**Check Sample Abstracts**

The following abstracts are compiled from Check Sample exercises published in 2008. These peer-reviewed case studies assist laboratory professionals with continuing medical education and are developed in the areas of clinical chemistry, cytopathology, forensic pathology, hematology, microbiology, surgical pathology, and transfusion medicine. Abstracts for all exercises published in the program will appear annually in *AJCP*.

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1  
**Fetal Lung Maturity Testing**  
**Clinical Chemistry No. CC 08-1 (CC-367)**  
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Neonatal respiratory distress syndrome (RDS) is a disorder of pulmonary immaturity with a high mortality characterized by low levels of pulmonary surfactant. Gestational age determines risk based on concentration of pulmonary surfactant, ie, as gestation progresses the concentration of pulmonary surfactant increases. As a result, newborns delivered at fewer than 28 weeks have a more than 60% risk of RDS, whereas those delivered at more than 34 weeks have a less than 5% risk of RDS. In situations where gestational age alone is not sufficient to determine RDS risk and preterm delivery is medically needed, amniotic fluid analysis can be performed to determine pulmonary surfactant concentration. Four common methods are the lecithin-sphingomyelin ratio, phosphatidylglycerol measurement, surfactant-albumin ratio, and lamellar body count. All of these tests have excellent negative predictive values but poor positive predictive values, ie, they are great at confirming maturity but poor at confirming immaturity.

2  
**Alkaline Phosphatase Isoenzyme Analysis: Guiding the Differential Diagnosis of Elevated Serum Total Alkaline Phosphatase**  
**Clinical Chemistry No. CC 08-2 (CC-368)**  
*David S. Bosler, MD,*¹ and *Raymond E. Karcher, PhD.*² ¹Department of Laboratory Medicine and Pathology, Mayo Clinic, Rochester, MN; and ²Department of Clinical Pathology, William Beaumont Hospital, Royal Oak, MI.

The measurement of alkaline phosphatase (ALP) has long been used in clinical medicine, primarily to aid the diagnosis and monitoring of liver and bone diseases. Its diagnostic utility is limited by the enzyme’s wide tissue distribution and by a variety of potential nonpathologic causes. Isoenzyme analysis is one of several tools available to the clinician hoping to further characterize an elevated total ALP. It provides differentiation among liver, bone, intestinal, placental, and tumor-related forms as the cause of an elevation. The case presents a patient with persistent elevated ALP and atypical bands in the isoenzyme electrophoresis gel. An atypical ALP may be the result of a macroenzyme, which, if present, complicates interpretation of the test result and may cause additional, unnecessary testing or procedures. Recognizing and reporting a macroenzyme is an important service the clinical laboratorian can provide a clinician.

3  
**Indirect Phlebotomy: Is It Good Practice?**  
**Clinical Chemistry No. CC 08-3 (CC-369)**  
*James Nichols, PhD, DABCC, FACB, Aparna Rajadhyaksha, MD, Sandra Camelo-Piragua, MD, and Carol Rauch, MD, PhD, FACP. Department of Pathology, Baystate Health, Springfield, MA.*

Indirect phlebotomy, the collection of blood samples through vascular infusion devices, is a common practice adopted to minimize needle-stick pain and discomfort in hospitalized patients. However, this practice can lead to alteration of the specimen and medical errors associated with misrepresentation of the blood test values. Among the possible problems, dilution or concentration of a particular analyte may occur, depending on the contents of the line’s infusate. Although some studies may indicate that blood collection from lines can be acceptable for isolated laboratory tests, there are insufficient data to demonstrate the reliability of line draws as routine practice. Use of lines for specimen collection should be reserved only for those patients with truly poor vascular access or those patients who require multiple phlebotomies in a short time period. Samples should be collected from lines only under a direct physician order, with careful attention to technique and established protocols that take many variables into account, including the analytes, contents of the line, type of line, discard blood volume, time interval between interruption of infusion and sampling, and catheter size. Even with careful attention to these details, clinicians must remain wary of the potential for medical errors related to misinterpretation of laboratory test results based on such samples.
The Biochemical Diagnosis of Pheochromocytoma
Clinical Chemistry No. CC 08-4 (CC-370)

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A 77-year-old woman had symptoms consistent with pheochromocytoma. The initial laboratory results for catecholamines failed to detect the tumor, but the appropriate additional tests were confirmatory. An algorithm for the biochemical diagnosis of pheochromocytoma is presented, and the role of plasma and urine metanephrine and catecholamine concentrations in the workup of this diagnosis is discussed. Plasma fractionated metanephrines determination is the most sensitive test to rule out a pheochromocytoma and is recommended as the initial test. A diagnostic dilemma is presented when plasma metanephrines are elevated but not to the very high levels usually associated with pheochromocytomas. Common causes of false-positives are discussed, and a strategy, which includes the clonidine test, to differentiate a true-positive from a false-positive is provided in the suggested algorithm.

Hirsutism and Hyperandrogenism
Clinical Chemistry No. CC 08-5 (CC-371)

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Many of the clinical and laboratory dilemmas associated with assessing hyperandrogenemia in women are illustrated in the case example. The patient had a long history of hirsutism and polycystic ovarian syndrome (PCOS) and a relatively rapid onset of intensified hirsutism with frontal balding. Changes in hormone levels are not necessarily specific and can present a challenging differential diagnosis that depends on a careful clinical evaluation. In discussing the differential diagnosis of hyperandrogenism and hirsutism in women, steroid biosynthesis and metabolism, technical issues associated with testosterone measurement in women, pathophysiological sources of androgens, and the classification of steroid-producing tumors are reviewed. Laboratory evaluation included dynamic testing based on an understanding of the hypothalamic-pituitary-ovarian endocrine axis. A combination of laboratory testing and anatomical assessment was used in making the diagnosis.

Laboratory Methods for Colorectal Cancer Screening
Clinical Chemistry No. CC 08-6 (CC-372)

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Annual fecal occult blood testing (FOBT) is 1 of several options recommended by the American Cancer Society for colorectal cancer (CRC) screening. Guaiac-based FOBT (G-FOBT) is the traditional laboratory method that has been shown to reduce overall CRC mortality by one third. However, its use remains limited by high false-positive rates due to dietary and medication effects or occult upper gastrointestinal bleeding. Immunochemical-based FOBT (I-FOBT) has been shown to be as effective as G-FOBT in detecting adenomatous polyps but without any dietary and pharmacologic restrictions.

Hepatocellular Carcinoma and Tumor Markers
Clinical Chemistry No. CC 08-7 (CC-373)

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Although a large number of potential tumor markers for hepatocellular carcinoma have been reported, 3 are commonly used worldwide: α-fetoprotein, α-fetoprotein fraction L3%, and des-γ-carboxy prothrombin. At this time, there is no definitive marker for early detection or a marker for diagnosis and/or prognosis of hepatocellular carcinoma. The combination of the 3 commonly used tumor markers measured simultaneously has increased sensitivity compared with individual markers or the markers used in pairs. Transcription expression assays and/or identification of molecules in the proteome that are up- or down-regulated using microarray detection systems will provide the tools for future progress in this field.

Osteoporosis and Bone Markers
Clinical Chemistry No. CC 08-8 (CC-374)

Catherine Hammett-Stabler, PhD, and Kristin A. Pierce, MD. Pathology and Laboratory Medicine, University of North Carolina, Chapel Hill.

Osteoporosis is an insidious disorder resulting from a derangement in bone remodeling. No longer considered a natural course for aging women, the disease is recognized in men and children. Remodeling is a complex process involving interactions among osteoblasts, osteoclasts, and osteocytes. Various biochemical compounds expressed by these cells or derived as bone is formed or degraded have proven useful in monitoring patient drug therapy and in assessing patient risk for developing osteoporosis.

