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# NEWSPath

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## **ANATOMIC PATHOLOGY**

### **A Simplified, Noninvasive Stool DNA Test for Colorectal Cancer Detection**

**Steven Itzkowitz, Randall Brand, Lina Jandorf, et al**

Background: As a noninvasive colorectal cancer (CRC) screening test, a multi-marker first generation stool DNA (sDNA V 1.0) test is superior to guaiac-based fecal occult blood tests. An improved sDNA assay (version 2), utilizing only two markers, hypermethylated *vimentin* gene (hV) and a two site DNA integrity assay (DY), demonstrated in a training set (phase 1a) an even higher sensitivity (88%) for CRC with a specificity of 82%.

Aim: To validate in an independent set of patients (phase 1b) the sensitivity and specificity of sDNA version 2 for CRC.

Methods: Forty-two patients with CRC and 241 subjects with normal colonoscopy (NC) provided stool samples, to which they immediately added DNA stabilizing buffer, and mailed their specimen to the laboratory. DNA was purified using gel-based capture, and analyzed for hV and DY using methods identical to those previously published.

Results: Using the same cutpoints as the 1a training set (N = 162; 40 CRCs, 122 normals), hV demonstrated a higher and DY a slightly lower sensitivity, for a combined sensitivity of hV + DY of 86%. Optimal cutpoints based on the combined phase 1a + 1b dataset (N = 445; 82 CRCs, 363 normals) yielded a CRC sensitivity of 83%. The vast majority of cancers were detected regardless of tumor stage, tumor location, or patient age. Assay specificity in the phase 1b dataset for hV, DY, and hV + DY was 82%, 85%, and 73%, respectively, using the phase 1a cutpoints. Optimal cutpoints based on the combined phase 1a + 1b dataset yield a specificity of 82%.

Conclusions: This study provides validation of a simplified, improved sDNA test that incorporates only two markers and that demonstrates high sensitivity (83%) and specificity (82%) for CRC. Test performance is highly reproducible in a large set of patients. The use of only two markers will make the test easier to perform, reduce the cost, and facilitate distribution to local laboratories.

*Am J Gastroenterol. 2008;103(11):2862-2870*

### **Lymphomas Involving the Breast**

**Talwalkar SM, Miranda RN, Valbuena JR, et al**

A nice review of 106 cases divided into two groups: localised disease and disseminated disease. Not surprisingly, DLBCL is the commonest (64%), presenting with a localised mass. In the disseminated lymphoma category, follicular lymphoma was the most frequent followed by other B, T and Hodgkin lymphomas in lower frequencies. Follicular lymphoma was not encountered as localised disease but only as part of disseminated disease. Localised disease carries a better prognosis than disseminated disease, unsurprisingly.

*Am J Surg Pathol 2008;32:1299–309.*

## **Diagnosis of Usual Interstitial Pneumonia and Distinction from Other Fibrosing Interstitial Lung Disease**

**Katzenstein ALA, Mukhopadhyay S.**

Idiopathic pulmonary fibrosis (UIP) is a life threatening disease with a high mortality and, as such, this diagnosis should be made with great caution. This excellent review revisits the criteria for diagnosis with superb photographs (spatial/temporal heterogeneity with architectural distortion and fibroblastic foci), and distinguishes UIP from non-specific IP (both cellular and fibrosing phases), chronic hypersensitivity pneumonitis and Langerhans cell histiocytosis (both acute and chronic phases). Also We have to remember that chemoradiation, collagen vascular diseases and smoker's lung must always be ruled out before a diagnosis of UIP is made. Lastly, there is no role for transbronchial biopsies in the diagnosis of UIP.

*Hum Pathol 2008;39:1275–94.*

## **Toker Cells of the Breast - Morphological and Immunohistochemical Characterization of 40 Cases**

**Di Tommaso L, Franchi G, Destro A, et al.**

Toker cells are epithelial cells with clear cytoplasm usually devoid of cytologic atypia that are localised to the epidermis of nipple. Rarely, they can be numerous and even atypical so that distinction from malignant cells of Paget disease is essential. This paper describes the morphology (usual scenario: bland, benign cells in the basal zones of the nipple epidermis that disappear on deeper sections), along with hyperplasia and even atypia. When one resorts to immunohistochemistry, Toker cells are: ER/PR positive, CD138 negative and p63 negative. In contrast, Paget disease is ER/PR negative, CD138 positive and p63 positive. Both Toker and Paget cells are CK7/EMA positive.

