the diagnosis of HCC showed 75% sensitivity, 100% specificity, 100% positive predictive value, and 86.6% negative predictive value.

Conclusions: Positive immunoreactivity for GPC3 is highly specific for HCC and can be reliably used to distinguish HCC from other benign and malignant hepatic lesions and most metastatic lesions. However, because GPC3 expression in HCC can be negative (25%) or focal (33%), a negative GPC3 expression in HCC can be negative (25%) or focal (33%), a negative

Gene Expression of SOX4 and Prothymosin α Are Positively Correlated in Esophageal and Gastric Adenocarcinomas
(Poster No. 17)

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Context: SRY related HMG box 4 (SOX4), a transcriptional regulatory protein, has been identified by microarray gene expression profiling as part of cancer signature of up-regulated genes for many types of human cancer. Previous work in our laboratory has shown that down-regulating SOX4 in cancer cell lines causes apoptosis, suggesting it confers prosurvival phenotype. RNAi knockdown experiments have identified prothymosin α (PTMA) as a potential target of SOX4 gene regulation. PTMA is known to negatively regulate apoptosome formation and is a likely mediator of the SOX4 prosurvival pathway. The present study is undertaken to determine the gene expression patterns of SOX4 and PTMA in esophageal and gastric adenocarcinomas.

Design: Formalin-fixed, paraffin-embedded tissues from 164 gastric and 64 esophageal adenocarcinomas and 20 benign gastroesophageal mucosa samples were obtained from the archives of the University of Virginia pathology department and made into tissue microarrays. Immunohistochemistry was performed for PTMA and SOX4 proteins, with interpretation of intensity and percent staining. Quantitative reverse transcriptase polymerase chain reaction (RT-PCR) analysis was performed on a subset of frozen gastric adenocarcinoma and normal mucosa samples to determine the relative levels of RNA transcripts for SOX4 and PTMA.

Results: Both SOX4 and PTMA proteins are significantly up-regulated in adenocarcinomas relative to normal mucosa. There is a strong positive correlation between SOX4 and PTMA expression (P < .001). The quantitative RT-PCR data correlated with the immunohistochemical findings.

Conclusions: Our results suggest that SOX4 and PTMA are involved in the tumorigenesis of gastroesophageal adenocarcinomas and are consistent with a functional relationship between SOX4 and PTMA protein levels.

Analysis of Morphologic Features and Oncogene Mutations in a Series of 52 Intraductal Papillary Mucinous Neoplasms
(Poster No. 18)

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Context: Pancreatic carcinomas may arise from pancreatic intraepithelial neoplasia by a series of morphologic changes and mutational events. A less well-described pathway for pancreatic carcinogenesis involves intraductal papillary mucinous neoplasms (IPMs).

Design: We studied 52 IPMNs for histologic features (dysplasia, subtype) and for the presence of K-ras, EGFR, p53, BRAF, and HER-2/neu mutations.

Immunophenotypic Findings in SPN and PET*

<table>
<thead>
<tr>
<th>SPN</th>
<th>PET</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chromogranin A</td>
<td>0/8 (0)</td>
</tr>
<tr>
<td>E-cadherin</td>
<td>0/8 (0)</td>
</tr>
<tr>
<td>CD31</td>
<td>8/8 (100)</td>
</tr>
<tr>
<td>Synaptophysin</td>
<td>5/8 (62.5)</td>
</tr>
<tr>
<td>CD56</td>
<td>6/6 (100)</td>
</tr>
<tr>
<td>Progesterone receptor</td>
<td>8/8 (100)</td>
</tr>
</tbody>
</table>

* SPN indicates solid-pseudopapillary neoplasm of the pancreas; PET, pancreatic endocrine tumor.

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Results: Sixteen cases had a gastric foveolar morphology. Seven contained low-grade, 8 moderate-grade, and 1 high-grade dysplasia. Six low-grade gastric IPMNs demonstrated K-ras mutations, and 1 had a HER-2/neu mutation. Six of 7 moderate dysplasia cases showed K-ras mutations. Twenty-seven cases revealed intestinal morphology. Six had low-grade, 13 moderate-grade, and 8 high-grade dysplasia. Three low-grade IPMNs demonstrated K-ras mutations. Seven of 13 intestinal type IPMNs with moderate dysplasia demonstrated K-ras mutations. Six high-grade intestinal IPMNs had K-ras mutations and 1 had a BRAF mutation. Nine IPMNs demonstrated pancreaticobiliary morphology. None were low grade. Two showed moderate dysplasia, 1 of which demonstrated a K-ras mutation. Seven pancreaticobiliary tumors revealed high-grade dysplasia, with 6 K-ras mutations, 3 p53 mutations, and 1 EGFR mutation.

Conclusions: Pancreaticobiliary IPMNs demonstrated higher degrees of dysplasia than other morphologic subtypes. Two of 3 cases demonstrating invasive adenocarcinoma were pancreaticobiliary type. The presence of K-ras mutations did not correlate with degree of dysplasia. p53 mutations were only found in high-grade dysplasia and only in the pancreaticobiliary subtype. The pancreaticobiliary subtype was more often associated with invasive adenocarcinoma. Two invasive carcinomas contained p53 mutations.

Cytomegalovirus Colitis in an Immunocompetent Man With Ischemic Bowel Disease

Poster No. 19

Sarat C. Khandavalli, MD (skhandav@yahoo.com); Mariam M. Haber, MD; Fernando U. Garcia, MD. Department of Pathology, Drexel University College of Medicine, Philadelphia, Pa.

Cytomegalovirus (CMV) colitis is a well-documented disease process affecting the gastrointestinal tract of immunocompromised individuals. Our case involved an immunocompetent patient who developed CMV colitis in a background of ischemic bowel disease. This case involved a 69-year-old immunocompetent man who suffered from coronary artery disease, hypertension, and peripheral vascular disease and who underwent placement of an aortobifemoral graft. Approximately 1 month later, the graft became infected, warranting surgical intervention. At the time of surgery, the sigmoid colon was noted to be perforated. A partial colectomy was performed and the resected specimen consisted of 2 short segments of bowel, each showing a reddish mucosal discoloration. Microscopic examination demonstrated changes consistent with chronic ischemic disease, including mucosal hemorrhage and fibrosis, ulceration, and perforation of the bowel wall. Cells with large intranuclear inclusions that stained strongly with CMV antibodies were noted, confirming the diagnosis. The latent form of CMV can persist in host tissues indefinitely and may reactivate under various circumstances. In patients who have inflammatory bowel disease, as many as 15% show CMV in gut tissue. A recent review of such patients has suggested that it is the localized inflammatory response rather than the immunosuppressive treatment that is responsible for the reactivation of CMV. Our case, as well as a few previously reported cases, illustrates that CMV colitis should be considered in the differential diagnosis of patients with newly intensified chronic ischemic bowel or other types of chronic colitis, regardless of immunocompetency (Figure 15).

A Neurofibromatosis Type 1 Patient With Multiple Concurrent Gastrointestinal Tumors

Poster No. 20

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Neurofibromatosis type 1 (NF1) is one of the most common inherited diseases with an estimated birth incidence of 1:3000 and autosomal dominant transmission. In addition to cutaneous, soft tissue, and visceral neurofibromas, patients with NF1 have an increased incidence of other tumors. The gastrointestinal manifestations of NF1 are not uncommon, although they are less frequent than neurocutaneous manifestations. The spectrum of NF1-associated gastrointestinal lesions includes hyperplastic lesions of gastrointestinal neural tissue and its supporting structures, gastrointestinal stromal tumors, and endocrine cell tumors of the duodenum and peripancreatic region. We present the clinical and pathologic findings in a 63-year-old woman NF1 patient with prior history of multiple cutaneous neurofibromas and a sarcoma of the thigh. The patient presented with obstructive jaundice. Endoscopy revealed an ampullary mass, which was subsequently resected. Pathologic evaluation of the pancreaticoduodenectomy specimen revealed multiple concurrent neoplasms. These included an obstructing ampullary carcinoma, a separate duodenedal mixed carcinoid/adenocarcinoid, multiple neurofibromas, and multiple c-kit-positive gastrointestinal stromal tumors (Figure 16). These lesions have been previously reported in association with NF1. However, to our knowledge, the concurrent nature of this patient's tumors is distinctly unusual. This case further highlights the importance of a thorough clinical and pathologic evaluation of NF1 patients, as they may show multiple concurrent gastrointestinal neoplasms.

Signet Ring Cell Sinus Histiocytosis of Lymph Node Mimicking Metastatic Signet Ring Cell Adenocarcinoma

Poster No. 21

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Signet ring sinus histiocytosis of lymph nodes is a reactive change that can mimic a metastatic poorly differentiated signet ring cell adenocarcinoma. This entity has not been described in lymph nodes of patients with colon adenocarcinoma but has only been reported in lymph nodes of patients with prostatic adenocarcinoma and breast carcinoma. We report on a 44-year-old man with a history of a stage III, pT3N2MX, moderately to poorly differentiated colonic adenocarcinoma, and 11 of 16 positive lymph nodes with extranodal extension. He developed a new retroperitoneal mass within 1 year after his primary colon cancer resection and chemotherapy. Evaluation of the retroperitoneal mass showed a recurrent poorly differentiated adenocarcinoma with signet ring cell features. The lymph node dissection revealed 56 pelvic lymph nodes, which all showed sinusoidal distention with signet ring–like cells. Examination on hematoxylin-eosin–stained slides showed signet ring–like cells with bland cytologic features closely resembling histiocytes. Special stains for mucicarmine and periodic acid–Schiff without diastase and immunohistochemical stains for pancytokeratin and CD68 confirmed a reactive signet ring sinus
hiopathy, they are widely regarded as unusual reactions to vegetable matter and the stomach in the setting of ulcers; however, these lesions fail rather than representing vasculopathy. Most pulse granulomas affect the following a motor vehicle accident and pulmonary contusion, a 69-year-old woman developed 

Signet Ring Cell Change in a Preexisting Tubulovillous Adenoma With Pseudomembranous Colitis

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Signet ring cell change is a nonneoplastic process associated with pseudomembranous colitis that can present a diagnostic dilemma when differentiating from signet ring cell carcinoma. We report a case of signet ring cell change occurring in a preexisting tubulovillous adenoma in a colon with pseudomembranous colitis. After being treated with antibiotics following a motor vehicle accident and pulmonary contusion, a 69-year-old woman developed Clostridium difficile toxin–positive pseudomembranous colitis. A computed tomography scan revealed diffuse colonic wall thickening, vascular enhancement, and inflammatory stranding of the pericolonic fat. A total colectomy with end ileostomy was performed. The surgical specimen consisted of an 86.5 × 5 × 4-cm segment of bowel filled with green mucus and a granular, edematous, hemorrhagic mucosa. There were 1 pedunculated polyp measuring 1.8 × 1.5 × 0.6 cm. On light microscopy, a tubulovillous adenoma with low-grade dysplasia and multiple small clusters of signet ring cells within a background of mucosal necrosis, transmural edema, and fibrinoinflammatory exudates was revealed. The signet ring cell changes were confined to intestinal crypts of the tubulovillous adenoma and the surrounding ischemic mucosa and did not infiltrate into the lamina propria. To the best of our knowledge, this is the second case of signet ring cell change presenting in a preexisting tubulovillous adenoma (Figure 17).

A Mixed Pancreatic Endocrine Tumor and Clear Cell Carcinoma Mimicking Renal Cell Carcinoma

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We report a case of a mixed pancreatic tumor consisting of endocrine tumor and clear cell carcinoma in a 76-year-old man. The patient was originally evaluated for hematuria and subsequently diagnosed with urinary bladder infection. During the initial workup, the computed tomography scan revealed a 2-cm solid mass in the pancreatic body. Endoscopic ultrasound showed a 2.2-cm round, sharply demarcated mass consistent with an endocrine tumor. The patient had no medical history of von Hippel-Lindau disease or renal cell carcinoma. A distal pancreatectomy was performed. Grossly, we found a solitary 2 × 1.8 × 1.6-cm yellow-brown well-circumscribed pancreatic mass with central hemorrhage. Microscopic findings revealed a mixed pancreatic tumor with 2 distinct areas of endocrine tumor and clear cell carcinoma components. The 2 components had different immunohistochemical staining patterns, consistent with neuroendocrine tumor and clear cell carcinoma, respectively, as summarized in the Table. Extensive workup did not show any evidence of primary renal cell carcinoma or other malignant neoplasm (up to 8 months after surgery). The molecular analysis performed on clear cell carcinoma derived from laser microdissection did not reveal K-ras mutation. To our knowledge, this is a new entity of mixed pancreatic endocrine tumor and clear cell carcinoma, which has never been reported. The clear cell carcinoma component mimics the histology and immunohistochemical profile of renal cell carcinoma, and it does not express the neuroendocrine markers as clear cell endocrine tumor does. It also does not express HMB-45, which differentiates it from sugar cell tumor.

True Gastric Pulse Granulomas: Report of the First Case

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Pulse granulomas are rare entities characterized by aggregates of thin, eosinophilic hyaline rings often admixed with vegetable matter, multinucleated giant cells, and other inflammatory cells. The rings vary in size and shape, and although they morphologically resemble hyaline vasculopathy, they are widely regarded as unusual reactions to vegetable matter rather than representing vasculopathy. Most pulse granulomas affect the oral cavity in association with oral pathology or dental procedures. Similar lesions have been reported to affect the lungs in the setting of aspiration and the stomach in the setting of ulcers; however, these lesions fail to meet strict morphologic criteria of pulse granulomas. For unknown reasons, extraoral alimentary pulse granulomas are extremely rare with 4 being reported and all intestinal. True gastric pulse granulomas have yet to be reported. We encountered a case with 2 gastric pulse granulomas, involving a 69-year-old woman who underwent gastroduodenectomy for a perforated ulcer that was preoperatively confirmed radiologically with barium sulfate. The pathologic specimen contained a prominent well-circumscribed perforated ulcer in the anterior wall of the pyloric antrum. Microscopy showed deeply invasive adenocarcinoma, intestinal type, low grade, and surrounding the perforation. Two small pulse granulomas occupied the adjacent subserosa with the largest measuring 0.5 mm in greatest diameter (Figure 18). The pulse granulomas were admixed with barium-laden histiocytes and were near polarizable fragments of botanical seeds and Candida species. To our knowledge, we present the first case of true gastric pulse granulomas. Pulse granulomas in gastric subserosa can help confirm perforation. Awareness of this entity is necessary to avoid confusion with hyaline vasculopathy.

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**Synchronous Renal and Adrenal Masses: An Analysis of 80 Cases**

**Poster No. 25**

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**Context:** Synchronous renal and adrenal masses are uncommon. Although adrenal tumors in the context of renal cell carcinoma (RCC) are often suspected as metastasis, other lesions of different therapeutic or prognostic implications have been described. However, pathologic characteristics of these lesions have not been investigated on a large scale.

**Design:** Five hundred fifty radical nephrectomies (including ipsilateral adrenalectomy) were reviewed for cases with grossly detected concurrent renal and adrenal masses. Pathologic features of coexisting renal and adrenal lesions were examined.

**Results:** Eighty (15%) of 550 radical nephrectomies had simultaneous renal and adrenal masses. The renal lesions included clear cell (79%), papillary (11%), and chromophobe (2.5%) RCC; oncocytoma (2.5%); and others (5%) (Table). The adrenal lesions were cortical adenoma/hyperplasia (46%), metastatic RCC (24%), direct extension from RCC (19%), pheochromocytoma (5%), and others (6%). There was a considerable overlap in the size of benign and malignant adrenal masses.

**Conclusions:** In most cases the preoperative radiographic impression of adrenal masses in the context of RCC was that of metastasis, histologically the majority (56%) of them represented other entities, including adenoma/hyperplasia (45%), pheochromocytoma (4%), and others (7%). In contrast, metastasis and contiguous spread from RCC were less common (25% and 19%, respectively). When an adrenal mass is seen concurrently with RCC, the likelihood of having an isolated adrenal lesion is at least comparable to that of metastasis or direct extension from the renal primary. Nonetheless, finding of metastatic RCC as small as 0.5 cm mandates thorough gross and microscopic evaluation of the adrenal gland.

**Table 1. Tumor Grades**

<table>
<thead>
<tr>
<th>Tumor Grade</th>
<th>No. of Cases</th>
<th>% of Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade 1</td>
<td>41</td>
<td>20.3</td>
</tr>
<tr>
<td>Grade 2</td>
<td>118</td>
<td>58.4</td>
</tr>
<tr>
<td>Grade 3</td>
<td>42</td>
<td>20.8</td>
</tr>
<tr>
<td>Grade 4</td>
<td>1</td>
<td>0.5</td>
</tr>
</tbody>
</table>

**Table 2. Histologic Subtypes of Renal Cell Carcinoma (RCC)**

<table>
<thead>
<tr>
<th>Histologic Subtype</th>
<th>No. of Cases</th>
<th>% of Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clear cell RCC</td>
<td>153</td>
<td>75.7</td>
</tr>
<tr>
<td>Papillary RCC</td>
<td>40</td>
<td>19.8</td>
</tr>
<tr>
<td>Chromophobe RCC</td>
<td>8</td>
<td>4</td>
</tr>
<tr>
<td>Unclassified RCC</td>
<td>1</td>
<td>0.5</td>
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</tbody>
</table>

**Expression of PAX2 and α-Methylacyl-CoA Racemase in Cystic Renal Neoplasms**

**Poster No. 27**

Hwajeong Lee, MD (hlee1@hfhs.org); Min W. Lee, MD; Mehsati Herawi, MD, PhD. Department of Pathology and Laboratory Medicine, Henry Ford Hospital, Detroit, Mich.

**Context:** Cystic renal neoplasms (CRNs) encompass a broad range of entities. The transcription factor PAX2 has been reported to be expressed in cystic renal disease, and α-methylacyl-CoA racemase (AMACR) appears to be a specific marker for neoplasms arising from proximal renal tubules. We studied the immunohistochemical expression and diagnostic utility of PAX2 and AMACR in a variety of CRNs and compared them with several other markers.

**Design:** Twenty-three cases of CRN from the surgical pathology archives at Henry Ford Hospital were included 12 cystic renal cell carcinomas (CRCCs), not otherwise specified (nosCRCCs). 9 CRCCs associated with acquired cystic or end-stage renal disease (aCRCCs); and 2 CRCCs associated with von Hippel-Lindau syndrome. Four cases of multicellular CRCC were included in nosCRCCs. All were of clear cell type except 2 papillary RCCs included in aCRCCs. Representative sections were immunostained with PAX2, AMACR/p63 cocktail, CD10, cytokeratin (CK) 7, CK20, and high-molecular-weight cytokeratin (HMWK).

**Results:** Only moderate or strong staining was considered positive (Table). CK20, HMWK, and p63 were negative in all cases.
Conclusions: (1) AMACR and CD10 were strongly positive in the great majority of aCRCCs (89%; 89%) compared with only 25% and 33% in nosCRCCs; (2) 33% of aCRCCs were negative for PAX2; (3) all papillary RCCs and 76% of clear cell RCCs stained positive for AMACR; (4) no significant immunohistochemical difference was observed between multiloculuar CRCCs and the remaining nosCRCCs; (5) CK20 and HMWK were negative in all cases, whereas CK7 was positive in most (87%) cases.

<table>
<thead>
<tr>
<th>Expression of PAX2, α-Methylacyl-CoA Racemase (AMACR), CD10, and Cytokeratin (CK) 7 in Cystic Renal Neoplasms*</th>
</tr>
</thead>
<tbody>
<tr>
<td>PAX2, %</td>
</tr>
<tr>
<td>--------</td>
</tr>
<tr>
<td>nosCRCC (n = 12)</td>
</tr>
<tr>
<td>aCRCC (n = 9)</td>
</tr>
<tr>
<td>VHL (n = 2)</td>
</tr>
</tbody>
</table>
* nosCRCC indicates cystic renal cell carcinoma, not otherwise specified; aCRCC, acquired cystic renal cell carcinoma; and VHL, von Hippel-Lindau syndrome.

Indications for Frozen Section Examination of Pelvic Lymph Nodes in Prostate Cancer

(Ihsane Ouansafi, MD, PhD; Aroob Shanaah, MD; Ann E. Anderson, MD; Gary Weiss, MD; Department of Pathology and Urology, Long Island Jewish Medical Center, New Hyde Park, NY.)

Context: In prostate cancer, pathologic examination of lymph nodes on paraffin section is the gold standard to determine if a lymph node has metastases. The role of frozen section examination of lymph nodes during total prostatectomy is controversial because of its high cost and low sensitivity.

Design: The objective of our study was to examine the clinical value and the cost effectiveness of intraoperative frozen section of lymph nodes before or during prostatectomy. Reports of patients who underwent pelvic lymphadenectomy for prostatic carcinoma with frozen section examination at Long Island Jewish Medical Center from 1995 to 2005 were reviewed. The cost of performing a frozen section was assessed.

Results: One hundred fifty-four patients underwent frozen section examination of pelvic lymph nodes. Three patients (1.9%) had positive lymph nodes. Two cases were diagnosed on frozen section and 1 case was diagnosed on paraffin section (false-negative on frozen section). The sensitivity of frozen section for determining lymph node metastases was 66%. The cost of performing a frozen section was subdivided into the operating room, professional, and technician cost ($1689).

Conclusions: Frozen section diagnosis of metastatic carcinoma in pelvic lymph nodes before radical prostatectomy is costly and may not be justified as a routine procedure because of its low sensitivity and the low incidence of lymph node metastasis. We propose a comprehensive approach to the controversial issue of indications for frozen section examination of lymph nodes in prostate cancer using Gleason score, prostate-specific antigen, and clinical stage as guidelines.

Automated Assessment of Growth Factor Expression in Renal Cell Carcinoma

(Zeenath Asma, MD, PhD; Anoja Attele, MD; Weihua Gao, MD; Craig Beam, PhD; Virgilia Macias, MD; Alexis Chesrow, MD; Alan Chernoff, MD; Suman Setty, MD, PhD; (setty@uic.edu). Department of Pathology, University of Illinois, Chicago.)

Context: Renal cell carcinomas (RCCs) express epidermal growth factor receptor (EGFR), a cell membrane receptor whose activation leads to tumor progression, and vascular endothelial growth factor (VEGF), which has a role in tumor-associated angiogenesis. The aim of this study was to characterize the expression of EGFR and VEGF and to assess their prognostic value.

Design: Thirty consecutive cases of RCC were evaluated by 2 pathologists for expression of VEGF (1:100; Neomarkers, Calif) and EGFR (1:50; Dako, Carpinteria, Calif), distribution (membrane or cytoplasmatic), and intensity (scale of 0 to 3). Five random areas selected from scanned hematoxylin-eosin–stained sections were quantitated using ImageScope software (Aperio) and the average compared with the manual method. The expression of EGFR and VEGF were correlated with Fuhrman grade and survival using the Spearman/Pearson correlational coefficient test.

Results: Twenty clear cell, 3 papillary (type I), and 7 papillary (type II) RCCs, with an average follow-up of 3.5 years, had membrane and cytoplasmatic EGFR positivity in 16 (80%) of 20 clear cell and 6 (60%) of 10 papillary RCCs. Intensity of EGFR staining was associated with a rising tumor grade and size (P < .05). A patient with a clear cell RCC having higher EGFR staining intensity (2 or 3) had a higher risk of dying (hazard ratio, 2.4; 95% confidence interval, 1.2–4.7; P < .05). Cytoplasmatic VEGF staining was more prevalent in type I and II papillary RCCs (70%).

Conclusions: Higher intensity of EGFR in clear cell RCC and lower intensity of VEGF in papillary RCC were correlated with poor survival. Quantitation by manual and automated methods was comparable.

p16 and p53 Immunoexpression in Urethral Carcinomas: Correlation With Stage and Ki-67 Index

(Jehimint Z. Ali, MD; (talil@umm.edu); Anil V. Parwani, MD, PhD; Department of Pathology, University of Maryland Medical Center, Baltimore; Department of Pathology, University of Pittsburgh Medical Center, Pittsburgh, Pa.)

Context: Inverse expression of p53 and p16 is seen in bladder urothelial carcinomas (UCs) and correlates with tumor stage and grade. This study specifically evaluates the expression of p16 and p53 and correlates it with Ki-67 percent and stage of urethral UCs.

Design: Fifteen high-grade urethral UCs, 10 invasive urethral UCs (NIUCs), 5 invasive urethral UCs (INUCs), and 4 bladder UCs were studied. Moderately intense staining with p16 was considered positive. p53 staining greater than 20% was scored positive, whereas p516 staining of less than 10% was considered abnormal. Ki-67 percent is the percentage of positive nuclei.

Results: Of the 10 NIUCs, decreased expression of p16 was seen in 5 (50%), whereas it was seen in 3 (60%) of 5 INUCs. In NIUCs with decreased and normal p16, mean Ki-67 percent was 66% (range, 40%–80%) and 38% (range, 25%–70%), respectively, whereas it was high in 5 (50%) of these only 2 showed decreased p16. In NIUCs with high and normal p53, Ki-67 percent was 50% (range, 30%–80%) and 54% (range, 25%–80%), respectively. Among 5 INUCs, high p53 was seen in 2 (40%) and both had low p16. Ki-67 percent in INUCs and NIUCs was 68% (range, 40%–90%) and 49% (range 25%–80%), respectively. Of the 4 bladder UCs, all showed normal p16 but increased p53 percent in 3 INUCs. One low-grade NIUC showed no increase in p53.

Conclusions: Urethral UCs did show the expected inverse relationship of p53 and p16 in a subset of cases. Abnormal p16 correlates with increased Ki-67 percent, as does the tumor stage. p53 expression did not correlate with Ki-67 percent. p16 and p53 immunoexpression did not correlate well with tumor stage.
Matriptase Is Overexpressed in Localized but Not in Aggressive Prostate Cancer
(Poster No. 32)
Matthew Ttwohig, MD1 (mtwohig@uwhealth.org); Miranda Warren, BS; Thomas Pier, BS; Jens Eickhoff, PhD; Wei Huang, MD.1 Departments of Pathology and Biostatistics and Medical Informatics, University of Wisconsin, Madison.

Context: Recent studies have suggested that matriptase and its inhibitor, hepatocyte growth factor inhibitor 1 (HAI), are important in the progression of many cancers. Limited data are available on prostate cancer.

Design: A prostate tissue microarray was constructed consisting of 35 localized prostate cancers, 15 aggressive prostate cancers, 15 metastases, 24 benign prostate hyperplasia, 18 high-grade prostate intraepithelial neoplasia, and 41 normal prostate tissues. Mean patient age was 63 years and Gleason scores ranged from 6 to 9. Target antigens were detected by anti-matriptase and anti-HAI and visualized by Alexa Fluor-567-tyramide and HRP-anti-mouse immunoglobulin. Intensities of matriptase and HAI in cytoplasmic compartment were quantified using AQUA system (HistoRx, New Haven, Conn). Statistical analysis was performed using analysis of variance method.

Results: Matriptase expression levels were significantly higher (P < .001) in localized prostate cancer compared with normal tissue and decreased in aggressive prostate cancer compared with metastatic cancer (P < .001) when compared with localized carcinoma (Table). When compared with normal prostate tissue, HAI expression levels were significantly higher (P < .001) in all proliferative prostate diseases (benign prostates, high-grade prostate intraepithelial neoplasia, localized and aggressive cancer, and metastases), among which no significant differences were found.

Conclusions: Matriptase is overexpressed in localized prostate cancer but decreased in metastases. HAI expression levels are elevated in all proliferative prostate diseases (benign prostate hyperplasia and prostate cancers), yet no significant differences were found among them.

### Table 1

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Matriptase</th>
<th>HAI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal tissue</td>
<td>470.1</td>
<td>491.2</td>
</tr>
<tr>
<td>Benign prostate hyperplasia</td>
<td>524.3</td>
<td>1136.2</td>
</tr>
<tr>
<td>High-grade prostate intraepithelial neoplasia</td>
<td>609.9</td>
<td>948.8</td>
</tr>
<tr>
<td>Localized cancer</td>
<td>645.7</td>
<td>904.6</td>
</tr>
<tr>
<td>Aggressive cancer</td>
<td>518.2</td>
<td>957.4</td>
</tr>
<tr>
<td>Metastatic disease</td>
<td>377.4</td>
<td>1228.8</td>
</tr>
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</table>

Presacral Masses: Clinical and Pathologic Correlates
(Poster No. 33)

Sonai N. Kamat, MBBS, MD1 (kamat.sn@hotmail.com); Morris Edelman, MD; Sherrie White, MD; Richard Glick, MD.2 Department of Pathology, North Shore Long Island Jewish Health System, New Hyde Park, NY; Department of Pediatric Surgery, Schneider Children's Hospital, New Hyde Park, NY.

Context: The presacral region of the pelvis is host to a variety of pathologic entities, some with unusual clinical associations and genetic implications. Presacral masses may be associated with the Curriano syndrome (autosomal dominant), which includes a spectrum of anorectal malformations, sacrococcygeal defects, and presacral mass lesions.

Design: Retrospective search of the pathology records, including pathology slides and clinical information, of the Long Island Jewish Medical Center from 1990 to 2006 revealed 31 patients with presacral lesions.

Results: Patient ages ranged from 2 days to 32 years with 14 patients younger than 1 year. There were 11 (35%) males and 20 (65%) females. Pathologic diagnoses were mature cystic teratoma (n = 21), mature cystic teratoma with carcinoma tumor (n = 1), Ewing/primitive neuroectodermal tumor (n = 2), and 1 case each of hamartoma, multicellular mesothelial cyst, differentiating neuroblastoma, ganglioneuroma, enteric duplication, extrarenal Wilms tumor, and mixed germ cell tumor with immature teratomatous and yolk sac elements. Associated anomalies included anorectal malformations (n = 5) and 1 case each with ureteric dudlephels, recto-vaginal fistula, tethered cord, and myelomeningocele. Three patients in this series were known to be family members with features of the Curriano syndrome, including 1 patient each with presacral hamartoma, mature cystic teratoma with carcinoma, and a presacral enteric duplication with hemiscirrump.

Conclusions: Presacral tumors show a preponderance of germ cell tumors. Six (30%) cases were malignant. We report the occurrence of a carcinoïd tumor arising rarely in a presacral teratoma. Identifying a presacral mass should prompt a search for other pelvic anomalies and potentially family counseling and screening to detect the Curriano syndrome.

A 2-Dimensional Approach to Glomerular Mesangial Expansion Measurement
(Poster No. 34)

Jesse Christ; Mona Papari, MD; Arun K. Setty, PhD; Suman Setty, MD (ssetty@uiuc.edu). Department of Pathology, University of Illinois, Chicago.

We investigated the correlation between the severity of diabetic nephropathy and expansion of the mesangium as characterized by the ratio of the mesangial and glomerular surface area. We investigated the feasibility of quantitating glomerular disease by light microscopy. Biopsy material was obtained from 2 clinically documented diabetic nephropathy patients (1 moderate and 1 severe glomerulosclerosis). Periodic acid-Schiff–stained sections were scanned using the Aperio setup and viewed at >200 magnification. Surface area of 10 nonsclerosed glomeruli was measured by the mesangial (M/G) area algorithm. Mesangial fractional area of the glomerulus (M/G area) was determined. Additionally, a limited number of glomeruli from the patient with moderate glomerulosclerosis were reconstructed from 3 parallel sections of the biopsy taken 16 μm apart. The patient with moderate disease has an average M/G area of 49.59 ± 0.09 and severe disease of 64.70 ± 0.12. Average glomerular volume in the patient with moderate disease was calculated to be 212000 μm³. This is a novel method to obtain near accurate measurements of volume by examining light microscopic sections instead of from the more laborious electron microscopic technique. Mesangial expansion detected by the M/G area calculation, in the patients with moderate and severe nephropathy, is commensurate with the severity of disease. There was little variation in the degree of mesangial expansion among the 10 nonsclerosed glomeruli. This suggests the possibility that sampling even fewer glomeruli may yield results reflective of the degree of disease.

