

TcPco₂ measurements may help in deciding the timing of arterial sampling and may therefore considerably reduce the frequency of painful invasive arterial sampling.

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doi: 10.1136/thx.2005.051664

Competing interests: none declared.

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Per lesion analysis is misleading

We read with interest the randomised controlled trial by Häußinger and co-workers¹ which compared autofluorescence bronchoscopy (AFB) plus white light bronchoscopy (WLB) with WLB alone for detecting precancerous lesions. The authors stratified their patients into four different risk groups before randomisation. They also excluded from analysis biopsy samples taken from or next to visible tumours. Their major findings suggested that WLB plus AFB was significantly superior to WLB alone for detecting precancerous lesions.

While we appreciate the clinical significance of their major findings, we found the per lesion analysis adopted in the paper misleading for evaluating the sensitivity, specificity, and predictive values of AFB plus WLB. They obtained biopsy tissue from all suspicious areas and at least two areas of non-suspicious appearance in each subject.¹ Thus, each study subject contributed an arbitrary number of biopsy samples which might also be dependent on each other when they were taken from the same subject. Other investigators also adopted a similar approach in a loose manner.^{2–4} Apart from causing confusion, a per lesion analysis does not inform clinical decision. It may also partly explain the high variability of sensitivity and specificity in different studies.¹

Sensitivity, specificity, and predictive values are clinically relevant because they inform us how well a test will perform in certain clinical contexts. The preferred approach for ascertaining these parameters is therefore a per subject analysis in which each subject is labelled as either test positive or test negative and the test status is matched against the representative histological result of the subject's biopsy. Study subjects should also be representative of those encountered in a typical clinical scenario.

To illustrate the potential flaw in a per lesion analysis, let us vary the number of biopsy samples taken arbitrarily from non-suspicious sites in both arms (WLB plus AFB arm versus WLB alone) of the quoted study¹ without changing negative predictive values and the number of biopsy samples from suspicious sites (table 1). When the number of non-suspicious biopsy samples is doubled or tripled, the sensitivity, specificity and prevalence in each arm change accordingly. The sensitivity of WLB plus AFB relative to that of WLB alone also changes from 1.42 (95% CI 0.94 to 2.15) to 1.72 (95% CI 1.04 to 2.83) and 1.94 (95% CI 1.13 to 3.33), respectively. Likewise, the prevalence of pre-invasive lesions detected by WLB plus AFB relative to that detected by WLB alone changes from 1.61 (95% CI 0.93 to 2.79) to 1.37 (95% CI 0.84 to 2.22) and 1.23 (95% CI 0.79 to 1.90), respectively. Thus, a per lesion approach could generate different sets of arbitrary values according to an arbitrary change in the number of biopsy samples taken from non-suspicious areas.

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Dr Häußinger was asked to comment but no reply had been received by the time this issue of *Thorax* went to press.

Funding: none.

Competing interests: none.

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A&E department: a missed opportunity for diagnosis of TB?

The World Health Organization declared tuberculosis (TB) to be a global emergency in 1993. Since then there has been a resurgence of TB in England and Wales, particularly in London.^{1,2} Early diagnosis, particularly of infectious cases, is a major factor in the success of control programmes.³ In the UK, TB continues to disproportionately affect vulnerable groups—including the homeless, illicit drug users, alcoholics, and immigrants recently arrived from high prevalence countries. These groups frequently find it difficult to access appropriate health care and often rely on Accident and Emergency (A&E) departments for health-care provision. We examined how frequently patients with TB attended the local A&E department before their diagnosis and whether their A&E attendances led to a diagnosis of TB being made.

From January 2001 to March 2002 there were 130 notifications of TB at University College London Hospitals. For each patient with TB the A&E department records were examined for the 6 month period before the date of diagnosis. Forty one (31%) of the 130 patients attended the A&E department on 51 occasions during the 6 months prior to diagnosis. Thirty six of the 41 (88%) had no access to a general practitioner; of the remainder, the majority self-referred to A&E. The demographic characteristics of patients attending A&E and the 130 patients were similar. Of A&E attenders, 17 were black African, 13 were Asian, and 11 were white. Eighteen had underlying risk factors

Table 1 Effects of varying the number of samples from non-suspicious areas in a per lesion analysis

Diagnostic test	Biopsy results		Sensitivity (%)	Specificity (%)	Prevalence (%)
	Positive	Negative			
WLB+AFB					
Test positive	28*	623*			
Test negative					
Original	6*	874*	82.3*	58.4*	2.2*
2 × Original	6 × 2	874 × 2	70.0	73.7	1.7
3 × Original	6 × 3	874 × 3	60.9	80.8	1.4
WLB alone					
Test positive	11*	514*			
Test negative					
Original	8*	843*	57.9*	62.1*	1.4*
2 × Original	8 × 2	843 × 2	40.7	76.6	1.2
3 × Original	8 × 3	843 × 3	31.4	83.1	1.1

WLB, white light bronchoscopy; AFB, autofluorescence bronchoscopy.

