

Diagnostic Tests for Pertussis

Pertussis caused by the bacterial pathogen *Bordetella pertussis* is a fairly common cause of respiratory tract infection. Children and others who lack immunity to pertussis present with a severe tracheitis called whooping cough. Adults who have some immunity to pertussis present with a chronic cough, and studies show that an adult with a cough lasting more than 2 weeks has a high likelihood of having pertussis if the disease is circulating in the community. Protective immunity to pertussis is short-lived, and pertussis tends to reappear in communities on 3 to 5-year cycles. Kalamazoo had a large increase in pertussis cases in 2006, and the numbers seem to be high again this year.

The best test for pertussis is to look for the organism's DNA in a calcium alginate nasopharyngeal swab specimen in a patient that has a characteristic cough using the polymerase chain reaction (PCR) test. The organism does not grow very well on culture, so most laboratories have

stopped doing culture for pertussis. *Bordetella* is not carried as normal flora by humans, so the presence of the organism in a symptomatic patient is diagnostic for pertussis. The PCR test is very sensitive for the first three weeks of the patient's cough. After 3 weeks or after antibiotic treatment, the amount of DNA in the specimen starts to drop and PCR testing will turn negative.

The Bronson laboratory sends the PCR test for pertussis to Mayo Medical Laboratories in Rochester, Minnesota, which performs the PCR test daily and ships specimens every night. The turn-around time for the PCR test is approximately 48 hours.

Serology can be used for retrospective epidemiologic studies after the pathogen has been eliminated from the patient and PCR test has gone negative, but it is not as sensitive or specific as the PCR test performed during the first 3 weeks of illness. Serum IgG against the main

pertussis toxin protein (PT) rises about 8 weeks after infection and drops about 6 months after infection, but most adults carry some antibodies to pertussis and it is not clear that any single measurement is diagnostic of current infection. Paired serum samples collected 4 weeks apart showing rising or falling levels may be suggestive of infection, but are not



Rick VanEnk, PhD

as good as an optimally collected PCR specimen.

Pertussis is a reportable disease of public health significance so physicians should perform the optimal diagnostic test for it if it is suspected.

Positive pertussis laboratory tests are reported automatically to the health department.

— Rick VanEnk, PhD

Update on Urothelial Tract Cancer Terminology

In an effort to bring Bronson's Department of Pathology urinary tract cancer terminology in alignment with the current World Health Organization (WHO) International Classification of Tumors (2004)^{1,8}, we will be updating our bladder terminology and grading system from transitional cell carcinoma (TCC) (papillary grades I, II, or III, carcinoma in situ, or invasive) to urothelial carcinoma (papillary low grade or high grade, carcinoma in situ, or invasive).

Epidemiology

Worldwide, bladder cancer is the seventh most common cancer, accounts for 3.2% of all cancers, and it is more common in males with a male:female ratio of 3.5:1.¹ The incidence of urothelial papilloma is very low.¹ The incidence of papillary urothelial neoplasm of low malignant potential (PUNLMP) is also low when strictly defined.¹ As defined by the WHO, it is a papillary urothelial tumor that resembles the exophytic urothelial

papilloma, but shows increased cellular proliferation exceeding the thickness of normal urothelium. The vast majority of the papillary urothelial tumors will fall into the categories of low or high grade non-invasive urothelial carcinoma. The remaining urothelial carcinomas are comprised of urothelial (flat) carcinoma in situ and infiltrating urothelial carcinoma.

Nomenclature

Almost all of the tumors previously called TCC grade I will be diagnosed as papillary urothelial carcinoma, low grade (with only a few now termed PUNLMP). Likewise, all of the tumors previously called TCC grade III will now be diagnosed as papillary urothelial carcinoma, high grade. It is the TCC grade II diagnosis where the bulk of inter-observer variability was noted. The TCC grade II tumors that have slightly more architectural and nuclear pleomorphism than allowed (*continued*)

Previous WHO	Current (2004) WHO classification of papillary urothelial tumors
Papilloma	Papilloma
TCC Grade I	Papillary urothelial neoplasm of low malignant potential (PUNLMP)
TCC Grade I	Non-invasive papillary urothelial carcinoma, low grade
TCC Grade II	Non-invasive papillary urothelial carcinoma, low grade
TCC Grade II	Non-invasive papillary urothelial carcinoma, high grade
TCC Grade III	Non-invasive papillary urothelial carcinoma, high grade

Update on Urothelial Tract Cancer Terminology

(continued) for TCC grade I tumors will now be diagnosed as papillary urothelial carcinoma, low grade. In contrast, the TCC grade II tumors with moderate architectural and cytologic atypia as well as an increase in mitoses will now be diagnosed as papillary urothelial carcinoma, high grade.

