

## Blair H Smith

Professor of Primary Care Medicine

## Nicola Torrance

Research Fellow, Aberdeen Pain Research

Collaboration, University of Aberdeen

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### ADDRESS FOR CORRESPONDENCE

#### Blair H Smith

Professor of Primary Care Medicine,  
University of Aberdeen, Department of  
General Practice and Primary Care,  
Foresterhill Health Centre,  
Westburn Road, Aberdeen, AB25 2AY.  
E-mail: blairsmith@abdn.ac.uk

# The new tuberculosis

## Raised awareness of tuberculosis is vital in general practice

Thirty years ago epidemiologists confidently predicted that tuberculosis (TB), like smallpox, would soon be eradicated. But TB is resurgent in places as diverse as sub-Saharan Africa, European cities, the former Soviet Union, central Asia and south America.<sup>1,2</sup> New York's TB epidemic of the 1990s cost £625m to control.<sup>3</sup> The World Health Organisation declared TB a global emergency in 1992.<sup>4</sup> Multidrug resistant (MDR-TB)<sup>5</sup> and rapidly fatal extremely drug resistant (XDR-TB) strains have made newspaper headlines. This re-emergence has rightly been dubbed 'the new TB'.<sup>6</sup>

Infectious diseases thrive in times of social and environmental upheaval — TB reached its (initial) peak during the industrial revolution. We have just completed the most barbaric century in recorded history,<sup>7</sup> human migration is unprecedented,<sup>8</sup> and climate change is a reality. Several factors are catalysing the re-emergence of TB: first, the advent of HIV,<sup>9</sup> coupled with the huge reservoir of latent TB infection (one-third of the world is estimated to be infected); second, rising levels of multiple drug resistance, stemming from inconsistent antibiotic use and treatment non-

completion; and third, disruption arising from conflicts, widening social inequalities and disrupted health systems.

The rise of TB in the UK continues: the annual UK figures from the Health Protection Agency show an 11% increase in cases for 2005 with the majority of the 8113 total occurring in young adults (61% between ages 15–44 years) and in the non-UK born population (72%).<sup>10</sup> Notification rates of TB in east London have exceeded 100/100 000 population which is approaching the average for India as a whole.<sup>11</sup> Nine per cent of UK cases are resistant to at least one first-line drug. Treatment completion rates at 79% are below the 85% target in the Chief Medical Officer's Action Plan.<sup>12</sup> Death is the commonest reason for not completing treatment in patients aged over 45 years, notably among white UK-born men.<sup>10</sup> The NHS has recently focused efforts on improving chronic disease management, but these data, and other problem infectious diseases — HIV, hepatitis C, sexually transmitted diseases — suggest they are ignored at our peril.

To stereotype TB as a disease of foreign-

born people is unwise and clinically inaccurate. TB remains first a disease linked to poverty and social exclusion.<sup>13</sup> North east London's ongoing outbreak of isoniazid-resistant TB has reached 292 cases, is the largest in Europe, and is focused on prisoners and crack cocaine abusers rather than a specific ethnic minority group (G Bothamley, personal communication, 2007). That two-thirds of TB cases occur in people born abroad suggests that migration is a factor, but to say that migrants bring TB to the UK is an oversimplification. In eight out of 10 cases active TB is diagnosed 2 years or more after their arrival in the UK, suggesting that factors related to migration predispose to reactivation of latent TB infection.<sup>10</sup> These might be nutritional, stress-related or environmental, such as suboptimal housing or overcrowding once in the UK. Interestingly, vitamin D levels fall after migration to the UK and vitamin D deficiency is an independent risk factor for TB.<sup>14</sup> Vitamin D was used as a treatment in the pre-antibiotic era (as was sunbathing or 'heliotherapy')<sup>15,16</sup> and recent data show the vitamin induces innate immunity to *Mycobacterium tuberculosis*.<sup>17</sup>

In this issue of the Journal Metcalfe *et al* use qualitative methods to describe the process of diagnosis in 16 cases of TB in Wales. This is interesting because TB has traditionally been seen as a disease managed in secondary care, with chest physicians diagnosing, notifying and providing treatment and follow up. Metcalfe's paper describes typical and atypical presentations of TB and the low level of suspicion among GPs. Herein is the key, highlighting raised awareness and early diagnosis as the most important contribution of primary care to TB control. GPs and practice nurses should no longer be surprised to diagnose TB in their patients, they should be expecting it and actively excluding it in patients with the varied symptoms with which it can present. Atypical presentations will become more common as the percentage of extra-pulmonary and HIV-related cases is increasing.<sup>10</sup> In Hackney, east London, GPs diagnose or refer for diagnosis almost half the cases of TB in the borough. A recent randomised screening programme, set in primary care and focused on simple verbal screening in the registration health check increased this further, identified more latent TB infection and increased sevenfold the rate of BCG (Bacille Calmette-Guérin) immunisation in people over age 5 years.<sup>18</sup> Such screening is acceptable to patients<sup>19</sup> and relatively cheap to carry out.<sup>20</sup> The impact was similar in magnitude to existing contact tracing activity and to new entrant screening clinics, regarded as the current mainstay of case-finding. While the prevalence of TB may not be high enough in other boroughs to justify a formal screening programme at the registration health check, the benefits of this intervention arose largely from raised awareness of TB in primary care. Pulmonary TB is often diagnosed after one or more failed courses of antibiotics prescribed in primary care. GPs and practice nurses need to lower their thresholds for requesting chest X-rays and sending sputum samples for acid fast bacilli examination, and (despite current financial disincentives) for referring those with unexplained symptoms. Greater use of these cheap investigations would reduce diagnostic delay, and lead to fewer patients ultimately presenting at accident and emergency departments. TB is more

common among the socially excluded, and people from such groups frequently either find it difficult to register in primary care, or if they are registered, find making and keeping appointments more difficult. A second, more general role for primary care not just in relation to TB, but also to equity, is to ensure ease of registration and subsequent access for groups such as the homeless, drug users, ex-prison population, refugees and asylum seekers.

DNA fingerprinting of TB strains causing disease in London suggests that reactivation of latent disease accounts for more new cases than infection arising from person to person transmission.<sup>21</sup> This suggests that identification and treatment of people with latent disease is a priority. Here again primary care may have a role through targeted screening, especially in areas of high TB incidence, since a key to controlling the UK's rising TB rates may be more comprehensive identification of, and treatment of, latent TB infection.<sup>22</sup> Latent disease is currently identified through tuberculin skin testing — the oldest screening test in medicine.<sup>23</sup> It suffers from poor specificity due to crossreactivity of purified protein derivative with BCG and is of little use in patients aged over 35 years. New immunodiagnostic tests based on TB-specific antigen-stimulated interferon- $\gamma$  secretion have the benefit of not being confounded by BCG immunisation or immunodeficient states such as HIV infection.<sup>24</sup> The exact role of these tests must be determined, but they may be crucial in identifying large numbers of patients with latent infection in the community, and in confirming (or excluding) infection in complex cases, particularly as the cost of the tests falls.

The relative contributions of improved social conditions and medical interventions to the decline in TB incidence through most of the 20th century have been a matter of considerable debate. Both will be needed if TB is to be brought under control whether in the UK or globally.

#### Chris Griffiths

Professor of Primary Care

#### Adrian Martineau

Clinical Lecturer

Centre for Health Sciences, Barts and the London, Queen Mary's School of Medicine and Dentistry

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## ADDRESS FOR CORRESPONDENCE

### Chris Griffiths

Centre for Health Care Sciences  
2 Newark Street, London E1 2AT.  
E-mail: c.j.griffiths@qmul.ac.uk