Risk Assessment Model for Noninvasive Papillary Urothelial Carcinoma
(Poster No. 35)

Lara R. Harik, MD1 (laraharik@gmail.com); Ahmad Shabsigh, MD; Satish Tickoo, MD; Samson W. Fine, MD; Anuradha Gopalakrishnan, MD; Guido Dalbagani, MD; Victor E. Reuter, MD.1 Departments of Pathology and Urology, Memorial Sloan-Kettering Cancer Center, New York, NY.

Context: Despite recent advances in pathologic grading of noninvasive papillary lesions, significant difficulty still exists in predicting which patients will progress or recur and might benefit from modified treatment modalities.

Design: This study was funded by the College of American Pathologists Foundation-Scholar Research Grant. Patients presenting with primary papillary noninvasive tumors (papillary urothelial carcinomas [PUCs]) between 1995 and 2003 were identified. All surgical specimens from each patient were evaluated for clinicopathologic parameters.

Results: Two hundred ninety patients were identified; initial data were available on 50 cases (150 specimens) in this ongoing study. Mean age is 69 years (range, 38–93 years); male-female ratio is 4:1. Primary specimen: 17 of 50 were low-grade (LG) PUC; 33 of 50 were high-grade (HG) PUC. LG-PUC: 4 (24%) of 17 recurred (2 recurred 1 time; 2 recurred 2 times), 1 recurred as HG-PUC; none progressed to higher stage; mean mitotic rate (per 10 high-power fields) was 1 (range, 0–6). HG-PUC: 22 (67%) of 33 recurred (18 recurred ≤3 times; 4 recurred >4 times), 8 HG-PUC recurred as LG-PUC; 1 progressed to pT1 disease; mean mitotic rate (per 10 high-power fields) was 8 (range, 0–57). Mean follow-up is 5 years (range, 3–9 years). Status at last follow-up: LG-PUC—17 of 17 no evidence of disease; HG-PUC—29 of 33 no evidence of disease, 4 of 33 alive with disease.

Conclusions: Initial data show that HG-PUCs show increased rates of recurrence and mitotic rates compared with LG-PUCs. In this limited series on PUC, there was no LG-PUC to very rare (HG-PUC) stage progression. Additional patient accrual, clinicopathologic correlation, and molecular analyses are underway, with the goal of integrating these prognostic factors into a risk assessment tool that may better identify patients at risk for adverse outcomes.

Complement Product C4d Deposits in Allograft Kidneys: Staining Patterns in Frozen Sections and Routinely Processed Tissue
(Poster No. 36)

Ibrahim Batal, MD1,2 (ibatali2@upmc.edu); Bassel Abou Saab, MD; Sean Stockhausen, BS; Ron Shapiro, MD; Amit Basu, MD; Henkie Tan, MD, 1440 Arch Pathol Lab Med—Vol 131, September 2007

Abstracts
Calculating the frequency and anatomic distribution of calcifications within different tissue compartments was correlated with other biopsy parameters.

**Results:** Within peritubular capillaries, C4d stain on FS was diffuse and focal in 22 (42%) and 7 (13.4%) of 52, respectively, versus 10 (19%) and 13 (25%) of 52 in PE, respectively. Within glomerular basement membrane, diffuse staining was observed in 21 (50%) of 42 FS versus 13 (25%) of 52 PE with 3 biopsies showing chronic transplant glomerulopathy. In TBM, staining was diffuse in 10% (5/52), focal in 38% (20/52), and negative in 52% (27/52) of FS and present in 2 (4%) PE of which 1 showed BK virus nephropathy. Arteriolar stain was diffuse in 73% of FS versus 40% of PE, whereas arteries stained similarly in both groups (48% vs 40%). Using Kruskal-Wallis 1-way analysis of variance test, the grade of tubular atrophy did not correlate with TBM staining (P = .46), whereas arteriolar hyalinosis score tended to be higher in biopsies with diffuse or focal arteriolar staining (P = .09).

**Conclusions:** Immunohistochemistry for C4d is more sensitive in FS compared with PE. Glomerular basement membrane and TBM staining was observed in biopsies that did not show chronic transplant nephropathy or BK virus nephropathy, respectively.

**Lymphoid Host Response in Clear Cell Renal Cell Carcinoma (Poster No. 37)**

Steven Garzon, MD; Zeenath Asma, MD; Andre K. Balla, MD, PhD; Vicki Macias, MD; Suman Setty, MD, PhD (Setty@uic.edu). Department of Pathology, University of Illinois, Chicago.

**Context:** Greater lymphocytic infiltration has been associated with a better prognosis in many tumor types. Whether lymphoid cells play a role in clear cell renal cell carcinoma (CRCC) is not clearly established in the literature. We enumerated the lymphoid nests in the CRCC and compared them to known prognostic indicators.

**Design:** Hematoxylin-eosin–stained sections of 25 CRCC cases were retrieved from our files, and the number of nests of lymphoid cells was counted in an average of 1000 low-power fields. A comparison of lymphocytic infiltration with tumor stage, grade, size, and extracapsular extension was performed. Cases with extensive necrosis and/or hemorrhage were excluded.

**Results:** Sixteen stage I, 4 stage II, 4 stage III, and 1 stage IV CRCCs were studied. All cases had peripheral lymphoid nests, and 24 of 25 had central nests. There were significantly more lymphoid nests in the periphery of stage I CRCCs and cases with no EE (P < .05). There were more lymphoid nests in central areas of CRCCs without EE. Markedly fewer aggregates were detected in Fuhrman III to IV RCCs compared with Fuhrman I to II CRCCs.

**Conclusions:** Higher stage tumors had significantly fewer lymphoid aggregates. In summary, host lymphoid response is associated with known prognostic factors such as Fuhrman grade, EE, and tumor stage.

**Calculating the relationship between calcifications and prostate cancer has not been clearly documented, as in breast cancer.**

**Design:** We reviewed whole mount tissue sections from 298 randomly selected radical prostatectomy and cryoprostatectomy specimens, which included 284 cases of prostatic adenocarcinoma. The presence and anatomic distribution of calcifications in prostate and ejaculatory system were evaluated, and their association with prostatic adenocarcinoma was also studied. The degree of calcification was quantified using 3 categories: mild, moderate, and severe.

**Results:** Calcification was most frequently identified in the transition zone (205/298) and less commonly in the peripheral and central zones. Calcifications were also commonly seen in the verumontanum (200/298) and the seminal vesicles (173/298) and less commonly in the ejaculatory ducts (51/298). Calcification is most commonly associated with benign prostatic tissue (264/298, 78%). Calcifications were rarely identified within prostatic adenocarcinoma (4/284, 1.4%). In all 4 cases, the adjacent benign prostate tissue also contained moderate or severe calcification.

**Conclusions:** Calcifications were very commonly seen in prostate tissue in patients with prostate or bladder carcinoma. They are present most often in the transitional zone and verumontanum. Calcifications are primarily seen associated with benign prostatic tissue and do not appear to have any association with prostate cancer.

**Unusual Myofibroblastic Proliferation in the Testis (Poster No. 39)**

Douglas J. Hartman, MD (douglas.hartman@uahs.edu); Fadi W. Abdu, MD; Thomas M. Ullman, MD; Donald B. Ruhland, MD; T. MacLeany, MD; Departments of Pathology and Urology, University Hospitals Case Medical Center, Cleveland, Ohio; Department of Pathology, Indiana University Medical Center, Indianapolis.

Myofibroblastic proliferations have been described in many body sites but only rarely in the testis. We report a case of a quadriplegic 36-year-old African American man who developed left scrotal swelling after an episode of epididymitis-orchitis and who had a hypoechogenic mass identified on ultrasound. The lesion was excised and histologically, the lesion consisted of a focus of intense lymphoplasmacytic inflammation in association with spindle cells and occasional large cells with atypical nuclei having prominent nucleoli. Many of these cells had dense, abundant cytoplasm. The differential diagnosis included Hodgkin lymphoma, inflammatory myofibroblastic tumor, a dendritic cell tumor, and a regressed germ cell tumor. The atypical cells showed negative immunostaining for CD15, CD30, ALK-1, smooth muscle actin, desmin, CD5, and CD20. None of the lesional cells showed positive immunostaining for CD21, CD35, S100, or OCT4. Instead, they stained positively for C4d, CD11c, and CD68, consistent with an inflammatory myofibroblastic proliferation. The lesion regressed after excision, and follow-up imaging showed no evidence of change. We conclude that this lesion likely represents an unusual case of myofibroblastic proliferation in the testis, which may be associated with fasciitis-like lesions.
Small Cell Carcinoma of the Urinary Bladder 4 Years Following Prostatic Brachytherapy
(Poster No. 41)

Cesar V. Reyes, MD; Joel N. Slutsky, MD; Walter E. Kelley, DO; Tehmina Z. Ali, MD.

A 74-year-old white woman presented with a 1-year history of chronic pelvic pain and intractable urinary frequency with urgency. Additional medical history was significant for weight loss of 70 lb. Computed tomography demonstrated a contracted, thickened bladder. Cystoscopy with ileal loop diversion was performed, following which the symptoms resolved.

Microscopic evaluation revealed a severe edematous surface. Cystectomy with ileal loop diversion was performed, following which the symptoms resolved. Gross examination of the bladder demonstrated a mucosal surface, which was polypoid, edematous, and hemorrhagic, with a cobblestone pattern. Microscopic evaluation revealed a chronic necrotizing arteritis of medium-sized vessels of the submucosa, muscularis propria, and perivesical adipose tissue, with a perivascular granulomatous response. Primary vasculitis of the urinary bladder is extremely rare. To our knowledge, chronic pelvic pain and urinary symptoms as the initial clinical presentation of chronic polyangiitis nodosa (MPA) has not been previously reported. The patient's weight loss is characteristic of MPA (present in 72% of MPA patients). Although not present at the time of cystectomy, the patient was subsequently noted to have evidence of mononeuritis multiplex (present in 57% of MPA patients) and was noted to be perinuclear antineutrophil cytoplasmic antibody positive (present in 60% of MPA patients). MPA is more common in African American men and has an approximate age of onset of 50 years. MPA should be considered in the differential diagnosis of chronic pelvic pain, as this diagnosis will lead to immunosuppressive therapy. With therapy, 90% of MPA patients had improvement and 75% reached complete remission. The relapse rate is 30% in 1 to 2 years (Figure 20).

Characterization of 2 Leydig Cell Tumors of the Testis Using Immunohistochemistry and Comparative Genomic Hybridization
(Poster No. 44)

Sharon L. Steinman, MD; Soojin Jung, MD, PhD; Albert G. Ayala, MD; M. S. Kwon, MD;

The presence of ectopic prostatic tissue (EPT) in the bladder neck and urethra is not an uncommon finding. However, EPT in the dome of bladder is a rare finding. Only 1 case of adenocarcinoma arising in EPT has been previously described. We report an additional case of adenocarcinoma arising in EPT that is the first case occurring in the dome of bladder. A 62-year-old man presented with persistent microscopic hematuria following a urinary tract infection. Cystoscopic examination revealed several papillary lesions throughout the bladder, which were diagnosed as invasive papillary urothelial carcinoma on biopsy. Radical cystoprostatectomy was performed, and the biopsy diagnosis was confirmed. Incidentally, 1 section from the dome of the bladder showed a focus composed of 3 adjacent, distinct types of glands within the submucosa. One type resembled benign prostate glands with basal cells. The second type resembled well-differentiated adenocarcinoma arising in the benign glands. Both benign and malignant glands were positive for prostate-specific antigen and prostatic acid phosphatase. The third type of gland was benign urachal remnant. Sections of the prostate also revealed adenocarcinoma of the prostate, with no invasion of the bladder or metastatic disease identified. In our case, the presence of normal prostatic glands adjacent to malignant prostatic glands in the dome of bladder supports the diagnosis of malignant transformation within the EPT, rather than a metastatic deposit from the prostate. The absence of lymph node metastases, distant metastases, or bladder invasion by the prostatic adenocarcinoma further supports this interpretation.

Systemic Microscopic Polyangiitis Presenting as Interstitial Cystitis
(Poster No. 43)

Walter E. Kelley, DO; Tehmina Z. Ali, MD.

A 74-year-old white woman presented with a 1-year history of chronic pelvic pain and intractable urinary frequency with urgency. Additional medical history was significant for weight loss of 70 lb. Computed tomography demonstrated a contracted, thickened bladder. Cystoscopy revealed a 6-cm urinary bladder SCC that was completely transurethrally resected. Two months later, transurethral resection of nodular medial lobe revealed a 6-cm urinary bladder SCC that was completely transurethrally resected. Two months later, transurethral resection of nodular medial lobe showed sparse, short, irregularly distributed microvilli. Mitochondria were abundant. Apical microvilli and basolateral cytoplasmic interdigitation were markedly reduced. Tubulocystic carcinoma is a recently described, rare, low-grade renal neoplasm. The immunohistochemical and electron microscopic features are suggestive of a proximal tubule origin. In this case, it arose in the clinical setting of lupus nephritis, and despite having low-grade morphology, grew rapidly during a short time and showed a high Ki-67 reactivity (Figure 19).
Leydig cell tumors with rhabdoid differentiation have never before been reported. Because distinguishing features in tumors may signify different clinical behaviors, it is important to characterize these tumors further. Two Leydig cell tumors with rhabdoid features from different geographical locations were compared with 3 conventional Leydig cell tumors from the Pathology Department at the Methodist Hospital in Houston, Tex. Immunostains for pancytokeratin, α-inhibin, calretinin, Melan-A, vimentin, and CD10 were performed on all tumors. Comparative genomic hybridization analysis was performed on the 2 Leydig cell tumors with rhabdoid differentiation and on 1 conventional-type tumor. Metaphase slides were prepared, and tumor DNA and normal DNA were labeled with biotin-16dUTP and digoxigenin-11dUTP, respectively, by nick translation. After denaturation and probe hybridization, the slides were treated with avidin-fluorescein isothiocyanate and antidigoxigenin-rhodamine. The metaphase slides were counterstained with DAPI, and the reverse banding images of 15 metaphase images were identified for each case. Average ratio profiles were calculated on selected metaphases. Gains and losses were defined as the theoretical values of 1.25 and 0.75, respectively. All 5 tumors showed negative pancytokeratin staining and positive staining for α-inhibin, calretinin, Melan-A, and vimentin. As shown in the Table, the comparative genomic hybridization results show chromosomal loss of 13p, 14p, 15p, and 22p in both the Leydig cell tumors with rhabdoid features and in the conventional-type tumor. In summary, these results demonstrate that, although Leydig cell tumors with rhabdoid differentiation are unusual, they belong in the same classification with conventional Leydig cell tumors.

Chromosome Loss as Determined by Comparative Genomic Hybridization in Leydig Cell Tumors With Rhabdoid Differentiation Versus Control

<table>
<thead>
<tr>
<th>Case No. 1</th>
<th>Case No. 2</th>
<th>Control Case</th>
</tr>
</thead>
<tbody>
<tr>
<td>1p</td>
<td>9p</td>
<td></td>
</tr>
<tr>
<td>5p</td>
<td>1p</td>
<td></td>
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<tr>
<td>13p</td>
<td>13p</td>
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<tr>
<td>14p,14q</td>
<td>14p</td>
<td>14p</td>
</tr>
<tr>
<td>15p,15q</td>
<td>15p</td>
<td>15p</td>
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<tr>
<td>21p</td>
<td>21p,21q</td>
<td>21q</td>
</tr>
<tr>
<td>22p,22q</td>
<td>22p,22q</td>
<td>22p</td>
</tr>
</tbody>
</table>

Clonal Evidence for the Progression of a Testicular Germ Cell Tumor to Angiosarcoma

(Poster No. 45)

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Testicular germ cell tumors (GCTs) may be composed of multiple histologic subtypes. Mature teratoma components are capable of malignant transformation, with only a few reports of possible transformation into angiosarcomas. It is currently unclear whether cases of angiosarcoma in patients with GCT represent natural tumor progression, radiation-induced carcinogenesis, or chemotherapy-induced carcinogenesis. We present a case of a male with mixed testicular GCT and numerous mature teratoma metas- tases whose tumor consisted of chemotherapy without radiation. Forty months after his original diagnosis, a mediastinal angiosarcoma was diagnosed. He is currently without radiologic evidence of metastatic angiosarcoma 42 months after its diagnosis. We performed laser capture microdissection and compared loss of heterozygosity (LOH) at multiple microsatellite polymorphic markers in all 3 cell types of his GCT, angiosarcoma along with the concurrently resected mature teratoma of the left lung, and multiple metastatic mature teratomas from various locations resected during additional surgeries. Each component of the primary testicular GCT showed allelic LOH on chromosomes 1p36 (D1S1648) and 18q22 (D18S543). These identical losses were identified in the angio- sarcoma and in the concurrently resected mature teratoma. The other mature teratomas sampled contained these identical losses and showed progressive LOH on chromosome 9p21 (D9S171). There was no LOH at 9p21 (IFNA), 9q21 (D9S303), or 18q21 (D18S60). These data support the conclusion that the angiosarcoma arose from a GCT. The patient's lack of therapeutic radiation alludes to tumor progression that may have been accelerated by chemotherapy but which unlikely resulted from chemotherapeutic carcinogenesis on cells of non-GCT origin.

Two Cases of Bilateral Germ Cell Tumors Composed of Seminoma and Embryonal Carcinoma

(Poster No. 46)

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Bilateral germinative testicular tumors are rare (1%-2% of germ cell tumors), and seminoma and embryonal carcinoma on each side of the testes are even more rare. We report here on 2 cases of bilateral testicular germ cell tumor (GCT) composed of seminoma and embryonal carcinoma that occurred successively. Medical records and histology of these 2 patients were reviewed retrospectively. A literature review of GCT was undertaken. One patient had seminoma at stage I in his left testis at age 22 years. He was treated with radical orchectomy and radiation therapy without chemotherapy. Five years later, he developed embryonal carcinoma at stage III in his right testis with involvement of the spermatic cord. He underwent orchectomy and completed chemotherapy. He is still alive at 7 years after his first orchectomy. The second patient had embryonal carcinoma at stage II with angiosarcomatous invasion in his right testis at age 27 years. One year later, he developed a seminoma at stage I in his left testis. He was again treated with orchectomy and chemotherapy. Up to now, he has been cancer free for 2 years after his second orchectomy. Although they are very rare, 2 different testicular GCTs consisting of embryonal carcinoma and classic angiosarcoma can metachronously develop in a patient bilaterally. Patients with a unilateral GCT are at high risk of a second GCT. Thus, all patients with GCT are advised to be under close surveillance for the maximal management and the longest survival time.

Adenomatous Hyperplasia of the Rete Testis

(Poster No. 47)

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Adenomatous hyperplasia of the rete testis (AHRH) is an uncommon lesion. It is usually incidentally discovered in surgical specimens from cases of cryptorchidism and testicular tumor. Some cases are identified in autopsy specimens from patients dying with various diseases and in newborns with kidney diseases. In this report, we document a case of AHRH in a 39-year-old man who presented with secondary infertility and severe azospermia. Ultrasound studies showed an ill-defined mass measuring 9 x 6 mm with mixed echogenicity in his left testicle along with varicocele, diffuse microtheliasis, and small epididymal cysts bilaterally. The mass was highly suspicious for malignancy and left radical orchiectomy was performed. The resected testicular specimen grossly demonstrated a white, fibrotic, and nonencapsulated area located at the mediastinum. No definitive testicular mass was identified. Microscopically, the rete testis showed diffuse complex interconnecting proliferation of tubulopapillary channels lined by low columnar cells without significant cytologic atypia. An adjacent area of relatively normal appearing rete testis was identified almost imperceptibly merging with the zone of proliferation. Immunohistochemical stains of the proliferating epithelial cells were positive for cytokeratin and negative for inhibin, which confirmed the morphologic impression. The remaining tests revealed focal atrophy and microcalcifications within the seminiferous tubules. The morphologic findings were consistent with the diagnosis of AHRH. The patient was healthy at 5-month follow-up. This case shows that, in addition to presenting as an incidental finding as in most previously reported cases, AHRH by itself can bring a patient to clinical attention.

A Rare Case of Renal Synovial Sarcoma

(Poster No. 48)

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Synovial sarcoma is a rare neoplasm in the kidney. It occurs in patients 12 to 59 years with a mean age of 35 years. It is characterized by t(X;
Adrenal Cortical Rests in the Kidney: A Mimic of Clear Renal Cell Carcinoma

(Poster No. 49)

Adebawole J. Adeniran, MD (deboadeniran@yahoo.com); Pheroze Tamboli, MD. Department of Pathology, The University of Texas M. D. Anderson Cancer Center, Houston.

Context: Ectopic adrenal cortical tissue has been described in various organs, although not widely reported to arise in the kidney. When present in the kidney, it may mimic clear cell renal carcinoma (CRCC), which could lead to an erroneous diagnosis. We report the clinicopathologic features of 4 cases of adrenal cortical rests seen in surgical pathology material. Three of these cases were received as consultation cases with a question of whether the lesion represented a small CRCC.

Design: Four cases (3 consultation and 1 in-house) were evaluated, including all hematoxylin-eosin slides. Immunohistochemical stains were performed on selected cases.

Results: Clinicopathologic characteristics of the 4 lesions are summarized in the Table. All 4 cases formed subcapsular nests of cells with clear bubbly cytoplasm and uniform, small, round nuclei with few nucleoli, resembling Fuhrman nuclear grade 1 or 2 CRCC. Positive immunohistochemical stain results are as follows: inhibin (3/3), Mart-1 (1/1), cytokeratin (1/1), vimentin (1/1), and synaptophysin (2/3). Negative stains are as follows: CD10 (0/2) and epithelial membrane antigen (0/1).

Conclusions: Clear cells of adrenal cortical rests in the kidney have the potential to mimic CRCC. Although rare, awareness of this unusual manifestation of an embryonic remnant is important to avoid a potential erroneous diagnosis of CRCC. Important features to consider are the subcapsular location, uniform bland appearance of the cells, and the bubbly cytoplasm as opposed to optically clear cytoplasm of CRCC cells. Finally, immunohistochemistry is a valuable tool in making the correct diagnosis.

### Clinicopathologic Characteristics

<table>
<thead>
<tr>
<th>Case No., Age, y/Sex</th>
<th>Location</th>
<th>Size, cm</th>
<th>Differential Diagnosis</th>
<th>Other Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>1, 54/M</td>
<td>Left, upper pole</td>
<td>0.2 × 0.1</td>
<td>Microscopic focus of CRCC</td>
<td>Papillary adenoma, cortical cyst</td>
</tr>
<tr>
<td>2, 45/M</td>
<td>Right, upper pole</td>
<td>0.2 × 0.1</td>
<td>Microscopic focus of CRCC</td>
<td>Papillary adenoma, cortical cyst</td>
</tr>
<tr>
<td>3, 64/M</td>
<td>Left, not specified</td>
<td>2.5 × 0.5</td>
<td>Adrenal cortex vs adenoma vs CRCC in kidney with end-stage renal disease (ESRD)</td>
<td>ESRD</td>
</tr>
<tr>
<td>4, 53/M</td>
<td>Left, upper pole</td>
<td>0.6 × 0.4</td>
<td>Adrenal cortical rest vs microscopic focus of CRCC</td>
<td>CRCC, papillary adenoma</td>
</tr>
</tbody>
</table>

* CRCC indicates clear renal cell carcinoma.
Cyclooxygenase 2 Expression in Breast Cancer

(Poster No. 2)

Young Choi, MD (young.choi@yale.edu); Ali Riba, MD. Department of Pathology, Yale University School of Medicine, Bridgeport, Conn.

Context: Cyclooxygenase 2 (COX-2) is up-regulated during chronic inflammation and neoplastic processes and has been considered to be important for the development of breast cancer and to decrease nonsteroidal anti-inflammatory drug consumption. We assess the association between COX-2 expression and the degree of chronic inflammation and other prognostic biomarkers.

Design: Tissue microarray sections prepared from 270 breast cancer surgical specimens were tested for COX-2, estrogen receptor, progesterone receptor, HER-2, vascular endothelial growth factor (VEGF), Bcl-2, CD3, CD20, CD1a, and CD68 by standard immunohistochemistry. Expression of COX-2 and VEGF was evaluated by combining the percentage of immunoreactive cells and the intensity.

Results: COX-2 was expressed in 67.4% (182/270) and not in 32.6% (88/270). COX-2 expression was markedly heterogeneous within the same tumor and between different histology types and strong in the adjacent hyperplastic epithelial cells and cancer cells but weak in the normal epithelium away from cancer. The chronic inflammatory cell infiltrates were prominent in 23.7% (64/270) and consisted of T cells, B cells, plasmacytoid lymphocytes, macrophages, and a few dendritic cells. Overall, COX-2 expression was not significantly associated with the degree of chronic inflammation (P < 0.10), histology types (P < 1.0), or stage (P < 1.0) but was significant with VEGF (P < 0.01), HER-2 (P < 0.01), and Bcl-2 (P < 0.01).

Conclusions: Strong COX-2 expression in the hyperplastic and benign epithelium adjacent to cancer and weak in benign epithelium away from cancer and a significant association between COX-2 and VEGF, HER-2, and Bcl-2 supports COX-2’s important role of cell proliferation, apoptosis, and angiogenesis in breast cancer. COX-2 expression does not appear to be directly correlated with the degree of inflammatory cell infiltrates.

Utility of the Mitosis-Specific Antiphosphohistone-H3 Marker in the Grading of Invasive Ductal Carcinoma of Breast

(Poster No. 3)

Munir Shahjahan, MD (mshahjahan@tmh.tmc.edu); Hema Khurana, MD; James Netreba, MD; Jae Ro, MD; Steven Shen, MD; Jim Zhai, MD. Department of Pathology and Laboratory Medicine, The Methodist Hospital, Houston, Tex.

Context: Mitotic figure count is important in the histoprognostic grading of infiltrating ductal breast carcinomas. We compared and tested the utility of mitosis specific marker phosphohistone-H3 (PHH3) in the grading of invasive ductal breast carcinomas and examined long-term follow-up data.

Design: Hematoxylin-eosin– and PHH3-stained slides from 31 cases of infiltrating ductal breast carcinomas in women (mean age, 55 years) were evaluated for mitotic counts in 10 consecutive high-power fields with time recorded. Follow-up data were obtained from the hospital cancer registry.

Results: Mitotic counts ranged from 0 to 48 per 10 high-power fields with average counting time of 2.2 minutes by hematoxylin-eosin and 0 to 80 per 10 high-power fields with average time of 1.1 minutes by PHH3 (48.4% reduction in time). A change to a higher grade was seen in 6 (19%) cases of PHH3 compared with hematoxylin-eosin. Twenty patients were alive without disease and 2 were alive with disease (median follow-up of 78 and 77 months, respectively). Seven patients died after a median of 40 months. Of the 6 cases reclassified to higher grade, 3 were alive without disease and 1 had central nervous system metastasis. One patient died 56 months after diagnosis. No follow-up data were available on 1 case.

Conclusions: PHH3 stain is a reliable and rapid method for enumerating mitotic count and is useful in the stratification of tumors into low, intermediate, and high grade. The change in grading by PHH3 observed in our series and its impact on clinical outcome needs validation in a larger cohort of patients.

Significant Down-Regulation of Human Tissue Kallikreins 8 and 6 From Benign to Ductal Carcinoma In Situ to Infiltrating Ductal Carcinoma: An mRNA In Situ Hybridization Analysis Suggesting Increased Survival in Women With Higher Human Kallikrein 8 Expression

(Poster No. 4)

Monica Goswami, MD* (monicagoswami@yahoo.com); Charles D. Sturgis, MD; Vinma Band, PhD. Departments of Pathology and Cancer Biology and Biochemistry, Evanston Northwestern Healthcare, Evanston, Ill; Department of Pathology, Evanston Northwestern Healthcare and Feinberg School of Medicine, Evanston, Ill.

Context: Human tissue kallikreins (hKs) are serine proteases encoded by 15 genes (KLKs) that colocalize to chromosome 19q13.4. Reduction of hK10 was reported by mRNA in situ hybridization in 50% ductal carcinoma in situ (DCIS) and 90% infiltrating ductal carcinoma (IDC). hKs may be involved in breast carcinogenesis. We investigate the potential of hK3, hK5, hK6, hK8, and hK10 as prognostic and predictive factors in breast cancer.

Design: One hundred forty-five nonconsecutive archived, paraffin-embedded blocks were retrieved from Evanston Northwestern Healthcare files. Samples included 19 reduction mammoplasties (mean age, 36.9 years), 41 DCISs (mean age, 59.88 years), and 85 IDCs (mean age, 59.6 years). Grade; stage; estrogen receptor, progesterone receptor, and HER-2/neu status; and survival data were recorded. mRNA in situ hybridization using biotinylated RNA probes for hKs was performed. Cases were scored using a 4-tiered scale from negative to intense positivity (0–3).

Results: Reduction mammoplasties had significantly higher hK levels than IDCs and DCISs (P < .001). hK8 was expressed at higher levels in DCISs compared with IDCs (P = .002). hK6 was expressed at higher levels in DCISs compared with IDCs (P = .04). Higher hK8 mRNA in DCISs directly correlated to longer survival, more than 9.2 years versus less than 5.5 years (P = .003).

Conclusions: We found a significant down-regulation of kallikreins, particularly hK8 and hK6, across the spectrum from reduction mammoplasties to DCISs to IDCs. Significant overall greater survival is noted in DCIS patients with high hK8 expression. Further studies may elucidate the exact involvement of hKs in mammary carcinogenesis, and measurement of mRNAs may be useful prognostic and predictive indicators.

Expression of Vascular Endothelial Growth Factor Subtypes in Mammary Invasive Ductal Carcinoma and Their Relationship to Tumor Progression

(Poster No. 5)

Katherine Maloney, MD1 (khana@ummhc.org); Judith Savageau, MPH; Tanya Pulver, MS2; Manju Prasad, MD1; Robert Quinlan, MD2; Ashraf Khan, MD. Departments of 1Pathology and 2Surgery, University of Massachusetts Medical School, Worcester.

Context: Multiple genes and proteins have been shown to be important in breast cancer progression. Vascular endothelial growth factor (VEGF) has been shown to be associated with lymphovascular invasion (LVI), lymph node metastases (LNM), and prognosis in various cancers, including breast cancer. The aim of our study was to correlate the expression of VEGF subtypes and their receptor with known prognostic factors and clinical behavior.

Design: Ninety (90) grade III invasive ductal carcinomas received during 1997 to 2001 were selected from our files. Immunohistochemistry was performed on formalin-fixed, paraffin-embedded tissue of both primary tumor and lymph node metastasis using VEGF-A, VEGF-C, VEGF-D, and VEGF-R antibodies. The staining was graded from 0 (no expression) to 3+ (high expression). These expression profiles were then compared via chi-square test with LVI, LNM, tumor stage, and recurrence.

Results: High level (3+) of VEGF-A, VEGF-D, and VEGF-R expression was seen in 43 (47.8%), 32 (35.6%), and 24 (26.7%) cases, respectively; expression of VEGF-C was seen in 7 (7.8%) cases. Normal residual breast tissue was either negative or showed 1+ to 2+ staining. High level of VEGF-A and presence of VEGF-C expression were both associated with tumor recurrence (P < .20). High level of VEGF-R expression was associated with LVI, LNM, and higher tumor stage (P < .50). No correlation was seen between high levels of VEGF-D expression and LVI, LNM, or tumor recurrence.