Insular Thyroid Carcinoma: Difficulties on Fine-Needle Aspiration Cytology and Its Diagnostic Importance
Cytology No. C 08-1 (C-403)

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A case of insular carcinoma of the thyroid is presented. Histologically, the diagnostic criteria for insular carcinoma are well defined. Definitive diagnosis on cytology is challenging because most cytological features are not specific to this particular tumor. Several morphologic entities are of assistance in its separation from other thyroid neoplasms, and, in retrospect, this case exhibited features of insular carcinoma on fine-needle aspiration. Insular carcinoma is a highly aggressive tumor with a propensity for metastases and recurrence and warrants an initial aggressive treatment. It is important to become familiar with and keep insular carcinoma in the
Primary Effusion Lymphoma (PEL)
Cytopathology No. C 08-2 (C-404)
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Lymphomatous effusions without associated malignant lymphoma tumor mass (primary effusion lymphoma [PEL]) were first reported in AIDS patients about 2 decades ago. Additional cases and further investigations established an association between human Kaposi sarcoma–associated herpesvirus/human herpesvirus type 8, Epstein-Barr virus, and PEL in these patients. Currently, PEL accounts for approximately 3% of all non-Hodgkin lymphomas that occur in persons with AIDS. Rarely, PEL has been described in HIV-seronegative individuals. PEL is part of a dynamic and still-evolving group of disease conditions. It can present a variety of differential diagnostic problems to cytologists and should be considered in the differential diagnosis of malignant effusions in appropriate clinical settings and especially in individuals who are HIV positive. Characteristic immunophenotypic and molecular features help distinguish PEL from lymphoma that secondarily involves an effusion.

Primary Effusion Lymphoma in the Adult Patient
Cytopathology No. C 08-7 (C-409)
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Primary effusion lymphoma (PEL) is an effusion-based extranodal non-Hodgkin lymphoma possibly related to human herpesvirus type 8 in HIV-infected and HIV-uninfected patients. This case presents a diagnostic dilemma in the appropriate handling of extranodal effusions. Two cases of PEL are discussed to highlight the diagnostic features of PEL in HIV-seronegative patients that should be considered by cytopathologists in the differential diagnostic spectrum of effusions.

Gastrointestinal Stromal Tumors: Cytologic Spectrum and Differential Diagnosis
Cytopathology No. C 08-3 (C-405)
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In this exercise, 3 cases illustrate the cytomorphology of gastrointestinal stromal tumors (GISTs), including spindle cell and epithelioid types. Histologic correlation is provided where available. The differential diagnoses of both morphologic forms are described, and the immunohistochemical findings are reviewed. A brief overview of the nature of this tumor, including molecular genetics, is provided. The role of cytology in managing GISTs is discussed.

Diagnosis of Sarcoïdosis in a Mediastinal Lymph Node Using EUS-Guided FNA
Cytopathology No. C 08-4 (C-406)
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Sarcoïdosis, a granulomatous disease of unknown etiology, is clinically on the differential diagnosis of malignancy because it presents with mediastinal and pulmonary lymphadenopathy. These enlarged lymph nodes are accessible for tissue sampling via a fine-needle aspiration (FNA) using endoscopic ultrasound (EUS). EUS-guided FNA is being used successfully in the diagnosis and staging of various gastrointestinal and lung malignancies. The advantages of this technique include assessment of very small, 3-mm to 4-mm lesions. In cases of mediastinal lymphadenopathy of unknown etiology, this is a useful and accurate procedure for procuring diagnostic material. After a diagnosis of granulomatous lymphadenitis is rendered, further support and ancillary studies, along with the clinical and radiological findings, can establish the diagnosis of sarcoïdosis.

The Role of Fine-Needle Aspiration Biopsy in Diagnosis of Pulmonary Fungal Infections
Cytopathology No. C 08-5 (C-407)
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Fine-needle aspiration biopsy (FNAB) of the lung is a fast, easy method of evaluating a localized mass or an infectious process. Fungal infections of the lung are among the most commonly encountered infections in patients who are immunocompromised. The ideal way of handling the material is by on-site cytologic evaluation. The most commonly encountered fungal infections include aspergillosis, zygomycosis, cryptococcosis, blastomycosis, histoplasmosis, and coccidioidomycosis. Most of these infections show a granulomatous reaction that varies in severity depending on the length of the infection and the immune status of the patient. The characteristics of the major growth forms of fungi—yeast forms, hyphae, pseudohyphae, arthroconidia, and chlamydoconidia; the use of special studies; and correlation with microbiology establish the correct diagnosis.

Fine-Needle Aspiration of Abdominal Masses in Young Women
Cytopathology No. C 08-6 (C-408)
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Fine-needle aspiration biopsies (FNABs) of abdominal masses in young women present unique differential diagnoses. While gender and age can often be helpful in assessing cytologic findings, it can at times be misleading. Cytologists who are aware of the common entities and the pitfalls in this age group will be able to render the most accurate diagnoses. Additionally, in some scenarios ancillary studies are paramount, and a definitive diagnosis should not be given based on cytologic features alone. An overview of epithelial, small round blue cell, and spindle cell lesions is provided with an emphasis on how age and gender alter the assessment of abdominal FNABs in this patient population.

Cytopathology of Adrenal Lesions in the Adult Patient
Cytopathology No. C 08-7 (C-409)
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Primary adrenal lesions are relatively common in the general population. Adrenal lesions are also frequent findings in patients being investigated for a primary malignancy arising at another site. Knowledge of the cytomorphology helps in accurately separating

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them from metastatic disease. A number of metastatic tumors can be confused with or may have overlapping features with normal, hyperplastic, or neoplastic adrenal tissue. Careful attention to nuclear and cytoplasmic features and immunohistochemical findings usually can distinguish metastatic from primary adrenal neoplasms.

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Diagnosis of Secondary Follicular Center Cell Lymphoma to Pancreas With Endoscopic Ultrasound–Guided Fine-Needle Aspiration Biopsy
Cytopathology No. C 08-8 (C-410)
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Endoscopic ultrasound (EUS) is increasingly used for the detection of pancreatic lesions. On-site evaluation of specimen adequacy by a trained cytopathologist facilitates obtaining adequate samples for ancillary studies leading to proper diagnosis. EUS coupled with fine-needle aspiration (FNA) is a powerful tool for the diagnosis of deep-seated lymphoma and leukemia. Follicular lymphoma is the most common adult non-Hodgkin lymphoma in the United States. It most commonly involves lymph nodes, but it may also involve spleen and bone marrow. Rarely, extranodal sites, such as the gastrointestinal tract or skin, may be involved. Involvement of the pancreas is even rarer. We demonstrate the diagnostic usefulness of EUS-FNA in the diagnosis of a secondary follicular center cell lymphoma to pancreas. Flow cytometry is a useful adjunct ancillary study for the diagnosis of deep-seated lymphoma coupled with EUS-FNA.

17

Xanthogranulomatous Pyelonephritis: An Important Lesion in the Differential Diagnosis of Renal Cell Carcinoma
Cytopathology No. C 08-9 (C-411)
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Xanthogranulomatous pyelonephritis (XGP) is a rare, chronic inflammatory lesion of the kidney that can present as either generalized or focal involvement of the kidney, mimicking a mass lesion. For this reason, XGP has been called the “great imitator.” XGP clearly has an infective origin and assumes its pathologic appearance due to massive parenchymal necrosis and obstruction, with resulting accumulation of foam cells and inflammation. Despite the fact that XGP does not have widely studied cytologic criteria for definitive diagnosis, several morphologic features are of assistance in its separation from other benign or malignant renal neoplasms. The case example illustrates features of XGP. It is important to be aware of and keep this specific entity in the differential diagnoses of aspirated renal masses because of its ability to radiologically, grossly, histologically, and cytologically mimic renal cell carcinoma.