The older three-tiered grading system as put forth by previous editions of the WHO was complicated by inter-observer variability.² In addition, there remained a strong need for a common system of terminology between urologic pathologists, urologists, and oncologists for pre-neoplastic and neoplastic lesions of the urinary system.^{2,6} Leading up to the publication of the most recent WHO classification there were studies that validated the clinical utility of the newer system.³ In addition, multiple long term clinical follow-up studies helped show that the vast majority of low grade papillary urothelial tumors behave in a benign fashion while the urothelial (flat) carcinoma in situ and the high grade papillary urothelial tumors give rise to the majority of invasive carcinomas.^{4-7,9}

Invasion, of course, can be present in both low and high-grade lesions, and accordingly non-invasive is removed from the diagnostic line and the depth of invasion is noted in the bladder staging checklist and/or in the microscopic description. We will continue to utilize the p53 immunohistochemical stain in an effort to help guide therapeutic decisions regarding the initial diagnosis of a papillary tumor in a given patient.



Jeff Hinson, DO

— Jeff Hinson, DO

References:

1. Eble JN, Sauter G, Epstein JI, Sesterhenn IA, (Eds.): World Health Organization Classification of Tumors. Pathology and Genetics of Tumors of the Urinary System and Male Genital Organs. IARC Press: Lyon 2004.
2. Reuter VE. The Urothelial Tract. In Sternberg's Diagnostic Surgical Pathology (Eds.) Lippincott Williams & Wilkins: Philadelphia 2004.
3. Malmstrom PU, Busch C, Norlen BJ. Recurrence, progression, and survival in bladder cancer. A retrospective analysis of 232 patients with greater than or equal to 5-year follow-up. Scand J Urol Nephrol 1987;21:185-195.
4. Miyamoto H, Brimo F, Schultz L, et al. Low-grade papillary urothelial carcinoma of the urinary bladder: a clinicopathologic analysis of a post-World Health Organization/International Society of Urological Pathology classification cohort from a single academic center. Arch Pathol Lab Med 2010 Aug;134(8):1160-3.
5. Pan CC, Chang YH, Chen KK, et al. Prognostic significance of the 2004 WHO/ISUP classification for prediction of recurrence, progression, and cancer-specific mortality of non-muscle-invasive urothelial tumors of the urinary bladder: a clinicopathologic study of 1,515 cases. Am J Clin Pathol 2010 May;133(5):788-95.
6. Miyamoto H, Miller JS, Fajardo DA, et al. Non-invasive papillary urothelial neoplasms: the 2004 WHO/ISUP classification system. Pathol Int. 2010 Jan;60(1):1-8.
7. Herr HW, Donat SM, Reuter VE. Management of low grade papillary bladder tumors. J Urol 2007 Oct;178(4 Pt 1):1201-5.
8. Epstein JI. Diagnosis and classification of flat, papillary, and invasive urothelial carcinoma: the WHO/ISUP consensus. Int J Surg Pathol 2010 Jun;18(3 Suppl): 106S-111S.
9. Fine SW, Humphrey PA, Dehner LP, et al. Urothelial neoplasms in patients 20 years or younger: a clinicopathological analysis using the world health organization 2004 bladder consensus classification. J Urol 2005 Nov;174(5):1976-80.

Gestational Glucose Tolerance Update

The American College of Obstetricians and Gynecologists (ACOG) has issued a recommendation to use a 1 hour post 50 gram glucose test to screen for gestational diabetes mellitus (GDM) and a 3 hour 100 gram glucose tolerance for diagnosis of GDM. This contrasts with the American Diabetes Association (ADA) recommendation for the "one-step" 2 hour 75 gram test. Bronson laboratory will offer all three options. The reference ranges are listed below:

Gestational Screen – 1 hour 50 gm (ACOG)

Normal range is 65-139 mg/dl for the single sample drawn one hour post ingestion of 50 gm glucose. If the glucose is greater than 140 mg/dl it is an indication for the Glucose Tolerance Gestational Diagnostic.

Gestational Diagnostic – 3 hour 100 gm (ACOG)

Fasting: 70-94 mg/dl
1 hour: 70-179 mg/dl
2 hour: 70-154 mg/dl
3 hour: 70-139 mg/dl

Two or more of these glucose values must exceed reference range to confirm a diagnosis of gestational diabetes mellitus.

Gestational One Step – 2 hour, 75 gm. (ADA)

Fasting: 70-91 mg/dl
1 Hour: 70-179 mg/dl
2 Hour: 70-152 mg/dl

The diagnosis of GDM is made when any of the three plasma glucose values exceed the reference range.

LabWire is published by Bronson Laboratory Services. If you have a topic you would like addressed in this publication, call 341-8997 or send your request to Jeff Pearson, MD (pearsonj@bronsonhg.org).