Conclusions: In high-grade breast cancer, VEGF-A, VEGF-C, and VEGF-R expression was associated with adverse prognostic factors, including...
Lack of Expression of Xanthine Oxidoreductase Enzyme in Poorly Differentiated Estrogen Receptor– and Progesterone Receptor–Negative Infiltrating Ductal Carcinomas of the Breast Is Associated With Worse Prognosis (Poster No. 7)

Allison T. Howard, MD (allison.howard@rush.edu); Kalliopi P. Sziros-pikou, MD, PhD; Vijaya B. Reddy, MD; Paolo Gattuso, MD. Department of Pathology, Rush University Medical Center, Chicago, III.

Context: Xanthine oxidoreductase (XOR) plays a role in milk globule secretion and is strongly expressed and regulated in normal breast epithelium. Previous publications reported that abnormal expression of XOR was seen in a variety of experimental tumorigenesis, including breast neoplasia. We examined XOR expression in a subgroup of breast carcinoma patients to see whether the expression of XOR protein correlated with clinical outcome.

Design: Our study consisted of 2 groups of patients diagnosed with estrogen receptor (ER)– and progesterone receptor (PR)–negative grade III infiltrating ductal carcinomas. Group 1 consisted of 16 women free of age, tumor size, and lymph node status. XOR, ER, and PR immunohistochemistry was obtained.

Results: All tumors were ER- and PR-negative infiltrating ductal carcinomas. The average age of group 1 patients was 52.4 years and of group 2 patients was 52.6 years. XOR was expressed in 69% of group 1 patients (long-term survivors) versus 25% of patients in group 2 (short-term survivors) (P < .01).

Conclusions: Seventy-five percent of the ER- and PR-negative infiltrating ductal carcinomas with poor prognosis lack XOR expression in contrast to long-term survivors (31%) with similar tumor characteristics, suggesting that breast carcinomas that lack cytoplasmic XOR expression are associated with a poor outcome. The mechanism through which loss of XOR is associated with poor prognosis is currently not well characterized. Further studies are needed to elucidate whether neoplasms lacking XOR respond differently to chemotherapy compared with those exhibiting XOR expression.

DNA-Binding Protein IMP3 Expression Correlates With Tumor Progression and Metastasis in Breast Cancer (Poster No. 9)

Tanya Pulver, MS1 (khana@umnhc.org); Katherine Maloney, MD; Manju Prasad, MD; Zhong Jiang, MD; Kathryn Edmiston, MD; Robert Quinlan, MD; Ashraf Khan, MD. Departments of Pathology, Medicine and Surgery, University of Massachusetts Medical School, Worcester.

Context: Breast cancer encompasses a heterogeneous group of neoplasms with diverse pathogenic origins and behaviors. IMP3 is a member of the insulin-like growth factor mRNA-binding protein family, whose plasmas with diverse pathogenic origins and behaviors. IMP3 is a member of the insulin-like growth factor mRNA-binding protein family, whose role in breast carcinomas with diverse pathogenic origins and behaviors. IMP3 is a member of the insulin-like growth factor and other parameters for each case was compiled. Data were subjected to chi-square analysis to compare IMP3 expression in PT versus MT as well as IMP3 expression in PT versus known prognostic factors mentioned previously.

Results: Thirty-three (26%) of the 127 PTs stained positive for IMP3 compared with 31 (60.8%) of the 51 MTs (P < .001). In PT, IMP3 positivity was also associated with other adverse prognosticators, such as high grade (P = .03), presence of necrosis (P < .001), and negative estrogen receptor (P < .001) and progesterone receptor (P < .001) status.

Conclusions: IMP3 expression in breast cancer is higher among MTs compared with PTs and is associated with a number of adverse prognostic factors, suggesting it plays a role in breast cancer progression and metastasis.

Identification of Basal Phenotype Markers in Medullary Breast Carcinoma: Correlation With Patient Outcome (Poster No. 10)

Gerard J. Oakley, MD (oakleyge@upmc.edu); Mamatha Chivukula, MD; Sudeshna Bandypadhyay, MD; Amin-Khanhour Shakeri, MD; David Dabbs, MD. Department of Pathology, University of Pittsburgh Medical Center, Pittsburgh, Pa.
Context: Medullary breast carcinomas (MCs) are morphologically similar to 'basal phenotype' carcinoma (BC). BC has worse prognosis and positive immunohistochemistry for at least 2 of cytokeratin (CK) 5/6, CK14, CK17, and epithelial growth factor receptor (EGFR) and 'triple negative' for estrogen receptor (ER), progesterone receptor (PR), and HER-2/neu. We assayed these markers in 17 triple-negative MCs and correlated the findings with overall survival and disease recurrence.

Design: Seventeen triple-negative MCs were identified strictly on syncytiotrophoblast growth pattern, high nuclear grade, geographic necrosis, 'pushing' margins, and lymphoplasmacytic response. Each was stained for CK5/6, CK14, CK17 (using a standard scoring scale), EGFR, ER, PR, and HER-2/neu. ER and PR were scored positive if staining more than 10% of tumor nuclei. HER-2/neu was scored 0 to 3+ per manufacturer's instructions. Fifteen- and 5-year overall survival and disease recurrence for all patients was independently obtained and deidentified. Statistical comparison between stage-matched MC–basal phenotype and MC–without basal phenotype was made.

Results: Twelve (71%) of the 17 triple-negative MCs were positive for at least 2 basal phenotype markers. Kaplan-Meier and LogRate analysis revealed a trend to worse 15- and 5-year survival and higher recurrence for MCs with basal phenotype than MCs without positive basal phenotype markers.

Conclusions: The majority of triple-negative MCs were positive for at least 2 of CK5/6, CK14, CK17, and EGFR with a trend to worse prognosis compared with MCs without these basal phenotype markers. This suggests that MC and BC are distinct, and immunohistochemistry can help differentiate the 2 to provide accurate prognosis.

Altered Threshold for 3+ HER-2 Immunohistochemistry: Result? Does It Matter? (Poster No. 11)

Tenley J. Rivera, AS* (riveraj@auralab.com); Gregory Snow, PhD; Elizabeth Hammond, MD; Department of Pathology and *Statistical Data Center, LDS Hospital, Salt Lake City, Utah.

Context: Currently there is a 13% to 18% false-positive rate for the US Food and Drug Administration (FDA)-approved testing methods for HER-2. The College of American Pathologists and American Society of Clinical Oncology experts have proposed increasing the threshold for positivity of the immunohistochemical test from the FDA-approved rate of 10% cells with complete dark membrane staining to a level of 30%. Oncologists and test manufacturers have concern that this change in threshold might neglect potentially eligible patients who may respond to trastuzumab. This study analyzes a single reference laboratory's experience to predict HER-2 fluorescence in situ hybridization positivity based on the original and altered threshold values.

Design: Between 2003 and 2007, 254 cases of HER 3+ positive cases were analyzed using DAKO HercepTest and ACIS image analysis, and the percentage of tumor cells exhibiting a complete dense uniform membrane staining was documented. The sensitivity and specificity of testing were determined for samples with greater than 10% and 30% of cells stained using fluorescence in situ hybridization amplification rate as the measure of true test positivity.

Results: The frequency of extent of dark membrane staining is illustrated (Figure 22). Only 2 cases have less than 30% staining. With a threshold of 10% cells, the calculated sensitivity for the sample was 73.7 and the specificity was 96.7, whereas an increased threshold of 30% cells yielded a sensitivity of 73.4 and specificity of 96.9.

Conclusions: Increasing the cutoff to 30% of tumor cells stained involved a minority of samples and the sensitivity and specificity of the testing is unchanged, providing support to increase the FDA-approved threshold.

Solid Papillary Carcinoma of the Breast: Analysis of 16 Cases (Poster No. 12)

Kliment Donev, MD (klimentdonev@hotmail.com); Hwa Jeong Lee, MD; Usha Raju, MD. Department of Pathology, Henry Ford Hospital, Detroit, Mich.

Context: Solid papillary carcinoma (SPC) of the breast is a distinctive tumor with unique morphologic and immunohistochemical features and can have overlapping features with benign usual hyperplasia. High-molecular-weight cytokeratin has a potential to distinguish SPC (negative) from usual hyperplasia (strongly positive).

Design: We analyzed architectural patterns and cytologic features of 16 cases of SPC. The epithelial proliferation was studied using immunostain for CK5/6 (high-molecular-weight cytokeratin). Immunostain for calponin, a muscle marker, was also performed to identify myoepithelial cells.

Results: Architectural patterns: All cases revealed ducts distended by solid papillary proliferations of neoplastic epithelial cells supported by thin fibrovascular cores (4 had hyalinized cores). Six cases had focal areas of cribiform arrangement. Cytologic features: Monotonous population of cells with low to intermediate nuclear grade was present in 15 cases. In 13 cases, cells had, at least focally, plasmacytoid appearance with ample eosinophilic cytoplasm and eccentric nucleus with prominent nucleolus. Streaming spindle cells were present in 10 cases. Immunostains: CK5/6 was uniformly negative in neoplastic epithelial cells in all cases. In 13 cases, scattered, CK5/6-negative epithelial cells were present either singly or in small clusters. Myoepithelial cells, present as a discontinuous layer along the fibrovascular cores, were positive for CK5/6 and calponin.

Conclusions: CK5/6 can reliably distinguish SPC from usual hyperplasia (CK5/6 negative). SPCs contain scattered, CK5/6-positive, benign epithelial cells among neoplastic epithelial cells. Presence of myoepithelial cells along the papillary cores suggests that SPC arises in benign papilloma.

Down-Regulation of Human Kallikrein 3 in Infiltrating Ductal Carcinoma: An mRNA In Situ Hybridization Analysis Suggesting Survival Trends (Poster No. 13)

Monica Goswami, MD* (monicagoswami@yahoo.com); Charles D. Sturgis, MD; Vimla Band, PhD; 1Department of Pathology, Evanston Northwestern Healthcare, Evanston, Ill; 2Department of Pathology, Evanston Northwestern Healthcare and Feinberg School of Medicine, Evanston, Ill; 3Departments of Cancer Biology and Biochemistry, Evanston Northwestern Healthcare and Northwestern University, Evanston, Ill.

Context: Human kallikreins (hKs) are secreted serine proteases encoded by 15 structurally similar steroid hormone regulated genes (KLKs) that colocalize to chromosome 19q13.4. Reduction of hK10 was reported by mRNA in situ hybridization in 50% ductal carcinomas in situ (DCISs) and 90% infiltrating ductal carcinomas (IDCs). Hypermethylation is potentially a cause for reduced expression in cancer cells. hKs may be involved in breast carcinogenesis. We investigate the potential value of hK3, hK5, hK6, hK8, and hK10 as prognostic and predictive factors in breast cancer.

Design: Archived, paraffin-embedded blocks from 145 consecutive patients were retrieved from the pathology files at Evanston Northwestern Healthcare. Samples included 19 reduction mammoplasties (mean age, 36.9 years), 41 DCISs (mean age, 59.88 years), and 85 IDCs (mean age, 59.6 years). Grade; stage; estrogen receptor, progesterone receptor, and HER-2/neu status; and survival data were recorded. mRNA in situ hybridization using biotinylated RNA probes for hK3, hK5, hK6, hK8, and hK10 was performed. Cases were scored using a semiquantitative 4-tiered scale from negative to intensely positive (0–3).

Results: Analysis showed hK5, hK6, hK8, and hK10 to be expressed at significantly higher levels in reduction mammoplasties than in IDCs and DCISs (P < .001). A trend toward greater overall survival was demonstrated in hK3-positive IDC patients (P = .08).

Conclusions: Our findings indicate significant down-regulation of hKs in IDCs compared with benign controls and overall trends toward greater survival in carcinomas with higher hK3. Further studies may help elucidate exact involvement of hK3 in mammary carcinogenesis and explain correlation between hK3 expression and survival.
Concordance and Stability of Histologic Features and Biomarker Studies in Needle Core Biopsy and Surgical Resection Specimens in Breast Cancer

(Poster No. 14)

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Context: The objective was to determine the percentage concordance between needle core biopsy (NCB) and surgical resection of breast cancer for histologic tumor type, tumor grade, estrogen receptor (ER), progesterone receptor (PR), epidermal growth factor receptor (EGFR), and HER-2/neu and to characterize quantitative differences between results obtained from the 2 specimen types.

Design: Histologic features and prognostic tumor biomarkers on preoperative NCB and surgical resection specimens were compared in 140 patients with breast cancer.

Results: Concordance between NCB and resection was 96% for histologic type, 73% for tumor grade, 96% for ER, 84% for PR, 96% for EGFR, and 96% for HER-2/neu. Quantitatively, staining for ER, PR, and HER-2/neu was decreased in the resection specimens (Table). Neither neoadjuvant treatment nor the time interval between NCB and resection affected quantitative staining for any marker. Tumor diameter related only to ER, with larger tumors associated with lower scores in the resection (P = .02 by linear regression).

Conclusions: Concordance of results obtained from NCB and surgical resections of breast cancer varies depending on the specific feature or biomarker type. Decreased quantitative staining in the resection specimen for multiple biomarkers suggests that the NCB may be superior to the resection specimen for evaluation of these markers.

<table>
<thead>
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</table>

The Effect of Selected Preanalytic Factors on Fluorescence In Situ Hybridization Testing for HER-2/neu: Are Friday Specimens Less Likely to be HER-2/neu Positive?

(Poster No. 15)

Jared Szymanski, DO (jszymanski@swmail.sw.org); V. O. Speighds, DO; Sheila Dobin, PhD. Department of Pathology, Scott and White Memorial Hospital, Temple, Tex.

Context: Preanalytic factors can influence the results of both immunohistochemistry (IHC) and fluorescence in situ hybridization (FISH) tests for HER-2/neu. Although FISH appears to be less affected by fixation time than IHC, the manufacturer of the Pathvysion HER-2 DNA probe kit recommends using specimens fixed in 10% buffered formalin for 24 to 48 hours. In our laboratory, about 20% of the specimens (those that are received on Friday) fix in formalin for 48 to 96 hours before being embedded. Another preanalytic variable that may affect results is the type of tissue submitted for analysis. Smaller tissue fragments such as core biopsies may be less likely to show amplification based on sampling error or artifacts.

Design: Statistical analysis was performed on 404 primary breast cancer cases from February 2004 to September 2006 at Scott and White Hospital that had FISH performed for HER-2 on formalin-fixed, paraffin-embedded tissue. Only cases that were originally processed at our laboratory were considered. Cases were categorized by specimen type (core biopsy vs excision specimens) and by fixation time (more than or less than 48 hours).

Results: There was no significant difference in amplification of core biopsies compared with other tissue types. The specimens fixed for more than 48 hours showed no statistically significant difference in amplification from specimens fixed less than 48 hours.

Conclusions: In our laboratory, preanalytic factors such as tissue type and formalin fixation time have no statistically significant effect on the results of FISH assays for HER-2/neu.

Pathologist Experience and Reproducibility in Histographic Grading of Infiltrating Ductal Carcinoma of the Breast

(Poster No. 16)

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Context: There have been only rare efforts to assess the respective roles of pathologist experience and adherence to well-defined morphologic criteria for histographic grading (HG) in relation to reproducibility.

Design: The 2 authors, 1 of whom (S.S.) was considerably more experienced in HG of infiltrating ductal carcinoma of the breast, used the Nottingham modification of the Bloom-Richardson (NMBR) criteria and independently reviewed 24 consecutive cases of infiltrating ductal carcinoma of the breast that had been previously diagnosed by an experienced pathologist who had based HG on a general visual impression rather than NMBR criteria. The median time from diagnosis to review by the 2 authors was 26 months (range, 20.5–90 months).

Results: Despite the experience gap, there was good agreement between the 2 pathologists using NMBR, with concordance in 19 (79.2%) of 24 cases (κ = .66). Agreement between the 2 experienced pathologists, 1 of whom did not use NMBR criteria, was poor with concordance in 10 (41.7%) of 24 cases (κ = .16). Use of the NMBR criteria detected a significant difference in the occurrence of metastases/local recurrence (M/LR) during the follow-up period between grade I and II tumors (4/13 with M/LR versus grade III lesions (8/11 with M/LR); χ² = 4.2, P = .04). With the HG results of the pathologist who has not used NMBR criteria, the relationship between HG and M/LR was lost.

Conclusions: Although this was a small study, it suggests that HG can supply useful prognostic information but only with consistently applied standardized criteria. Under these circumstances, good reproducibility can be obtained despite differences in experience between pathologists.

Cyclin D1 and GATA3 Expression Correlate With Estrogen Receptor Status in Invasive Breast Carcinoma

(Poster No. 17)

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Context: Conflicting results on the prevalence of cyclin D1 overexpression and its correlation with estrogen receptor (ER) expression and outcome have been reported. In addition, a recent meta-analysis performed in breast carcinoma identified a new potentially prognostic marker for breast cancer: GATA3. The aim of this study was to simultaneously assess the prevalence of cyclin D1 and GATA3 expression in breast carcinoma and their association with ER status.

Design: Twenty-five ER-positive and 20 ER-negative invasive ductal (n = 37) and lobular (n = 8) breast carcinomas were selected. For all cases, immunohistochemical staining for ER, progesterone receptor (PR), HER-2/neu, cyclin D1, and GATA3 was performed. The extent of staining was graded based on intensity and proportion of positive cells. Tumors were categorized into 3 groups: negative/weak (score 0–2), intermediate (score 3–5), and strong expression (score 6–8).

Results: The great majority of ER-positive breast carcinomas expressed both cyclin D1 (96%) and GATA3 (96%), whereas only 35% and 15% of ER-negative cases, respectively, were positive. There is a stronger correlation of GATA3 expression and ER and PR negativity compared with cyclin D1. HER-2/neu was positive in an equal number (40%) of both ER-positive and ER-negative breast carcinoma, and there was no correlation with cyclin D1, GATA3, ER, or PR expression.

Conclusions: Low expression of GATA3 and cyclin D1 is strongly associated with invasive breast carcinoma with negative ER and PR status. There is no association between cyclin D1 or GATA3 expression and HER-2/neu positivity by immunohistochemistry.

Lymphoepithelioma-like Carcinoma of the Breast: A Rare Entity Diagnosed on Core Biopsy and Confirmed by Segmental Mastectomy

(Poster No. 18)

Emerald D. O’Sullivan-Mejia, MD (emeralduva@yahoo.com); Margaret M. Grimes, MD; Michael O. I dovu, MD, MPH. Department of Pathology, Virginia Commonwealth University, Richmond.

Lymphoepithelioma-like carcinoma is an undifferentiated carcinoma consisting of epithelial tumor cells associated with a dense lymphocytic
infiltrate. This entity has been identified in a variety of locations including the larynx, salivary glands, lungs, stomach, thyroid, thymus, skin, uterine cervix, urinary tract, and prostate but has very rarely been diagnosed in the breast. We report a case of a 55-year-old woman with a 3.1-cm oval hypoechoic mass in the upper outer quadrant of the left breast. Ultrasonound-guided needle core biopsy was performed and histologic examination revealed isolated, as well as clustered, mildly pleomorphic epithelial cells within a dense lymphoid infiltrate (Figure 23). Immunohistochemically, the tumor cells were positive for cytokeratin AE1/AE3 and E-cadherin and demonstrated an intermediate proliferation index using Ki-67. The cells were negative for estrogen and progesterone receptors, as well as Epstein-Barr virus latent membrane protein. Fluorescence in situ hybridization demonstrated HER-2 gene amplification. Markers for CD3, CD15, CD20, CD30, and ALK-1 showed a mixed reactive lymphocytic population, with no evidence of lymphoma. A similar appearance was confirmed on the subsequent segmental mastectomy. The tumor showed no circumscription and no syncytial growth pattern. Two sentinel lymph nodes were examined and were negative for metastasis. Although previous reports have suggested that this pattern is a variant of lobular carcinoma, our results suggest a possible ductal cell origin. Similar to previous reports, association with Epstein-Barr virus was not found.

Bilateral Invasive Lobular Breast Cancer Presenting as Carcinomatosis in a Man
(Poster No. 19)

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Invasive lobular breast carcinoma represents only 1.5% of all male breast cancers. However, it should remain on the differential diagnosis in a patient with metastatic carcinoma of unknown origin. We report a case of a 58-year-old man with a medical history of prostate cancer following a radical prostatectomy in 1994 who presented with increasing abdominal girth and a 10-lb weight loss during a 3-month interval. A computed tomography scan of the abdomen revealed massive ascites and vague peritoneal nodularity suspicious for carcinomatosis. A peritoneal biopsy revealed a malignant epithelial neoplastic process focally arranged in a single-file pattern. There was immunohistochemical reactivity for cytokeratin 7 and a negative mesothelial immunophenotype. Prostatic-specific antigen and cytokeratin 20 immunostains were negative. Subsequent gastric and right iliac bone biopsies revealed a poorly differentiated carcinoma similar in histology and immunophenotype to the previous peritoneal biopsy. On a more thorough physical examination, bilateral breast masses and nipple retraction were noted. Biopsies of the masses revealed estrogen receptor–positive invasive lobular carcinomas with similar histology to all the previous biopsies (Figure 24). This case is unusual in that to our knowledge, it represents the first reported case of bilateral lobular carcinoma of the breast presenting as carcinomatosis. The fact that the patient was a man prolonged the identification of the primary site. Although a rare neoplasm in a man, breast cancer should be included in the differential diagnosis of a metastatic carcinoma of unknown origin.

MART-1–Positive Breast Carcinoma: Immunohistochemical and Ultrastructural Features
(Poster No. 20)

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MART-1 is a melanosome specific protein. Since it was first cloned in 1994, MART-1 has become a standard immunohistochemical stain used in the diagnosis of melanoma. To the our knowledge, MART-1–positive breast cancer has not yet been described. Using standard immunohistochemical methods and electron microscopy, we evaluated a primary and metastatic ductal breast adenocarcinoma that was strongly reactive for MART-1. Immunohistochemical staining for MART-1 on the primary ductal breast adenocarcinoma (Figure 25) and on metastases to the anterior chest wall and brain showed strong positivity. Other melanoma markers, including S100 and HMB-45, were negative. GCDFP-15, cytokeratins AE1/AE3, and cytokeratin 7 were positive, typical of breast carcinoma. Electron microscopy performed on the brain metastasis showed features typical of adenocarcinoma, including desmosomes, intracellular lumens, and microvilli, and failed to demonstrate any evidence of melanosomes. We report a case of metastatic ductal breast adenocarcinoma having strong immunoreactivity for MART-1. To our knowledge, this association has not been previously described. This case has important implications for diagnosing patients with melanoma or other MART-1–positive cancers, particularly in locations where primary or metastatic breast cancer might be a consideration.
Synchronous Presentation of Primary Breast Diffuse Large B-Cell Lymphoma and Invasive Ductal Carcinoma as Well as High-Grade Ductal Carcinoma In Situ in the Same Breast
(Poster No. 21)

Ziying Zhang, MD (zzhang2@hfhs.org); Rashmi K. Shamanna, MD; Adrian Ormsby, MD; Usha Raju, MD; Osama Alassi, MD. Department of Pathology, Henry Ford Hospital, Detroit, Mich.

Synchronous occurrence of carcinoma and primary breast lymphoma is extremely rare. We report a patient with synchronous occurrence of diffuse large B-cell lymphoma (DLBL) and invasive ductal carcinoma (IDC) with high-grade ductal carcinoma in situ (HG-DCIS). A 65-year-old woman, on screening mammogram, had heterogeneously dense breast with suspicious linear, pleomorphic calcifications spanning an area of 9 cm. A core needle biopsy showed HG-DCIS. Because of extensive calcifications, the patient underwent simple mastectomy and sentinel lymph node excision. A 2.2-cm mass was found, which was composed of 2 intermixed but distinct cell populations and larger discohesive cells with pleomorphic hyperchromatic nuclei surrounded by small mature lymphocytes. Almost in contact with the mass was a classic HG-DCIS with discontinuous foci of IDC. Initial impression was poorly differentiated carcinoma heavily infiltrated by lymphocytes. Immunohistochemistry showed the larger, discohesive tumor cells strongly positive for CD20 and negative for cytokeratin. Additional lymphoma markers were kept in keeping with DLBL. Sentinel lymph node was negative for both carcinoma and lymphoma. IDC and DCIS were negative for estrogen receptor, progesterone receptor, and HER-2/neu. The patient was in remission for lymphoma after 6 cycles of R-CHOP chemotherapy. After 17 months, the patient developed metastatic carcinoma in 19 of 20 axillary lymph nodes. Because carcinoma is much more frequent than lymphoma, the diagnosis of lymphoma may not be considered in routine pathology. This case emphasizes the importance of careful review when the tumor is heavily infiltrated by atypical lymphocytes or is poorly differentiated carcinoma. Although extremely rare, synchronous lymphoma and carcinoma does occur (Figure 26).

Renal Cell Carcinoma Presenting as a Solitary Breast Mass: A Diagnostic Pitfall on Aspiration Cytology of Clear Cell Tumors of the Breast
(Poster No. 22)

Yahya Daneshbod, MD, MIAC1 (daneshbk@yahoo.com); Sohrab Atefi, MD; Habib Noorani, MD1 1Department of Pathology; Dr Daneshbod Pathology Laboratory, Shiraz, Islamic Republic of Iran; 2Department of Surgery, Saadi Hospital, Shiraz, Islamic Republic of Iran; 3Department of Oncology, Nemazi Hospital, Shiraz, Islamic Republic of Iran.

Metastasis to the breast from extrammary primary is rare. We describe the cytologic findings of a case of metastatic renal cell carcinoma (RCC) presenting as a solitary breast mass together with the diagnostic pitfalls of aspiration cytology of clear cell tumors of the breast. A 65-year-old woman presented to her oncologist after noticing an enlarging, solitary, painless, right-sided breast mass. She has been a known case of RCC for 8 years. Fine-needle aspiration was performed, which was reported as suspicious for malignancy, and excisional biopsy was recommended. Cytologic findings were papillary clusters, loose clusters, and mostly isolated single cells. Individual cells were large with relatively low nuclear-cytoplasmic ratio. The cytoplasm was abundant and vacuolated. The nuclei were round with fine chromatin and slight pleomorphism. Immunocytochemical staining showed dual positivity for vimentin and keratin. A preliminary diagnosis of suspicious for malignancy and suggestive of metastatic RCC was made. Cell block preparation showed aggregates of clear cells with eccentric nuclei. Excisional biopsy was performed and imprint smears were made. The diagnosis of metastatic RCC in the breast was confirmed. Clinically and cytologically, metastatic RCC to the breast can be confused with benign or malignant breast primaries. The previous clinical history and ancillary studies, such as histochemical and immunohistochemical study, are essential to arrive at a correct diagnosis.

Discordant Results by 2 Widely Used Anti–Platelet Factor 4/Heparin Enzyme-Linked Immunosorbent Assay Tests
(Poster No. 23)

Naomi Montague, PhD, MD1 (NMontague@med.miami.edu); Diana Morla, MD; Saleh Alazemi, MD; Daniel Seckenger, MD; Phan Nguyen, MS; Michelle Rodriguez, MS; Daniel Kett, MD; David Andrews, MD1 Departments of Pathology and Internal Medicine/Pulmonary and Critical Care, and Special Coagulation Laboratory, Miller School of Medicine at the University of Miami, Miami, Fla.

Context: The accurate diagnosis of heparin-induced thrombocytopenia requires both clinical criteria and laboratory assessment of serum antibodies to platelet factor 4 (PF4). Accurate diagnosis is essential as overdiagnosis may result in alternative anticoagulation medication with increased bleeding risk and treatment cost. Underdiagnosis places patients at risk for significant clinical sequelae, such as life- and limb-threatening thrombosis.

Design: Forty-nine archived patient sera (26 consecutive positive and 23 negative) originally sent for GTI platform anti-PF4 status were retested in parallel at identical freeze-thaw cycles with both the GTI and STAGO platforms. Patient records were reviewed, and the 4Ts pretest clinical scores (J Thromb Haemost. 2006;4:759–765) were calculated.

Results: Retested samples negative for anti-PF4 antibodies agreed well between the GTI and STAGO methods (25/26; 96%). Discordance was observed between the GTI and STAGO anti–PF4–positive specimens (12/23; 52%). In the discordant specimens, the average GTI optical density was significantly lower (P < .02) than the average GTI optical density seen in the anti–PF4–positive discordant specimens (Table). The 4Ts pretest clinical score for the discordant group was low to intermediate (4.1 ± 0.7).

Conclusions: The GTI platform incorporates PF4 directly onto plastic as a PF4/polyvinylsulfonate complex, whereas the STAGO platform couples preformed PF4/heparin to plastic. For low optical densities (<1.1), discordance may be due to difference in reagents. For high optical densities (>1.1), the diagnosis of heparin-induced thrombocytopenia requires greater dependence on clinical judgment until better agreement between enzyme-linked immunosorbent assay laboratory results and clinical parameters is achieved.

Optical Density (OD) of Discordant Versus Concordant GTI/STAGO Specimens

<table>
<thead>
<tr>
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<th>GTI OD</th>
<th>Range</th>
<th>STAGO OD</th>
<th>Range</th>
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<td>GTI</td>
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<td>0.20 ± 0.12</td>
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<tr>
<td>STAGO</td>
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<td>0.80–3.49</td>
<td>1.71 ± 1.08</td>
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</table>

Associations Between Oxidative Stress and Red Blood Cell Deformability
(Poster No. 24)

You Kyoung Kim, MD; Se Hyun Shin, PhD; Won-Kil Lee, MD1 (leewk@knu.ac.kr); Jang-Soo Suh, MD; Kyung-Eun Song, MD1 1Department of Laboratory Medicine, Kyungpook National Hospital, Daegu-Gu, Republic of Korea; 2School of Mechanical Engineering, Kyungpook National University, Daegu-Gu, Republic of Korea.

Context: Chronic hyperglycemia may result in increased peroxidation in erythrocyte membrane. Oxidative stress might cause abnormalities of red cell membrane that alter the rheologic properties of blood. We tried to examine the association of oxidation status and rheologic properties by measuring thiobarbituric acid–reactive substance (TBARS), superoxide dismutase, and red cell deformability in diabetic patients.

Design: We studied 31 patients of type 2 diabetes mellitus without complications and 34 healthy subjects. Red blood cell (RBC) deformability...
was assessed by a Rheoscan-D ectactometry. The activity of superoxide dismutase in the erythrocytes was determined by monitoring the inhibition of the autoxidation of pyrogallol. Lipid peroxidation in the erythrocytes and plasma was estimated as evidenced by the formation of TBARS. Statistical significance was analyzed by Student t test, and correlations between variables were performed by using Pearson correlation coefficient test.

Results: The values of RBC deformability and erythrocyte superoxide dismutase levels were significantly decreased compared with those of controls (P < .01 and P < .05, respectively). Plasma TBARS (P < .01) was significantly increased compared with those of controls. Correlation analysis revealed a significant negative correlation between RBC deformability and plasma TBARS (r = −0.4204, P < .01).

Conclusions: The serum levels of TBARS were significantly increased in diabetic patients. We observed a decrease in erythrocyte superoxide dismutase activity and RBC deformability in diabetic patients compared with controls. We can conclude that oxidative stress is elevated and impaired RBC deformability is observed in patients with diabetes mellitus, and there was significant negative correlation between RBC deformability and plasma oxidation.