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Cytologic Diagnosis of Lymphoid Lesions of the Thyroid Gland
Cytopathology No. C 08-10 (C-412)
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When a lymphocyte-predominant smear is encountered in the cytologic evaluation of thyroid aspirates, the main differential diagnosis is that of inflammatory disorders, specifically, chronic lymphocytic thyroiditis (Hashimoto thyroiditis), and lymphoma. The cytologic diagnosis of malignant lymphoma involving the thyroid follows the same principles as diagnosis of lymphoma at other body sites but is complicated by the fact that many primary malignant lymphomas of the thyroid arise in a background of Hashimoto thyroiditis. This fact makes identification of a monomorphic lymphoid population difficult if not impossible in some cases and results in a failure to recognize the lymphomatosus population. Pure morphologic analysis of cytologic preparations may be insufficient to establish a diagnosis of lymphoma arising in the background of Hashimoto thyroiditis. However, immunocytochemistry and flow cytometric analysis combined with routine cytomorphology (rapid Romanowsky stain) generally allow separation of chronic lymphocytic thyroiditis (Hashimoto thyroiditis) from lymphoma.
in the smears. At the edges of these and interspersed throughout the smears, individual cells with high nuclear-cytoplasmic ratios, coarse chromatin, and angulated nuclei were present. A diagnosis of “involvement by malignant lymphoma” was rendered and confirmed by ampullary biopsy.

When the smear pattern consists of dispersive, individual malignant cells admixed with ductal epithelial cells, differential diagnostic consideration includes a variety of uncommon neoplasms. Non-Hodgkin malignant lymphoma can present as a population of single lymphoid cells with reactive ductal cells on bile duct smears. Unusual carcinomas, neuroendocrine neoplasms, malignant melanoma, and metastatic carcinomas should be included in the diagnostic considerations.

21
Peripartum Death and Cardiovascular Disease
Forensic Pathology No. FP 08-1 (FP-332)
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Indigestion, chest pain, and shortness of breath are common complaints reported during the last trimester of pregnancy. These unpleasant symptoms are usually benign, but they may be a consequence of severe cardiovascular disease. Approximately 7% of pregnancy-related deaths are attributed to cardiovascular disease; however, most pregnancy-related cardiovascular deaths are not due to atherosclerosis. Among the entities to be considered at autopsy are coronary artery dissection, peripartum cardiomyopathy, myocarditis, and acute myocardial infarction. The physiologic changes of pregnancy create a greater myocardial oxygen demand, thus lowering the tolerance for additional cardiac insults such as coronary artery spasm. The exercise reviews the differential diagnosis of peripartum cardiovascular disease and associated autopsy findings by means of a case presentation and subsequent discussion.

22
Genetic Evaluation of Aortic Dissections
Forensic Pathology No. FP 08-2 (FP-333)
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An aortic dissection, defined as a separation of the layers within the aortic wall, is an often fatal disorder that occurs most often in people aged 40 to 70 years. Certain heritable diseases, such as Marfan syndrome and Ehlers-Danlos syndrome, make the aorta more prone to dissection due to weaknesses in the media layer. Most commonly, though, dissections occur because the aortic wall has deteriorated due to long-standing hypertension. In a small group of individuals, no known history of hypertension or genetic syndrome accounts for the dissection. In this group, it is important to rule out a heritable nonsyndromic genetic abnormality that predisposes affected individuals to thoracic aortic aneurysms and dissections. These individuals will often have a family history of sudden deaths at an early age or multiple family members with aneurysms of various blood vessels. A good, detailed family history from surviving family members is important. Genes causing familial thoracic aortic aneurysms and dissections have been mapped to 4 loci: 5q13-14 (TAAD1), 11q23 (FAA1), 3p24-25 (TAAD2), and 16p12.2-13.13. Genetic testing can be performed on postmortem samples, as well as on surviving family members. Regular screening for aortic aneurysms in genetically predisposed individuals will allow for surgical repair of the aneurysm before it fatally dissects.

23
Asphyxiation Following Inhalation of Cat Litter
Forensic Pathology No. FP 08-3 (FP-334)
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Asphyxiation is a commonly encountered cause of death in forensic practice. A wide variety of scenarios can interfere with the body’s uptake or utilization of oxygen. One such mechanism is upper-airway obstruction. In the case example, upper-airway obstruction followed inhalation of small granules of cat litter. Due to the particular physical qualities of cat litter, the small granules coalesced into a solid mass that completely occluded the upper airway. A complete and thorough postmortem examination is necessary to delineate the cause of death in asphyxia-related cases. Reporting appropriate cases to the US Consumer Product Safety Commission should be considered by medical examiners’ offices.

24
Living Forensic Examination of a Strangulation Victim
Forensic Pathology No. FP 08-4 (FP-335)
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The reported case entails the historical account and the physical examination of an adult female who survived an attempted strangulation and possible sexual assault. Clinical forensic examinations are performed on living pediatric and adult victims of trauma. Physical sequelae of their trauma are assessed and documented to reveal, if possible, the mechanism(s) used to cause the injuries or simply to concur or dispute if the reported history is consistent with the injuries.

25
Clinical and Pathologic Manifestations of Congenital Ichthyosiform Disorders
Forensic Pathology No. FP 08-5 (FP-336)
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Congenital ichthyoses are a relatively rare group of skin disorders associated with abnormal cornification of the skin. The disorders share a final common pathway of morbidity and mortality related to septicemia and pneumonia. A substantial overlap of clinical, histologic, and genetic characteristics makes arriving at a correct diagnosis a challenge. A case of autosomal recessive congenital ichthyosis illustrates common diagnostic complexities, the heterogeneity of the disorder, and the importance of communicating accurate genetic implications to the decedent’s family.

26
Understanding Status Asthmaticus
Forensic Pathology No. FP 08-6 (FP-337)
Asthma is an inflammatory disorder that causes constriction of the airways resulting in wheezing, chest tightness, and coughing. It is a common disease in adults and children and is generally reversible by treatment with bronchodilators and corticosteroids. Status asthmaticus is an acute, unrelenting exacerbation of underlying asthma. The symptoms are usually very similar to asthma, including bronchospasms, airway inflammation, mucus plugging, and difficulty breathing; however, the patients experiencing status asthmaticus are not responsive to typical treatment with bronchodilators and need to be treated more aggressively. We present a case of an inmate with status asthmaticus that led to respiratory failure and death. Mitral valve stenosis due to rheumatic heart disease was an incidental finding on autopsy.

27
Suicidal Asphyxiation by Helium Intoxication and Plastic Bag Suffocation
Forensic Pathology No. FP 08-7 (FP-338)
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Derek Humphry’s Final Exit: The Practicalities of Self-Deliverance and Assisted Suicide for the Dying, third edition, detailed a painless and legal procedure of ending life by plastic bag suffocation in conjunction with helium gas intoxication. This asphyxial method involves the depletion of oxygen with the replacement of helium in an assured and expeditious fashion. We present 2 unique cases of suicidal asphyxiation by plastic bag with helium. In 1 case, the chapter specifying suicide via inert gases in Final Exit was found lying next to the victim, a patient with metastatic colon cancer. The other decedent had suffered from severe depression. In both cases, the victims’ heads were completely covered by a plastic bag, and the adjoining helium gas apparatus remained in close proximity. Determination of cause and manner of death in these rare cases depends primarily on the scene investigation because many of the physical indications of asphyxiation may not be present at autopsy, and routine toxicological analysis does not incorporate helium testing.

