On Ruling Out PE, Guidance on School Dismissals, Obtaining Urine from Young Children, and Travel and VTE

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Each month, Dr. Nahum Kovalski reviews a handful of abstracts from, or relevant to, urgent care practices and practitioners. For the full reports, go to the source cited under each title.

Another Validation of Clinical Assessment and D-Dimer to Rule Out PE

Key point: Among patients with low or intermediate risk, the sensitivity and negative predictive value of D-dimer testing were 100%.

Citation: Gupta RT, Kakarla RK, Kirshenbaum KJ, et al. D-dimers and efficacy of clinical risk estimation algorithms: Sensitivity in evaluation of acute pulmonary embolism. *AJR Am J Roentgenol*. 2009;193:425-430.

Despite research showing that clinically important pulmonary embolism (PE) can be excluded when patients with low clinical probabilities have negative D-dimer test results, many clinicians continue to order pulmonary computed tomography angiograms (CTAs) in virtually every patient with suspected PE.

Researchers conducted this study at a community teaching hospital in Chicago to determine the accuracy of clinical risk assessment plus D-dimer testing in 627 emergency department patients in whom clinicians considered PE as a diagnostic possibility.

According to Geneva scores, the proportions of patients with low, intermediate, and high probability of PE were 45%, 53%, and 3%, respectively. Outcomes were as follows:

- Among 69 low-probability patients with negative D-dimer test results (<1.2 mg/L), CTA showed no PE cases.
- Among 103 intermediate-probability patients with negative D-dimer test results, CTA showed no PE cases.
- Among 212 low-probability patients with positive D-dimer test results, CTA showed six cases of PE.
- Among 227 intermediate-probability patients with positive D-dimer test results, CTA showed 17 cases of PE.

Among patients with low or intermediate risk for PE, the sensitivity and negative predictive value of D-dimer testing were 100% (i.e., no false-negatives were reported).

For patients with high clinical probability, the current consensus is to skip D-dimer testing and go directly to imaging.

[Published in *J Watch Gen Med*, August 13, 2009–Allan S. Brett, MD.] ■

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CDC Issues Guidance for School Districts for Upcoming Academic Year

Key point: Social disruption should be considered in decisions to dismiss students due to H1N1 flu.

Citation: Updated guidance for schools for the fall flu season. Centers for Disease Control and Prevention. 2009. Available at: *www.pandemicflu.gov/plan/school/schoolguidance.html*.

When contemplating school dismissals for flu, officials should balance the goal of reducing exposure to H1N1 virus against the social disruption associated with sending students home, the CDC recommends in new guidance issued for the upcoming academic year (grades K–12).

If H1N1 severity *is the same* as during the spring outbreak, the CDC advises that:

- ill students and staff should remain at home for 24 hours

8.3 Nursing Mothers: Studies in rats have demonstrated that zanamivir is excreted in milk. However, nursing mothers should be instructed that it is not known whether zanamivir is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when RELENZA is administered to a nursing mother.

8.4 Pediatric Use: Treatment of Influenza: Safety and effectiveness of RELENZA for treatment of influenza have not been assessed in pediatric patients less than 7 years of age, but were studied in a Phase III treatment study in pediatric patients, where 471 children 5 to 12 years of age received zanamivir or placebo [see Clinical Studies (14.1) of full prescribing information]. Adolescents were included in the 3 principal Phase III adult treatment studies. In these studies, 67 patients were 12 to 16 years of age. No definite differences in safety and efficacy were observed between these adolescent patients and young adults.

In a Phase I study of 16 children ages 6 to 12 years with signs and symptoms of respiratory disease, 4 did not produce a measurable peak inspiratory flow rate (PIFR) through the DISKHALER (3 with no adequate inhalation on request, 1 with missing data), 9 had measurable PIFR on each of 2 inhalations, and 3 achieved measurable PIFR on only 1 of 2 inhalations. Neither of two 6-year-olds and one of two 7-year-olds produced measurable PIFR. Overall, 8 of the 16 children (including all those under 8 years old) either did not produce measurable inspiratory flow through the DISKHALER or produced peak inspiratory flow rates below the 60 L/min considered optimal for the device under standardized in vitro testing; lack of measurable flow rate was related to low or undetectable serum concentrations *[see Clinical Pharmacology (12.3), Clinical Studies (14.1) of full prescribing information]*. Prescribers should carefully evaluate the ability of young children to use the delivery system if prescription of RELENZA is considered.

Prophylaxis of Influenza: The safety and effectiveness of RELENZA for prophylaxis of influenza have been studied in 4 Phase III studies where 273 children 5 to 11 years of age and 239 adolescents 12 to 16 years of age received RELENZA. No differences in safety and effectiveness were observed between pediatric and adult subjects *[see Clinical Studies (14.2) of full prescribing information]*.

8.5 Geriatric Use: Of the total number of patients in 6 clinical studies of RELENZA for treatment of influenza, 59 patients were 65 years of age and older, while 24 patients were 75 years of age and older. Of the total number of patients in 4 clinical studies of RELENZA for prophylaxis of influenza in households and community settings, 954 patients were 65 years of age and older, while 347 patients were 75 years of age and older. No overall differences in safety or effectiveness were observed between these patients and younger patients, and other reported clinical experience has not identified differences in responses between the elderly and younger patients, but greater sensitivity of some older individuals cannot be ruled out. Elderly patients may need assistance with use of the device.