Establishment of eGFR Reference Ranges in Geriatric Population Using the Modification of Diet in Renal Disease Study Equation (Poster No. 25)

Rita H. Khoury, MD (rkhoury@aculabs.com); Bernard P. Salmon, MS; Asha Gandhi, BS; Irina Y. Ryzhkova, BS; Peter Gudaitis, BS; Dauna Gudaitis, BS; A. V. Gudaitis, MS. Aculabs, Inc, East Brunswick, NJ.

Context: Glomerular filtration rate (GFR) is an important tool in the management of patients who need clinical assessment of kidney function. The National Kidney Disease Education Program encourages laboratories to automatically report eGFR when serum creatinine is reported, and eGFR is based on the Modification of Diet in Renal Disease Study equation, which has been shown to be reliable in estimating GFR from serum creatinine when the patient’s age, sex, and race are also known.

Design: We analyzed eGFR data collected from 63500 samples of patients tested in our laboratory; the Roche/Hitachi Modular P was used to measure serum creatinine (modified Jaffe). Patient data were separated into 6 age groups: younger than 50, 51 to 65, 66 to 75, 76 to 85, 86 to 99, and older than 100 years. In addition, each group was separated based on sex. The prevalence of eGFR of less than 60 or less than 90 mL/min/1.73 m² in each group was calculated. Reference intervals were calculated using nonparametric analysis.

Results: The mean value of eGFR decreased with age in both sexes. The percentage of patients with eGFR values less than 60 and less than 90 mL/min/1.73 m² increased with age for both males and females. Reference ranges for both sexes ranged from 16 to 229 mL/min/1.73 m² in each group was calculated. Reference intervals were calculated on sex. The prevalence of eGFR of less than 60 or less than 90 mL/min/1.73 m² in each group was calculated. Reference intervals were calculated on sex. The prevalence of eGFR of less than 60 and less than 90 mL/min/1.73 m² was significant compared with those of controls.

Conclusions: Kidney dysfunction based on eGFR is more common in elderly people and increases with age. More than 20% of the population older than 90 years will reach critical value of eGFR, requiring extensive management of patients who need clinical assessment of kidney function.

The Prevalence of eGFR

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Galactosemia and Falsely Elevated Glucose Values by Point-of-Care Testing (Poster No. 26)

Erin Bamhart, MD (eabamhr@utmb.edu); Anthony Okorodudu, PhD; Diana Dehoyos, MS, MT; John Petersen, PhD. Department of Pathology, University of Texas Medical Branch, Galveston.

Point-of-care testing (POCT) is intended to provide laboratory testing at or near a patient’s bedside by nonlaboratory personnel, thereby providing a faster turnaround time and shorter time to therapeutic intervention. University of Texas Medical Branch has a large, decentralized POCT program of which glucose monitors play a major part. In our institution, the POCT glucose monitors use the glucose dehydrogenase pyrroloquinolinate-nequinnine (GDH-PQQ) method, which is known to be falsely elevated in the presence of maltose, galactose, or xylose. We report the case of a neonate with markedly abnormal liver and coagulation values, critically elevated POCT glucose, and normal clinical laboratory glucose levels. This issue of inaccurate POCT glucose results was brought to the attention of the clinical laboratory. Because of the clinical laboratory’s awareness of the potential interference by maltose, galactose, and xylose when using the GDH-PQQ method, and the presence of large amounts (+4) of reducing sugars in the baby’s urine, the possibility of galactosemia was raised with the treating pediatricians. Galactosemia was confirmed shortly thereafter. To our knowledge, only 1 previous case report addresses the use of these monitors coincident with galactosemia. Because of a single case of galactosemia, the institution advocated switching POCT monitors to a type that was not affected by galactose. In contrast, because of our awareness that increased galactose levels can cause a false elevation of glucose when using our POCT glucose monitor, our patient was diagnosed with galactosemia several days prior to the availability of required state testing results.

Age-Based Distribution and Follow-up of High-Risk Human Papillomavirus–Positive Atypical Squamous Cells of Unknown Significance in a Nondysplasia Clinic Population (Poster No. 27)

Douglas Kim, MD (djk949@gmail.com); Jane Dancer, MD; Anna Nunez, BS; Deborah Smith, CT(ASCP); Dina Mody, MD. Department of Pathology, The Methodist Hospital, Houston, Tex.

Context: The aim was to identify any trends in high-risk human papillomavirus (HR-HPV)–positive results following a diagnosis of atypical squamous cells of unknown significance (ASC-US).

Design: The patient population consisted of 337 women, with ASC-US diagnosis on Papanicolaou test in 2006, who were triaged using HR-HPV testing via Hybrid Capture II assay from ThinPrep and SurePath samples. Dysplasia clinic patients were excluded. The age-related groups were categorized as follows: younger than 20 years (group 1), 21 to 30 years (group 2), 31 to 40 years (group 3), 41 to 50 years (group 4), and older than 50 years (group 5).

Results: Group 1 had 10 (42%) of 24 HPV-positive cases and none of these had documented follow-up. In group 2, 39 (48%) of 81 were positive for HPV. Of these, 9 had follow-up, with 1 diagnosed as HPV-related changes and 2 diagnosed as cervical intraepithelial neoplasia (CIN) I. In group 3, 19 (21%) of 91 cases had positive HPV results. One patient had documented follow-up with HPV-related changes. Group 4 had 13 (16%) of 80 cases with positive HPV results. One had documented follow-up with HPV-related changes. Lastly, group 5 had 61 ASC-US cases and 7 (11%) were positive for HPV. Two of these had follow-up, with 1 diagnosed as HPV-related changes and the other as CIN I. No patients in our study had a high-grade lesion on subsequent colposcopy and biopsy.

Conclusions: The percentage of HR-HPV positivity declined as the age of the patient population increased. From this, one can surmise that the ASC-US type changes seen on cytology in older patients are related to factors other than HPV infection.

Distinguishing Gastric Mucosal Contamination From Intraductal Papillary Mucinous Neoplasm in Endoscopic Ultrasound-Guided Fine-Needle Aspiration Biopsies of the Pancreas (Poster No. 28)

Sandra L. White, MD (whitesa@ohsu.edu); Dornald Myles, BS; Terry Morgan, MD, PhD. Department of Pathology, Oregon Health & Science University, Portland.

Context: Endoscopic ultrasound-guided fine-needle aspiration biopsy
is a sensitive and specific method for diagnosing pancreatic neoplasia. The approach is through the duodenum or stomach, which introduces contaminating mucinous intestinal or gastric mucosa, respectively. Contamination is especially a problem when sampling cytologically bland intraductal papillary mucinous neoplasms (IPMNs) because gastric mucosa closely resembles IPMN cytopathology. We hypothesized that Alcian blue and Alcian yellow staining may distinguish gastric mucosa contamination from IPMN.

Design: Representative sections of IPMNs without atypia (n = 4), normal pancreas (n = 3), normal gastric antrum mucosa (n = 4), and reactive antral mucosa (n = 3) from surgical pathology archives were stained for Alcian blue and Alcian yellow (Ventana, Tucson, Ariz) using routine methods. Sections were scored for the presence or absence of intracytoplasmic staining by 2 independent pathologists (S.L.W. and T.M.).

Results: Alcian yellow and Alcian blue staining reliably differentiated gastric mucosa from normal pancreatic ductal epithelium. Gastric mucosa was positive for Alcian yellow and negative for Alcian blue. Pancreatic ductal epithelium was positive for Alcian blue and negative for Alcian yellow. IPMNs, 3 of 3, variably stained for Alcian blue ranging from diffuse to only focally positive. IPMN epithelium showed positive staining for Alcian yellow when negative for Alcian blue.

Conclusions: We conclude that positive Alcian blue staining supports a diagnosis of pancreatic mucosal differentiation; however, the absence of staining, by itself, does not exclude the diagnosis. Changes in normal mucin production in neoplastic pancreatic mucosa may explain our observation.

A Comparison of Saccomanno Preservative, CytoRich Red Preservative, and SurePath Preservative in Body Fluid Cytology (Poster No. 29)

Marsha Moler, BS, MT, ASCP(CT); Charlotte Myers, CT(ASCP); Timothy C. Allen, MD, JD (timothy.allen@uthc.edu). Department of Pathology, The University of Texas Health Center, Tyler.

Context: Body fluid cytology specimens are often processed as smears using Saccomanno preservative (SMP). Studies have evaluated the efficacy of various preservatives in gynecologic cytology, but their comparison in nongynecologic cytology has not been fully examined. We compared the cytologic quality of body fluid specimens with conventional SMP with that of CytoRich Red Preservative (CRP) and SurePath Preservative (SPP).

Design: Sixteen fresh body fluid specimens (11 pleural, 2 peritoneal, 1 pericardial, 2 breast) were each divided into 3 portions with 10 mL of SMP, CRP, and SPP added to their cell buttons. Smears were prepared from the SMP portion and stained with modified Papanicolaou stain. CRP portions were prepared and stained on the TriPath slide processor using manufacturer’s nongynecologic protocol. SPP portions were prepared and stained on the TriPath slide processor using manufacturer’s gynecologic protocol. Slides were reviewed by 2 experienced cytopathologists and a pulmonary/thoracic cytopathologist for differences in the preparation quality, including artifact, background, and cellular characteristics, specifically nuclear, cytoplasmic, and chromatin detail and nucleolar distinction than the other fixatives, average 2.31. CRP and SPP scored highest overall for all cellular characteristics averaging 3.13 and 3.08, respectively. SMP gave a cleaner background than SMP or CRP because of the gynecologic processing protocol.

Conclusions: CRP and SPP yielded best overall cytologic detail. Further comparison of these preservatives with body fluid cytology would help determine the best preservative for routine use.

The Use of Epithelial Membrane Antigen, Desmin, and Ki-67 in Distinguishing Reactive From Neoplastic Mesothelial in Effusions (Poster No. 30)

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Context: We investigate the diagnostic utility of desmin, epithelial membrane antigen (EMA), and Ki-67 to differentiate reactive from neoplastic mesothelial cells in effusions.

Design: Archival paraffin-embedded cell blocks of cytologic effusions were retrieved to obtain 57 cases of malignant mesothelioma and 34 cases of florid reactive mesothelial hyperplasia. The blocks were stained with desmin, EMA, and Ki-67.

Results: The malignant mesotheliomas were immunoreactive to EMA in 37 (100%) of 37 and to desmin in 4 (11%) of 37 cases. The pattern of EMA positivity was diffuse with membranous accentuation; the desmin reactivity was focal in malignant cases. Reactive mesothelial cases showed focal and weak cytoplastic positivity to EMA in 3 (9%) of 34 and diffuse positivity to desmin in 27 (78%) of 34 cases. Proliferation marker (Ki-67) immunoreactivity was less than 5% (10 vs 10), 5% to 25% (6 vs 11), 26% to 49% (10 vs 9), and 50% and above (2 vs 5) reactive versus malignant, respectively. None of the reactive cases exceeded 50%; 4 of the malignant did.

Conclusions: Positive EMA and negative desmin correctly identified 91% of malignant mesotheliomas. However, positive desmin and negative EMA was seen in only 75% of reactive mesothelial cells. In cases that showed positive reaction to both markers, a strong membranous EMA positivity would be more suggestive of a malignant process. However, it is important to recognize that rare cases may strongly coexpress both markers and that these findings should be interpreted in correlation with the clinical and radiologic findings. Ki-67 was not helpful in separating florid hyperplasia from malignant mesothelioma, as both are highly proliferative.

Evaluation of Solid Pancreatic Lesions by Endoscopic Ultrasound-Guided Fine-Needle Aspiration: 5-Year Experience at Northwestern Memorial Hospital (Poster No. 31)

Songlin Zhang, MD, PhD (songlin-zhang@northwestern.edu); Maria Ramos, MD; Denise V. S. De Frias, MD; Marina Ivanovic, MD; Ritu Nayar, MD. Department of Cytopathology, Northwestern University, Chicago, Ill.

Context: Endoscopic ultrasound-guided fine-needle aspiration (EUS-FNA) has been in use for more than a decade and has gained widespread popularity as a diagnostic and tumor staging modality. Pancreatic lesions, both cystic and solid, are one of the main targets of EUS-FNA.

Design: A computer-based search for EUS-FNA was performed in the pathology and gastrointestinal database from January 2002 to October 2006 for pancreatic solid lesions, and the surgical pathology reports were reviewed.

Results: A total of 279 EUS-FNAs were performed on 244 patients, including 147 males and 97 females. The ages ranged from 17 to 90 years (mean, 63 years). The cytology diagnoses included 150 (53.8%) malignant, 14 (5%) suspicious for malignancy, 28 (10%) neuroendocrine tumors, 7 (2.5%) neoplasms, 49 (17.6%) negative, 11 (3.8%) descriptive diagnosis, and 20 (7.2%) unsatisfactory. Eighty-eight cases had histologic follow-up (53 malignant, 23 neuroendocrine, 3 neoplasms, and 9 negative), and the corresponding cytology diagnosis included 43 malignant, 8 suspicious for malignancy, 21 neuroendocrine, 5 neoplasms, 4 negative, 1 descriptive diagnosis, and 6 unsatisfactory. There were no false positives and 4 false negatives. The sensitivity for solid pancreatic malignant lesions was 94.3% and for neuroendocrine tumors was 95.7%.

Conclusions: We achieved a very high sensitivity and a low unsatisfactory rate for both malignant and neuroendocrine tumors with a 100% positive predictive value and 0% false-positive rate. In summary, with experienced intervention gastroenterologists and cytopathologists, EUS-FNA is a powerful tool for evaluation of pancreatic solid lesions.

Human Papillomavirus–Related Cervical Disease in Women With Posttraumatic Stress Disorder or Depressive Symptoms (Poster No. 32)

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Context: Associations of posttraumatic stress disorder (PTSD) and depression with human papillomavirus (HPV) infection and cervical cyto logic abnormalities in human immunodeficiency virus (HIV)–positive Rwandan women.

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Abstracts
Design: HPV was typed by polymerase chain reaction on cervicovaginal lavage specimens, and cervical smears were classified from 710 HIV-positive women naïve to antiretroviral therapy and previously unscreened for cervical dysplasia. Of these women, 683 were screened for PTSD with the Harvard Trauma Questionnaire (≥2.5 considered PTSD) and 612 for depression by the Center for Epidemiologic Studies Depression Scale (CESD; ≥20 considered depressive symptoms). Groups were compared by exact tests for contingency tables and Wald tests for logistic regression.

Results: Women screening positive for depressive symptoms were more likely than those screening negative (n = 228) to harbor any HPV (75% vs 67%, odds ratio [OR] = 1.50, P = .02). In multivariate models adjusted for CD4 category (OR = 350), age, and any sexual activity in the last 6 months, the association of harboring HPV with CESD 20 or greater was attenuated (OR = 1.28, P = .07). A higher CESD score had a small (P = .16) but significant inverse correlation with lower CD4 cell count (P < .001), and lower CD4 count was associated (P < .001) with HPV infection. PTSD did not have notable or significant associations with HPV infection or with cervical cytology in univariate or multivariate models. Among women harboring HPV, neither CESD nor PTSD scores were associated with abnormal cytology in adjusted or unadjusted models.

Conclusions: Depressive symptoms were associated with HPV infection, which may reflect residual confounding from higher measures of CESD in women with more advanced HIV disease.

Low-Grade Squamous Intraepithelial Lesion Is the Most Common Abnormality on Follow-up of Atypical Glandular Cervical Papanicolaou Tests in Pregnant and Postpartum Women

(Poster No. 33)

Laura J. Tafe, MD (laura.tafe@hitchcock.org); Jean-Ann Selleck, BS, CT, ASCP; Vijayalakshmi Padmanabhan, MD. Department of Pathology, Dartmouth-Hitchcock Medical Center, Lebanon, NH.

Context: Pregnancy and postpartum (PP) are ideal times for screening Papanicolaou tests (PTs). Hormonal stimulation and reactive and repair changes can pose a diagnostic challenge for the cytopathologist. Few studies have examined the significance of atypical glandular cells (AGC) in pregnant and PP women compared with the general population (GP); this was the primary aim of our study. Also, we wanted to see if reviewers differed in interpretation of AGC in both groups.

Design: A computer-assisted search of abnormal PTs (January 2003 to May 2006) was performed. Twenty-three pregnant and PP women with AGC were identified; 50 random cases of AGC from the GP were used for control. Follow-up data were collected in Microsoft Excel format. Blinded review of PTs from both groups and random cases of no abnormal PTs (NAP) were more likely than those screening negative (n = 228) to harbor any HPV (75% vs 67%, odds ratio [OR] = 1.50, P = .02). In multivariate models adjusted for CD4 category (OR = 350), age, and any sexual activity in the last 6 months, the association of harboring HPV with CESD 20 or greater was attenuated (OR = 1.28, P = .07). A higher CESD score had a small (P = .16) but significant inverse correlation with lower CD4 cell count (P < .001), and lower CD4 count was associated (P < .001) with HPV infection. PTSD did not have notable or significant associations with HPV infection or with cervical cytology in univariate or multivariate models. Among women harboring HPV, neither CESD nor PTSD scores were associated with abnormal cytology in adjusted or unadjusted models.

Conclusions: Depressive symptoms were associated with HPV infection, which may reflect residual confounding from higher measures of CESD in women with more advanced HIV disease.

Comparison of the Pregnant/Postpartum and General Population Groups

<table>
<thead>
<tr>
<th>Adequacy Score Designation</th>
<th>Adequacy Score</th>
<th>Specimen Description</th>
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</thead>
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<tr>
<td>0</td>
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<td></td>
</tr>
<tr>
<td>1</td>
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<tr>
<td>2</td>
<td>Diagnostic, borderline cellular material</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>Diagnostic, abundant cellular material</td>
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</table>

Papanicolaou Test Requisitions: A Snapshot of Current Practice

(Poster No. 35)

Sonya Narayshkin, MD, FLAC, FCAP (drsa1981@ucd.net); Brenda L. Schultz, BA, SCT(ASCP). Department of Pathology, Mercy Hospital, Janesville, Wis.

Context: The Papanicolaou (Pap) test requisition is recognized as an important communication tool. However, the reliability of patient history and clinical information provided on requisitions is unknown, and the effect of incomplete or inaccurate information on quality of patient care has not been previously quantified.

Design: Clinicians and assistants were surveyed to determine how they viewed and completed Pap test requisition slips. Patient history and clinical information from 500 consecutive requisition slips (preliminary sample of 1000) were compared with data from our laboratory information system and/or electronic patient medical records. Specifically, we determined whether or not a Pap test qualified for a “high-risk rescreen,” as defined by our laboratory, based on the requisition alone and compared that determination with one based on data from the computerized records.

Results: Ninety-four surveys were returned. Most (84%) respondents did not realize that negative high-risk Pap tests underwent a second screen. Of the 385 (of 500; 77%) Pap tests with applicable computerized records, 71 (of the 385; 18%) qualified for high-risk rescreen based on the requisition alone. Twenty-four other Pap tests (24/385; 6%) were discovered to be high-risk after review of additional information from the electronic records.

Conclusions: Our requisition slip check boxes did not elicit all the information expected. Additional education of those completing requisitions is warranted. Twenty-five percent of high-risk Pap tests would not have undergone a high-risk rescreen if the laboratory had relied solely on data from the requisition. This study launches development of benchmarks for this important preanalytical aspect of Pap testing.
Is There a Difference in the Results of High-Risk Human Papillomavirus Testing in Atypical Squamous Cells of Unknown Significance Cases With the Modifier “Rare” Compared With Unselected Atypical Squamous Cells of Unknown Significance Cases?  
(Poster No. 36)

Michael E. Smith, MD (msmith126270@hotmail.com); James F. Sikle, MD. Department of Pathology, Eisenhower Army Medical Center, Evans, Ga.

Context: A fraction of atypical squamous cells of unknown significance (ASC-US) cases are signed out as “rare” ASC-US (R-ASC). This study was designed to see if there was a difference in the high-risk human papillomavirus (HR-HPV) results in cases of R-ASC versus cases of atypical squamous cells (ASC).

Design: Papanicolaou (Pap) smears classified as ASC or R-ASC with HR-HPV results from 2005 were reviewed. Calculations were performed to determine the difference in the HR-HPV and colposcopy results in R-ASC versus ASC.

Results: A total of 897 Pap smears classified as ASC were analyzed. HR-HPV was positive in 47% (422/897) overall; 21.1% (189/897) were cases of ASC of which 31.2% (59/189) were HR-HPV positive. Of the remaining ASC cases, 51.3% (963/708) were HR-HPV positive. Chi-square analysis demonstrated a statistically significant difference (P < .001) between the groups. Colposcopy data were available in 44% (26/59) of HR-HPV R-ASC; 53.8% (14/26) were negative, 38.5% (10/26) were positive for low-grade squamous intraepithelial lesion, and 7.7% (2/26) were positive for high-grade squamous intraepithelial lesion.

Conclusions: The rate of HR-HPV positivity was lower in R-ASC cases compared with unmodified ASC-US and was statistically significant. The reasons for this smaller fraction in R-ASC needs further study.

Is There a Difference in the Results of High-Risk Human Papillomavirus and Biopsy Proven Dysplasia in Atypical Squamous Cells of Undetermined Significance Upgraded by Pathologists Versus Atypical Squamous Cells of Undetermined Significance Affirmed by Pathologists?  
(Poster No. 37)

Keith E. Thompson, MD; Aaron R. Huber, DO (aaron.huber@med.navy.mil); James F. Sikle, MD. 1Department of Pathology, Naval Medical Center, San Diego, Calif; 2Department of Pathology, Eisenhower Army Medical Center, Fort Gordon, Ga.

Context: Some Papanicolaou (Pap) smears diagnosed as negative for intraepithelial lesion or malignancy (NILM) by cytootechnologists are reviewed by pathologists and a fraction of these cases are upgraded to atypical squamous cells of undetermined significance (ASC-US). High-risk human papillomavirus (HR-HPV) DNA testing is performed on all ASC-US cases.

Design: Pap smears classified as ASC-US with HR-HPV testing results from 2005 were reviewed to determine the HR-HPV and dysplasia rates when the pathologist upgraded a NILM diagnosis or affirmed an ASC-US diagnosis. The cytotechnologist diagnosis, pathologist diagnosis, patient age, HR-HPV results, and biopsy results were tabulated.

Results: A total of 1066 Pap smears classified as ASC-US with HR-HPV testing results were analyzed. HR-HPV was positive (POS) in 46% (493/1066) with 134 biopsies performed (134/493). When NILM was upgraded to ASC-US, 35% (105/304) were HR-HPV POS and 62% (18/29) were POS for dysplasia. When ASC-US was affirmed, 51% (388/762) were HR-HPV POS and 55% (58/105) were POS for dysplasia (Figure 27). Chi-square analysis demonstrated a statistically significant difference (P < .001) in the rate of HR-HPV between the 2 groups but no significant difference in the rate of dysplasia (P < .39).

Conclusions: The reasons for the smaller fraction of positive HR-HPV cases in the upgraded group needs further study but may be related to subtle cytologic findings. The similar rates of dysplasia between the 2 groups stress the importance of the recognition of ASC-US using strict criteria, so that those women originally classified as NILM are not missed.

Saccomanno and CytoRich Red Preservatives With Fresh Sputum Specimens: A Comparative Study  
(Poster No. 38)

Charlotte Myers, CT(ASCP); Marsha Moler, BS, MT, ASCP(CT); Timothy C. Allen, MD, JD (timothy.allen@uthct.edu). Department of Pathology, The University of Texas Health Center, Tyler.

Context: Typically, sputum is submitted fresh to the cytology laboratory for processing as smears using Sacomanno (SAC). Although studies have evaluated the efficacy of various preservatives in gynecologic cytol- ogy, the comparison of preservatives for sputum cytology has not been widely studied. We compared SAC with the newer CytoRich Red (CRR) for use with fresh sputum specimens.

Design: Fourteen fresh sputums were divided into 2 portions each and processed using SAC or CRR in a heavy-duty blender for 5 to 6 seconds, centrifuged, and the supernatant decanted. SAC or CRR was then added to each cell box. A pair of smears was prepared from the SAC portion and manually stained with Papanicolaou stain. CRR portions were prepared and stained on the TriPath slide processor using the manufacturer's nongynecologic protocol. Two cytootechnologists and a pulmonary/tho- racic cytopathologist reviewed all preparations. Differences in the quality of the preparations, including artifact, background, and cellular characteristics, specifically nucleus, nucleolus, and cytoplasm, were evaluated. Each fixative was scored from 1 to 4, respectively, as poor, fair, good, or excellent according to cellular characteristics.

Results: SAC fixation yielded some air-drying artifact and less chromatin detail (average score, 2.57). CRR preparations scored slightly higher for nuclear and cellular characteristics. No major differences between the preservatives were identified with regard to background or artifact.

Conclusions: Only a slight difference in cytologic detail was obtained using the CytoRich Red preservative. Further evaluation of fresh sputum cytology is needed to fully evaluate the benefits or deficiencies of these preservatives.

Cytologic Findings in Allogeneic and Autologous Bone Marrow Transplant Patients: A 9-Year Follow-up Study  
(Poster No. 39)

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Context: Bone marrow transplant (BMT) patients and correlates them with pertinent clinical information, flow cytometry studies, and histologic follow-up when available.

Design: We reviewed all cytology reports on BMT patients with pulmonary symptoms from 1998 to 2007 at The Methodist Hospital, Houston, Tex. The cytologic findings were reviewed for the presence of malignant neoplasms, infectious organisms, inflammatory responses, reactive changes, and cellular atypia because of treatment.

Results: Three hundred thirteen patients had undergone BMT including 89 patients (71 allogeneic, 18 autologous) with pulmonary symptoms (43 women, 46 men). The mean age at BMT was 49.9 years (range, 20–75 years). Forty-seven specimens from 28 patients had positive cytologic diagnosis. The most common microorganism was Candida found in 21 specimens. Cytomegalovirus was found in 1 specimen, Aspergillus species and polyomavirus in 2 specimens, respectively. Acute inflammation was present in 6 specimens. Reactive bronchial epithelial cells were found in 4
High-Risk Human Papillomavirus DNA Test Is Useful in the Triage of Women Aged 35 Years and Older With Atypical Squamous Cells, Cannot Exclude High-Grade Squamous Intraepithelial Lesion

(Paper No. 42)

Howard H. Wu, MD1 (hhjwu@yahoo.com); Angie Schultz, MD; Allison Morris, CT; Joseph L. Kirkpatrick, CT.1 Department of Pathology, Ball Memorial Hospital, Muncie, Ind; 2Department of Cytology, PA Labs, Indianapolis, Ind.

Context: High-risk human papillomavirus (HR-HPV) DNA testing has been found to be useful to triage women with atypical squamous cells, cannot exclude high-grade squamous intraepithelial lesion (ASC-H) on Papanicolaou (Pap) tests in recent studies. Approximately 30% (range, 17%-45%) of patients with ASC-H were found to have worse than grade 2 cervical intraepithelial neoplasia (CIN 2+) lesions in the follow-up biopsies. However, most studies found that HPV-negative patients, even with ASC-H diagnosis, are usually negative for CIN 2+.

Design: In our laboratory, reflex HPV DNA testing using Hybrid Capture II methods were carried out in 408 women with a diagnosis of ASC-H during a 2½-year period. Corresponding follow-up of colposcopic histologic diagnoses were available in 155 patients. The age of the patients and results of the HPV testing and corresponding biopsy results were tabulated.

Results: Among patients 35 years and older, 40% (55/136) were HR-HPV positive, which compared with 75% (204/272) for women younger than 35 years. Follow-up biopsies of HR-HPV–positive patients and 0% (0/59) of HR-HPV–negative patients. The sensitivity and negative predictive rate for HR-HPV DNA testing to detect CIN 2+ lesions were both 100% (Table).

Conclusions: HR-HPV DNA testing is a highly sensitive test in detecting high-grade cervical dysplasia. For women 35 years and older with ASC-H diagnosis, HR-HPV positive rate is only 40%. Therefore, reflex HR-HPV DNA testing is a useful method to triage women with an ASC-H diagnosis, especially for women 35 years and older.

| Correlation of HR-HPV Results With Age in Patients With ASC-H* |
|----------------------|-----------------|-----------------|-----------------|
| Age, y               | HPV+, No. (%)   | HPV-, No. (%)   | Total           |
| <35                  | 204 (75)        | 68 (25)         | 272             |
| ≥35                  | 55 (40)         | 81 (60)         | 136             |
| Total                | 259             | 149             | 408             |

* HR indicates high risk; HPV, human papillomavirus; and ASC-H, atypical squamous cells, cannot exclude high-grade squamous intraepithelial lesion.

Ultrasound-Guided Fine-Needle Aspiration of a Thyroid Abscess Caused by Salmonella Species in a Patient With Acquired Immunodeficiency Syndrome

(Paper No. 43)

Jing Liu, MD, PhD1 (jing.liu1@uth.tmc.edu); Susan Zachariah, MSCT (ASCP); Anuradha T. Rao, MD.2 Departments of Pathology and Laboratory Medicine and Radiology, University of Texas Health Science Center at Houston Medical School, Houston; 2Cytology Laboratory, Memorial Hermann Hospital, Houston, Tex.

Acute suppurative thyroid lesion is a rare disease. To our knowledge, use of ultrasound-guided fine-needle aspiration (US-FNA) in thyroid abscess caused by Salmonella species in acquired immunodeficiency virus (AIDS) patients has not been reported in the literature. A 78-year-old African American man with a history of AIDS was admitted to our hospital for fever, neck pain, dysphagia, urosepsis, and altered mental status with a blood culture positive for Salmonella species. On physical examination, he was found to have a large left neck mass that was suspicious for malignancy. A US-FNA was performed. The ultrasound examination revealed a diffusely enlarged thyroid with several complex cysts and nodules in both lobes and the isthmus. The left lobe was asymptomatically enlarged and contained a 7-cm dominant nodule, which was heterogeneous in echo texture and had liquefied hypoechoic areas. This dominant nodule was aspirated. An immediate assessment during the FNA showed numerous degenerated neutrophils, some degenerated macrophages, and necrotic granular debris without thyroid follicular cells. The preliminary diagnosis was abscess. Then, a portion of specimen was submitted for culture. A US-FNA was also performed on a right thyroid nodule that showed features of a benign nodular goiter. The thyroid aspirate culture grew Salmonella species. The patient was treated for the infection. Thyroid abscess can be caused by Salmonella species in AIDS patients. US-FNA is a diagnostic tool for acute suppurative thyroid lesion. The immediate as-
Core Biopsy Diagnosis of Intraductal Papilloma of the Breast: Do They Need To Be Excised?
(Poster No. 44)

Christopher T. Rossi, MD (wanax2@yahoo.com); Jamie Shutter, MD. Department of Pathology, The George Washington University, Washington, DC.

Context: Standard of care has been to excise an intraductal papilloma when the lesion is diagnosed on core biopsy for a presumed increased risk of the development or the presence of concurrent intraductal or invasive carcinoma. However, more recent studies indicate that solitary intraductal papillomas without atypia might not need to be excised and can be managed more conservatively. We evaluated follow-up excisions of an intraductal papilloma diagnosis by core biopsy.

Design: Our case files during a 4-year period identified 23 excisions that had a previous diagnosis by core biopsy of a solitary intraductal papilloma without atypia or a previously or concurrently diagnosed in situ or invasive carcinoma. Mean time to follow-up excision was 59 days, with a range of 11 to 310 days.

Results: Subsequent excision revealed evidence of only residual intraductal papilloma in 20 (87%) of 23 cases. One case showed only fibrocystic changes, and another showed a fibroadenoma without a residual intraductal papilloma. Only 1 (4%) case showed ductal carcinoma in situ arising within the intraductal papilloma. No excisions identified an invasive carcinoma (Table).