28
Coxsackie B Viral Infection With Myocarditis
Forensic Pathology No. FP 08-8 (FP-339)
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Viral myocarditis is a relatively common infectious process that typically remains subclinical or resolves spontaneously following minor symptomatology. Rarely, viral myocarditis is severe enough to result in death. Not infrequently, the death is unexpected. As such, the medicolegal autopsy is the setting in which many lethal cases of viral myocarditis are first diagnosed. Although viral myocarditis can be quite obvious histologically, it is not uncommon for the associated myocardial inflammatory infiltrate to be sparse and subtle. A case of sudden death in a 7-day-old infant due to coxsackie B myocarditis is described. An overview of myocarditis is presented with specific attention to viral myocarditis and coxsackie B myocarditis. The tests available to render such a diagnosis are discussed.

29
Lethal Varicella Pneumonia
Forensic Pathology No. FP 08-9 (FP-340)
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The herpes varicella-zoster virus is associated with both chickenpox (varicella) and shingles (herpes zoster) in the immunocompromised and the partially immune individual, respectively. Varicella begins as a discrete erythematous maculopapular rash that advances through vesicular, pustular, and crusted stages. Lesions are generally located on the trunk and proximal extremities and are found in various stages of progression. Chickenpox during childhood is a common, well-tolerated, self-limiting disease. Serious complications may occur in select population groups such as neonates, immunocompromised patients, pregnant women, and, rarely, normal adults. Respiratory manifestations are the most common complications of adult-onset varicella infections. Pneumonia, a potentially lethal sequela, occurs early in the course of an infection in the immunocompetent host. Prompt diagnosis and treatment may be lifesaving in these individuals.

We report a case of a previously healthy 26-year-old female who died suddenly from varicella pneumonitis after brief treatment for disseminated varicella-zoster infection presenting as chickenpox. The clinical and autopsy findings of the case are accompanied by a discussion of the symptoms, risk factors, and complications associated with varicella infections. Specific consideration of varicella pneumonia are also presented.

30
Identifying Injuries Associated With Airbag Deployment
Forensic Pathology No. FP 08-10 (FP-341)
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Air bags were first patented in 1952, and dual frontal air bags became required equipment for all passenger vehicles in the United States in 1997. In addition, side air bags are now offered as optional features in many vehicles. When used in conjunction with lap/shoulder safety belts, air bags have been shown to be the most effective protection available for the occupants of passenger vehicles. However, their deployment can result in serious and sometimes fatal injuries, with 276 confirmed airbag-related deaths in the United States as of January 2007. Persons most at risk are those with short stature, particularly children. Airbag-related injuries have been well documented, with the most frequently injured body areas being the face (42%), wrists (17%), forearms (16%), and chest (10%). Skull fractures, injuries to the cervical spine due to hyperextension, and trauma to the abdominal organs have also been documented.
Understanding the mechanism of airbag-related injuries is key to differentiating these injuries from injuries resulting from impact with other parts of the vehicle. This differentiation may prove to be critical to the outcome of a case. The use of additional autopsy dissection techniques, such as facial and posterior neck dissections, and cutting into soft tissues to document the presence/absence of trauma can be instrumental in identifying the source of the injuries, eliminating the possibility of controversial alternative interpretations to the pathologist’s conclusions.

31
ALK+ Diffuse Large B-Cell Lymphoma, Plasmablastic Type
Hematology No. H 08-1 (H-316)
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Large B-cell lymphomas with plasmablastic differentiation are a heterogeneous group of neoplasms. While these tumors exhibit overlapping features, distinguishing clinical, histologic, and phenotypic features allow the identification of individual disease entities. One of the most interesting and unusual of these tumors is anaplastic lymphoma kinase (ALK)-positive diffuse large B-cell lymphoma. This tumor is defined by the characteristic ALK positivity. Two subtypes, plasmablastic and anaplastic, are currently recognized. Because this is an extremely rare lymphoma, additional cases and large series of cases are still needed to better delineate this highly aggressive lymphoma.

32
To Bleed or Not To Bleed…Which FVIII Assays to Use
Hematology No. H 08-2 (H-317)
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Factor VIII (FVIII) abnormalities are common, and accurate assessment of functional levels is important clinically. The relative level of deficiency or elevation correlates to the bleeding or thrombotic risk, respectively. The measurement of FVIII activity is also critical for the diagnosis and monitoring of allo- and auto-FVIII inhibitors. Factor VIII can be measured with 1-stage or 2-stage clotting assays, with a chromogenic activity assay, or with antigenic assays that measure the amount of protein present but not its procoagulant function. Clot-based activity assays are more affected than chromogenic and antigenic assays by interferents such as lupus anticoagulant and therapeutic anticoagulants, and, thus, these functional assays may give incorrect values leading to misdiagnoses and erroneous treatment. Understanding the principles and interferences associated with each type of FVIII assay will allow the most appropriate testing choice in various patient populations.

33
Sickle Cell Disease
Hematology No. H 08-3 (H-318)
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A case of sickle cell disease (SCD) complicated by priapism is presented. The patient’s history was significant for veno-occlusive disease, acute chest syndrome, and gallstones. The epidemiology, etiology, clinical manifestations, diagnostic modalities, and treatment options of SCD are discussed. Because pneumococcal sepsis, the most serious complication of SCD in young infants, can be reduced dramatically with prophylactic oral penicillin initiated by the age of 3 months, programs for universal screening for SCD have assumed increased importance.

34
Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma: Clinical and Pathological Features
Hematology No. H 08-4 (H-319)
Ryan Gill, MD, PhD, William Karlon, MD, PhD, and Joan Etzell, MD. University of California San Francisco.

Chronic lymphocytic leukemia (CLL)/small lymphocytic lymphoma (SLL) is a common mature B-cell neoplasm characterized by clonal expansion of small lymphocytes with clumped chromatin and aberrant expression of CD5. CLL may involve the blood, bone marrow, peripheral lymphoid organs, and extranodal tissue, while SLL lacks leukemic involvement. Patients with CLL are often discovered on routine examination but occasionally display constitutional symptoms. Morphologic differential diagnosis includes other mature B-cell malignancies, in particular mantle cell lymphoma, as well as less-common T- and natural killer–cell malignancies. Combining morphologic examination with immunophenotyping generally allows accurate diagnosis. Prognosis is variable, and the presence of unmutated immunoglobulin V\textsubscript{H} genes or expression of related surrogate markers, CD38 and/or ZAP-70, confers a poorer prognosis. The important role of cytogenetic abnormalities in prognostication has also recently been established with 11q– and 17p– associated with poorer prognosis and 13q– with better prognosis. Treatment options have similarly advanced, though CLL remains largely an incurable disease of the elderly.

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Hypereosinophilic Syndrome/Chronic Eosinophilic Leukemia: Clinical and Pathologic Features
Hematology No. H 08-5 (H-320)
Michael Deftos, MD, PhD, William J. Karlon, MD, PhD, and Joan E. Etzell, MD. University of California San Francisco.

Eosinophilia is caused by both reactive and neoplastic conditions. Reactive conditions include allergic diseases, helminth infections, collagen vascular/autoimmune disorders, and various pulmonary processes. Neoplastic proliferation of eosinophils occurs in chronic eosinophilic leukemia (CEL) or as a component of other hematologic malignancies, particularly myeloid disorders. Blurring the line between reactive and neoplastic causes, both hematologic and nonhematologic malignancies can cause reactive eosinophilia. Eosinophilia is considered idiopathic if no evidence for either a reactive or neoplastic process is found and, when associated with end-organ damage, particularly involving the heart, skin, and nervous system, is termed hypereosinophilic syndrome (HES). Some patients with HES have unrecognized clonal proliferation of eosinophils, such as a cryptic FIP1L1-PDGFR\textalpha fusion gene, and may develop acute leukemia. Imatinib therapy results in remission in a subset of patients with CEL/HES, including FIP1L1-PDGFR\textalpha-positive cases. Distinguishing the causes of eosinophilia requires careful integration of clinical and laboratory data and is important because the prognosis and treatment of these conditions differ.
Juvenile Myelomonocytic Leukemia

Hematology No. H 08-6 (H-321)
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Juvenile myelomonocytic leukemia (JMML) is a rare pediatric hematopoietic neoplasm that is characterized by clonal proliferation of myeloid/monocytic lineages. It comprises about 2% of all childhood leukemia but accounts for 30% of childhood cases of myelodysplastic syndrome and myelodysplastic/myeloproliferative diseases. The majority of cases occur before the age of 3 years. JMML has been noted to be associated with neurofibromatosis type 1 and Noonan syndrome. Patients usually present with leukocytosis, monocytosis, hepatosplenomegaly, and other extramedullary involvement. Bone marrow is typically hypercellular with myeloid hyperplasia and fewer than 20% blasts. Elevation of fetal hemoglobin and hypersensitivity to granulocyte-macrophage colony-stimulating factor are 2 features that are helpful in establishing the diagnosis. Mutations of NF1, Ras, and PTPN11 genes have been detected in the majority of JMML cases, which are largely mutually exclusive. JMML carries a poor prognosis, and allogeneic hematopoietic stem cell transplant is the only modality that may lead to long-term survival.