*Figures as reported in the study by Häußinger et al.[1]

Table 1 Patients in whom TB was not diagnosed as a result of their A&E attendance (12 attendances in 10 patients)

Patient	Ethnic group	Age (years)	Risk factor for TB	Admitted to hospital	Site of TB	Microbiologically confirmed diagnosis	Time from A&E attendance to diagnosis of TB (days)	Reason for presentation to A&E
1a	White	65	HIV+	Yes	Pleural	No	178	Dyspnoea, ankle oedema
1b				Yes			155	Dyspnoea, ankle oedema
2	Asian	53	Dialysis	Yes	Pleural	No	122	Sepsis, MRSA bacteraemia
3	Black African	25	HIV+*	Yes	Meningitis	No	45	Headache, malaise, right iliac fossa pain, Dyspnoea, bronchiectasis
4a	Asian	59	No	Yes	Pulmonary	Smear positive, sensitive	126	
4b				No	Pulmonary	Smear positive, sensitive	134	Power failure at home
5	Asian	3	No	No	Pulmonary	No	166	Mouth ulcers
6	Asian	24	No	No	Pulmonary	Smear positive, sensitive	100	Malaise, weight loss
7	Asian	16	No	No	Pulmonary	Smear positive, MDR	2	Haemoptysis
8	Black African	30	No	No	Pulmonary	Smear negative, sensitive	184	Cough, diagnosed as LRTI
9	Black African	22	No	No	Pulmonary	No	12	Foreign body in ear
10	Asian	40	No	No	Pulmonary and psoas abscess	No	82	Cough

*HIV infection only diagnosed after admission to hospital. MRSA, methicillin resistant *Staphylococcus aureus*; HIV+, infected with human immunodeficiency virus; LRTI, lower respiratory tract infection; MDR, multidrug resistant.

for TB (HIV infection in 10, alcohol abuse in five, illicit drug use in one, and renal dialysis in two). The site of infection was pulmonary in 27 (17 smear positive), pleural in five, lymph node in three, meninges in three, abdominal in two, and spinal in one. Of 30 patients who were culture positive, 24 had sensitive TB, two had isoniazid monoresistant disease, two had streptomycin monoresistant disease, and two had multidrug resistant TB.

Patients were admitted to hospital on 35 of the 51 attendances at the A&E, three directly to the intensive care unit. TB was not diagnosed on five of the 35 occasions (three patients, table 1). Patients were not admitted following the remaining 16 attendances but in three patients a diagnosis of TB was made at the time of A&E attendance. Five patients were referred to (and one already had) an appointment for the TB clinic. In seven patients TB was not diagnosed (table 1).

At this centre almost one third of patients with TB attended the A&E department in the 6 months prior to diagnosis. The diagnosis of TB was missed in 10/41 A&E attendees (24.3%). This may represent an underestimate as patients may have attended other A&E departments, or may have been seen in our A&E department but treated for TB at another hospital. The reason for this high rate of A&E attendance may reflect the inability of this patient group to access appropriate health care. This suggestion is supported by

the finding that 69% of patients in whom TB was subsequently found required admission to hospital compared with an overall figure of 6.7% of all A&E attendances during this period.

The diagnosis of TB was made as a direct result of the A&E attendance in three quarters of patients. Possible reasons for missed diagnosis in the remainder include failure to suspect TB, presenting symptoms not typical of TB, other diagnoses being more clinically apparent, and some patients may not have had TB at the time of their A&E presentation.

A&E departments serving vulnerable populations represent an opportunity for the early diagnosis of TB.⁴ Staff working in this environment should have a high index of suspicion for this diagnosis, particularly in patients at risk of infection, regardless of their reason for A&E attendance.

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This study was carried out within the guidelines of the University College Hospitals research ethics committee.

Funding: none.

Competing interests: R F Miller is Editor of *Sexually Transmitted Infections*, part of the BMJ Publishing Group. The other authors declare no competing interests.

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