Conclusions: This study shows a very low risk of concurrent ductal carcinoma in situ in patients with the core biopsy diagnosis of an intraductal papilloma without atypia on follow-up excision. No cases of invasive carcinoma were identified. Our experience confirms the more recent literature suggesting that solitary intraductal papillomas without atypical features can be managed more conservatively and might not require excision.

<table>
<thead>
<tr>
<th>Follow-up Excisions</th>
<th>No. (%)</th>
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<tbody>
<tr>
<td>Invasive carcinoma</td>
<td>0 (0)</td>
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<tr>
<td>In situ carcinoma</td>
<td>1 (4)</td>
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<tr>
<td>Benign, nonpapilloma</td>
<td>2 (9)</td>
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<tr>
<td>Residual intraductal papilloma</td>
<td>20 (87)</td>
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<tr>
<td>Total</td>
<td>23</td>
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</table>

Correlation Between Core Needle Biopsy and Follow-Up Excision for Radial Scar
(Poster No. 45)

Katherine N. Kimmelshue, MD (kimmelshue@mcvh-vcu.edu); Marie C. Do, MD, H. D. Massey, MD, PhD; Michael O. Idowu, MD, MPH; Margaret M. Grimes, MD. Department of Pathology, Virginia Commonwealth University Health Systems, Richmond.

Context: Previous studies suggest that radial scar (RS) may be associated with an increased risk of breast carcinoma. This study evaluated the incidence of carcinoma on follow-up excision (FUE) after a diagnosis of RS on core needle biopsy (CNB).

Design: Our surgical pathology records were searched for diagnoses of RS between 1999 and the present. Sixty-six women were found with RS or probable RS on CNB. Half of these patients were excluded because of no record of FUE, CNB diagnoses that included lesions other than fibrocystic changes, or a history of previous carcinoma in the same breast. Only the highest grade findings are presented in the Table.

Results: Of patients not excluded from review, 24 were diagnosed with RS and 9 with probable RS on CNB. Of these, only 1 (3%) had infiltrating carcinoma, 2 (6%) had in situ carcinoma, and 2 (6%) had atypical ductal hyperplasia on FUE. More common was papilloma (9%), RS (21%), or fibrocystic changes (55%). The findings are independent of probable RS versus RS.

Conclusions: In this series, fibrocystic changes were the most common finding on FUE after a diagnosis of RS or probable RS on CNB. The results suggest that radial scar on CNB does not present an increased risk of infiltrating or in situ carcinoma on FUE.

FUE Diagnosis

<table>
<thead>
<tr>
<th>RS (n = 24)</th>
<th>Probable RS (n = 9)</th>
<th>Total RS (n = 33)</th>
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<tr>
<td>Infiltrating ductal carcinoma</td>
<td>1 (3)</td>
<td>0 (0)</td>
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<tr>
<td>Lobular in situ</td>
<td>1 (3)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Ductal carcinoma in situ and lobular carcinoma in situ</td>
<td>0 (0)</td>
<td>1 (3)</td>
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<tr>
<td>Atypical ductal hyperplasia</td>
<td>1 (3)</td>
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</tr>
<tr>
<td>Radical scar</td>
<td>7 (21)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Papilloma</td>
<td>2 (6)</td>
<td>1 (3)</td>
</tr>
<tr>
<td>Fibrocystic changes</td>
<td>12 (36)</td>
<td>6 (18)</td>
</tr>
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</table>

* FUE indicates follow-up excision; RS, radial scar.

Human Epidermal Growth Factor Receptor 2 Immunohistochemistry and Fluorescence In Situ Hybridization Testing at the McGill University Health Center: A Retrospective Study of 199 Cases
(Poster No. 46)

Shachar Sade, MD1 (shachar.sade@mail.mcgill.ca); Parisa Momta, BSc 3; Louise Quenneville, MD 4; Catalin Mihalciou, MD2; Atilla Omeroglu, MD. 1Department of Pathology and 2Medical Oncology, McGill University Health Center, Montreal, Quebec, Canada; 3Faculty of Medicine, McGill University, Montreal, Quebec, Canada; 4Department of Pathology, Jewish General Hospital, Montreal, Quebec, Canada.

Context: HER-2 testing is routinely performed in the pathologic evaluation of invasive breast carcinoma. Numerous algorithms with established scoring criteria exist to optimize testing; nevertheless, the best approach remains unknown.

Design: One hundred ninety-nine consecutive HER-2 fluorescence in situ hybridization (FISH) studies and corresponding immunohistochemical results were retrieved from the McGill University Health Center database. FISH was scored for both number of HER-2 signals and HER-2–chronosome 17 signal ratio (HER-2/Chr17) and categorized according to American Society of Clinical Oncology and College of American Pathologists guidelines. Immunohistochemistry was also categorized per recommended guidelines. Cases not suitable reported were retrieved and rescored.

Results: Negative, equivocal, and positive immunohistochemical cases represent 3.5%, 64.8%, and 31.7%, respectively, of FISH studies performed (see FISH analysis, Table).

<table>
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<tr>
<th>Immunohistochemical Score</th>
<th>Amplification Status</th>
<th>HER-2 Interpretation</th>
<th>HER-2/Chr17 Interpretation</th>
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<tr>
<td>Negative (0, 1+)</td>
<td>Nonamplified</td>
<td>7 (100)</td>
<td>7 (100)</td>
</tr>
<tr>
<td></td>
<td>Borderline/amplified</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Equivocal (2+)</td>
<td>Nonamplified</td>
<td>87 (68.0)</td>
<td>95 (74.2)</td>
</tr>
<tr>
<td></td>
<td>Borderline* (P = .02)</td>
<td>21 (16.4)</td>
<td>9 (7.0)</td>
</tr>
<tr>
<td></td>
<td>Amplified</td>
<td>20 (15.6)</td>
<td>24 (18.8)</td>
</tr>
<tr>
<td>Positive (3+)</td>
<td>Nonamplified</td>
<td>2 (3.2)</td>
<td>1 (1.6)</td>
</tr>
<tr>
<td></td>
<td>Borderline</td>
<td>0 (0)</td>
<td>1 (1.6)</td>
</tr>
<tr>
<td></td>
<td>Amplified</td>
<td>61 (96.8)</td>
<td>61 (96.8)</td>
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Fluorescence In Situ Hybridization Subgroup Analysis for HER-2 Signal Counts and HER-2/Chr17 Signal Ratio

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Abstracts
Ultrasound-Guided Fine-Needle Aspiration Biopsy of Thyroid Nodules 1.5 cm or Smaller: Is It Useful?  
(Poster No. 48)
Nadiya Shafi, MD (hanan.farghaly@yahoo.com); Hanan Farghaly, MD. Department of Pathology, University of Louisville, Louisville, Ky.

Context: Clinical management of palpable thyroid nodules larger than 1.5 cm is well established; however, the evaluation of small thyroid nodules is controversial, and the necessity to perform fine-needle aspiration (FNA) is frequently discussed. The aim of our study was to assess the usefulness of ultrasound-guided FNA (USG-FNA) of thyroid nodules measuring 1.5 cm or less.

Design: Retrospective review of computerized data and charts of 377 patients who underwent FNA for nodular thyroid disease between June 2001 and August 2006 was conducted. Only patients with available ultrasound findings, FNA diagnosis, and histologic follow-up were included. Fifty-four patients (46 women, 8 men) with a mean age of 47 years (range, 21–73 years) were divided into 2 groups. Group 1 included 14 patients with thyroid nodules 1.5 cm or smaller (range, 0.8–1.5 cm; mean, 1.2 cm). Group 2 included 40 patients with thyroid nodules larger than 1.5 cm (range, 1.7–8.0 cm; mean, 3.5 cm).

Results: FNAs from group 1 were diagnosed as benign (7/14), neoplasm (5/14), nondiagnostic (2/14), suspicious for malignancy (0/14), and malignant (0/14). Sensitivity of 57.1%, specificity of 83.3%, and accuracy rate of 85.7% for USG-FNA of nodules 1.5 cm or smaller were determined. FNAs from group 2 were diagnosed as neoplasm (17/40), benign (14/40), malignant (4/40), nondiagnostic (4/40), and suspicious for malignancy (1/40). Sensitivity of 82.6%, specificity of 58.3%, and accuracy rate of 79.1% for USG-FNA of nodules larger than 1.5 cm were seen.

Conclusions: Our results confirm that USG-FNA is a useful initial evaluation tool for thyroid nodules measuring 1.5 cm or less.

<table>
<thead>
<tr>
<th>Turnaround Times (Minutes)</th>
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<tr>
<td>Order to Routine</td>
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<tr>
<td>Baseline</td>
</tr>
<tr>
<td>Autoverification</td>
</tr>
<tr>
<td>Automation</td>
</tr>
</tbody>
</table>

Cytotechnologists Interpretation for Thyroid Fine-Needle Aspirations  
(Poster No. 49)
Ibrahim Mansoor, MD (ibm979@gmail.com); Farhan Zahid, BS; Danita Beckman, CT(ASCP); Idris T. Ocal, MD. Department of Cytopathology, Yale University School of Medicine, Hamden, Conn.

Context: CLIA-88 outlined in detail requirements for cytotechnologist (CT) performance in gynecologic cytopathology. However, the role of the CT in nongynecologic cytopathology is not clearly defined. The aim of our study is to analyze the interpretation skills of CTs in thyroid fine-needle aspirations. The intent of our study is promotion of quality improvement through enhanced education.

Design: The cytology archives of Yale New Haven Hospital were searched for all consecutive fine-needle aspirations of thyroid nodules with a surgical follow-up performed from 2002 to 2006. CT cytologic interpretations in these cases were compared with the final surgical diagnosis. Cases with nondiagnostic cytology were excluded from calculations. Clinical and surgical follow-ups were also reviewed.

Results: We reviewed 466 fine-needle aspirations of thyroid nodules from 362 patients. Surgical diagnosis of these nodules on thyroid resection was follicular or Hurthle cell adenoma (follicular lesions) in 81, follicular/Hurthle cell carcinoma follicular lesions in 11, papillary thyroid carcinoma in 189, miscellaneous malignancy (medullary, poorly differentiated or anaplastic carcinomas, lymphomas, mets, etc) in 22, and negative/benign in 163 cases.

| Comparison of Fine-Needle Aspiration Biopsy of Thyroid Nodules ≤1.5 cm and >1.5 cm |
|-----------------------------|------------------|-------------------|
| Sensitivity, % | Specificity, % | Positive Predictive Value, % | Negative Predictive Value, % |
| Group 1: nodules ≤1.5 cm (n = 14) | 57.1 | 83.3 | 80.0 | 62.5 |
| Group 2: nodules >1.5 cm (n = 40) | 82.6 | 58.3 | 79.1 | 63.6 |

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Correlating the CT’s interpretation with the final surgical diagnosis revealed true-negative interpretation in 122 cases, true-positive/suspicious in 211, false-negative in 65, and false-positive/suspicious in 43 cases (Table).

**Conclusions:** CTs suggested neoplastic/suspicious for neoplastic process in 151 (88%) of 171 papillary thyroid carcinoma cases and in 47 (53%) of 89 follicular lesions. There were 20 cases of papillary thyroid carcinoma that were undercalled by CTs as benign. Review of these 20 cases showed chronic lymphocytic thyroiditis in 11 of 20 cases, and 9 of 20 were hypocellular with very few epithelial cells. The predominant reason for undercalling follicular lesions was hypocellularity.

<table>
<thead>
<tr>
<th>Correlation of Cytotechnologist’s Cytological Interpretation (Rows) Versus Final Surgical Diagnosis (Columns)</th>
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<tbody>
<tr>
<td>Cytotechnologist’s Cytological Interpretation*</td>
</tr>
<tr>
<td>---------------------------------------------------------------</td>
</tr>
<tr>
<td>Atypical cytology</td>
</tr>
<tr>
<td>FN/HCN</td>
</tr>
<tr>
<td>PTC</td>
</tr>
<tr>
<td>Miscellaneous malignancy</td>
</tr>
<tr>
<td>S/F FN/HCN</td>
</tr>
<tr>
<td>S/F PTC</td>
</tr>
<tr>
<td>Negative/benign</td>
</tr>
<tr>
<td>Nondiagnostic</td>
</tr>
<tr>
<td>Total</td>
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</table>

* FN/HCN indicates follicular neoplasm Hürthle cell neoplasm; PTC, papillary thyroid carcinoma; and S/F, suspicious for.

**POSTER SESSION 500: TUESDAY, OCTOBER 2, 2007, 10 AM–12:30 PM**

**Administrative and Regulatory Affairs; Autopsy and Forensic Pathology; Bone and Soft Tissue Pathology; Cardiovascular Pathology; Clinical Immunology; Endocrine Pathology**

**Essential Elements of a Transfusion Medicine Consultation Report**

(Poster No. 1)

Stephen Samuel, MD (ssamuel@swmail.sw.org); William Koss, MD; Walter Linz, MD, MBA. Department of Pathology, Scott and White Memorial Hospital–Texas A&M Health Science Center College of Medicine, Temple.

**Context:** Clinical pathology has an important consultative role for the optimal practice of medicine. This is particularly true for transfusion medicine. A successful consultation practice requires practitioners to have command of expert level knowledge; be readily accessible for clinical service needs, and have a mechanism that reimburses consultative activity and generates meaningful consultation reports. The first two attributes are specific to a pathology group and its setting. The Centers for Medicare and Medicaid Services (CMS) currently addresses the third attribute by providing three Current Procedural Terminology (CPT) codes for transfusion medicine consultative services. However, although the consultation report itself is critical to both conveying relevant information and securing payment, no published generally acceptable standards exist to define the essential elements of an adequate consultative report.

**Design:** We propose that we have identified the five essential elements of an acceptable transfusion consultation report for CPT 86077 “physician service—difficult crossmatch.”

**Results:** First, an accurate clinical history is necessary in order to substantiate medical necessity. Second, a transfusion history is included in order to integrate current serologic findings with historic findings. Third, a serologic evaluation is provided to offer evidence to support the conclusion of the study. Fourth, a diagnostic interpretation communicates the conclusion. Finally, a comment section conveys nuances of the study and recommendations to the clinician.

**Conclusions:** We have identified five essential elements that address these essential elements and describe the prevalence and distribution of coccidioidal lesions identified in all autopsies performed in an endemic region during a 20-year period.

**Implementing Public Health Recommendations for Rapid Human Immunodeficiency Virus Testing: The Role of the Hospital Laboratory**

(Poster No. 2)

Evan M. Cadoff, MD (cadoff@umdnj.edu); Sindy M. Paul, MD, MPH; Eugene G. Martin, PhD; Gratian Salaru, MD. 1Department of Pathology and Laboratory Medicine, Robert Wood Johnson Medical School, New Brunswick, NJ; 2Division of HIV/AIDS Services, New Jersey Department of Health and Senior Services, Trenton.

**Context:** The Centers for Disease Control and Prevention (CDC) recommends rapid human immunodeficiency virus (HIV) testing both for women in labor with undocumented HIV status and in occupational exposures. New CDC recommendations encourage rapid testing in episodic care settings: hospital emergency departments (EDs) or clinics with little continuity of care.

**Design:** The hospital laboratory is a natural resource for developing effective strategies to implement CDC recommendations. In many jurisdictions, the laboratory has regulatory and accreditation responsibilities for quality assurance oversight. The New Jersey Department of Health and Senior Services and the Robert Wood Johnson Medical School provide a central resource for rapid testing sites throughout the state. To implement CDC recommendations, we helped hospitals customize rapid testing programs.

**Results:** Systems were adapted from the statewide testing program, resulting in several models for rapid testing for labor and delivery, employee health, and EDs. Some hospitals needed coaxing and more than one model: hospital counselors providing testing in the ED under the auspices of the hospital laboratory; nonhospital staff providing testing in the ED under an external laboratory license; hospital clinicians providing counseling, with rapid testing performed in the main laboratory; hospital counselors providing testing under an independent laboratory license; hospital counselors providing bedside testing for inpatients; and rapid testing done offsite by special arrangement. At one site, 56% of patients agreed to be tested; one site had a seroprevalence of more than 10%; and 83% of positives were new HIV diagnoses at one site.

**Conclusions:** Multiple strategies allow hospital laboratories to implement the CDC’s HIV testing goals successfully.

**Coccidioidomycosis: Autopsy Prevalence and Patterns of Dissemination in an Endemic Region**

(Poster No. 3)

John B. Carpenter, MD (jbc2@email.arizona.edu); Jeffrey T. Henderson, MD; John R. Davis, MD; Richard E. Sobonya, MD. Department of Pathology, University of Arizona, Tucson.

**Context:** Coccidioidomycosis is an endemic fungal disease with increasing prevalence in the Sonoran Desert region of North America. Clinical patterns of infection are being increasingly reported. However, the full spectrum of organ involvement remains largely unknown due to the often subclinical nature of the disease process. Coccidoidal infections are considered “isolated” if pulmonary involvement is the only feature and “disseminated” if the disease spreads beyond the lungs. Our purpose was to describe the prevalence and distribution of coccidioidal lesions identified in all autopsies performed in an endemic region during a 20-year period.

**Design:** All autopsies performed at the University of Arizona Health Sciences Center between 1986 and 2006 were reviewed for diagnostic lesions of coccidioidomycosis. Distribution of organ involvement for each patient was recorded.

**Results:** A total of 3150 autopsies were reviewed. Among these, we identified 136 patients (4.3%) with coccidioidal lesions, 104 (3.3%) with pulmonary lesions only, and 32 (1.0%) with disseminated disease. Cases with dissemination involved spleen (n = 19; 59%), liver (n = 17; 53%), central nervous system (n = 11; 34%), kidneys (n = 9; 28%), heart (n = 8; 25%), thyroid (n = 7; 22%), bone marrow (n = 5; 16%), pancreas (n = 3; 9%), adrenal (n = 2; 6%), skin (n = 2; 6%), mediasinum (n = 2; 6%),
esophagus (n = 2; 6%), bone (n = 1; 3%), prostate (n = 1; 3%), colon (n = 1; 3%), and parathyroid (n = 1; 3%).

Conclusions: Coccioidiomycosis shows remarkable variation in its pattern of infection. Solitary pulmonary granulomas are the most frequent finding, but dissemination to uncommon sites, such as spleen, liver, kidneys, heart, and thyroid, may be more common than is clinically recognized.

Adult T-Cell Leukemia and Myelopathy in a Patient With Chronic Human T-Cell Leukemia/Lymphotropic Virus Type 1 Infection
(Poster No. 4)

Jeremy P. Crim, MD (jpcrim@utmb.edu); Gerald A. Campbell, MD, PhD. Department of Pathology, The University of Texas Medical Branch, Galveston.

Human T-cell leukemia/lymphotropic virus type 1 (HTLV-1) is an unusual complex retrovirus. Two types of disease may be caused by HTLV-1 infection: the highly aggressive adult T-cell leukemia/lymphoma (ATLL) and HTLV-1–associated myelopathy/tropical spastic paraparesis (HAM/TSP). Infection does not necessarily result in disease, with a lifetime risk of 5% for ATLL and 1% to 2% for TSP. We present the case of a patient with prolonged neurologic and cutaneous sequelae during a 20-year period as a result of infection with HTLV-1. The patient was a 60-year-old man with a medical history significant for multiple neurologic problems that included gait imbalance, urinary incontinence, seizure disorder, polyneuropathy, and hyperflexia, all clinically attributed to neurosyphilis. The patient was admitted to the hospital due to hypercalcemia (total calcium: 20.2 mg/dL) and confusion, and he then developed a large maculopapular rash that began on his hip and spread extensively over his body. The patient died, and a complete autopsy was performed. Histologic examination revealed a proliferation of large atypical lymphocytes in the skin and lymph nodes. Extensive calcifications were visible in the larger pulmonary blood vessels and alveolar capillaries. The spinal cord demonstrated a myelopathy characterized by demyelination and axonal loss in the anterior and lateral funiculi, with relative preservation of the posterior columns. A blood sample was seropositive for HTLV-1. Complications of HTLV-1 infection are rare but have potentially severe consequences. We present a case in which both HTLV-1 infection and the complications of ATLL and TSP were identified and confirmed by autopsy.

Phosphorylated β-Arrestin 1 Expression in Normal Human Tissue
(Poster No. 6)

Mansoor Nasim, MD, PhD (Pathoram@yahoo.com); Wanghai Zhang, MD; Payam Arya, MD; Edward Lee, MD. Department of Pathology, Howard University, Washington, DC.

Context: Arrestin is a group of proteins involved in regulation of 7-membrane-spanning receptor signaling pathway. The gene for this protein has been mapped to 11q13. The Arrestin protein family has 4 isoforms, 2 of which are expressed specifically in the visual system (visual and cone Arrestin), and expression of the other 2 molecules, β-Arrestin 1 and 2, in the human body needs clarification. Protein x-ray structure of β-Arrestin 1 molecule was found to have binding sites that could be hypothetically used to inhibit its function, providing an opportunity for new drug development. This molecule is known to activate MAP kinases. We are investigating the molecular bioexpression in normal human tissue of this molecule in its active phosphorylated form.

Design: We tested 99 cores of human tissue and examined 33 types of normal human organs (tissue microarray slide). The β-Arrestin 1 expression was examined qualitatively and semiquantitatively using immunohistochemistry.

Results: Focal staining was observed in adrenal cortical cells, neurons, oligodendroglial cells, stroma of ovary, stroma of endometrium, muscularis mucosa of gastrointestinal tract, stroma of the prostate, endothelial cells, lymphoid tissue, pneumocytes, Sertoli-Leydig cells, myoepithelial cells in breast tissue, blood vessels (tunica media), weak staining of bone marrow constituents. In other organs the staining was negative.

Conclusions: This indicates that the β-Arrestin 1 molecule expression in normal organs is focal and weak and is restricted to mainly blood vessels, myoepithelial cells, stroma, Sertoli-Leydig cells, oligodendroglial cells, and neurons. This expression may reflect the functionality of this molecule. Further studies are required to elicit its function in pathologic states.

Disseminated Cryptococcosis With Pulmonary Lymphangioleiomyomatosis
(Poster No. 7)

Sanam Husain, MD (sanam-husain@ouhc.edu); Ranjana Gotti pattii, MD; Willard Aronson, MD. Department of Pathology, University of Oklahoma, Health Sciences Center, Oklahoma City.

Lymphangioleiomyomatosis of the lungs is a rare, progressive, cystic lung disease that primarily affects young women. The disease is characterized by nonneoplastic peribronchial, perivascular, and perilymphatic proliferation of smooth muscle cells, resulting in airway and vascular obstruction. Occurrence is sporadic or more commonly associated with tuberous sclerosis complex. We present an autopsy case of a 31-year-old white woman who presented with complaints of severe dyspnea, cough, and bleeding. She was admitted for possible sepsis due to methicillin-sensitive Staphylococcus aureus and was started on appropriate antibiotics.

Her medical history was significant for diabetes mellitus, deep venous thrombosis, rheumatoid arthritis, and chronic renal failure. Physical examination revealed tachycardia, tachypnea, bilateral rales on chest auscultation, and weakness in the lower limbs. Her course in the hospital was complicated by renal failure and she developed cardiopulmonary arrest 12 days after admission. An autopsy restricted to the chest and abdomen was performed. Major autopsy findings included bronchi filled with blood and multiple small cysts distributed bilaterally throughout the lung parenchyma. Microscopic examination of the lungs revealed abnormal proliferation of smooth muscle cells around cystic spaces, lymphatics, and blood vessels (Figure 28). The smooth muscle cells stained positive...
Fibromuscular dysplasia (FMD) is a segmental noninflammatory, non-atherosclerotic vascular disease that has been described in almost every organ system of the body. It involves arterial beds, including the cerebral and coronary arteries. FMD of cerebral arteries is a rare entity that is usually associated with fatal complications, especially in immunocompromised patients. Our findings reveal the potential for involvement of several vascular beds in a single patient—a ruptured anterior communicating artery aneurysm and a right coronary artery dissection occurring in a 38-year-old woman. At autopsy, FMD was found in multiple vascular beds. Our findings reveal the potential for involvement of several vascular beds in patients with FMD resulting in multiple vascular complications.
Pathologic Findings in Wolman Disease
(Poster No. 14)

Kenata A. Joffe, MD (k2186@columbia.edu); Brett Lauring, MD, PhD; Suzanna Aiaian, MD; Hermann Schubert, MD Department of Pathology, Columbia University, New York, NY.

Wolman disease, first described by Wolman in 1956, is a severe, rare lipid storage disorder due to the deficiency of lysosomal acid lipase. This autosomal recessive disease is marked by accumulation of cholesteryl esters and triglycerides in multiple organs. It affects both males and females. There is no specific treatment for this condition, and it is usually fatal by the age of 2. We report an interesting autopsy case of a 10-week-old boy with confirmed Wolman disease in which electron microscopy and ocular pathology were performed. Previous case reports including ocular changes in Wolman disease are limited. Hepatosplenomegaly, calcification of the adrenal glands, and yellow-orange discoloration of the internal organs were among the main gross findings. Microscopically, lipid deposits and foamy macrophages were seen in virtually every organ, although they were more prominent in the small bowel, liver, spleen, adrenal glands, lymph nodes, and endothelial cells. The liver showed marked diffuse steatosis, cholestasis, and pericellular fibrosis. Iron and Oil Red O stains highlighted the diffuse Kupffer cell hemosiderosis and the extensive deposits of lipid in the hepatic parenchyma, respectively. Electron microscopy demonstrated the characteristic elliptical cholesterol clefts, predominantly in the Kupffer cells of the hepatocytes. Ocular pathology revealed vacuolization of multiple structures of the eye, including the epithelial layer of the cornea, the iris pigment epithelium and nonpigmented layer of pars plana, the iridal constrictor muscle, ganglion cell layer, inner nuclear layer, and optic nerve. The coroidal vessels also showed vacuolization of the endothelial cells, with macrophages in the lumen.

Hemophagocytic Lymphohistiocytosis in a Newborn Associated With Neonatal Giant Cell Hepatitis
(Poster No. 15)

Alex John, MD (alex-john@uhsce.edu); Eric Harp, DO; Willard Aronson, MD; Nasir Bakshi, MD. Department of Pathology, University of Oklahoma, Oklahoma City.

Hemophagocytic lymphohistiocytosis (HLH) is an uncommon syndrome characterized by fever, rash, splenomegaly, and multiple cytopenias. Because of the overlap of clinical symptoms with more common neonatal diseases, the diagnosis is often delayed, allowing for rapid disease progression. We present a case of a male neonate born at 37 weeks of gestation with mild neonatal hyperbilirubinemia. He was treated with phototherapy and discharged after 48 hours. At 6 weeks of age, he became febrile and was investigated for sepsis, which was negative. Shortly after, fever returned with a maculopapular rash, anemia, thrombocytopenia, and elevated liver transaminases. Routine bacteriology and virology were negative. Because of hepatic symptoms, a liver wedge biopsy was performed which showed necrosis, giant cell change and mild chronic inflammation. A diagnosis of neonatal giant cell hepatitis was made. A bone marrow biopsy at that time was nondiagnostic. As the disease progressed, he developed massive hepatosplenomegaly, worsening pancytopenia, and persistent fever. Further diagnostic workup, including elevated bilirubin, ferritin, lactate dehydrogenase, and triglycerides later combined with his current presentation were supportive of HLH. He was treated, but he ultimately died 2 months after his initial fever. Clinical laboratory and postmortem anatomic findings in bone marrow, liver, and spleen demonstrated a classic case of HLH. Liver involvement of HLH is well described and leads to the hepatomegaly seen clinically. The histology is characteristically described as a portal lymphohistiocytic infiltrate, with fulminant hepatocyte necrosis being less common. To our knowledge, premortem, biopsy-proven, neonatal giant cell hepatitis seen in association with HLH has not been previously reported.

Histiocytoid Cardiomyopathy: A Case Report and Review of the Literature
(Poster No. 16)

Dana L. Altenburger, MD (dlaltenb@neoucom.edu); Thomas J. Bollinger, MD, MPH; Orlando Gonzalez, MD. Department of Pathology, Orlando Regional Healthcare System, Orlando, Fl.

Histiocytoid cardiomyopathy is a rare condition of unknown etiology, with fewer than 100 cases reported worldwide. This condition usually presents with sudden death in girls younger than 2 years. The autopsy was performed by the 2 residents on autopsy service and was supervised by our institution’s pediatric pathologist. A 2-week-old female infant presented to an urgent care facility with a vague medical history of vomiting,
diarrhea, and heart murmur. The patient was in extremis and had inau-
dible heart sounds. Resuscitative efforts were unsuccessful. Her autopsy
was significant for an 83-g heart with a pale yellow myocardium and
three 0.2-cm tan-yellow subendocardial nodules on the tricuspid valve.
Histologically, the myocardium and subendocardial nodules contained
large foamy granular cells consistent with histiocytoid cardiomyopathy.
Histiocytoid cardiomyopathy is an unusual autopsy finding; however, this
rare entity must be considered in cases of infant sudden death. A thor-
ough inspection of heart valves and myocardium should be conducted in
all infant sudden death cases, as the gross and histologic pathologic find-
ings of this entity are subtle. A literature review and case comparison will
be discussed (Figure 30).

**Diffuse Pulmonary Ossification and Pulmonary Tumor Thrombotic Microangiopathy**

(Poster No. 19)

Sonal N. Kamat, MBBS, MD1 (kamatson@hotmail.com); Jela Bandovic,
MD2 Department of Pathology, North Shore Long Island Jewish Health
System, New Hyde Park, NY; 2Department of Pathology, North Shore Uni-
versity Hospital, Manhasset, NY.

Pulmonary tumor thrombotic microangiopathy (PTTM) is characterized
by widespread fibrocollascular intimal proliferation of the small pulmonary
arteries and arterioles in patients with metastatic carcinoma. A rare case of
PTTM with gastric adenocarcinoma has been identified, including chronic
lymphedema, prior irradiation, and exposure to environmental carcino-
gens, such as Thorotrast. Rare cases of angiosarcoma have been reported
in association with foreign materials, such as synthetic graft material (usu-
ally Dacron), surgical sponges, and steel. We report a case of epithelial
angiosarcoma involving the lung and ovary 2 years after insertion of an
ileofemoral Dacron bypass graft. To our knowledge, there are no pub-
lished reports of epithelial angiosarcoma in these 2 locations in associ-
ation with Dacron graft material. We discuss the clinical and pathologic
findings of angiosarcoma and review the literature regarding foreign
body tumorgenesis.

**Sudden Death Following Recent Onset Pulmonary Hypertension Related to Pulmonary Arterial Tumor Microemboli From an Undiagnosed Breast Carcinoma**

(Poster No. 20)

Prabhakar D. Borge, MD, PhD (dayandborg@yahoo.com); John
Wurzel, MD, Department of Pathology and Laboratory Medicine, Temple
University Hospital, Philadelphia, Pa.

Pulmonary arterial tumor microemboli are a recognized but rare cause
of pulmonary hypertension. In this case, a 67-year-old woman with a
recent onset of pulmonary hypertension died suddenly. Gross autopsy
examination showed scattered small pulmonary infarcts and scars but no
pulmonary artery atheromas or thromboemboli. Cardiomegaly with bi-
ventricular hypertrophy and right atrial and ventricular dilation were
also noted. Histologic examination of the lungs confirmed the presence
of the infarcts and scars. Small elastic and muscular arteries showed me-
 vantricular hypertrophy and right atrial and ventricular dilatation were
also noted. Histologic examination of the lungs confirmed the presence
of the infarcts and scars. Small elastic and muscular arteries showed me-

tive for CK7, CK20, and carcinoembryonic antigen and negative for TTF-
1. PTTM is a rare entity and is observed in 0.9% to 3.3% of autopsies with
malignant tumors. Few cases are diagnosed antemortem, but they should
be considered in the differential diagnosis of pulmonary hypertension.
Diffuse pulmonary ossification is also a rare finding. Even more rare is
diffused pulmonary ossification and pulmonary tumor thrombo-
ictic microangiopathy.