Factor XI Deficiency

Hematology No. H 08-7 (H-322)
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A 15-year-old boy had recurrent, mild epistaxis after minor trauma. Family history did not include a bleeding disorder. The initial differential diagnosis and laboratory evaluation of possible bleeding disorders, including factor deficiencies, are reviewed. The diagnostic criteria for factor XI deficiency, the biochemistry of factor XI, and its role in the coagulation cascade as both a procoagulant and antifibrinolytic agent are summarized. Factor XI deficiency, including its pathogenesis, clinical features, genetics, and treatment are reviewed. The risk of developing factor XI inhibitors after fresh frozen plasma replacement therapy is presented. The clinical effects of elevated factor XI levels are briefly examined.

Refractory Cytopenia With Multilineage Dysplasia and Ringed Sideroblasts

Hematology No. H 08-8 (H-323)
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Myelodysplastic syndrome (MDS) is a group of heterogeneous clonal hematopoietic neoplasms of the elderly. It is characterized by morphologic dysplasia and ineffective hematopoiesis in 1 or more of the myeloid lineages with various risks to evolve to acute myeloid leukemia. MDS was classified into 8 groups by the World Health Organization Leukemia Working Group, including refractory anemia (RA), refractory anemia with ringed sideroblasts (RARS), refractory cytopenia with multilineage dysplasia (RCMD), RCMD with ringed sideroblasts (RCMD-RS), refractory anemia with excess blasts–1 (RAEB-1), refractory anemia with excess blasts–2 (RAEB-2), 5q–syndrome, and MDS, unclassifiable. Refractory cytopenia with multilineage dysplasia and ringed sideroblasts (RCMD-RS) is a subtype of RCMD, with ringed sideroblasts comprising more than 15% of marrow erythroid precursors. RCMD-RS is in the intermediate-risk group for survival and evolution to acute leukemia. Compared with RA and RARS, patients with RCMD and RCMD-RS have a significantly worse prognosis. The treatment decision for MDS is guided by International Prognostic Scoring System risk assessment. Although a variety of treatment modalities are now available, the only potentially curative treatment is allogeneic stem cell transplantation.
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**Bacillus Bacteremia**

**Microbiology No. MB 08-3 (MB-352)**

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The taxonomy of the group of aerobic, spore-forming, gram-positive bacilli of the genus *Bacillus* species is discussed. The case example is an immunocompromised patient who had a catheter infection with *Bacillus cereus*. The diagnostic algorithm of ruling *Bacillus anthracis* in/out is emphasized. *B. anthracis* as a potential bioterrorism agent requires additional safety precautions during workup. Identification of *Bacillus* requires visualization of spores. *B. cereus* is an environmental bacterium and often represents contamination of the specimen. It can be associated with serious infections such as bacteremia, endocarditis, ocular infections, musculoskeletal infections, and a variety of opportunistic infections in patients who are immunocompromised. Contamination of food leads to short- or long-incubation gastroenteritis due to production of different toxins; the gastroenteritis is usually benign and self-limiting.

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**Cryptococcus neoformans var gattii: Changing Epidemiology in an Emerging North American Pathogen**

**Microbiology No. MB 08-4 (MB-353)**

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*Cryptococcus neoformans var gattii* emerged in 1999 as a pathogen on Vancouver Island, British Columbia, Canada. Unlike *C. neoformans* var *neoformans* and *Cryptococcus var grubii*, it tends to infect hosts with normal immunity, causing pneumonia or meningoencephalitis. This organism should be ruled out in HIV-negative travelers returning from southwestern British Columbia who develop pulmonary or neurologic symptoms. Routine imaging may miss central nervous system disease; lumbar puncture is crucial to diagnosis, and cerebrospinal fluid cryptococal-antigen testing is highly sensitive. In pulmonary disease, X-ray findings of nodules, infiltrates, or even obstructing endobronchial lesions may be seen. The fungus is easily cultured in the laboratory, but distinguishing the varieties requires specialized canavanine-glycine-bromthymol blue (CGB) agar and/or genotyping. For treatment, consultation with an infectious disease specialist is recommended. Further information may be obtained from the BC Centre for Disease Control (www.bccdc.org).

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**Rat Bite Fever and Haverhill Fever Due to Streptobacillus moniliformis: Recognition of the Clinical Syndromes, Laboratory Diagnosis, and Treatment**

**Microbiology No. MB 08-5 (MB-354)**

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Infection due to *Streptobacillus moniliformis* is relatively rare, with fewer than 300 cases reported in North America. We present a case of a previously healthy 14-year-old male who had a 1-day history of fever, petechial rash (involving the face, torso, and palms and soles of the feet), vomiting, diarrhea, and progressive drowsiness. He had no history of ill contacts, recent travel, or unusual animal exposures. On presentation to the emergency department, he was treated empirically for meningococccemia, and laboratory investigation including blood cultures and a lumbar puncture were performed. *S. moniliformis*, the agent of rat bite fever and Haverhill fever was isolated from blood cultures, and the patient eventually recovered after being treated with intravenous penicillin. We review the epidemiology, clinical syndromes, diagnosis, and treatment of infection due to *S. moniliformis*.

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**Septic Arthritis in Patients With Systemic Lupus Erythematosus**

**Microbiology No. MB 08-6 (MB-355)**

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An immunosuppressed woman with systemic lupus erythematosus developed septic polyarthritis for which no bacterial etiology could be identified until specific cultures were performed that demonstrated the presence of *Mycoplasma hominis* that was resistant to doxycycline. Despite treatment with various antimicrobials, resolution of symptoms was achieved only when surgical debridement of the knee was completed and a series of intravenous immunoglobulin G injections were administered in addition to a 6-month course of levofloxacin. This case history illustrates the potential for fastidious bacteria such as *M. hominis* to cause systemic illness in a susceptible host, the laboratory procedures that are necessary to detect and characterize this organism in clinical specimens, and the difficulties faced by clinicians who must provide treatment to manage compromised hosts who become infected with *M. hominis*.

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**Ochrobactrum Infections**

**Microbiology No. MB 08-7 (MB-356)**

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Cleveland Clinic, Cleveland, OH.