In 2 additional studies of RELENZA for prophylaxis of influenza in the nursing home setting, efficacy was not demonstrated *[see Indications and Usage (1.3) of full prescribing information]*.

10 OVERDOSAGE

There have been no reports of overdosage from administration of RELENZA.

17 PATIENT COUNSELING INFORMATION

See FDA-Approved Patient Labeling (17.6).

17.1 Bronchospasm: Patients should be advised of the risk of bronchospasm, especially in the setting of underlying airways disease, and should stop RELENZA and contact their physician if they experience increased respiratory symptoms during treatment such as worsening wheezing, shortness of breath, or other signs or symptoms of bronchospasm [see Warnings and Precautions (5.1)]. If a decision is made to prescribe RELENZA for a patient with asthma or chronic obstructive pulmonary disease, the patient should be made aware of the risks and should have a fast-acting bronchodilator available.

17.2 Concomitant Bronchodilator Use: Patients scheduled to take inhaled bronchodilators at the same time as RELENZA should be advised to use their bronchodilators before taking RELENZA.

17.3 Neuropsychiatric Events: Patients with influenza (the flu), particularly children and adolescents, may be at an increased risk of seizures, confusion, or abnormal behavior early in their illness. These events may occur after beginning RELENZA or may occur when flu is not treated. These events are uncommon but may result in accidental injury to the patient. Therefore, patients should be observed for signs of unusual behavior and a healthcare professional should be contacted immediately if the patient shows any signs of unusual behavior *[see Warnings and Precautions (5.3)]*.

17.4 Instructions for Use: Patients should be instructed in use of the delivery system. Instructions should include a demonstration whenever possible. For the proper use of RELENZA, the patient should read and follow carefully the accompanying Patient Instructions for Use.

If RELENZA is prescribed for children, it should be used only under adult supervision and instruction, and the supervising adult should first be instructed by a healthcare professional *[see Dosage and Administration (2.1)]*.

17.5 Risk of Influenza Transmission to Others: Patients should be advised that the use of RELENZA for treatment of influenza has not been shown to reduce the risk of transmission of influenza to others.

17.6 FDA-Approved Patient Labeling and Instructions for Use: See separate leaflet.

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after they are free of fever (without use of fever-lowering drugs);
- those who are sick at school should be separated from others until they can be sent home.

If the virus shows *increased* severity compared with the spring outbreak:
- students and staff should be screened on arrival at school and sent home if ill;
- people at high risk for complications or with ill household members should stay home;
- sick people should stay home for at least 7 days, even if they become asymptomatic. ■

Obtaining Urine Specimens in Young Children: Bag vs. Catheter

Key point: Don't rely on bag-obtained specimens alone.

Citation: Etoubleau C, Reveret M, Brouet D, et al. Moving from bag to catheter for urine collection in non-toilet-trained children suspected of having urinary tract infection: A paired comparison of urine cultures. *J Pediatr*. 2009;154:803.-806.

Urine collection methods in young children who are not toilet trained are difficult and unreliable. In this prospective cohort study, researchers from two emergency departments in France collected urine specimens by bag and then by catheter in 192 children (age <3 years; 72% girls) who had unexplained fever and positive urinalysis results from bag-obtained specimens.

Catheter-obtained specimens were positive (defined as $\geq 10^3$ CFU/mL, one species only) in 53% of children, negative in 38%, and contaminated in 8%.

Corresponding results for bag-obtained specimens were 48% positive, 21% negative, and 30% contaminated. Compared with results from catheter-obtained specimens, bag-obtained specimen cultures had a false-positive rate of 7.5% and a false-negative rate of 29%.

[Published in *J Watch General Med*, July 7, 2009—Howard Bauchner, MD.] ■

Travel and Venous Thromboembolism

Key point: Results of a meta-analysis showed a significant elevation in risk that increased with the duration of the journey.

Citation: Chandra D, Parisini E, Mozaffarian. Travel and risk for venous thromboembolism. *Ann Intern Med*. 2009;151(3): 180-190.

Concern about travel-related venous thromboembolism (VTE) has recently attracted public attention. To examine the risk for VTE in travelers, these investigators conducted a literature analysis of 14 studies (two cohort, 11 case-control, and one case-crossover) with a total of 4,055 cases of VTE. The mode of travel in the studies varied (five air-only, nine air or surface), and the outcomes evaluated were deep venous thrombosis alone in seven, pulmonary embolism (PE) or DVT in five, and PE alone in two.

Compared with non-travelers, the pooled relative risk for VTE in travelers across all studies was 2.0 ($P<0.001$). However, significant heterogeneity resulted from differences in study design—specifically, in the selection criteria for controls.

The pooled risk estimate was somewhat higher for air travel than for surface travel. When duration of travel was assessed, the risk for VTE rose at a statistically significant 18% per two-hour increase in travel duration.

[Published in *J Watch Cardiol*, August 12, 2009—Joel M. Gore, MD.] ■