**Epithelioid Angiosarcoma of Bladder and Ovary After Ileofemoral Bypass Graft: A Case Report and Review of the Literature**

(Poster No. 18)

Alma R. Reyes, MD (alma.reyes@beaumont.edu); Mariza DePeralta-
Venturina, MD Department of Anatomic Pathology, William Beaumont
Hospital, Royal Oak, Mich.

Angiosarcoma is a malignant vascular tumor that comprises less than
1% of all soft tissue tumors. They can occur anywhere in the body but
have a predilection for skin and superficial soft tissue. Several predispos-
ing factors for angiosarcoma have been identified, including chronic
lymphedema, prior irradiation, and exposure to environmental carcino-
gens, such as Thorotrast. Rare cases of angiosarcoma have been reported
in association with foreign materials, such as synthetic graft material (usu-
ally Dacron), surgical sponges, and steel. We report a case of epithelial
angiosarcoma involving the lung and ovary 2 years after insertion of an
ileofemoral Dacron bypass graft. To our knowledge, there are no pub-
lished reports of epithelial angiosarcoma in these 2 locations in associ-
ation with Dacron graft material. We discuss the clinical and pathologic
findings of angiosarcoma and review the literature regarding foreign
body tumorgenesis.
Acute Hemorrhagic Leukoencephalopathy: A Case Report of an Autopsy Diagnosis (Poster No. 21)

Elizabeth L. Gilmore, DO1 (elizabeth.gilmore@ttuhsc.edu); Alek Milovanovic, MD2; Thomas Bearer, MD; Surender Bodhireddy, MD3.1 Department of Pathology, Lubbock County Medical Examiner, Texas Tech University Health Science Center, Lubbock; 2Department of Pathology, Lubbock; 3Department of Pathology, Covenant Health System, Lubbock, Tex.

After having a short upper respiratory illness, a 63-year-old white man lying supine in his bed and had brown, dried emesis on his face and shirt. His medical history was significant for congestive heart failure. He rarely left his home and had not been seen for a week prior to his discovery. At autopsy, the most striking finding was numerous petechial peri-vascular hemorrhages limited to the white matter of the brain. The white matter hemorrhages distinctly spared the meninges, gray matter, and U-fibers (Figure 3). There was no skin rash, and the general autopsy findings were otherwise noncontributory. Microscopically, the perivascular hemorrhages of the white matter were accompanied by very scant inflammation. Luxol fast blue stain revealed areas of demyelination throughout the life span. This case is unique due to the prominent petechial hemorrhages within the white matter. It is an important diagnosis to consider in cases of sudden death or severe acute illness. We will discuss the autopsy diagnosis and differential diagnosis and present a literature review of this condition.

Solitary Synovial Osteochondroma of the Knee: A Clinicopathologic Review of 4 Cases With Radiographic Correlation (Poster No. 22)

Rania Abadeer, MD1 (rania.a.abadeer@uth.tmc.edu); Emanuela Veras, MD2; Alberto Ayala, MD; Dongfeng Tan, MD3.1 Department of Pathology and Laboratory Medicine, University of Texas Southwestern Medical Center, Dallas; 2Department of Pathology, Hospital, Houston, Tex; 3Department of Molecular Genetics and Pathology, The University of Texas M. D. Anderson Cancer Center, Houston.

Context: Solitary synovial osteochondroma (SSO) is a rare variant of extraskeletal osteochondroma, with only few individual cases reported in the literature to date. A systematic study of SSO has not been documented.

Design: Four cases of SSO were retrieved from our departmental files. Histopathology was reviewed. A radiographic and clinicopathologic correlation was obtained and evaluated.

Results: Patient ages ranged from 33 to 59 years. All patients presented with a knee mass. Painful mass and limitation of joint motion were the main complaints. Mass size ranged from 4.5 to 6.5 cm. Two of the cases were suspicious for chondrosarcoma on imaging studies. Grossly, all cases demonstrated a well-demarcated mass consisting of multiple cartilaginous lobules surrounded by fibro-adipose tissue. Histologically, all 4 SSOs consisted of lobulated adult-type hyaline cartilage with central sotty calcification and ossification, features similar to those seen in the osteochondroma of the bone. Cytological atypia, including hypercellularity and binucleation, was noted in 1 case. However, no infiltrating borders, mitosis, or adjacent bone involvement was identified. All 4 patients underwent surgical excision only, with no recurrences documented to date.

Conclusions: The knee is a frequent site of SSO. Radiographically and, to some degree, histologically, SSO may mimic a chondrosarcoma. Histologic features distinguishing these 2 entities are absence of mitosis, infiltrating borders, and bone permeation in SSO. The correct recognition of SSO depends on a combined radiographic and clinicopathologic correlation.

Expression of Master Transcription Factors (Osterix, Runx2, and Sox9) in the Osteoid Osteoma, Osteoblastoma, Chondroblastoma, and Chondromyxoid Fibroma (Poster No. 23)

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Context: Progress in skeleton molecular biology has lead to clarification of the transcriptional mechanisms of chondrocytes and osteoblast differentiation in bone growth. Three master transcription factors (Osterix, Runx2, and Sox9) play pivotal roles in early mesenchymal condensation and determination of osteo-chondrogenic fate.

Design: The aim of the present study was to evaluate the expression of these 3 master transcription factors in 4 rare types of the following benign bone tumors: chondromyxoid fibroma, chondroblastoma, osteoblastoma, and osteoid osteoma. Immunohistochemical stain method utilizing a tissue microarray and Western blot analysis were used.

Results: Osteoid osteoma and osteoblastoma showed 100% (12/12) strong nuclear expression of Osterix and Runx2, whereas 3 (38%) of 8 chondroblastoma showed positive nuclear expression of Osterix. Strong nuclear expression of Sox9 was detected in all 8 (100%) chondroblastoma. Five (of 12; 41%) osteoblastomas showed diffuse cytoplasmic Sox9 staining. Focal nuclear Sox9 expression was demonstrated in 1 osteoblastoma. This is the first report implicating these 3 essential transcription factors (Sox9, Runx2, and Osterix) in the regulation of cartilage and osseous differentiation pathways in benign bone tumors.

Conclusions: These findings confirm that osteoblastoma and osteoid osteoma have phenotypic features corresponding to the early condensational phase of osteogenic differentiation. In contrast, chondroblastoma and chondromyxoid fibromas have phenotypic features corresponding to the early condensational phase of cartilaginous differentiation. A subset of osteoblastoma and chondroblastoma appears to have biphasic phenotypic features of both osteogenic and cartilaginous differentiation.

Myxoid Areas and Delicate Vascular渠道 Pitfalls in Diagnosis of Massive Localized Lymphedema (Poster No. 24)

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Massive localized lymphedema (MLL) is a recently described rare lesion that presents most often as a large soft tissue mass affecting the extremities of morbidly obese adults. Diagnosis of this entity can be challenging, and it is often mistaken for well-differentiated liposarcoma and fibromatosis. Recognition of the unique features of MLL will help in making the correct diagnosis, thus impacting significantly on the management of the patient. We present a 40-year-old morbidly obese woman with a recurrent, long-standing, large soft tissue mass in the posterior-medial aspect of her right thigh. There was no skin or bone involvement. Following surgical excision, a full gross and microscopic examination was performed. The specimen consisted of a 1.0-kg, 50-cm, poorly circumscribed, lobulated mass. Histologic exam revealed a homogenous lesion with abundant mature adipose tissue compartmentalized by fibrous septa containing rare atypical stromal cells. Myxoid and edematous areas with fluid-filled cysts were also observed. Of particular interest were myxoid ar-
Serous Atrophy of Bone Marrow

(Poster No. 25)

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Context: Serous atrophy is a degenerative/reactive change in the bone marrow classically observed in states of malnutrition, acquired immunodeficiency deficiency syndrome, neoplasia, and other systemic illnesses. Histopathologically, it manifests as homogeneous extracellular eosinophilic material deposited in hematopoietic and fatty marrow in a focal or diffuse distribution associated with adipocyte atrophy and loss of hematopoietic elements.

Conclusions: Serous atrophy is associated with a wide variety of systemic and localized disease processes and is not specific for any one disorder. This likely reflects the limited repertoire of marrow to respond to the demands of systemic and localized disease processes. Serous atrophy is a common finding in bone marrow specimens and is not specific for any one disorder. It likely reflects the limited repertoire of marrow to respond to the demands of systemic and localized disease processes.

Vascular Endothelial Phenotype in Mesenchymal Cells in a Lipoblastoma

(Poster No. 26)

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Phenotypic plasticity between adipocytic cells and vascular endothelial cells has been shown in a variety of adipocytic tumors and in normal adipose tissue. To our knowledge, this has not been previously investigated in lipoblastomas. Routine histologic staining, lipoid stains, and immunohistochemical staining for vascular endothelial markers (CD34, CD31, factor VIII–related antigen) were variably positive for CD34, CD31, and factor VIII–related antigen. Mesenchymal cells and lipoblasts in lipoblastoma can exhibit phenotypic markers characteristic of vascular endothelium. This adds further support to the concept of phenotypic plasticity in adipocytic tumors and suggests further study of a larger series of lipoblastomas.

Malignant Perivascular Epithelioid Cell Tumor in a Child: Clinical, Histologic, and Immunohistochemical Features of a Rare Tumor

(Poster No. 27)

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Most neoplasms demonstrating perivascular epithelioid cell differentiation (PEComas) are benign; however, a small subset behaves in a malignant fashion. A 6-year-old girl presented with intermittent abdominal pain; computed tomography scan showed dispersed necrotic masses in the pelvis, liver, spleen, and right adrenal. Serum CA 125 was mildly elevated; AFP, β-HCG, and urinary VMA and HVA were normal. Light microscopy of a biopsy demonstrated sheets of epithelioid cells divided into nests by thin fibrovascular septa. The cells had large, round nuclei, prominent eosinophilic nucleoli, stippled chromatin, abundant granular eosinophilic cytoplasm, and distinct cytoplasmic membranes. A few cells contained periodic acid-Schiff–positive/diastase-resistant hyaline globules but no crystalline inclusions. There were occasional mitotic figures and focal vascular invasion; necrosis was absent. Most tumor cells stained for HMB-45 and TFE3; occasional cells stained for desmin and smooth muscle actin. The cells showed normal staining for BAP1 and were negative for Myo-D1, Melan-A, S100, caldesmon, cytokeratin AE1/AE3, EMA, AFP, PLAP, CD30, inhibit, CA 125, Hepar-1, synaptophysin, and chromogranin. A diagnosis of malignant PEComa was rendered. Malignant PEComas are rare in children. The differential diagnosis includes germinoma, carcinoma, amelanotic melanoma, clear cell sarcoma, and alveolar soft part sarcoma. Nuclear staining for TFE3 is typically associated with pediatric renal cell carcinoma and alveolar soft part sarcoma; however, the profile of nuclear TFE3 and cytoplasmic HMB-45 staining appears to be unique to PEComa. TFE3 should be included in the immunohistochemical panel to evaluate epithelioid neoplasms of uncertain histogenesis.
of paraffin-embedded tissue was performed and finally revealed the presence of the SYT-SSX chimeric fusion transcript specific for synovial sarcoma. This case report highlights the equivocal immunohistochemical staining pattern left for diagnosis. In a synovial sarcoma arising in an unusual, nonsoft tissue location. This case report also presents a 3′ sequence deletion involving the SYT gene not previously reported for synovial sarcoma and emphasizes the importance of utilizing a combination of molecular and cytogenetic techniques when confronted with a particularly challenging sarcoma.

**Cardiac Synovial Sarcoma: A Clinicopathologic Analysis of 3 Cases**

(POSTER NO. 32)

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**Context:** Cardiac primary sarcomas (CPSs) are rare and represent less than 25% of primary cardiac tumors. Rarer are cardiac synovial sarcomas (CSSs), and what is known is limited to case reports. Therefore, the clinicopathologic features of 3 patients with this neoplasm who were seen and treated at our institution during a 13-year period are presented.

**Design:** Our files yielded 3 cases of primary CSSs of 25 CPSs. The clinical records and pathology materials were reviewed. In addition to routine examination of hematoxylin-eosin material, immunohistochemistry was performed with pan-cytokeratin, epithelial membrane antigen (EMA), BCL-2, vimentin, and CD138. All patients had a pacemaker prior to initial diagnosis. Two patients had a ventricular septal defect and one had a patent ductus arteriosus. None of the patients had a prior history of a synovial sarcoma.

**Results:** All 3 patients were men. Their ages were 35, 51, and 53 years, respectively. Dyspnea was the most common symptom at presentation. The tumors arose from right ventricle, left atrium, and right atrium, respectively. Histologically, 2 CSSs were biphasic and 1 was monophasic. All tumors stained strongly for vimentin and focally for cytokeratin and EMA. Focal staining for BCL-2 was seen in the monophasic CSS. All CSSs were negative for S100 protein, desmin, smooth muscle actin, and CD34. No metastases were seen at the time of diagnosis. Two patients developed recurrences 1 year after initial surgery but have survived 6 months and 9 years, respectively. The remaining patient, who had local extension into lung and mediastinum of his tumor, died of complications 1 month after surgery.

**Conclusions:** CSSs are rare and very aggressive neoplasms that may recur if incompletely excised. Early diagnosis and complete surgical resection with adjuvant chemotherapy and radiotherapy may improve the survival.

**Clinical Presentation and Patterns of Lymphocytic Myocarditis: The Challenge of Establishing a Viral Etiology**

(POSTER NO. 33)

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**Context:** True prevalence of viral myocarditis is unknown; because its clinical presentation varies from mild to even fatal cardiac dysfunction, early diagnosis is critical yet challenging. We review several cases of lymphocytic myocarditis and discuss methods used to increase diagnostic sensitivity.

**Design:** A database search from 2001 to 2007 identified 5 autopsies and 1 endomyocardial biopsy with lymphocytic myocarditis. Histologic findings were analyzed in the context of clinical presentation, comorbidities, laboratory data, and molecular studies.

**Results:** Review of all 6 cases revealed common clinical presentations of respiratory distress and prodromal symptoms. All had evidence of myocarditis of variable degree according to the Dallas criteria. Comorbid conditions included hypertension (2), diabetes (2), human immunodeficiency virus (2), and pulmonary hypertension (2). Other findings included cardiomyopathy (6), cardiac dilatation (4), and pericardial effusion (4). Infection was suspected in all 6 cases, although definitive etiologies were not determined. Two cases were suggestive of cytomegalovirus and human herpesvirus 6 infection, with positive immunofluorescence and electron microscopy findings, respectively.

**Conclusions:** Establishment of the diagnosis remains the diagnostic gold standard of acute myocarditis, despite low sensitivity. Revived interest in noninvasive imaging to identify potential biopsy patients and revised Dallas criteria may facilitate diagnosis. Establishing etiology can then permit essential, even virus-specific, therapy. Serology and immunohistochemistry can help, but viral genomic detection using molecular methods significantly increases sensitivity. Thus, viral myocarditis must be included in the differential diagnosis of disease of uncertain etiology. Obtaining op-
timal serum and tissue samples at biopsy or autopsy increases the like-
lihood of making a definitive, specific diagnosis of viral myocarditis.

**Histogenesis of Cardiac Myxomas: The Methodist Hospital Experience**  
(Poster No. 34)

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**Context:** Myxomas are the most frequent benign cardiac tumors. There 
is considerable controversy regarding their histogenesis, and previous 
studies have suggested a primitive mesenchymal, endothelial, and sub-
endocardial cell origin. We performed a panel of immunohistochemical 
markers to elucidate the histogenesis of cardiac myxomas.

**Design:** A total of 17 myxoma cases (10 women and 7 men, median 
age 58 years) diagnosed between 2000 and 2005 at The Methodist Hospital 
were identified, and tissue microarray blocks were prepared from the 
original paraffin-embedded blocks. Immunohistochemical study was 
performed with antibodies to CD31, CD34, FLI-1, OCT-4, D2-40, smooth 
muscle actin (SMA), E-cadherin, and CD117. Stromal cells, vascular endo-
thelial cells, surface lining cells, and cells around the vascular spaces 
were assessed separately for each marker.

**Results:** In all 17 cases, stromal cells failed to reveal immunoreactivity 
and focally, the surface lining cells. Focal positivity of the endothelial 
and surface lining cell was observed with CD31 in 2 cases. In all of the cases, 
SMA highlighted the vascular smooth muscle cells and the majority of the 
markers stained the granular hemosiderin pigment present within tumor cells.

**Conclusions:** The morphologic pattern of the myxomas was character-
ized by the presence of polygonal or stellate stromal cells within a myxoid 
background, with hemosiderin-laden macrophages and numerous ves-
cular structures. No heterologous component was identified. Our results 
show that cardiac myxomas do not follow a consistent pattern of immu-
noreactivity to these markers and reaffirm that a candidate marker for 
these tumors is yet to be identified.

**Rapid Cardiac Failure and Death Due to Giant Cell Myocarditis Associated With Myositis, Thymoma, and Myasthenia Gravis**  
(Poster No. 35)

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Giant cell myocarditis is a rare cause of acute heart failure with variable 
clinical presentation. It occurs independently, but a rare association with au-
timmune processes exists. The patient's medical records and available pa-
thology case were reviewed. A full gross and microscopic autopsy was per-
formed. A 39-year-old white woman with a history of thymoma, myositis, 
and myasthenia gravis presented with mideast chest pressure radiating to 
her left shoulder, neck, and jaw following 3 weeks of cough, progressive short-
ness of breath, and fever. The patient was transferred to our institution for 
cardiac catheterization. She rapidly decompensated, developed cardiogenic 
shock with mitral valve failure, and died despite aggressive treatment. At 
autopsy, severe pericardial adhesions were present. The heart was diffusely 
soft and boggy, with right and left ventricular dilatation. Histology showed 
excessive myocardial necrosis with a lymphohistiocytic infiltrate containing 
numerous CD68-positive giant cells (Figure 34). Skeletal muscle examination 
revealed a mild to moderate active inflammatory myopathy with isolated 
multinucleated giant cells. Metastatic thymoma was present in pleural-based 
lesions within the posterior thorax and over the diaphragm. This case is un-
usual, as it represents a rare presentation of giant cell myocariditis associated 
with giant cell myositis, thymoma, and myasthenia gravis. Its addition to the 
10 previously reported cases adds to the strength of this clinical association 
and further supports the idea of an underlying autoimmune cause linking 
the various entities.

**Eosinophilic Arteritis of the Temporal Artery**  
(Poster No. 37)

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We present an unusual case of segmental eosinophilic arteritis of the 
temporal artery. Review of the records reveals that the patient was a 66-
year-old white man who presented to his doctor with symptoms suggestive 
of giant cell arteritis. At that time, his erythrocyte sedimentation rate 
was 44, and a temporal artery biopsy was performed. Step sections 
through a serially sectioned muscular artery were examined. Vasculitic 
was present, with focal areas of numerous eosinophils ringing the artery 
and present within the arterial wall. There was a focus of intimal prolif-
eration with fibrovascular tissue containing lymphocytes and numerous 
eosinophils. Focal destruction of the elastic membrane was noted, but gi-
ant cells at the level of the elastic membrane with ingestion of elastica 
were not seen. A giant cell was noted within the intimal plaque. Eosin-
ophils are unusual in giant cell arteritis. We will explore the differential 
diagnosis for patients presenting with the clinical syndrome of temporal 
arthritis, which includes Churg-Strauss-related vasculitis (including iso-
lated Churg-Strauss vasculitis), drug reaction (including but not limited to 
Dapsone, Minocycline, and nonsteroidal anti-inflammatory drugs), ANCA-
associated vasculitis, isolated eosinophilic vasculitis, systemic hyper-
pereosinophilia with vasculitis, and vasculitis associated with lympho-
proliferative (primarily T-cell lymphoma) or myeloproliferative (primarily 
acute myelocytic with eosinophilia) disorders. It is important for pathol-
ologists to keep this variant of arteritis in mind when reviewing cases of 
potential giant cell arteritis.
Aging and devise a simple neutrophil function test protocol for use in a clinical setting. (Poster No. 38)

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Aortic dissection has a high mortality rate. In younger individuals, it is most commonly associated with Marfan syndrome. *Clostridium septicum* infection is a rare cause of aortic dissection that is typically seen in elderly patients with colonic neoplasms. Here we present an unusual autopsy case of a young individual. A 22-year-old white man with morbid obesity and hypertension presented with acute onset of sensory and motor dysfunction in the lower extremities. No pedal pulses were palpable. Computed tomography scan of the abdomen revealed occlusive thrombosis of the distal aorta with extension to the iliac arteries. The patient died before an arteriogram could be performed. Postmortem examination revealed acute aortic dissection involving the entire length of the aorta with occlusion of the distal portion by a large blood clot in the false lumen. There was a transverse intimal tear in the ascending aorta, rupturing into the pericardial sac with massive hemopericardium. No evidence of Marfan syndrome was present. No neoplasm was identified. Microscopic section showed aortitis with gram-positive rods in the aortic wall. Postmortem blood culture was positive for *C. septicum*. Review of the literature revealed that there are only 21 reported cases of *C. septicum* aortitis; all patients were elderly, and 15 of them had an associated colonic neoplasm. To the best of our knowledge, this is the first report of such a condition causing death in a young individual.

**Age-Related Decrease and a Simple Flow Cytometric Assay of Neutrophil Function** (Poster No. 39)

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**Context:** We intended to confirm a decline in neutrophil function with aging and devise a simple neutrophil function test protocol for use in a clinical setting. Conversely, the reliability of this protocol was to be confirmed by detectability of a decline in neutrophil function with aging.

**Design:** Whole-blood samples from young (30s, n = 32) and old (60s, n = 32) healthy subjects were incubated with the 7-aminoactinomycin D-stained *Escherichia coli*. The mixture was stained by dihydrodohamide 123 as an oxidative probe. Two kinds of fluorescence were measured by flow cytometry.

**Results:** Phagocytosis declined with aging, as indicated by a decrease in the percentage (from 28.2% ± 9.5% to 21.9% ± 10.9%; P < .05) and the mean fluorescence intensity ratio (from 1.67 ± 0.27 to 1.51 ± 0.27; P < .05). Oxidative burst had a trend toward a decrease with aging, but the differences were not significant (percentage: from 35.3% ± 13.2% to 32.1% ± 14.1%; P = .36; mean fluorescence intensity ratio: from 5.26 ± 3.23 to 5.08 ± 3.55; P = .84).

**Conclusions:** The devised protocol in this study could detect a significant decline in neutrophil function with aging, and this protocol may be useful for the assessment of neutrophil function in a clinical setting.

**High-Performance Liquid Chromatography Analysis of the Hemoglobin Fractions: Effects of Specimen Processing on the Accuracy of Measurements** (Poster No. 40)

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**Context:** High-performance liquid chromatography is currently used as a major analytical procedure in hemoglobin studies. For practical purposes it is important to know whether specimen exposure to room temperature could affect the accuracy of hemoglobin fractions' measurements.

**Design:** To answer this question we conducted repeated hemoglobin measurements on blood specimens that after the initial analysis were deliberately exposed to room temperature conditions for 24 hours and 7 days.

**Results:** We found that even after 24 hours' exposure to room temperature, the measured levels of hemoglobin A, A2, and F were essentially the same. The minor fluctuations that were seen could not affect the clinical interpretation of the results. A minimal decrease was observed in the level of the P2 fraction representing the hemoglobin A2 component. The P3 fraction showed about 15% elevation comparative with the initial level. After 7 days' exposure to room temperature there was a further increase in the level of P3 (about 90%). At this point the clinically significant fractions (F and A2) started showing more substantial changes that could interfere with the clinical interpretation.

**Conclusions:** Our findings indicate that the P3 hemoglobin fraction is the most sensitive fraction to room temperature exposure. Elevation of this fraction could be used as an indicator of inappropriate handling of the blood specimen. At the same time, the A2 fraction demonstrated that accurate and acceptable measurements of clinically relevant fractions (F and A2) could be obtained even after 24-hour specimen exposure to room temperature conditions.

**BRAF Mutational Status in the Cribriform Morular Variant of Papillary Thyroid Carcinoma** (Poster No. 41)

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**Context:** The cribriform morular variant of papillary thyroid carcinoma (CMVPTC) is a rare variant of papillary thyroid carcinoma that occurs sporadically and in association with familial adenomatous polyposis. This morphologically distinct variant of papillary thyroid carcinoma is characterized by a cribriform architecture that is coupled with squamous or spindleled morules. Few prior studies have characterized the molecular genetic abnormalities in CMVPTC. APC tumor suppressor gene inactivation, β-catenin gene mutations, and ret/PTC oncogene activation have been reported. BRAF and ret/PTC alterations are frequently associated with conventional papillary thyroid carcinoma. The mutational status of the BRAF gene has not been reported in CMVPTC.

**Design:** Four cases of CMVPTC were identified and included in this study; 1 occurred in association with FAP, whereas the other 3 were sporadic. The tissue in all cases was formalin fixed and paraffin embedded. DNA from 3 cases was extracted using the High Pure PCR Template Preparation Kit, amplified via primerase chain reaction (PCR) and purified using ExoSAP-IT (USB 78200). DNA sequencing was performed using the BigDye Terminator kit and analyzed using the ABI Prism 310 Genetic Analyzer.

**Results:** The 4 cases demonstrated characteristic morphologic features of CMVPTC. The lesions ranged in size from 1 to 3 cm. Only 1 case had amplifiable DNA and successful sequencing reaction. This case was negative for the BRAF mutation.

**Conclusions:** CMVPTC is a morphologically distinct variant of papillary thyroid carcinoma that occurs sporadically and in association with familial adenomatous polyposis. Mutation of BRAF does not appear to play a role in the tumorigenesis of CMVPTC.

**Mutually Exclusive Mutations of Men1 and Rb in Neuroendocrine Neoplasia** (Poster No. 42)

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**Context:** Inactivation of multiple endocrine neoplasia (MEN) type 1 gene (*Men1*) results in development of multiple endocrine tumors in *Men1/-/-* mice and in humans. Intriguingly, loss of the wild-type retinoblastoma 1 (*Rb*) gene also leads to MEN-like phenotype in *Rb/-/-* mice. Since loss of function of *Men1* or *Rb* specifically targets cells with neuroendocrine differentiation, we aimed to evaluate potential genetic interactions between them.

**Design:** Neoplastic phenotypes of *Men1/-/-* and *Rb/-/-* compound mice were characterized in parallel with their parental genotypes, followed by functional testing of interactions between menin and Rb in cell culture.

**Results:** *Men1* and *Rb* did not cooperate in tumor suppression, as demonstrated by comparable developmental rates of *Men1/-/-* and *Rb/-/-* mice. Down-regulation of *Men1* targets p18 and p27, and increased presence of phosphorylated-Rb was observed in menin-deficient pheochromocytomas of *Men1/-/-* and *Men1/-/-* mice. At
Chronic Pancreatitis Increases Adult Beta Cell Regeneration
(Poster No. 43)

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Context: Juvenile (type 1) diabetes, an autoimmune disease with $100 billion in annual medical costs, affects 1 in 250 Americans. Patients require exogenous insulin and experience increased morbidity/mortality. Interest in regenerative capabilities of pancreatic cells leads to hope that a patient’s remaining cells can be induced to self-renew. This study assesses cell generation rates in patients with secondary chronic pancreatitis or hypergastrinemia and examines biomarkers for potential precursor cells.

Design: Paraffin blocks from 24 patients treated at our institution were selected. Patients were chosen as follows: 14 with primary diagnosis of pancreatic adenocarcinoma with or without secondary chronic pancreatitis, 5 with primary gastrinomas treated by pancreatic resection, and 5 autopsy patients with no clinical history of diabetes and with normal histopathology. Nontumor pancreas tissue was graded as severe (n = 4), mild (n = 4), or no (n = 6) pancreatitis. Immunolocalization was performed for cell replication (insulin/Ki-67), apoptosis (insulin/cleaved caspase-3), islet endocrine cells (glucagon, somatostatin), and precursor cells (Pdx-1, NeuroD1, Ngn3). Location of positive cells (islets, acini, or ducts) was analyzed and reported within islets as clusters (2-6 cells) or single cells.

Results: In patients with severe chronic pancreatitis, beta cell replication, along with Pdx-1 and NeuroD1 expression, was significantly increased. Hypergastrinemia also resulted in an increase in Pdx-1– and Ngn3-positive islet cells.

Conclusions: Findings indicate that chronic severe pancreatitis is associated with increased cell replication and cell turnover with expression of developmental markers for this lineage. Identification of the specific factors responsible for cell regeneration could provide a novel means for treatment of diabetes.

Indeterminate Fine-Needle Aspirations of Thyroid Are Not Clarified by Intraoperative Frozen Section
(Poster No. 44)

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Context: Fine-needle aspiration (FNA) of the thyroid is established as a sensitive and specific means of diagnosing papillary thyroid carcinoma. Less clear is the appropriate evaluation of indeterminate (nondiagnostic) FNA.

Design: Results of consecutive frozen sections (FSs) of the thyroid were examined to determine those patients with a previous diagnosis of indeterminate on FNA. Comparison was made with FNA biopsy results, FS diagnosis, and final diagnosis.

Results: Thirty-four consecutive indeterminate FNA biopsies were later followed by intraoperative FS. Of these, 20 resulted in a diagnosis of follicular lesion–defer, 9 were other benign diagnoses, 3 were deferred, and 1 showed high-grade thyroid carcinoma. On permanent sections, 5 cases showed papillary carcinoma, 2 were occult (1 mm or less, not grossly visible or sampled for FS), and 3 were evaluated at the time of FS and were deferred (n = 2), or given another diagnosis (n = 1: hyperplastic nodule). Only 1 case was interpreted as malignant on FS; the FNA diagnosis in this case was “hemorrhagic and inflammatory cells, insufficient for specific diagnosis,” and the patient had enlarged regional nodes clinically suspicious for metastatic disease. Overall, FS in cases of indeterminate FNA of the thyroid was not only not definitive, but in 5 cases the final diagnosis included papillary carcinoma (false negatives) that could not be diagnosed by FS.

Conclusions: These results support the evolving consensus that intraoperative FS of FNA “nondiagnostic” thyroid nodules is generally not beneficial.

In fact, a negative result on FS may be misleading, since extensive sampling on permanent sections can reveal occult papillary carcinoma.

Treatment Directed at Orthotopic Human Pancreatic Cancer by Subcutaneous Administration of a Novel Polyamine Analog, PH125
(Poster No. 45)

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Context: Polyamine metabolic pathway is investigated as a potential target for cancer treatment, since polyamine metabolism is frequently dysregulated in neoplastic tissue.

Design: A derivative of polyamine analog, PH125, is administered subcutaneously, producing an antineoplastic effect on human pancreatic cancer, L3.6pl, growing orthotopically in nude mice.

Results: To determine the optimal dose schedule of PH125, 2 separate experiments were performed, the first with larger doses injected daily and the second with smaller doses injected tri-weekly. Pancreatic tumor cells were injected into the pancreas of nude mice. Seven days later, treatment with PH125 was initiated in groups of mice (n = 10), with a saline control, at 100 mg/kg, 50 mg/kg, and 25 mg/kg daily doses. The 100 mg/kg and 50 mg/kg doses were highly toxic, with histologic changes predominately noted in the liver with increased reparative changes of the hepatocytes. The exocrine pancreas had mild decreases of cytoplasmic granules in the acinar epithelium. In contrast, the mice receiving the 25 mg/kg daily dose had notable tolerance to therapy without significant histologic changes, producing 87% decrease of pancreatic tumor volume and reduced metastasis from 8 of 10 to 2 of 10. The second experiment explored smaller doses injected tri-weekly, including 25 mg/kg, 15 mg/kg, and 5 mg/kg. Tumor volume decreased 48% with administration of 25 mg/kg dose.

