but is also dependent on many host variables (eg, age, immune function, etc). Vancomycin MICs tend to "creep" upward with recurrent exposure to the drug. Patients who require multiple rounds of vancomycin tend to be sicker and suffer from other underlying conditions such as end-stage renal disease, which could easily explain the observed mortality differences. Although vancomycin is certainly not the most effective antistaphylococcal antibiotic, it is relatively inexpensive and well-studied. Before we routinely recommend the use of alternative therapies, which may cost >1,000% of vancomycin's acquisition cost, for susceptible organisms, we should demand evidence that (1) any failure is truly due to antibiotic issues and not simply a function of host factors and (2) that other drugs are truly superior in such patients. While not cheap, it should be possible to design a study of patients with MRSA bacteremia or pneumonia with MICs ≥1 μg/mL and randomize them to continued vancomycin vs switching to comparator antibiotics. If it is indeed a vancomycin issue, comparator drugs should be able to prove their superiority and thereby validate the excess cost associated with these medications. If the higher failure rates and increased mortality are due to host issues, however, changing the antibiotic will not have the desired effect. Recommendations to change a treatment paradigm should not be based on observational studies, animal studies, and pharmacokinetic modeling when randomized trials are feasible. I actually believe that other drugs should be able to outperform vancomycin, but until companies making these drugs actually complete relevant studies, we should be careful to preempt a new standard of care, as is recommended by the authors of this study.

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Diffuse Alveolar Hemorrhage in Infectious Diseases

To the Editor:

We read with great interest the article by Lara and Schwarz1 in a recent issue of CHEST (May 2010), in which they discuss the diagnosis of the underlying histologic and clinical entities responsible for diffuse alveolar hemorrhage (DAH) as well as treatment options. The authors reviewed the different causes of DAH, but they did not mention the infectious diseases that can lead to this manifestation. Thus, we would like to report the case of a patient with 2009 influenza A(H1N1) (A[H1N1]) who presented with DAH. A 59-year-old man was admitted with a 2-day history of fever and headache followed by dry cough and progressive dyspnea. He also reported an episode of hemoptysis 6 h earlier. Physical examination revealed fever, oxygen saturation on room air of 91%, and crackles in both lungs. Laboratory tests revealed a WBC count of 3,400/mm³ with absolute lymphopenia, a C-reactive protein level of 7.0 mg/dL, and a lactate dehydrogenase level of 600 IU/L; HIV serologic results were negative. High-resolution CT scans performed 3 h after admission showed diffuse ground-glass opacities bilaterally. Bronchofibroscopy revealed blood-tinged secretion coming from both lungs. BAL results were negative for mycobacteria, fungi, and malignancy. Real-time polymerase chain reaction tests confirmed infection with A(H1N1) virus. The patient was treated with oseltamivir and was discharged on the seventh day.

DAH is a clinical syndrome that often leads to respiratory failure. Once the diagnosis is made, the underlying cause must be established in order to initiate treatment.1 Pulmonary infections have been unusually associated with DAH. The etiologic diagnosis of the infection relies upon clinical history, chest imaging, BAL, microbiologic and serologic tests, and histopathologic exams. The pulmonary infections with which DAH has been associated include those caused by viruses (dengue fever, Cytomegalovirus, Hantavirus, A[H1N1]), bacteria (leptospirosis, TB), fungi (invasive aspergillosis), and others agents (Mycoplasma, Legionella, Strongyloides).2,3

Gilbert et al4 described pulmonary hemorrhage as a complication of A(H1N1) viral infection. They have suspected that severe cases of A(H1N1) pneumonia had a higher incidence of alveolar hemorrhage than previously reported. This suspicion is supported by the findings of Mauad et al, who found an intense hemorrhagic component in five of 21 patients with A(H1N1) infection who had undergone autopsy.

In conclusion, infectious causes should be considered in the diagnostic work-up of DAH cases because of the obvious therapeutic implications. In the current context of the A(H1N1) outbreak, this infection should be particularly included in the differential diagnosis of DAH.

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On the Role of Chest CT Scanning in a TB Outbreak Investigation

To the Editor:

A recent article in CHEST (May 2010) by Lee et al.1 reported the use of high-resolution chest CT (HRCT) scanning during a TB outbreak investigation. They found that nine of 18 (50%) cases diagnosed with active TB would have been missed without the use of HRCT scanning and concluded that inclusion of HRCT scanning seems helpful to reliably identify cases with active TB during an outbreak investigation. Routine use of HRCT scanning will add cost, increase radiation exposure, and undermine confidence in existing screening tools where HRCT scanning is unavailable, but the most important reason for caution is the likely absence of clinical relevance.