*Ochrobactrum anthropi* is a nonfermentative, nonfastidious, aerobic, oxidase-positive, indole-negative, and motile gram-negative rod that is commonly found in the environment and is occasionally pathogenic in humans. It is highly resistant to β-lactam antibiotics except carbapenems, but pathogenicity is low. Risk factors for a clinically significant infection include the presence of foreign material, especially central venous catheters, surgery or instrumentation, chronic illness, and an immunocompromised or debilitated state. Depending on the clinical scenario, a single positive blood culture should strongly be considered a contaminant, particularly in a stable, immunocompetent host. The most common infections it causes are bacteremias and, less frequently, endophthalmitis and chronic sinusitis, as part of a polymicrobial infection. Rarely, it can cause pyogenic infections and septic shock. Patients generally have a benign clinical course with an uneventful recovery. Appropriate antimicrobial therapy includes ciprofloxacin, imipenem, and meropenem and, possibly, trimethoprim-sulfamethoxazole and aminoglycosides. Some cases of persistent catheter-related bloodstream infections require catheter removal. Most cases involving infections with other types of foreign material require device removal.
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Staphylococcus saccharolyticus: A Rare but Important Cause of Anaerobic Endocarditis  
Microbiology No. MB 08-8 (MB-357)  
Lulleth Tricia C. Bravo, MD, and Margaret D. Oethinger, MD, PhD, D(ABMM), D(AB Path-MM). Cleveland Clinic, Cleveland, OH.

Staphylococcus saccharolyticus is 1 of only 2 known anaerobic Staphylococcus species; the other species is Staphylococcus aureus subsp. anaerobius. It is an organism that characteristically grows on primary anaerobic culture only, but it exhibits aerotolerance on subculture under aerobic 10% CO₂ conditions. Because of its fastidious nature and its difficulty in isolation, evaluation of its clinical significance is often challenging. We present a case of proven prosthetic valve endocarditis caused by S saccharolyticus that illustrates this organism’s potential to cause morbidity and mortality as a cause of anaerobic endocarditis. Similar reports in the literature confirm further its capacity to cause disease, namely, subacute endocarditis and spondylodiscitis. Familiarity with the key microbiologic characteristics of S saccharolyticus will enable accurate identification and differentiation from other anaerobes and microaerophiles and, ultimately, will aid in the treatment of infection.

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Mucinous Borderline (Low Malignant Potential) Tumor of the Ovary  
Surgical Pathology No. SP 08-1 (SP-353)  
Emanuela Veras, MD, and Elvia Silva, MD, Johns Hopkins Hospital, Baltimore, MD; and M.D. Anderson Cancer Center, University of Texas Houston, Houston.

Mucinous borderline tumors of the ovary are reported to represent approximately 15% of all ovarian tumors. Clinically, they tend to present as large, unilateral masses. Histologically, they have been classically divided into 2 categories: gastrointestinal type and endocervical-like type. The majority of these tumors are comprised of an atypical proliferation of mucinous epithelium with overall bland cytologic features and without stromal invasion. However, a subset of mucinous borderline tumors displays marked epithelial atypia, either focal or diffuse, designated as intraepithelial carcinoma. Another subset demonstrates stromal microinvasion characterized by single cells, glands, or small clusters of mucinous epithelium or a confluent glandular growth within the stroma. In general, these 2 groups of mucinous borderline tumors follow an overwhelmingly benign course. Mucinous tumors metastatic to the ovary often mimic a primary mucinous borderline tumor. Bilaterally, smaller size, surface involvement, and a cytokeratin (CK) 7-/CK 20+ immunoprofile favor metastasis over a primary lesion.

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Cellular Fibroma of the Ovary  
Surgical Pathology No. SP 08-2 (SP-354)  
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Cellular fibroma (CF) is defined by the World Health Organization as a stromal tumor composed of packed cells that exhibit, at most, mild cytological atypia with no more than 3 mitoses per 10 high-power fields (HPF). A 51-year-old woman presented with a pelvic mass on the right side diagnosed as CF. A total abdominal hysterectomy with bilateral salpingo-oophorectomy and a vaginal wall biopsy were performed. Grossly, the ovary measured 9.7 × 6.2 cm and was almost entirely encompassed by a solid, firm, pink-tan tumor. Microscopically, the tumor was composed of a solid proliferation arranged in bundles with focal storiform pattern. Cells were spindle shaped with scant cytoplasm and wavy nuclei with tapered ends without cytological atypia. The tumor had no necrosis and fewer than 3 mitoses per 10 HPF. The differential diagnosis included fibroma, low-grade fibrosarcoma, leiomyoma, and metastases with spindle growth pattern. The most important and challenging differential was low-grade fibrosarcoma, an infrequent neoplasm with strict diagnostic criteria first defined by Prat and Scully by the presence of more than 4 mitoses per 10 HPF and significant nuclear atypia. CF is an infrequent ovarian tumor, with only few cases and short series reported in the literature. Even though most had an excellent outcome, a few cases with recurrences have been reported; therefore, it is considered a tumor of uncertain malignant potential, and the treatment of choice is surgical resection.

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An Unusual Dural-Based Tumor  
Surgical Pathology No. SP 08-3 (SP-355)  
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The vast majority of dural-based tumors are meningiomas. However, other entities, like this presented case of Rosai-Dorfman disease, can occur in the dura and may mimic meningioma, both clinically and radiographically. Rosai-Dorfman disease is a reactive histiocytic proliferation of unknown etiology characterized by a background of lymphocytes and plasma cells with nodular aggregates of S-100– and CD68-positive histiocytes exhibiting emperiploisis. Central nervous system involvement by Rosai-Dorfman disease, either as an extranodal manifestation of classic Rosai-Dorfman disease or as an isolated lesion, is being increasingly recognized. The histologic differential diagnosis includes lymphoplasmacyte-rich meningioma, inflammatory pseudotumor, Langerhans cell histiocytosis, lymphoma, and infectious processes. Appropriate use of immunohistochemistry is necessary to resolve this differential diagnosis.

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Chondrosarcoma: Clinical and Pathologic Features  
Surgical Pathology No. SP 08-4 (SP-356)  
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Chondrosarcoma (CS) is the third most frequent primary malignancy of bone after multiple myeloma and osteosarcoma. CSs mainly occur in patients older than 40 years. CSs are a heterogeneous group of tumors with distinct clinical and pathologic features. The conventional type of CS represents the majority of the cases; other subtypes are encountered less frequently. CSs can occur de novo or after secondary malignant transformation of preexisting benign lesions, especially in patients with Ollier (multiple enchondromas) and Maffucci (multiple enchondromas and associated cutaneous, soft tissue, or visceral hemangiomatous) syndromes. The grading of these tumors provides important prognostic information. While there are
several different grading systems, most use a 3-tier scale. Because chemotherapy and radiation therapy do not provide therapeutic advantage in cases of conventional CS, surgical excision remains the mainstay of treatment.

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Clear Cell Sarcoma of Tendons and Aponeuroses: A Review With Discussion of Molecular Techniques in Diagnosis
Surgical Pathology No. SP 08-5 (SP-357)
Jason W. Nash, DO. Department of Pathology, University of Texas M.D. Anderson Cancer Center, Houston.

Clear cell sarcoma of tendons and aponeuroses (CCS), also known as melanoma of soft parts, is an aggressive sarcoma of presumed neural crest origin frequently arising on an extremity of adolescents or young adults. This sarcoma is prone to local recurrences and metastasizes involving lymph nodes and distant solid organs, frequently with a dismal prognosis. The histologic differential is broad and includes metastatic melanoma with which CCS shares many pathologic characteristics. The discovery of a fairly unique translocation involving the EWS and ATF1 genes on chromosomes 22 and 12, respectively, has allowed for distinction of this tumor from many of its mimics. A discussion of CCS including other entities in the differential diagnosis and molecular diagnostic techniques is illustrated by a case report.

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Cellular Mesoblastic Nephroma
Surgical Pathology No. SP 08-6 (SP-358)
Olca Basturk, MD, Mary Ann Perle, PhD, Alba Greco, MD, and Peng Lee, MD, PhD. New York University School of Medicine, New York, NY.