Conclusions: The optimal biologic dose of PH125 at 25 mg/kg administered tri-weekly significantly inhibited the growth of human pancreatic carcinoma in the pancreas of nude mice. Tolerance at this dose was evident without total body weight loss of the mice or visible histologic discrepancies.

Clinical Utility of Frozen Section Evaluation in Patients Undergoing Surgery for Nodular Thyroid Disease With Inconclusive Fine-Needle Aspiration Diagnosis
(Poster No. 46)

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Context: The controversy continues among surgeons about whether or not a frozen section (FS) of thyroid lesions would alter the operative decision that would justify a change in surgical management. We reviewed our experience to determine the role of FS of thyroid lesions with inconclusive fine-needle aspiration (FNA) diagnoses and their utility in intraoperative decision making.

Design: A retrospective review of computerized data of patients who had undergone FNA between June 2001 and August 2006 and in whom inconclusive FNA diagnoses were rendered. From this set, 3 categories were defined: follicular neoplasms, suspicious for malignancy, and nondiagnostic. We divided patients into 2 groups according to the availability of intraoperative FS. The FS group included 28 patients, and the non-FS group included 10 patients.

Results: The study included 38 patients (37 women and 1 man) with a mean age of 54 years (range, 21-69 years) who had preoperative FNA interpreted as either neoplasm (n = 19), suspicious for carcinoma (n = 7), or nondiagnostic (n = 12). FS group intraoperative consultations were diagnosed as benign (n = 5), deferred (n = 21), and malignant (n = 2). In the FS group, lobectomy was performed in all cases, and none had total/subtotal thyroidectomy. In the non-FS group, lobectomy was performed in 8 cases, and a total/subtotal thyroidectomy was performed in 2 cases. In the latter group, none had an associated neck dissection.

Conclusions: FS did not alter the operative decision in any patient with preoperative inconclusive FNA diagnoses (Table).

Surgical Management of Frozen Section Group of Patients With Preoperative Inconclusive Fine-Needle Aspiration Diagnoses

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>FS group (%)</th>
<th>Non-FS group (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lobectomy</td>
<td>All cases (100%)</td>
<td>None (0%)</td>
</tr>
<tr>
<td>Total/subtotal thyroidectomy</td>
<td></td>
<td></td>
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</tbody>
</table>
Carcinoid Tumors Arising in Tailgut Cysts May Be Associated With Estrogen Receptor Status

(Poster No. 47)

John Liang, MD (liangj02@yahoo.com); Sadir Alrawi, MD; Gregory Fuller, MD; Dongfeng Tan, MD. Department of Pathology, The University of Texas M. D. Anderson Cancer Center, Houston.

Tailgut cysts are uncommon developmental cysts that form in the presacral space. To date, 6 cases of carcinoid tumors arising in tailgut cysts have been reported in the literature. Here we present another case of carcinoid tumor arising in a tailgut cyst. Since all 7 cases occurred in childbearing females, we postulate that hormones may play a role in the pathogenesis of this disease. A 34-year-old African American woman presented with a 3-year history of left hip pain. Magnetic resonance imaging of the hip revealed a demarcated soft tissue lesion, 5 cm in size, located anterior to the sacrum and coccyx. The mass was separated from the rectal wall by a plane of fibroadipose tissue. No other lesion was found by a full staging evaluation. Microscopically, the tumor was composed of cystic and solid components. The former were multiple small cysts lined by benign squamous columnar epithelium (tailgut cysts), and the latter were classic neuroendocrine tumor consisting of uniform oval or round cells with fine chromatin but without necrosis or increased mitosis. The tumor cells were diffusely positive for synaptophysin, chromogranin, and cytokeratin, confirming a diagnosis of carcinoid tumor. Furthermore, there was strong estrogen receptor immunoreactivity in cyst-lining cells as well as in tumor cells. Progesterone receptor revealed focally weak positivity. The present study supports our hypothesis that carcinoid tumors arising in tailgut cysts may be hormone driven and indicates that estrogen receptor plays a role in the pathogenesis of this disease.

Expression of Osteopontin in Benign and Malignant Thyroid Nodules

(Poster No. 48)

Jane Dancer, MD (YDancer@tmh.tmc.edu); Hema Kurana, MD; Jae Ro, MD, PhD; Alberto Ayala, MD; Mojghan Amrikachi, MD. Department of Pathology, The Methodist Hospital, Houston, Tex.

Context: Osteopontin (OPN) is a 34-kd extracellular matrix protein with cell-binding domain. It has been shown to be associated with the progression of several cancer types and to play an important functional role in various aspects of malignancy, particularly tissue invasion and metas- tasis. OPN has also been reported as a major RET/PTC-induced transcrip- tional target in thyroid follicular cells. In this study we evaluated the role of immunohistochemical (IHC) staining for OPN in differentiating benign thyroid lesions from thyroid carcinomas.

Design: Fifty-one cases of thyroid follicular lesions were selected from pathology archives of our department. The surgical diagnosis included 18 papillary carcinomas (PCs), 8 follicular adenomas (FAs), 7 follicular carcino- mas (Fcs), 7 Hürthle cell neoplasms (Hcs), 9 adenomatous nodules (ANs), 1 insular carcinoma (IC), and 1 mucoepidermoid carcinoma (ME). IHC staining of OPN was performed on formalin-fixed, paraffin-embedded sections. Intensity of staining was arbitrarily graded as negative, weak, moderate, and strong.

Results: The intensity of IHC staining in different follicular lesions is shown in the Table.

<table>
<thead>
<tr>
<th>Surgical Diagnosis</th>
<th>Negative/ Weak</th>
<th>Moderate</th>
<th>Strong and Diffuse</th>
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<tbody>
<tr>
<td>Papillary carcinomas (n = 18)</td>
<td>2 (11)</td>
<td>1 (5)</td>
<td>15 (83)</td>
</tr>
<tr>
<td>Follicular carcinomas (n = 7)</td>
<td>1 (14)</td>
<td>1 (14)</td>
<td>5 (72)</td>
</tr>
<tr>
<td>Insular carcinoma (n = 1)</td>
<td>0</td>
<td>0</td>
<td>1 (100)</td>
</tr>
<tr>
<td>Mucoepidermoid carcinoma (n = 1)</td>
<td>0</td>
<td>0</td>
<td>1 (100)</td>
</tr>
<tr>
<td>Follicular adenomas (n = 8)</td>
<td>2 (25)</td>
<td>5 (63)</td>
<td>1 (12)</td>
</tr>
<tr>
<td>Hürthle cell neoplasms (n = 7)</td>
<td>3 (43)</td>
<td>3 (43)</td>
<td>1 (14)</td>
</tr>
<tr>
<td>Adenomatous nodules (n = 9)</td>
<td>9 (100)</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

The staining pattern was cytoplasmic, except for 3 cases of PC that showed apical localization of the OPN expression.

Conclusions: OPN is intensely and diffusely expressed in 82% (22/27) of thyroid carcinomas as opposed to 8% (2/24) intense staining in benign lesions. These results indicate that antibodies to OPN may be useful in distinguishing benign from malignant thyroid nodules.

Diagnostic Utility of Galectin-3, HBME-1, Cited-1, and Cytokeratin 19 Immunostaining in Thyroid Lesions

(Poster No. 49)

Hema Kurhana, MD (hkhurana@tmh.tmc.edu); Alberto Ayala, MD; Jae Ro, MD, PhD; Mojghan Amrikachi, MD. Department of Pathology, The Methodist Hospital, Houston, Tex.

Context: A precise pathologic diagnosis is essential for management of patients with thyroid nodules. Despite well-described criteria, the diagnostic agreement for follicular thyroid neoplasms among expert pathologists is less than 60%. The goal of this study was to investigate the role of immunohistochemical markers in improving our diagnostic ability.

Design: A total of 64 cases were selected for this study, which included 20 papillary thyroid carcinomas (PTCs), 10 follicular carcinoma (Fcs), 5 Hürthle cell carcinomas (Hcs), 1 insular carcinoma, 8 follicular adenomas (FAs), 2 Hürthle cell adenomas, and 18 nodular goiters. Immunohistochemical studies for galectin-3, HBME-1, Cited-1, and cytokeratin (CK) 19 were performed on formalin-fixed, paraffin-embedded sections. The staining results were interpreted based on the proportion (P) of reactive cells within tumors and staining intensity (I). The proportion score was described by the estimated fraction of positively stained cells (0, no visible reaction; 1+, <20%; 2+, 20%–75%; 3+, >75% of tumor cells stained). The intensity score represented the estimated staining intensity (0, no staining; 1+, weak; 2+, moderate; 3+, strong).

Results:

Table of Results

<table>
<thead>
<tr>
<th></th>
<th>Benign</th>
<th>Papillary Thyroid Carcinoma</th>
<th>Follicular Carcinoma*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Negative/Positive</td>
<td>Negative/Positive</td>
<td>Negative/Positive</td>
</tr>
<tr>
<td>HBME-1</td>
<td>26/27 (96)</td>
<td>3/19 (16)</td>
<td>16/19 (84)</td>
</tr>
<tr>
<td>Cited-1</td>
<td>24/26 (92)</td>
<td>5/20 (25)</td>
<td>15/20 (75)</td>
</tr>
<tr>
<td>Galectin-3</td>
<td>23/24 (96)</td>
<td>1/24 (1)</td>
<td>4/19 (21)</td>
</tr>
<tr>
<td>CK19</td>
<td>20/23 (87)</td>
<td>4/20 (5)</td>
<td>17/20 (85)</td>
</tr>
</tbody>
</table>

* Follicular carcinoma also includes Hürthle cell carcinoma and insular carcinoma.

CK19 and Cited-1 showed higher rates of diffuse staining in carcinomas than benign lesions and CK19. HBME-1 and galectin-3 showed more diffuse staining in PTC than FC and FA.

Conclusions: Our series demonstrates the advantage of combining galectin-3, Cited-1, HBME-1, and CK19 immunostains to differentiate the various types of thyroid nodular lesions. Although focal HBME-1, galectin-3, Cited-1, and CK19 staining may be found in benign lesions, diffuse positivity is seen more often in malignant neoplasms, especially PTC.

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Quik cytosmear method. We recommend this rapid, inexpensive, and accurate method for rapid and reliable with the Diff-Quik cytologic architecture of routine pathology. Skin biopsies are well suited for virtual microscopy because most specimens are easily digitized. The purpose of this study was to evaluate the diagnostic accuracy of virtual microscopy versus conventional microscopy in routine dermatopathology specimens. In this study, diagnostic accuracy of virtual microscopy in routine dermatopathology specimens was not significantly different than intraobserver variability by conventional light microscopy. The number of clinically significant and insignificant discrepancies by virtual microscopy was 14% (11 minor and 3 major discrepancies). Intraobserver variability by light microscopy was also 14% (12 minor and 2 major discrepancies); \( \chi^2 = .56 \) for the same observer. Cross validation of virtual microscopy and virtual light microscopy may be a viable option for the evaluation of routine dermatopathology specimens.

Dr. Weinstein is a member of the Board of Directors of DMetrix Inc and owns stock in this company. Ms. Richter has exercised stock options for DMetrix Inc. All other authors have no relevant financial interest in the products or companies described in this abstract.

Immunohistochemical Staining to Aid in the Diagnosis of Infantile Digital Fibromatosis (Poster No. 3)

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Context: Infantile digital fibromatosis (IDF) is a rare benign tumor composed of spindle cells arranged in interlacing fascicles embedded in a collagenous stroma. Tumor cells contain perinuclear eosinophilic inclusion bodies (EIBs) that appear bright red with trichrome staining. IDF presents as solitary or multiple masses on the digits of children. Recent case reports describe unusual clinical and histologic presentations. As therapy ranges from observation to excision, differentiation from malignant entities is imperative. Differential diagnoses include infantile myofibromatosis (smooth muscle actin [SMA]-), fibrosarcoma (abundant mitoses), dermatofibroma (factor 13a/\( \alpha \)), angiofibroma (CD34\(^+\)), and neurofibroma (SI00\(^+\)). Although myofibroblastic in origin, the immunohistochemical profile of IDF varies in the literature. This study describes the immunophenotype of IDF in 3 classic cases.

Design: Three histologically classic (EIB\(^+\)) cases of IDF (size range, 1.4–2.3 cm) removed from the digits of children were evaluated. The number of EIBs per high-power field (HPF) was quantitated on trichrome-stained slides. Vimentin (Ventana, Tucson, Ariz), SMA (Zymed, San Francisco, Calif), factor 13a, CD34, and SI00 stains (Cell Marque, Hot Springs, Ariz) were performed.

Results: The number of EIBs ranged from 15 to 25 per HPF, and all cases were characterized by absence of mitotic figures. In all 3 cases, spindle-shaped tumor cells were negative for SMA, factor 13a, CD34, and SI00, and were positive for vimentin.
Malignant Melanoma Presenting as a Cardiac Mass: A Series of 4 Cases and a Review of the Literature
(Poster No. 5)

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Context: Cardiac metastases are detected in 1.5% to 21% of patients with malignant disease, and intracardiac masses are uncommon. Melanoma exhibits a remarkable propensity for cardiac involvement, documented in 50% of patients with disseminated disease at autopsy. Cardiac involvement by melanoma is rarely identified antemortem due to a paucity of cardiac symptoms, and there are only a small number of case reports with melanoma presenting as a cardiac mass.

Results: A search of the Mayo Clinic archives revealed 4 cases of malignant melanoma presenting as a cardiac mass. The authors conducted a retrospective clinicopathologic analysis of these cases with a literature review.

Results: All 4 institutional patients presented with dyspnea and other symptoms of outflow obstruction. The male-to-female ratio was 1:1, with an age range of 31 to 79 years. Echocardiography revealed a right heart mass in all 4 cases (3 atrial and 1 ventricular). Histopathologic analysis demonstrated malignant melanoma in each case. Two patients had a remote history (>10 years) of cutaneous malignant melanoma. The others exhibited cardiac masses as the initial presentation of melanoma, and subsequent dermatologic workup revealed previously undetected cutaneous malignant melanoma.

Conclusions: Malignant melanoma is known to have an unpredictable and often prolonged clinical course. Cardiac metastases from melanoma are common and can occur without overt clinical manifestations. Symptomatic cardiac involvement by melanoma appears to be uncommon, but it can occur. Neoplastic involvement of the heart should be considered in patients with cardiac symptoms when a documented malignancy exists, no matter how remote.

Gastrointestinal Melanoma or Clear Cell Sarcoma? Molecular Evaluation of 7 Cases Previously Diagnosed as Malignant Melanoma
(Poster No. 4)

Pamela L. Lyle, MD1 (pamelalyle@centura.org); Carol M. Amato, MS2; James E. Fitzpatrick, MD3; William Robinson, MD, PhD.1 1Department of Pathology, Penrose Hospital, Colorado Springs, Colo; 2Departments of Medical Oncology and Dermatology/Dermatopathology, University of Colorado Health Sciences Center, Aurora.

Context: Clear cell sarcoma (CCS) is a rare tumor classically associated with the tendons and aponeuroses of the distal extremities of young adults. CCS is indistinguishable from malignant melanoma (MM) by morphology, immunohistochemical profile, and ultrastructural features. CCS is genetically distinct from cutaneous melanoma, as CCS is consistently associated with a t(12;22)(q13;q12) chromosomal translocation leading to the formation of the EWS-ATF1 fusion transcript, which has never been documented in cutaneous melanoma, and thus is regarded as specific for CCS. Recent evidence suggests that primary “malignant melanomas” in unusual anatomic sites, most notably in the gastrointestinal (GI) tract, may be CCS. Additionally, 10 cases of primary GI CCS have been reported in recent literature. We utilized reverse transcription polymerase chain reaction (RT-PCR) to examine whether a proportion of cases diagnosed as either primary GI MM, or as metastatic MM to the GI tract in patients without a history of cutaneous MM, represent primary GI CCS.

Design: GI tumors from 7 patients diagnosed as MM identified from the University of Colorado and Penrose Hospital were tested for the EWS-ATF1 fusion transcript by RT-PCR.

Results: Review of medical records revealed that 5 of 7 patients carried no antecedent or concurrent diagnosis of cutaneous MM. Five of the cases studied (71%) harbored the EWS-ATF1 fusion transcript.

Conclusions: When evaluated by RT-PCR and sequencing studies, a significant percentage of GI tumors diagnosed as MM by conventional histopathologic evaluation represent CCS. Molecular studies may be warranted in cases that otherwise appear to represent MM of unusual primary locations.

Malignant Melanoma Based on Immunofluorescence Performed on Formalin-Fixed, Paraffin-Embedded Tissue After Antigen Retrieval With Proteases
(Poster No. 6)

Monica R. Ianosi-Irminie, MD, PhD (ianosimon@umdnj.edu); GRATIAN S. SARLARU, MD; ANGELA MINSON, HT, HTLIA(ASCP); NICOLO J. BARNARD, MD. Department of Pathology, Robert Wood University Hospital, New Brunswick, NJ.

The appearance on hematoxylin-eosin sections in correlation with direct immunofluorescence (IF) on frozen tissue is the method of choice used for pemphigus vulgaris (PV) diagnosis. When no frozen tissue is available, IF can be performed on the formalin-fixed, paraffin-embedded tissue allocated for light microscopy after antigen retrieval with proteases. A 55-year-old woman with a 10-year history of PV presented to the emergency department with several episodes of hematemesis. Because her disease had been quiescent, she stopped treatment in 2003 of her own accord. An esophageal endoscopy was performed, revealing circumferential erythema, excoriation, and several areas suggestive of ruptured blisters. The biopsy specimen was received in formalin and was submitted entirely for histologic examination. The hematoxylin-eosin sections revealed reparative and reactive-appearing squamous cells with suprabasal acantholysis and tombstone appearance. IF performed on the formalin-fixed, paraffin-embedded tissue allocated for light microscopy after antigen retrieval with proteases (proteinase bacterial type XXIV; Sigma P8038) showed positive direct immunofluorescence for immunoglobulin G in a netlike pattern (Figure 37). The patient was diagnosed with PV, and treatment was started. The patient was discharged after 48 hours and was in stable condition. We conclude that IF performed on formalin-fixed, paraffin-embedded tissue allocated for antigen retrieval with proteases is a valuable salvage immunohistochemical technique regularly used in renal pathology that can be extended to any specimens received in formalin. To our knowledge, there are no prior publications showing the use of this technique for PV diagnoses.

A Case of Mycosis Fungioides and Anaplastic Large Cell Lymphoma From 2 Separate Clones
(Poster No. 7)

Anita Sebastian, DO1 (anita.sebastian@yahoo.com); Colette Terry, MD2; Mandana Mahmoodi, MD; Steve Hou, MD; Carrie Cusack, MD3. Departments of Pathology and Dermatopathology, Drexel College of Medicine, Philadelphia, Pa; 3Department of Dermatology/Dermatopathology, Hahnemann University Hospital, Philadelphia, Pa.

Cutaneous T-cell lymphomas, such as mycosis fungoides and CD30+ anaplastic large cell lymphoma, overlap clinicopathologically and form a spectrum of lymphoproliferative diseases. Although large-cell transformation in mycosis fungoides is a well-defined entity, there have not been many reports in pathology literature that document the association of systemic large cell lymphoma with mycosis fungoides. We report on a case of both mycosis fungoides and anaplastic large cell lymphoma arising in the same patient but evolving from two separate clones. A 45-year-old African American man presented with widespread dryness and pruritus, which had started 30 years ago as several hyperpigmented spots on...

Andrew H. Fletcher, MD (*fletcher@pathology.ufl.edu); Jacqueline A. Knapik, MD; Cynthia W. Garvan, PhD; Edward J. Wilkinson, MD. Department of Pathology and *Statistics, University of Florida, Gainesville.

Context: According to 2001 American Society for Colposcopy and Cervical Pathology consensus guidelines, management of most patients with atypical glandular lesions (AGCs), low-grade squamous intraepithelial lesions (LSILs), or high-grade squamous intraepithelial lesions (HSILs) includes colposcopy with directed cervical biopsy and endocervical sampling. The diagnostic utility of endocervical curettage (ECC) has been debated. This study aims to determine the diagnostic utility of ECC versus directed biopsies of the cervical transformation zone (CBX) in colposcopy patients during a 1-year period.

Design: We conducted a search of the University of Florida Department of Pathology electronic database for ECC and CBX accessioned in 2005. The diagnosis on each was recorded as benign/reactive, CIN 1, CIN 2, CIN 3, or invasive squamous cell carcinoma (ISCA).

Results: A total of 714 colposcopy patients were identified: 524 had concomitant ECC and CBX (n = 118 had ECC only; and 72 had CBX only). Of those having ECC and CBX (n = 52), 8 had high-grade lesions (CIN 2, CIN 3) on ECC with concomitant low-grade (CIN 1) CBX (n = 4) or benign CBX (n = 41). Prior cytologic interpretation prompting colposcopy for these patients demonstrated HSILs (n = 6) and AGCs (n = 2); none had prior LSILs. Of those having ECC only (n = 118), 5 had CIN 3 (n = 5). Prior cytologic interpretation prompting colposcopy for these patients demonstrated HSILs (n = 3) and AGCs (n = 2); none had prior LSILs.

Conclusions: In a consecutive sample of our patient population, if patients with LSILs were excluded from ECC, no CIN 2, CIN 3, or ISCA would have been missed; however, ECC is required in patients with prior HSILs and AGCs.

Mucocoeplidemoid Carcinoma of the Cervix: Another Tumor With a t(11;19)-Associated MECT1-MAML2 Gene Fusion (Poster No. 11)

Joe K. Lennerz, MD (Jlennerz@path.wustl.edu); Arie Perry, MD; John Pfeifer, MD PhD. Department of Pathology, Washington University, St Louis, Mo.

Context: Mucocoeplidemoid carcinoma (MEC) of the cervix, a controversial entity, is characterized by nests composed of three cell types (epidermoid, intermediate, and mucin producing) and the absence of overt glandular differentiation. A subset resembles MEC of the salivary glands, a tumor type that often harbors the t(11;19)(q21;p13) translocation, resulting in fusion of the CAMP coactivator MECT1 to the NOTCH coactivator MAML2. This diagnostically useful molecular event leads to a fusion protein that activates NOTCH target gene transcription. Given morphologic similarities between MEC of the cervix and the salivary glands, we evaluated the former for the t(11;19) translocation.

Design: The departmental archives were searched for “mucocoeplidemoid”

his upper arms. Even though the initial diagnosis of his skin biopsy in 1997 was mycosis fungoides, a skin biopsy of another area demonstrated a dense dermal lymphocytic infiltrate composed of predominantly medium to large atypical lymphoid cells with an immunohistochemical profile consistent with cutaneous anaplastic large cell lymphoma. The patient later developed lymphadenopathy. Although the relationship between these two diseases is unclear, our case is unique because molecular studies confirmed that they are two unrelated malignant T-cell lymphomas.

Human Papillomavirus In Situ Hybridization for the Detection of High-Risk Human Papillomavirus in Eosinophilic Dysplasia of the Cervix (Poster No. 8)

Angela N. Bartley, MD (abartley@email.arizona.edu); Wencong Zheng, MD. Department of Pathology, University of Arizona, Tucson.

Context: Eosinophilic cervical dysplasia (CED) is a newly identified intraepithelial neoplasia equivalent to cervical intraepithelial neoplasia 2. The lesion is believed to arise from metaplastic cervical squamous epithelium subsequently infected with high-risk human papillomavirus (HR-HPV). Previously, we demonstrated that the lesion is highly associated with p16 overexpression and high-risk HPV by polymerase chain reaction. We sought to evaluate CED lesions using HPV in situ hybridization (HPV-ISH) to examine the cellular localization.

Design: HPV-ISH performed on 68 cases of cervical squamous epithelium included 8 benign cervical specimens, 15 cervicitis with squamous metaplasia, 14 low-grade squamous intraepithelial lesions (LSILs), 15 high-grade squamous intraepithelial lesions (HSILs), and 16 cases of CED. Nuclear staining was scored as positive or negative. A cervical cancer case with known HPV 16 expression served as a positive control. Negative controls were performed by replacing the high-risk HPV with nonspecific DNA.

Results: A total of 12 (75%) of 16 cases of CED and 10 (67%) of 15 cases of HSILs showed positive nuclear staining. The cellular localization of HPV DNA was directly related to atypical squamous cells in the lesions of CED. Metaplastic cells without significant nuclear atypia were mostly negative. All other cases were negative for HPV detection.

Conclusions: The rate of HPV positivity utilizing HPV-ISH in lesions of CED is similar to that of HSILs of the cervix. This further supports that CED is a variant of high-grade cervical squamous intraepithelial dysplasia. HPV-ISH is useful to help assess cervical biopsies that are histologically indeterminate for dysplasia in these lesions.

Role of p16 and Extracellular-Regulated Kinase in Ovarian Serous Tumorigenesis (Poster No. 9)

Delaram Fatemi, MD; Liane Deligdisch, MD; Rui Qiao, MD; Hao Shen, BS; Jianli Dong, MD, PhD; Frederique Penault-Llorca, MD; Peter Schlosshauer, MD (*fatemimd@yahoo.com). Department of Pathology, Mount Sinai School of Medicine, New York, NY; Department of Pathology, University of Texas Medical Branch, Galveston; Department of Pathology, Centre Jean Perrin, Clermont-Ferrand, France.

Context: Evidence suggests that ovarian atypical proliferative serous tumors (APSTs) may progress to intraepithelial and invasive low-grade carcinomas. These lesions are characterized by frequent KRAS and BRAF mutations. High-grade serous carcinomas show a different molecular genetic profile, including frequent p53 mutations, and are thought to be a genetically indeterminate for dysplasia in these lesions.

Design: Formalin-fixed, paraffin-embedded tissue sections of 24 regular APSTs, 14 micropapillary tumors, 7 low-grade invasive serous tumors, and 22 high-grade invasive serous carcinomas from the archives of the Mount Sinai Medical Center from 1995 to 2006 were stained immunohistochemically for p16, total ERK, and phosphorylated ERK. Stains were visually evaluated, assigned a score, and statistically analyzed using analysis of variance and Tukey post hoc tests.

Results: There was a decline in p16 expression from regular APSTs to micropapillary tumors (P < .001) and to low-grade invasive carcinomas (P < .001). High-grade invasive carcinomas had a variable p16 expression pattern. No correlation was found between p16 and phosphorylated ERK expression.

Conclusions: Loss of p16 expression may be a pathogenetic factor in the progression from APSTs to micropapillary tumors and low-grade carcinomas. ERK is activated to variable degrees in all 4 tumor types. The divergent expression pattern of high-grade carcinomas supports the theory that they are unrelated to APSTs or low-grade carcinomas.

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Role of p16 and Extracellular-Regulated Kinase in Ovarian Serous Tumorigenesis (Poster No. 9)

Delaram Fatemi, MD; Liane Deligdisch, MD; Rui Qiao, MD; Hao Shen, BS; Jianli Dong, MD, PhD; Frederique Penault-Llorca, MD; Peter Schlosshauer, MD (*fatemimd@yahoo.com). Department of Pathology, Mount Sinai School of Medicine, New York, NY; Department of Pathology, University of Texas Medical Branch, Galveston; Department of Pathology, Centre Jean Perrin, Clermont-Ferrand, France.

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and “cervix.” We identified 7 cases that fit the above-mentioned diagnostic criteria and performed molecular analysis by reverse transcripase polymerase chain reaction (RT-PCR) and fluorescent in situ hybridization (FISH).

**Results:** RT-PCR identified a fusion between exon 1 of the **MEC** and exon 2 of the **MAML2** gene in a single MEC of the cervix. Break-apart FISH analyses using home brew probes for both the **MEC** (Figure 38) and **MAML2** loci confirmed the presence of this chromosomal rearrangement.

**Conclusions:** While the diagnosis “MEC of the cervix” is controversial and not acknowledged by the World Health Organization, we demonstrate that in a small subset of cases, the (11;19) translocation targets the same genes and results in identical gene fusions as MEC of the salivary gland.

**Context:** MUC4 is a heterodimeric glycoprotein that plays an important role in the protection of epithelial surfaces and is involved in cellular signaling through its interaction with HER-2/neu. The aim of this study is to analyze MUC4 and HER-2/neu protein expression in endometrial carcinoma and to determine their relation to clinical outcome.

**Design:** We identified 124 patients who underwent surgical staging for endometrial cancer between July 2001 and July 2005 using the institutional tumor registry. Retrospective chart review was used to collect demographic and clinical data. MUC4 monoclonal antibody and HER-2/neu polyclonal antibody was applied to formalin-fixed, paraffin-embedded tissue. Two investigators who were blinded to the patient clinical history qualified the immunostains as positive or negative.

**Results:** The specimens included 92 endometrioid and 32 nonendometrioid carcinomas. MUC4 and HER-2/neu expression was seen in 57% and 30% of tumors, respectively. MUC4 and HER-2/neu were more likely to be co-expressed in nonendometrioid tumors (P < .001). There was a significant association between HER-2/neu expression and the following prognostic factors: FIGO stage (P < .001), nonendometrioid subtypes (P < .001), high grade (P < .001), lymphovascular invasion (P < .001), depth of invasion (P = .02), positive washings (P = .02), and positive pelvic lymph nodes (P < .001). MUC4 expression was associated with FIGO stage (P = .03) and positive washings (P < .001). Patients with tumors overexpressing HER-2/neu had decreased survival (P = .007). Survival in HER-2/neu-positive tumors was affected by MUC4 status (P = .04).

**Conclusions:** HER-2/neu expression is associated with poor prognosis. MUC4 is co-expressed in a significant number of HER-2/neu-positive endometrial tumors. Survival in HER-2/neu-overexpressing endometrial cancers may be affected by MUC4 status.

**Expression of p16 in Primary Ovarian Tumors** *(Poster No. 13)*

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**Context:** Ovarian and endocervical adenocarcinomas, there was no significant association between tumor type and p16 expression (Fisher exact test P = .33). All 5 nonendometrioid adenocarcinomas (100%) expressed p16.

**Conclusions:** The high rate of p16 expression in primary ovarian carcinomas indicates that p16 expression may play a role in primary ovarian carcinomas and that immunohistochemical staining for p16 is not a reliable indicator of metastatic endocervical adenocarcinoma to the ovary.

**Diagnosis of Unsuspected Coccidioidomycosis by Placental Examination** *(Poster No. 14)*

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**Coccidioides immitis** and **posadasii** are the causative agents of coccidioidomycosis. Disease incidence is highest in the southwestern United States and in parts of Central and South America. A total of 150,000 new cases occur annually in the United States. While most infections are asymptomatic, 40% of infections may present with flu-like respiratory symptoms; disseminated disease is uncommon. A 30-year-old pregnant Mexican woman in her third trimester presented in Dallas with a 4-month history of cough, nodular skin lesions on the face, and postauricular lymphadenopathy. Chest radiographs were unremarkable. Aspiration cytology of the lymph nodes showed granulomatous inflammation; special stains for acid-fast bacilli and fungal and mycobacterial culture were negative. A healthy 3560-g boy was delivered at term. The placenta was large but otherwise grossly unremarkable. Histologic examination showed mild acute chorioamnionitis and 2 small foci of supplicative granulomatous vililits/perivillitis associated with several thick-walled, endosperm-containing spherules. A subsequent biopsy from the mother’s lip lesion demonstrated similar spherules, and immunohistochemistry revealed positive titers of total Coccidioides antibodies in both the mother and infant. The lymph node aspirate was replated onto potato dextrose agar; this and a culture of the lip biopsy grew a mold confirmed as **C immitis** by DNA probe. The mother was treated with fluconazole. The mother and infant are doing well. This first report of disseminated coccidioidomycosis diagnosed by placental examination in a nonendemic region highlights the importance of “exotic” infectious disease awareness as well as placental histologic examination.