*Hum Pathol 2008;39:1295–300*

## **FIGO Staging of Endometrial Adenocarcinoma: A Critical Review and Proposal**

**Zaino, Richard**

The optimal staging of tumors would reflect their biology and patterns of spread, permit accurate prognostication, and facilitate therapeutic decision-making. The last revision of the International Federation of Obstetricians and Gynecologists (FIGO) staging of uterine corpus tumors was in 1988, and it represented the transition from a clinical to a surgico-pathologic system. With 20 years of experience, we can now review the accuracy, reproducibility, and utility of this system. Pathologists are in a unique position to study each of these characteristics, comment on their ability to apply the criteria in daily practice, and offer suggestions to further improve the FIGO system. This paper selectively reviews some of the more problematic aspects of the current FIGO system, including the following: the distinction of tumors confined to the endometrium from those which are superficially myoinvasive; the method and utility of histologic grading of endometrial adenocarcinoma; the utility and reproducibility of the diagnosis of cervical epithelial and stromal invasion; the striking heterogeneity within and among stage III A, B, and C tumors and their differing prognostic significance. It concludes with recommendations for changes in a future revision of the FIGO staging of endometrial carcinoma.

*International Journal of Gynecological Pathology. 28(1):1, January 2009.*

## **Nested Variant of Urothelial Carcinoma of the Renal Pelvis**

**Lau SK.**

The nested variant of urothelial carcinoma is an uncommon form of urothelial carcinoma with distinctive histopathologic features. The majority of cases of this unusual type of urothelial carcinoma have been described in the urinary bladder, with examples of this neoplasm involving the upper urinary tract being extremely limited. The present report details the clinical and pathologic features of an unusual case of a nested variant of urothelial carcinoma occurring in the renal pelvis of a 71-year-old woman. The tumor was characterized by a nested pattern of growth and relatively bland cytologic features, and presented with locally advanced disease at the time of nephroureterectomy. Although rare, awareness that the nested variant of urothelial carcinoma may occur at this particular site is important so as not to confuse this unusual form of urothelial carcinoma with other pathologic lesions of the renal pelvis.

Nested variant of urothelial carcinoma is a rare neoplasm that is histologically characterized by large numbers of small, closely packed, haphazardly arranged, poorly defined, confluent irregular nests of bland-appearing urothelial cells infiltrating the lamina propria and the muscularis propria. Due to the cells' deceptively bland appearance,

the tumors are sometimes misdiagnosed as benign lesions, leading in some cases to a significant delay in establishing the correct diagnosis and thus contributing to this neoplasm's advanced stage. Nested variant of urothelial carcinoma must be differentiated from the benign proliferative lesions of urothelium, such as von Brunn nests, cystitis cystica, cystitis glandularis, nephrogenic adenoma, inverted papilloma, and paraganglioma.

*Pathol Res Pract. 2009 Jan 24. [Epub ahead of print]*

## **MICROBIOLOGY**

### **Serological Diagnosis of Tuberculosis**

**Dayal R, Singh A, Katoch VM, Joshi B et al**

**Objective:** To evaluate the efficacy of ELISA for the detection of IgG antibodies against antigen 85 complex (Ag 85 complex) of Mycobacterium tuberculosis.

**Methods:** Children of either sex, 0-18 years of age, attending the outpatient department and admitted in the casualty and wards of the Department of Pediatrics, S.N. Medical College, Agra, were included in present study. The study was carried out on children with pulmonary and CNS tuberculosis along with matching controls (83 cases and 32 controls). Informed consents of their parents or guardians were taken. They were subjected to clinical examination, relevant laboratory investigations, tuberculin test and chest radiograph. Relevant body fluids were subjected to bacteriological tests; ELISA was applied to serum samples for detection of IgG antibodies against antigen 85 complex (Ag85). The result of ELISA was compared with bacteriological tests [Ziehl Neelson (ZN) staining for acid-fast bacilli, culture on Lowenstein Jensen (LJ) medium and culture on BacT/Alert 3D system].

**Results:** ELISA tests showed a significantly higher sensitivity (59.1%) as compared with LJ medium culture method (19.3%), BacT/Alert 3D system (24.1%) and ZN staining (16.9%) in all patients ( $p < 0.001$ ). Specificity of ELISA test was 71.9%.

**Conclusion:** In view of the convenience, low cost and good sensitivity, ELISA tests have a promising future in the diagnosis of childhood tuberculosis.

*Indian J Pediatr. 2008 Dec 4. [Epub ahead of print]*