We describe a 7-month-old male with an abdominal mass diagnosed as mesoblastic nephroma. Computed tomographic scan of a unilateral, firm, fixed mass showed a heterogeneous mass in the upper quadrant of the left kidney extending to the pelvis compatible with a Wilms tumor. Grossly, the tumor was 8 × 5.5 × 4.5 cm, solid, yellowish gray to tan, with foci of hemorrhage, necrosis, and cystic degeneration. Microscopically, the tumor was cellular, composed of fascicles of oval to spindle cells with numerous mitoses, and rich in vasculature. Immunohistochemistry revealed that the tumor cells were positive for vimentin and desmin and negative for keratins, smooth muscle, and muscle-specific actins, c-kit, and myogenin. CD31 and CD34 highlighted the blood vessels and were negative for tumor cells. Ki-67 was strongly positive indicating a high proliferation rate. Electron microscopic studies revealed immature mesenchymal cells with large nuclei. The cytoplasm contained many mitochondria and some intermediate-type filaments. These features are diagnostic of mesoblastic nephroma.

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Sporadic Microsatellite Instability–High Colon Carcinoma with hMLH1 Promoter Methylation
Surgical Pathology No. SP 08-7 (SP-359)
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DNA mismatch repair gene alterations have introduced a new paradigm in colon cancer. Microsatellite-unstable (MSI) tumors with alterations in DNA repair genes have some unique clinical and pathologic characteristics and a better prognosis as compared with microsatellite-stable tumors. DNA mismatch repair gene alterations are caused either by germline mutation in the target genes or by methylation of promoter of the target genes. A portion of MSI-high tumors show some distinct histologic features. One of these tumors is described in the case example.

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Pulmonary Adenocarcinoma, Micropapillary Pattern
Surgical Pathology No. SP 08-8 (SP-360)
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Micropapillary pattern (MPP) in pulmonary adenocarcinoma confers an unfavorable prognosis in early stage, node-negative adenocarcinomas compared with tumors lacking this pattern. This pattern consists of club-like, avascular, tumor-cell-cluster extensions from parent papillae, and the nuclei typically show high-grade features. Tumor cell clusters appear to “float” freely in alveolar spaces, potentially mimicking aerogenous spread of bronchioloalveolar carcinoma (BAC). The MPP needs to be distinguished from BAC, however, because the latter represents a tumor of excellent prognosis in comparison with a tumor with MPP.

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Internal Iliac Vein Leiomyosarcoma
Surgical Pathology II No. SPII 08-1 (SPII-317)
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Vascular leiomyosarcomas are extremely rare, accounting for 2% of all sarcomas, with more than 50% of cases arising in the inferior vena cava (IVC). Other leiomyosarcomas include those originating in deep soft tissue, of which the retroperitoneum is the most common site, and those that originate in cutaneous and subcutaneous tissue, which carry the best prognosis. These tumors are more common in women, slow-growing, firm, gray-white, multinodulated masses that can have focal areas of necrosis and hemorrhage. Most patients present with an abdominal mass arising in the middle or lower segment of the IVC. Favorable prognoses include tumors arising in the middle segment of the IVC, complete tumor resection, abdominal pain at the time of presentation, and the absence of an abdominal mass. Unfavorable prognoses include tumors arising in the upper segment of the IVC and those associated with Budd-Chiari syndrome. The recurrence rate is high; most patients die from their disease. Preoperative and postoperative radiation and/or chemotherapy provide no survival advantage and only play a palliative role.

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Evaluation of Testicular Borderline Serous Tumors
Surgical Pathology II No. SPII 08-2 (SPII-318)
H. James Williams, MD; and Brock J. Oliverio, MD. Department of Pathology, West Virginia University, Morgantown.
Borderline serous tumors are rare, low-grade lesions of the tests. Arising from remnants of müllerian tissue, they have the exact histologic appearance as the ovarian counterparts, showing multiple cysts with papillary projections lined by cuboidal epithelium and with fibrovascular cores, abundant calcifications, mild to moderate cellular atypia, and no stromal invasion. Immunohistochemically, the tumors express CA-125, Leu-M1, estrogen receptors, progesterone receptors, cytokeratin 7, weak cytokeratin 20, and, occasionally, carcinoembryonic antigen. Complete excision is curative; however, the presence of invasion must be thoroughly evaluated because papillary serous carcinoma may have identical histology except for areas of destructive invasion. Other lesions important in the differential include metastatic adenocarcinoma, rete testis adenocarcinoma, and malignant mesothelioma of the tunica vaginalis. The case example demonstrates the characteristic histology necessary for diagnosis in a tumor detected incidentally during workup for nephrolithiasis.

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Central Giant Cell Granuloma: An Overview of Multinucleated Giant Cell Lesions of the Bone
Surgical Pathology II No. SPII 08-3 (SPII-319)
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The clinical, radiological, and histopathological findings of a central giant cell granuloma (CGCG) arising in the mandible are depicted. CGCG is a relatively uncommon, benign, cystic, intraosseous lesion that was first described in 1953. Multinucleated giant cells are a prominent feature of this bone lesion. Important issues of CGCG with regard to diagnostic histopathology, differential diagnosis, and clinicopathologic correlation are discussed. The current knowledge about its pathogenesis and treatment is presented. Because multinucleated giant cells can be an important diagnostic clue in a number of osseous lesions, bone lesions with multinucleated giant cells as a diagnostically important component are reviewed, and their diagnostic features are listed. Pathologists examining a bone lesion featuring multinucleated giant cells need to be aware of the spectrum of these entities.

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A 16-Year-Old Female With Maxillary Sinus Mass
Surgical Pathology II No. SPII 08-4 (SPII-320)
Kyle L. Eskue, MD, Shawn D. Newlands, MD, PhD, MBA, FACS, and Mahmoud A. Eltorky, MD, PhD. University of Texas Medical Branch, Galveston.

A 16-year-old female with a 1-year history of recurrent sinusitis presented with headache and a paranasal sinus mass on computed tomography. A biopsy of the left maxillary sinus mass showed a diffuse, vascular growth pattern with spindle and polygonal-shaped cells, rare mitoses, giant cell reaction, and calcifications. Immunohistochemical stains were uniformly positive for vimentin and partially positive for smooth muscle actin. Both markers CD34 and CD31 were expressed in the endothelial component of the mass, while CD34 showed positivity in some tumor cells. The reticulin stain was positive for the intact reticulin fibers, while markers for cytokeratin (AE1/3), epithelial membrane antigen, glial fibrillary acidic protein, desmin, actin, progesterone receptor, and S-100 were all negative. The diagnosis of hemangiopericytoma was confirmed following excision. After 4 years of multiple questionable episodes of residual/recurrent disease on radiology, another nasopharyngeal/skull base mass was discovered, and a diagnosis of recurrent hemangiopericytoma was made.

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Cutaneous Spindle Cell Neoplasms
Surgical Pathology II No. SPII 08-5 (SPII-321)
Puja K. Puri, MD,1 Michael C. Royer, MD, LTC, MC,2 and Walter L. Rush, MD, MD, MD,3 1Geisinger Medical Center, Danville, PA; 2Walter Reed Army Medical Center, Washington, DC; 3Armed Forces Institute of Pathology, Washington, DC.

This review provides an understanding of the differential diagnosis of cutaneous spindle cell neoplasms. The discussion focuses on the presence of both dermatofibrosarcoma protubersans and giant cell fibroblastoma and discusses the relationship between these 2 entities on a clinical, pathological, and molecular level. Additional entities that would be considered in the histologic differential diagnosis are briefly discussed.

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Large Cell Neuroendocrine Carcinoma of the Lung: Pathological Assessment and Differential Diagnoses of Neuroendocrine Carcinomas
Surgical Pathology II No. SPII 08-6 (SPII-322)
Fabio Tavora, MD,1 Jeffrey R. Galvin, MD,1,2 and Teri J. Franks, MD, MD,1,1 Armed Forces Institute of Pathology, Washington, DC, 2University of Maryland School of Medicine, Baltimore.