**Congenital Neuroblastoma Metastasis to Placenta** *(Poster No. 15)*

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Neuroblastoma is one of the most common malignancies of neonates, and placental metastases have been described in rare cases. We report a case in which neuroblastoma was primarily diagnosed after pathologic examination of the placenta. A 26-year-old woman, gravida 3, para 2, at 37.4 weeks of gestational age, presented with polyhydramnios, pre-eclampsia, and multiple congenital abnormalities. She underwent a cesarean delivery, and a 3.26-kg female infant was delivered. The infant had a palpable liver and petechial lesions on the nose, trunk, arms, and legs. The placenta weighed 1034 g and measured 22 cm in diameter and 4.5 cm in thickness. The umbilical cord contained 3 vessels, and the cotyledons were edematous and pale tan. No discrete masses were identified. Microscopy revealed tight clusters of small blue cells in many of the villous vessels that were positive for neuron-specific enolase and peripherin with focal positivity for synaptophysin, confirming the diagnosis of neuroblastoma. Computerized tomography revealed a 4.27 × 4.29 × 4.6-cm left suprarenal mass. The baby girl underwent an adrenalectomy and wedge resection of liver metastases. Microscopy of the tumor revealed a poorly differentiated neuroblastoma. It was a stage IV tumor, graded as prognostically favorable using the Shimada criteria. Cytogenetics showed negative amplification of the N-MYC gene. Our case emphasizes the importance of a detailed histologic examination of the placenta. Management decisions for the neonate (i.e., surgery) were based on preliminary placental examination followed by subsequent radiology; thus, a noninvasive, accurate and timely diagnosis was provided.
Uterus-like Mass of the Retropertioneum  
(Poster No. 16)

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A uterus-like mass is a rare entity that consists of a cavity lined with endometrium surrounded by smooth muscle bundles mimicking the architecture of a normal uterus. We report a case of a uterus-like mass of the retropertioneum in a 69-year-old woman with a history of total abdominal hysterectomy and bilateral salpingo-oophorectomy 5 years prior and right nephrectomy for renal cell carcinoma stage I. The mass was firmly attached to the left internal iliac vessels. Grossly, it was a 127-g, 14 × 12 × 6-cm, pink, round, and encapsulated mass. Upon opening the mass, there was a cavity filled with old hemorrhagic material. Multiple cross sections revealed a pink whorled surface. Microscopic examination of the mass showed benign smooth muscle proliferation accompanied by endometrial-type glands and stroma. The benign smooth muscle was lacking atypia. Mitotic activity was very low to nil. The smooth muscle compartment resembled myometrium both grossly and microscopically. The endometrial glands and stroma were microscopically unremarkable. Immunohistochemical studies showed immunoreactivity for caldesmon, CD10, and estrogen receptor. Uterus-like mass represents a cavity lined by endometriallike mucosa surrounded by bundles of smooth muscle cells and may show a striking macroscopic and microscopic resemblance to the uterus. Notably, an embryologic müllerian abnormality, stem cell origin, or heterotopia are among theories proposed to explain the presence of this process. To the best of our knowledge, this is the second case that presents in retropertioneum.

Placental Mesenchymal Dysplasia: A Potential Misdiagnosed Entity  
(Poster No. 17)

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Placental mesenchymal dysplasia (PMD) is a rare placental entity often misdiagnosed as molar pregnancy because of its multicystic appearance on ultrasound and large edematous villi on gross findings. Definite molecular pathogenesis in PMD is still unknown. The possible role of insulin growth factor 2 in placental overgrowth and involvement of vascular endothelial growth factors in increased angiogenesis have been suggested. Correct diagnosis will avoid unnecessary termination of pregnancy. A 31-year-old woman, gravida 2, para 1, was admitted for vaginal bleeding. Ultrasound revealed a thick, multicystic placenta previa. Amnioncetesis showed normal female karyotype. She underwent preterm labor and delivered vaginally to a 24-week-old female infant with a birth weight of 660 g (mean weight ± SD: 579 ± 115 g). The infant developed respiratory distress, necrotizing enterocolitis, retinopathy, grade II intraventricular hemorrhage, and sepsis. The placenta was large for gestational age (440 g), with multiple, grapelike, clear cystic vesicles within normal-appearing villi. Histologically, the trivascular umbilical cord and chorionic vessels were unremarkable. Acute chorioamnionitis grade III was present. The villi showed hydropic changes with cистern formation but without trophoblastic hyperplasia. Placental infarction, chorangiosis, and vessel abnormalities were absent. This is a case of PMD characterized by hydropic villi with cистern formation but without abnormalities in the chorionic plate vessels, as previously reported. The fetus had a normal female karyotype and appropriate weight for gestational age. Further studies are granted in order to elucidate its wide spectrum of clinicopathologic findings and determine its pathogenesis.

Spontaneous Resolution of Isolated Coccidioidal Salpingitis  
(Poster No. 18)

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Coccidioidal salpingitis is a distinctly unusual entity and has never been described without concurrent disseminated coccidioidomycosis involving the peritoneum. We present a case of isolated coccidioidal salpingitis that resolved after surgical resection and without antifungal medication. The patient had no known pulmonary involvement or other sites of dissemination. To our knowledge, a similar case has never been described. A 64-year-old Hispanic woman from southern Arizona was diagnosed with a right pelvic mass and bilateral hydroalpinx, without signs or symptoms of peritonitis. She had a history of diabetes mellitus and was 10 years posthysterectomy for fibroid uterus. A bilateral salpingo-oophorectomy was performed. Examination of the uterine tubes showed bilateral granulomatous salpingitis with viable Coccidioides immitis spherules containing endospores. Granulomata were present in the tubal mucosa but absent on the serosal and peritoneal surfaces. An uninvolved 2.0-cm right ovarian serous cystadenoma was also present. She had no pulmonary symptoms or signs of wider dissemination. Preoperative chest x-ray was normal. Complement fixation titer was not performed. Following surgery, she was followed regularly for 5 years and was never treated with antifungal medication. There has been no recurrence of pulmonary or disseminated coccidioidomycosis. Coccidioidomycosis displays striking variability in its clinical behavior and should be considered in the differential for granulomatous processes of uncertain etiology, particularly if the patient has lived in or traveled through an endemic region.

Renal Cell–Like Sinonasal Adenocarcinoma  
(Poster No. 19)

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Context: We have described an unusual sinonasal neoplasm that is histologically indistinguishable from metastatic renal cell carcinoma (RCC): we term it renal cell-like sinonasal adenocarcinoma. Three additional cases have since been reviewed. We report on clinicopathologic features and extended outcome data.

Design: Four patients were identified. Slides and immunohistochemistry results were reviewed. Updated clinical follow-up was obtained from the clinicians.

Results: This group consisted of 3 women and 1 man ages 22 to 69 years, with a mean age of 46. Three tumors were in the nasal cavity and 1 was in the nasopharynx. Histologically, these tumors were composed of clear, cuboidal to polyhedral cells forming solid or glandular patterns (Figure 39). Spindle cells were seen in 1 case. Nuclear pleomorphism was present in 1 case. No perineural/vascular invasion, necrosis, mucinous, or squamous elements were seen. The immunohistochemical profile was cytokeratin (CK) 7+ (4/4), CK20+ (focal 1/4), S100+ (1/4), CD10+ (1/2). Staining was absent for vimentin (0/4), RCC (0/2), thyroglobulin (0/2), actin (0/2), and calponin (0/2). Three patients were treated surgically; 2 of them received adjuvant radiotherapy. The fourth patient received primary radiotherapy. All patients were disease free based on endoscopy and/or radiography at 2, 4, 5, and 8 years after diagnosis. No patient was ever found to have RCC.

Conclusions: Renal cell–like sinonasal adenocarcinoma is a rare tumor with remarkable resemblance to RCC. However, immunohistochemistry can easily aide in the distinction. Clinical follow-up has revealed that no patient developed recurrence, metastasis, or RCC to date. Greater expe-
Androgen Receptor Gene Amplification Is Not a Feature of Salivary Duct Carcinoma as Demonstrated by Fluorescence In Situ Hybridization Analysis

Ilan Weinreb, MD

And Detection of Human Papillomavirus in Upper Aerodigestive Tract Squamous Cell Carcinoma of Human Immunodeficiency Virus–Positive Individuals

Michael S. McLemore, MD, MPH

Context: Human immunodeficiency virus (HIV) infection increases susceptibility to opportunistic infections and malignancies. Infection with high-risk human papillomavirus (HPV) is associated with uterine cervical carcinoma and oral tonsillar squamous cell carcinoma. The relationship between HPV and upper aerodigestive tract squamous cell carcinoma (UADT-SCC) in HIV-positive patients is unclear. Our objective is to evaluate the frequency of HPV infection in UADT-SCC of HIV-positive individuals.

Design: Tissue microarrays were constructed from 25 UADT-SCC lesions (24 primary tumors and 1 lymph node metastasis) in patients reporting HIV infection. In situ hybridization was performed to detect infection with HPV types 6/11, 16/18, or 31/33.

Results: A total of 13 patients were men and 12 were women, with median age (range) at diagnosis of 50 (33–61) years; 88% were smokers. The primary tumor site was larynx in 13 patients, oropharynx in 10, nasal cavity in 1, and unknown in 1 (cervical lymph node). HPV 31/33 infection was detected in 11 (85%) of 13 laryngeal tumors, 8 (80%) of 10 oropharyngeal tumors, the nasal cavity tumor, and the nodal metastasis; prevalence was 84%. HPV 16/18 infection was detected in 3 (23%) of 13 laryngeal and 5 (50%) of 10 oropharyngeal tumors. All cases with HPV 16/18 hybridization showed cobybridization for HPV 31/33. HPV 6/11 infection was detected in 1 oropharyngeal and 1 laryngeal tumor.

Conclusions: The frequency of HPV 16/18 detection in oropharyngeal tumors is consistent with previous reports. The unexpectedly high frequency of HPV 31/33 detection is novel and suggests an association between HPV 31/33 and UADT-SCC in HIV-positive patients. Further study is necessary.

Malignant Giant Cell Tumor of the Larynx

Deborah Y. Cova, MD

Giant cell tumors (GCTs) are rare in the larynx. Fewer than 30 cases of laryngeal GCTs have been reported in the literature, and all were histologically benign. Malignancies in GCTs are uncommon and consist mostly of osteosarcomas and malignant fibrous histiocytomas. Primary malignant GCT consists of a sarcoma arising within a GCT, whereas secondary malignant GCT represents a sarcoma arising at the site of a previously diagnosed and treated GCT. To our knowledge, this is the first case of a malignant GCT in the larynx. A 34-year-old man presented with a 3-month history of a rapidly growing mass compromising his airway. A computed tomography scan revealed a large heterogeneous mass involving the right thyroid lobe and cartilage with pharyngeal extension. The patient underwent a right hemilaryngectomy. Immunohistochemistry for keratin, S100, TTF-1, thyroglobulin, calcitonin, CD68, and CD34 was performed using LSAB detection system. The tumor was composed of multinucleated osteoclast-like giant cells evenly distributed within a stroma composed of plump, oval mononuclear cells. Mitotic activity was increased at 10 to 12 per 10 high-power fields. Atypical spindle cells and delicate lacelike trabeculae of malignant osteoid with osteosarcomatous transformation were present. Necrosis and vascular invasion were identified. The tumor giant cells and stromal cells were positive for CD68 by immunohistochemistry. To the best of our knowledge, this is the first reported case of an osteosarcoma arising within a GCT of the larynx. The patient is doing well 2 years later.

And Oncocytic Mucoepidermoid Carcinoma: A Clinicopathologic Description of a Series and Use of p63 to Differentiate From Potential Mimics

Ilan Weinreb, MD

Context: Salivary duct carcinoma is a high-grade adenocarcinoma of the salivary gland with a poor prognosis and which nearly always has high expression of nuclear androgen receptors (ARs) as demonstrated by immunohistochemistry. The reason for this overexpression is not known. The presence or absence of amplification of the AR gene as a possible explanation for this finding, akin to HER-2/neu amplification in the breast, has never been investigated.

Design: Three cases of salivary duct carcinoma were retrieved from the archives of the Cleveland Clinic. All 3 were stained with AR by immunohistochemistry with appropriate positive and negative controls and showed strong and diffuse nuclear expression. AR gene amplification was then investigated with fluorescence in situ hybridization (FISH) using an orange AR gene probe and a green centromeric probe for chromosome X. The ratio of the 2 was calculated in at least 100 cells for each tumor, and a result greater than 2 was considered positive for AR gene amplification.

Results: All 3 tumors gave informative information and showed a ratio of 1.00, indicating that there was no AR gene amplification.

Conclusions: AR gene amplification is not a feature of salivary duct carcinoma and does not serve as an explanation for AR immunohistochemical expression in these tumors. Further work will be needed to clarify if there are AR gene mutations or epigenetic phenomena that would explain this finding.

Expression of Cytokeratin 7, Cytokeratin 20, and Different Types of Mucins in Acinic Cell Carcinoma of Salivary Glands: An Immunohistochemical Study of 14 Cases

Mousa A. Al-Abbadi, MD

Context: Acinic cell carcinoma is one of the common carcinomas of salivary glands. Expression of cytokeratin (CK) 7, CK20, and different types of mucins is not well characterized.

Design: Well-controlled immunohistochemical stains for CK7, CK20, MUC1, MUC2, MUC4, MUC5ac, and MUC6 were performed on 14 well-documented cases of acinic cell carcinoma of salivary glands.

Results: The total number of cases was 14. The average patient age was 42 years, with a range of 11 to 70 years. There were 10 women and 4 men. The tumors were positive for CK7 in 11 (79%) of 14 cases, with variable staining frequency and positive staining of normal salivary ducts. MUC4 and MUC6 showed similar staining distribution but stained 9 (64%) of 14 and 8 (57%) of 14 cases, respectively. MUC1 stained only 4 (29%) of 14 cases and was negative in all components of normal tissue. The tumor cells as well as the normal tissue components were completely negative for CK20, MUC2, and MUC5ac.

Conclusions: CK7, MUC4 and, to a certain extent, MUC6 are expressed in acinic cell carcinoma and thus may help in the differential diagnosis of this tumor with a built-in positive control of salivary ducts. MUC1 was only expressed in 20% of the cases and is essentially negative in all normal components of salivary gland tissue. CK20, MUC2, and MUC5ac are essentially negative in tumor cells as well as normal tissue.
iant that displays a prominent oncocytic epidermoid component with isolated mucous cells. When the mucous component is sparse, it may be confused with other oncocytic salivary gland neoplasms, squamous carcinoma, and metastases, particularly from the kidney. p63, a nuclear marker recently shown to be useful in separating oncocytomas/oncocytic carcinomas (positive peripheral staining) from metastatic renal cell carcinoma (negative), has not been evaluated in O-MEC. Most cases reported are low grade, but the biology of this variant is not well characterized.

**Limited Wegener Granulomatosis of the Orbit** (Poster No. 25)

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Wegener granulomatosis (WG) is a severe, noninfectious, granulomatous and necrotizing vasculitis classically affecting the respiratory tract and kidneys. The classic morphologic triad of WG includes vasculitis, necrosis, and granulomatous inflammation. WG can present as a systemic or limited disease. Commonly, WG is limited to organs of the head and neck region, including organs of the nervous system, skin, and heart. We present the case of a 26-year-old woman with progressive, painless eyelid swelling that occurred over the course of 1 year. Intraocular evaluation revealed a 1.0-cm, poorly differentiated medullary carcinoma with heterotopic ossification within the primary thyroid carcinoma, and the presence of mixed inflammation with areas of liponecrosis, vasculitis, fibroplastic changes, and poorly formed granulomas in the appropriate clinical and radiologic settings are highly characteristic of limited WG.

**Medullary Carcinoma of the Thyroid With Heterotopic Ossification Presenting as an Intracranial Metastasis** (Poster No. 27)

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Medullary carcinoma of the thyroid presenting as an intracranial metastasis has not been previously reported. In this case, the primary medullary carcinoma also exhibits heterotopic ossification, which has not been described within a primary thyroid carcinoma. We report a case of medullary carcinoma of the thyroid presenting as a parietal brain lesion. Identification of the primary lesion with heterotopic ossification occurred 21 months after presentation. A 70-year-old woman presented with syncpe. Evaluation revealed a cystic right parietal mass. Extensive imaging did not elucidate a primary neoplasm. A calcified mass consistent with a retrosternal thyroid was noted, and fine-needle aspirate of this was interpreted as a benign thyroid nodule. Histologic examination of the intracranial lesion revealed a metastatic, poorly differentiated neuroendocrine carcinoma that was immunohistochemically strongly reactive for calcitonin (polyclonal; Dako, Carpinteria, Calif), synaptophysin (SNAP8; Biogene, San Ramon, Calif) chromogranin (LK2H10; Hybritech, San Diego, Calif), and TTF-1 (SPT24, Vision Biosystem, Burlingame, Calif). The thyroid mass remained unchanged for the next 15 months. Serum calcitonin, which was initially undetectable, began to rise. A total thyroidectomy revealed a 1.0-cm, poorly differentiated medullary carcinoma with heterotopic ossification in the retrosternal right lobe. There was no capsular or vascular invasion. This case illustrates a potential pitfall in the diagnosis of medullary thyroid carcinoma. The striking features of this case include the initial presentation of intracranial metastasis, the presence of heterotopic ossification within the primary thyroid carcinoma, and the challenging retrosternal location of the primary tumor.

**Immunohistochemical Studies of Cell Cycle–Associated Proteins in Mandible Central Giant Cell Tumor** (Poster No. 28)

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Central giant cell tumor (CGCT) is a rare bony lesion that usually affects maxilla, mandible, and occasionally cranial bones. CGCTs are characterized by proliferation of fibroblasts and multinucleated giant cells. Although considered benign, CGCTs often exhibit an aggressive clinical course and have the potential for extensive bone destruction, recurrence, and even metastasis. CGCT is rare: only 3 reports (with very few cases) regarding the possible mechanism underlying its aggressive biologic behavior have been published, and the results are controversial. In our case, immunohistochemistry was performed on CGCT of mandible from a 50-year-old woman to examine the expression profile and cellular distribution of cell cycle–associated proteins cyclin D1, p53, proliferating cell nuclear antigen (PCNA), MIB-1, and factor XIIa. Our results demonstrated that high-level expression of cyclin D1 was predominantly in the nuclei of 85% of giant cells, whereas cyclin D1 staining was noticed in only 20% of mononuclear cells. Expression of PCNA and MIB-1, on the other hand, was observed in 70% and 40% of mononuclear cells, respectively, with less than 10% positive staining present in the giant cells. Protein p53 did not appear to be overexpressed in either mononuclear or giant cells, and factor XIIa was detected only in isolated stromal fibroblasts. These results support the hypothesis of Adel et al. (2004) that overexpression of cyclin D1 in giant cells may play a role in the pathogenesis of CGCTs and that the differential expression pattern of cyclin D1 and PCNA may be involved in the formation of multinucleated giant cells.

Unusual Parotid Tumors: Rare Combination of Sebaceous Lymphadenoma With Other Neoplasms

(Poster No. 29)

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Primary sebaceous lymphadenomas of the parotid gland are unusual benign tumors. In combination with other lesions, they are very rare. An 86-year-old man had a stable parotid mass for 20 years. The specimen showed a well-circumscribed, 3-cm, tan nodule and a separate 7-mm brown nodule. Microscopically, the larger nodule showed nests of bland sebaceous-like epithelial cells surrounded by dense lymphoid stroma, identified as sebaceous lymphadenoma (Figure 41). The smaller nodule showed an unencapsulated collection of cells with abundant eosinophilic granular cytoplasm and a small, round, bland central nucleus. More such smaller collections were seen, identified as oncocytosis with a dominant nodule. A 72-year-old man had a slowly growing, mobile, asymptomatic parotid mass. Fine-needle aspiration diagnosis was epidermal inclusion cyst. The specimen showed 2 lesions: a 2-cm, firm, well-circumscribed brown nodule and a 3.5-cm cystic lesion. Microscopically, the smaller nodule showed a partly cystic tumor lined by a bilayered papillary oncocytic epithelium with lymphoid stroma, identified as Warthin tumor. The larger lesion showed keratin-filled cysts lined by bland squamous cells with focal sebaceous differentiation and dense lymphoid stroma, identified as sebaceous lymphadenoma. There was no evidence of malignancy in either of these cases. Although sebaceous glands are present in the parotid, primary sebaceous tumors are rare. To our knowledge, very few cases of sebaceous lymphadenoma have been reported in literature. They are benign, have a very low recurrence rate, and are amenable to conservative surgery. It is important to recognize them to avoid overtreatment.

Papillary Thyroid Carcinoma With Heterotopic Ossification and Parathyroid Adenoma: Are They Related?

(Poster No. 30)

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Heterotopic bone formation within a primary thyroid carcinoma is a unique feature that has not been previously described. Ossification was noted within a benign thyroid nodule as well as in a lymph node metastasis of follicular carcinoma of the thyroid. We report a case of a 46-year-old man who presented with a well-differentiated papillary carcinoma of the thyroid with heterotopic mature bone formation, a micropapillary carcinoma, a Hurthle cell neoplasm, and a parathyroid adenoma. The man presented with hyperparathyroidism. Evaluation revealed a single enlarged parathyroid gland as well as bilateral thyroid nodules. Aspirates of the nodules were suspicious for a Hurthle cell neoplasm. Total thyroidectomy revealed a background of chronic lymphocytic thyroiditis with 1.2-cm, well-differentiated papillary carcinoma with heterotopic ossification and mature bone formation in the right lobe. The right lobe also demonstrated a 1.5-mm papillary microcarcinoma. The left lobe contained a 2.9-cm Hurthle cell neoplasm. One of three paratracheal lymph nodes was positive for metastatic papillary thyroid carcinoma. A 5.3-g parathyroid adenoma was identified in the left inferior parathyroid gland. Postoperative calcium levels returned to normal with supplementation. The patient was subsequently treated with radioactive iodine ablation therapy. This highly unusual case demonstrates four distinct pathologic entities within a single thyroid gland, including one that has not been described. With an initial presentation of a parathyroid adenoma, the incidental findings within the thyroid gland are not only surprising, but are of much greater diagnostic importance.

Sudden Death in Complete Upper Airway Obstruction Due to Bilateral Retropharyngeal Abscess

(Poster No. 31)

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A healthy 31-year-old African American man with a recent history of sore throat was found dead in his kitchen. He had never sought any medical attention. His brother saw him approximately 6 hours before he was found dead. There is no history of local trauma or odontogenic infections. Upon autopsy the significant findings included: complete upper airway obstruction due to massive edema of the epiglottis and vocal cords and bilateral small retropharyngeal abscess (RPA) with 2.5 cm in the greatest dimension (Figures 42 and 43). There was no rupture or compression to the retropharyngeal space. RPA culture showed growth of streptococci, β hemolytic nongroup A. Neuropathology examination disclosed cerebellar tonsils herniation and hyposemic neuronal injury of the hippocampus. Multiple organs demonstrated congestion, indicative of sudden cardiac arrest. The cause of the sudden death was due to acute upper airway obstruction from massive edema of the epiglottis and vocal cords, secondary to bilateral RPA. Traditionally, RPA has been recognized for more than 17 centuries and has been found most often in children. In the United States, it is relatively uncommon because of the widespread use of antibiotics. RPA in adults can occur as a result of local trauma (foreign body ingestion or instrumental procedures) and odontogenic infections. This case demonstrates an adult sudden death from unnoted bilateral RPA with massive edema of the epiglottis and vocal cords as an indirect complication. Awareness of the immediate life-threatening and other catastrophic complications of RPA are essential.
Patterns of Perineural Invasion in Cutaneous Neoplasms

(Mark Chan, MD (mmchan@bidmc.harvard.edu); Steven Tahan, MD. Department of Pathology, Beth Israel Deaconess Medical Center, Boston, Mass.)

Context: Perineural invasion is a well-recognized but poorly understood route of tumor extension in cutaneous neoplasms that portends increased morbidity. To understand the mechanisms responsible for perineural invasion, we investigated patterns of neural involvement in cutaneous neoplasms.

Design: Histologic sections of invasive squamous cell carcinomas (n = 25), basal cell carcinomas (n = 7), malignant melanomas (n = 5), granular cell tumors (n = 2), and a microcystic adnexal carcinoma (n = 1) with perineural invasion were classified as follows: intratumoral (I) versus extratumoral (E), and then circumferential (D) (completely surrounding nerve), incomplete (focally adjacent to nerve), and intraneural.

Results: Tumors had perineural invasion limited the tumor parenchyma (14/40), deep to the tumor (17/40), or both (9/40 [23%]). The pattern of 144 involved nerves is summarized in the Table.

Abstracts
Squamous cell carcinomas showed a wide range of patterns, including circumferential, incomplete, and intraneural invasion in both I and E locations. Basal cell carcinomas tend ed toward I perineural invasion in a circumferential pattern. Intraneural invasion was seen in malignant melanomas (4/10 cases) and squamous cell carcinomas (6/25 cases), usually in an E location (15/17 nerves). Incomplete involvement was seen in 22% (31/144) of nerves in all tumor types. Clinical follow-up in 6 cases reported that 6 had recurrence. No patient with incomplete involvement had a recurrence. Intraneural invasion was seen in 3 patients with recurrence.

Conclusions: Cutaneous neoplasms have patterns of perineural invasion that may be characteristic of tumor type and related to the risk of recurrence. Not only may these patterns assist in the diagnosis of perineural invasion, they may hold both prognostic and mechanistic significance.

### Value of CD138 in Normal and Pathologic Endometrium

(Poster No. 37)

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Context: CD138 is a marker of plasma cells that has recently been documented to be expressed in carcinomas like renal cell and hepatocellular carcinomas.

Design: A total of 35 cases of benign endometrium (5 proliferative, 5 secretory, 5 chronic endometritis, and 5 atrophic), endometrial hyperplasia (5 cases without atypia and 5 cases with atypia), and endometrial carcinoma (5 cases) were reviewed for their clinicopathologic findings and stained for CD138.

Results: A consistent pattern of membranous staining of surface epithelium was seen in all cases. Proliferative endometrium showed focal and weak membranous staining of the glandular epithelium. Secretory endometrium showed focal but strong staining of the glandular epithelium. Areas with tubal metaplasia showed strong and diffuse staining. Atrophic endometrium did not stain for CD138. Endometrial hyperplasia showed strong and diffuse staining in atypical glands. Endometrial carcinoma showed diffuse and strong staining. In all cases, there was no staining in the endometrial stroma. Cases with chronic endometritis stained plasma cells as well as benign endometrial glands (Table).

Conclusions: CD138 strongly stains surface endometrial glandular epithelium in secretory phase, with tubal metaplasia, atypical hyperplasia, and carcinoma. Inactive and proliferative endometrium show absent and weak focal staining, respectively. The diagnosis of chronic endometritis should be made if incidental staining of plasma cells is noted. Endometrial carcinoma should be included in the differential diagnosis of carcinomas expressing CD138.

### CD138 Staining in Various Endometrial Disease Conditions

<table>
<thead>
<tr>
<th>No. Group</th>
<th>Age</th>
<th>Pathology</th>
<th>CD138 Staining Intensity</th>
<th>CD138 Staining Pattern</th>
</tr>
</thead>
<tbody>
<tr>
<td>5</td>
<td>25–38</td>
<td>Proliferative</td>
<td>Weak, focal</td>
<td>Membranous</td>
</tr>
<tr>
<td>5</td>
<td>52–68</td>
<td>Atrophic</td>
<td>Strong, diffuse</td>
<td>Membranous</td>
</tr>
<tr>
<td>5</td>
<td>25–38</td>
<td>Secretory</td>
<td>Absent</td>
<td>Not applicable</td>
</tr>
<tr>
<td>10</td>
<td>32–45</td>
<td>Endometrial hyperplasia (simple and complex, with and without atypia)</td>
<td>Diffuse staining; strong at the site of atypical glands</td>
<td>Membranous</td>
</tr>
<tr>
<td>5</td>
<td>42–59</td>
<td>Endometrial carcinoma</td>
<td>Diffuse and strong</td>
<td>Membranous</td>
</tr>
<tr>
<td>5</td>
<td>25–35</td>
<td>Chronic endometritis</td>
<td>Staining of glands and plasma cells</td>
<td>Membranous staining in both the glands and plasma cells</td>
</tr>
</tbody>
</table>

### Alveolar Soft Part Sarcoma of the Uterine Cervix With Immunoreactivity for TFE3

(Poster No. 38)

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Alveolar soft part sarcoma is an uncommon neoplasm; in adults, the principal location is the anterior thigh. Alveolar soft part sarcoma has rarely been reported in the female genital tract. We report a case of alveolar soft part sarcoma arising in the cervix of a 37-year-old woman who presented with amenorrhea and irregular heavy menstrual bleeding. Ultrasound examination showed a possible solid mass with markedly increased vascularity in the peripheral margin of the cervix and a fibroid uterus. The patient underwent a cervical mass excision and total hysterectomy. The pink-red polypoid firm mass was received in multiple fragments, measuring 3.5 × 2.6 cm in aggregate. The tumor was composed of large, round, and polygonal cells with distinct cell borders and abundant clear/eosinophilic granular cytoplasm. The tumor cells had vesicular nuclei with prominent nucleoli and were arranged in nests separated by delicate fibrovascular septa in a pseudoalveolar pattern. The tumor cells were negative for CAM 5.2, AE1/AE3, epithelial membrane antigen, 5000, HMB-45, Melan A, desmin, neurofilaments, vimentin, thyroid transcription factor 1, and chromogranin. The tumor cells exhibited positive nuclear immunoreactivity for TFE3, consistent with previous reports documenting positivity for the TFE3 gene chromosomal translocation in alveolar soft part sarcoma. Computed tomography of the abdomen did not reveal a renal mass, ruling out the possibility of renal cell carcinoma, which is another tumor that may be positive for TFE3. To our knowledge, this is only the second case of alveolar soft part sarcoma of the cervix studied for immunoreactivity for TFE3 (Table).
### Immunohistochemical Staining of Alveolar Soft Part Sarcoma of the Female Genital Tract

<table>
<thead>
<tr>
<th>Cases</th>
<th>Cytokeratin</th>
<th>S100</th>
<th>Chromogranin</th>
<th>TFE3</th>
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<tbody>
<tr>
<td>Foschini et al</td>
<td>–</td>
<td>–</td>
<td>Not performed</td>
<td>Not performed</td>
</tr>
<tr>
<td>Abeler and Nesland</td>
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<td>–</td>
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<td>Sahin et al</td>
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</tr>
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<td>Morimitsu et al</td>
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<td>–</td>
<td>–</td>
<td>Not performed</td>
</tr>
<tr>
<td>Chang et al</td>
<td>–</td>
<td>–</td>
<td>Not performed</td>
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</tr>
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<td>Burch et al</td>
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<td>Not performed</td>
<td>Not performed</td>
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<tr>
<td>Nielsen et al</td>
<td>–</td>
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<td>–</td>
<td>Not performed</td>
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<tr>
<td>Roma et al</td>
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<tr>
<td>Our case</td>
<td>–</td>
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<td>+</td>
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