Patients with asymptomatic “HRCT confirmed active TB” present a case-definition dilemma, because the natural history of Mycobacterium tuberculosis infection demonstrates that transient phenomena, such as parenchymal consolidation and/or hilar adenopathy (even M tuberculosis excretion), occur quite frequently after recent primary infection.2,3 Only a small percentage of these asymptomatic “patients” progress to active disease on long-term follow-up.2,3 Therefore, it is not unexpected that HRCT scanning identifies a subset of recently exposed individuals with visible parenchymal and/or lymph node involvement despite being asymptomatic and having a normal chest radiograph. However, the clinical relevance of these findings remains questionable—whether it represents transient phenomena or is truly indicative of active disease, and whether treatment with combination therapy is warranted.

None of the patients with a normal chest radiograph and lesions suggestive of active TB on HRCT scan were sputum smear or culture positive for M tuberculosis, indicating uncertain diagnosis and/or low organism loads. The United States Public Health Service Tuberculosis Prophylaxis Preventive therapy trial conducted in the 1950s demonstrated that isoniazid monotherapy prevented progression to symptomatic disease in child TB contacts, despite the presence of radiologic signs suggestive of recent primary infection and/or minimal disease.4 This provides the rationale for symptom-based screening approaches in children.5 In certain high-risk groups the use of sensitive screening tools may well be warranted, but because subclinical transient phenomena may be detected and treated with increased regularity the routine use of HRCT scanning to screen asymptomatic TB contacts for active disease requires rigorous scrutiny. Given the current evidence, cost, and potential risks involved, there is no role for HRCT scanning as a routine screening test during TB outbreak investigations.

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References

Elevation of IL-6 Solely Is Not Sufficient to Infer Systemic Inflammation

To the Editor:

In an excellent study in CHEST (July 2010), Sabit et al. showed that a 2-h hypoxic challenge in patients with mild COPD who are clinically stable results in an elevation of serum IL-6 and some coagulation markers, such as prothrombin activation fragments 1 + 2 and thrombin-antithrombin complex. The authors concluded that a strong association exists between hypoxia, coagulation activation, and systemic inflammation and that patients with COPD may be at increased risk of VTE during air travel.

However, elevation of IL-6 solely cannot be used to infer the presence of systemic inflammation due to the pleiotropic action of IL-6 involving a variety of systems and diseases. IL-6 has been mostly studied in the context of the acute inflammatory response, although growing evidence shows IL-6 also plays a vital role in the pathogenesis of aging and chronic disease.6 In addition, IL-6 is also a “myokine,” a cytokine produced from muscle, and is elevated in response to exercise.5 Previous studies have demonstrated IL-6 levels can increase up to 100-fold during exercise, in a duration- and intensity-dependent manner.6

In the study by Sabit et al., subjects in the group with hypoxia experienced a hypoxic challenge with a mean oxygen saturation decline from 94% ± 2% to 90% ± 3%. When the oxygen concentration in the arterial blood fell, the chemoreceptors were stimulated and the ventilation increased, as shown by a rising respiratory rate (RR) and tidal volume.7 The muscle must be loaded with additional respiratory work, possibly contributing to a surge of IL-6. Although ventilation was not measured, the findings of higher RR and heart rate (HR) in the subjects receiving the hypoxic challenge were also in part compatible with our concern. (In the group with hypoxia, the RR increased from 14 ± 1 per min to 16 ± 3 per min, and the HR increased from 86 ± 6 per min to 94 ± 4 per min; in the control group, the RR increased from

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Elevation of IL-6 Solely Is Not Sufficient to Infer Systemic Inflammation

To the Editor:

In an excellent study in CHEST (July 2010), Sabit et al. showed that a 2-h hypoxic challenge in patients with mild COPD who are clinically stable results in an elevation of serum IL-6 and some coagulation markers, such as prothrombin activation fragments 1 + 2 and thrombin-antithrombin complex. The authors concluded that a strong association exists between hypoxia, coagulation activation, and systemic inflammation and that patients with COPD may be at increased risk of VTE during air travel.

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