Large cell neuroendocrine carcinomas of the lung are tumors with distinct histomorphological characteristics. We report a 59-year-old woman who presented with symptoms of superior vena cava syndrome and who was found to have a large pulmonary mass with extension into the mediastinum. We discuss the histological criteria for the diagnosis of large cell neuroendocrine carcinoma and the key features that separate large cell neuroendocrine carcinoma from other neuroendocrine tumors of the lung.

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Cutaneous Cryptococcosis
Surgical Pathology II No. SPII 08-7 (SP-323)
James Elliot Carter, MD, and Andrea Graciela Kahn, MD. Department of Pathology, University of South Alabama, Mobile.

Cryptococcus spp, a soil-dwelling, encapsulated, yeast form that is especially prevalent in avian settings, is a morphologically distinct fungal pathogen that can usually be readily identified based on appropriate culture methods and tissue examination. Its thick polysaccharide capsule stains strongly with mucicarmine stains and is a classic distinguishing feature, but unencapsulated strains can be more difficult to identify. The possible clinical presentations of cryptococcal infection fall into basic categories: pulmonary cryptococcosis, cebromeningeal cryptococcosis, and, much more rarely, primary cutaneous cryptococcosis unrelated to dissemination from a pulmonary source. We present the case of a 70-year-old female who developed cutaneous cryptococcosis at the site of a Marjolin ulcer on her left arm. Oral fluconazole therapy was successful in controlling the infection. In more advanced cases involving cebromeningeal infection, amphotericin B may be required for successful treatment.
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Myeloid Sarcoma of the Vulva: An Unexpected Tumor
Surgical Pathology II No. SPII 08-8 (SPII-324)

A 40-year-old woman presented to her gynecologist with a vulvar ulcer. She was otherwise asymptomatic. The ulcer was biopsied using the standard H&E stain and a panel of immunohistochemical stains that included myeloperoxidase and lymphoid markers. A diagnosis of myeloid sarcoma was rendered. The patient was asymptomatic, which is not inconsistent with the reviewed medical literature. The prognosis of the tumor is uncertain. Its behavior should be extrapolated from the clinical experience in extragenital sites.

63
West Nile Virus
Transfusion Medicine No. TM 08-1 (TM-301)
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Prior to the late 1990s, West Nile Virus (WNV) was limited to the Eastern hemisphere, with a wide distribution in Africa, Asia, the Middle East, and Europe. In 1999, WNV arrived in New York, where it caused disease in 62 patients and 7 deaths. Since that time, WNV has rapidly spread westward in the United States, causing documented illness in more than 27,000 people and resulting in more than 1,000 fatalities. Today, WNV is the most dominant vector-borne disease in North America. The scientific community responded quickly. Nationwide surveillance policies put into place early in the epidemic included surveillance of human and veterinary patients, avian and mosquito populations, and volunteer blood donor screening. Utilizing the Centers for Disease Control and Prevention Web site as a common clearinghouse for information, updates from multiple disciplines were freely available within a short period of time. It now appears that WNV will continue to be endemic at low levels in the United States. There is still much to learn about WNV.

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Granulocyte Transfusions
Transfusion Medicine No. TM 08-2 (TM-302)
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Granulocyte transfusions have received renewed interest because the possibility of increasing granulocyte dose has arisen. This review highlights considerations for the donor who agrees to granulocyte transfusion and administration of granulocyte colony-stimulating factor. Potential adverse effects of transfusion for the recipient are also noted. Indications for granulocyte transfusion are discussed, and data on clinical utility are reviewed. Note is made of an upcoming trial that attempts to resolve the question of utility of granulocyte transfusion in neutropenic patients.

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Acquired Platelet Disorders
Transfusion Medicine No. TM 08-3 (TM-303)
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A variety of conditions can cause acquired platelet function disorders. These include drug use, uremia, and liver failure. Because platelets play an essential role in hemostasis, impaired platelet function may lead to clinically relevant bleeding. Platelet transfusion decisions for patients with suspected platelet dysfunction can be difficult because the clinical manifestations can vary from patient to patient, even when the underlying etiology is similar. Familiarity with the causes, treatment modalities, and tests for platelet dysfunction is necessary to make correct transfusion decisions. The article reviews platelet function, some of the most common mechanisms of acquired platelet dysfunction, and platelet function tests.

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Transfusion Evaluation and Management of Patients With IgA Deficiency
Transfusion Medicine No. TM 08-4 (TM-304)
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IgA deficiency is one of the most common primary immunodeficiencies in whites. IgA-deficient patients may develop anti-IgA antibodies, which can predispose them to anaphylactic reactions upon exposure to IgA in transfused blood products. The pathophysiology of IgA deficiency and the development of anti-IgA antibodies are discussed. The laboratory investigation of anaphylactic reactions and proposed algorithms for managing the transfusion needs of patients with a history of anaphylaxis or IgA deficiency are presented.

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A Primer on Antiphospholipid Syndrome
Transfusion Medicine No. TM 08-5 (TM-305)
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Antiphospholipid syndrome (APS) is a systemic autoimmune disease that demonstrates a thrombophilic state and obstetrical complications. The definite mechanisms in APS are unclear. Special clinical and laboratory criteria are required in order to consider the APS diagnosis. Thrombosis in APS may occur in venous and/or arterial circulations and small- or large-sized vessels and tends to recur. Deep venous thrombosis is the most common thrombotic event in patients with APS. Arterial thromboses are primarily seen in the central nervous system. The diagnosis of APS requires constant presence of medium to high levels of anticardiolipin (aCL) (IgG or IgM isotype), lupus anticoagulant (LA), or both. β-2-Glycoprotein-1–based enzyme-linked immunosorbent assay is required for aCL testing, whereas 2 screening and 1 confirmatory test are required for LA. Oral anticoagulants are the main treatment in APS. Although some patients may require a short course of oral anticoagulation, cases with recurrence require indefinite treatment with oral anticoagulation.

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Drug-Induced Immune Hemolytic Anemia
Transfusion Medicine No. TM 08-6 (TM-306)
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Two cases are presented to illustrate the different clinical and serologic presentations of drug-induced immune hemolytic anemia. Other conditions to consider in the differential diagnosis are discussed.

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Minimizing Blood Transfusions in Medicine and Surgery: Current Considerations
Transfusion Medicine No. TM 08-7 (TM-307)
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A 54-year-old female Jehovah’s Witness with a diagnosis of Philadelphia chromosome–positive acute lymphocytic leukemia received an allogeneic stem cell transplant without transfusion support. Successful engraftment was achieved with infusion of peripheral blood stem cells from a 6/6 HLA-matched sibling, which was considered to be acceptable treatment according to her religious beliefs. However, when she was in need of a donor lymphocyte infusion, it was considered unacceptable, and she eventually died from bleeding complications secondary to recurrent leukemia.

This case presents 1 of several scenarios in which patients may refuse blood products. Besides the religious context, patients may decline transfusions or consider them as a last resort due to fear of transfusion reactions or contracting blood-borne diseases. A summary of available alternatives and techniques to minimize blood transfusions in today’s practice is presented.

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Autologous Transfusion Practices
Transfusion Medicine No. TM 08-8 (TM-308)
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The primary concern for patients who have decided to donate autologous blood is fear of infectious disease transmission, in spite of improved screening methods over the past 30 years. Additional benefits of autologous donation are a decreased risk of alloimmunization and creation of a blood source for those patients who are unable to accept allogeneic donation or for whom it is difficult to find compatible blood prior to elective surgical procedures.

Three methods of autologous donation—preoperative, intraoperative, and postoperative—are outlined along with their limitations and benefits, the federal regulations overseeing preoperative autologous donation, and pharmacologic agents available for use to maximize the benefit of autologous donation or minimize exposure to allogeneic donations.