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, 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.4 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 Trial conducted in the 1950s demonstrated that isoniazid monotherapy prevented progression to symptomatic disease in childhood TB contacts, despite the presence of radiologic signs suggestive of recent primary infection and/or minimal disease.5 This provides the rationale for symptom-based screening approaches in children.6 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.

Ben J. Marais, MD, PhD
Tygerberg, South Africa

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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.

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. In addition, IL-6 is also a “myokine,” a cytokine produced from muscle, and is elevated in response to exercise. Previous studies have demonstrated IL-6 levels can increase up to 100-fold during exercise, in a duration- and intensity-dependent manner.

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) or tidal volume. 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 companies/organizations whose products or services may be discussed in this article.

Correspondence to: Ben J. Marais, MD, PhD, Department of Paediatrics and Child Health, Faculty of Health Sciences, Stellenbosch University, PO Box 19063, Tygerberg, 7505, South Africa; e-mail: bjamin@sun.ac.za

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DOI: 10.1378/chest.10-1775
14 ± 1 per min to 15 ± 1 per min, and the HR increased from 82 ± 4 per min to 87 ± 6 per min. In this study, the role of muscle-derived IL-6 should be further clarified in order to accurately document the effect of hypoxia on IL-6.

Yi-Fong Su, MD
Kun-Ta Chou, MD
Taipei, Taiwan

Affiliations: From the Chest Department, Taipei Veterans General Hospital.

Financial/nonfinancial disclosures: The authors have reported to CHEST that no potential conflicts of interest exist with any companies/organizations whose products or services may be discussed in this article.

Correspondence to: Kun-Ta Chou, MD, Chest Department, Taipei Veterans General Hospital, No. 201, Section 2, Min-Pei Rd, Taipei 112, Taiwan; e-mail: ale1371@yahoo.com.tw

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DOI: 10.1378/chest.10-1821

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Response

To the Editor:

We thank Drs Su and Chou for their interest in our recent article in CHEST (July 2010), and submit our response to the comments made. We would like to clarify that although our study did demonstrate a rise in markers of coagulation and serum IL-6 in response to hypoxic challenge, such an association does not necessarily imply a causal relationship. We accept that the rise in serum IL-6 in response to hypoxia is not clear and, moreover, may not necessarily reflect a rise in IL-6 at the tissue level. We agree with the authors that respiratory muscles may be a possible source for increased IL-6 release as a consequence of hypoxia stimulating ventilation. Indeed, our department has demonstrated a rise in serum IL-6 in response to exercise in patients with cystic fibrosis. However, given the modest rise in respiratory rate in the patients undergoing hypoxic challenge, it would seem unlikely that the increased load on respiratory muscles could solely account for the rise in serum IL-6. A number of other studies have similarly demonstrated a rise in serum IL-6 and other inflammatory markers in response to hypoxia, although the exact mechanism for this association is yet to be elucidated.

Of possible greater interest is whether this rise in serum IL-6, regardless of its origin, contributes to the rise in markers of coagulation, as is postulated in other disease states associated with chronic systemic inflammation. Such a question only can be answered by future studies examining the relationship among hypoxia, systemic inflammation, and coagulation in patients with systemic inflammation and healthy control subjects.

Ramsey Sabit, MD
Paul Thomas, HTec
Dennis J. Shale, MD, FCCP
Vale of Glamorgan, Wales
Peter Collins, MD
Cardiff, Wales
Seamus J. Linnane, MB, BCh
Dublin, Ireland

Affiliations: From the Department of Respiratory Medicine (Drs Sabit, Shale, and Linnane), Academic Department, and Department of Lung Function (Mr Thomas), University Hospital Llandough; Department of Haematology and Coagulation (Dr Collins), University Hospital of Wales; and The Blackrock Clinic (Dr Linnane).

Financial/nonfinancial disclosures: The authors have reported to CHEST that no potential conflicts of interest exist with any companies/organizations whose products or services may be discussed in this article.

Correspondence to: Ramsey Sabit, MD, Department of Respiratory Medicine, University Hospital Llandough, Penarth, Vale of Glamorgan, CF64 2XX; e-mail: ramsey-sabit@gmail.com

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DOI: 10.1378/chest.10-2099

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Turning the Dial to Futility

To the Editor:

In a recent editorial in CHEST (April 2010), Hubmayr and Farmer questioned the rationale of “rescuing” patients with 2009 influenza A(H1N1) by using extracorporeal membrane oxygenation (ECMO) when they are failing using conventional treatment. The argument was made that results similar to what has been reported in New Zealand with the use of ECMO can be achieved without ECMO or other critical-care interventions (eg, nitric oxide [NO], prone positioning). The authors argue that physiologic end