25th anniversary of the BTS

The BTS and our 25th anniversary

Sheila Edwards

An organisation "fit for purpose"

As the British Thoracic Society (BTS) comes to the end of its 25th anniversary year, several articles in this issue of *Thorax* have been commissioned to provide accounts of some of the important developments in respiratory medicine that have impacted on practice.

As well as the developments described in these articles, it is a suitable time to reflect on the changes that have taken place in the management and governance of the Society's affairs. These have provided a strong frame, a sturdy heart and a healthy set of bellows to fuel the drive and enthusiasm of all those colleagues over the last 25 years who have contributed to the Society's achievements. There have been several key events since Dr Martin MacNicol and Dr Harry Gribbin led a highly significant "think tank" in the early 1990s. This gave shape and structure to the Society's constitution and set up the Standing Committee structure which has remained in broadly similar format until the present day.

In 1998 a management review proposed by the Society's auditors resulted in clearer definition of the Trusteeship of the Society and the establishment of a more effective head office, with the appointment of the Society's first Chief Executive. The Charity Commission agreed to the necessary changes in the Memorandum and Articles of Association and therefore the elected Council became an advisory body for the Executive Committee, which became the Board of Trustees (ie, the Chairs of Standing Committees and Honorary Officers). A more recent change was agreed in 2006, which enabled the appointment of up to three Trustees who have no affiliation

with a Standing Committee but who bring specific skills and experience as and when required (such as the recent appointment of a lay member).

The Society has for many years been a broad church, and there is a genuine commitment to inclusivity and team working across all levels. A significant change in the way in which interested members could be involved in the governance of the Society was introduced while Dr Jim Catterall was Honorary Secretary. His influential "democratisation" paper in 1999 still holds sway today—there is an annual call for volunteers for Committees in the summer each year, and we also encourage the participation of representatives of a number of allied professional organisations on Committees and Guideline Groups.

Those who were present to hear Professor Stephen Holgate's Presidential address at the December 2006 Winter Meeting heard him speak with passion and eloquence about the "Big Tent"—the need to continue to work towards the goal of bringing the voices of all respiratory health professionals and patients under one powerful umbrella. This pulled together several themes which had been actively pursued within the Society for several years, and work has continued in the past year with a number of organisations to provide practical and other support towards this goal. BTS has provided secretariat and other assistance to the Association of Respiratory Nurse Specialists since January 2006; is about to provide membership and other administrative support to the Association of Chartered Physiotherapists in Respiratory Care (ACPRC); has established a very

important committee with primary care colleagues to look at maintaining standards of care across traditional boundaries as care moves into the community (IMPRESS); and is delighted to have been the catalyst and support mechanism for the development of the British Associations of Stop Smoking Practitioners (BASSP). This was launched at the House of Commons in July 2007 with a formal reception sponsored by its Patron, Kevin Barron MP.

All of the Society's activities are dedicated to improving standards of patient care. We must ensure that the Society's policies and recommendations are represented to policymakers and regional and local health providers as well as to our members. As we move into the new year, plans are well in hand to ensure that the Society has in place a leaner and more responsive structure with effective communication channels in place. The system of Specialist Advisory Groups, more strategic links with national and regional Thoracic Societies, plans for a more effective website, the ability to gather meaningful and targeted data about services, a streamlined and reformed Committee structure, a revised strategic planning cycle, and a newly-expanded head office team should all see the Society in good shape for the next 25 years, as the challenges from the external environment require more nimble responses.

Governance, management and communications issues are not the basis of heated or enthusiastic discussion over refreshments breaks during the Winter Meeting or at clinic team meetings. The best way to make sure that this happy state continues is for Trustees and others to continue to work together on our core activities and projects but remembering, from time to time, to review the Society's structures, to ensure that they always remain "fit for purpose".

Thorax 2007;62:1019.
doi: 10.1136/thx.2007.091116

Correspondence to: Sheila Edwards, British Thoracic Society, 17 Doughty Street, London WC1N 2PL, UK; sheila.edwards@brit-thoracic.org.uk

Tuberculosis

Tuberculosis and its future management

John C Moore-Gillon

Will we do better in the next 25 years?

Twenty-five years ago, most writers on tuberculosis (TB) would, if asked to predict what the position would be by

2007, have anticipated better diagnostics, safer drugs, shorter treatment times, a better vaccine, the near eradication of TB

in the developed world and falling rates in the developing world. Some perceptive individuals were sounding the warning bells, but most pundits would have been profoundly wrong. They would have been closest to the mark if they had simply summed up their prediction of the position 25 years later, in 2007, as "Much the same, really—except where it's much worse."

Predictions about TB are particularly fraught with difficulty because the impact of factors beyond the control of clinicians, researchers and the pharmaceutical industry is far greater with TB than it is

in diseases like asthma, chronic obstructive pulmonary disease and lung cancer. These views on TB and its future management are therefore contingent upon three assumptions—all, some or none of which may come to pass: a modest increase in overall global prosperity, wars and political instability being at least no worse than they are at present, and the development of a reasonably effective AIDS vaccine. We can be completely confident of only one thing: 25 years from now, the December 2032 issue of *Thorax* (whether on paper or not) will reproduce these December 2007 editorials with a commentary on the extent to which I (and my co-authors) got it wrong.

The Stop TB partnership, coordinated by the World Health Organisation, has set out the actions—and the funds—needed for TB control.¹ Targets include the halving, by 2015, of TB prevalence and deaths compared with 1990 levels, and the elimination of TB as a global public health problem by 2050. Progress in vaccines, diagnostics and drugs is needed, but so is “advocacy, communications and social mobilisation” to ensure that an appropriate political and social—as well as medical—infrastructure is in place. There are clear milestones: a new TB drug (the first for 40 years) by 2010, a new and effective vaccine by 2015 and a 1–2 month duration treatment regimen soon after. But achieving these will cost big money—US\$56 billion—and that is US\$31 billion more than the funds currently identified. At last, though, there are signs that industry, the academic world and philanthropy are coming together, to varying degrees, in bodies like the Aeras Global TB Vaccine Foundation, the Global Alliance for TB Drug Development (the TB Alliance) and the Foundation for Innovative New Diagnostics (FIND). Backed up with money direct from the Gates Foundation (a name which keeps recurring in the TB field) and governments (including the USA, UK, Netherlands and the European Union), TB research and development is moving ahead.

Apart from the efforts of a few dedicated research groups, vaccine development had languished in the wilderness since BCG was introduced 80 years ago. BCG has at very best 80% efficacy—far less than this in many parts of the world—and there are some concerns about its use with the rising prevalence of HIV/AIDS. Approaches to vaccine development can use BCG as the starting point to produce modified recombinant BCG strains with higher immunogenicity, or may use *Mycobacterium tuberculosis* itself to develop knock-out mutants with the antigenic profile of TB but without (the researcher hopes) its pathogenicity. A further alternative is to use subunit

vaccines containing antigens which confer additional protection by boosting the response occurring after priming by conventional BCG.² Up to six vaccine candidates will enter phase I trials in 2007, one should enter phase II in 2008, and phase III trials may begin as early as 2010.

Constrained by resources, TB control programmes in resource-poor countries understandably must concentrate on detecting active pulmonary disease that is infectious to others. Sadly, politicians (and the newspapers) in some wealthier countries seem to believe that mass chest x rays would eradicate TB. The problem is that about *one-third* of the global population is already infected with TB, each with the potential for developing active disease. Intervention with chemoprophylaxis reduces that risk, but identification of those with latent TB infection using the tuberculin skin test is unreliable, particularly in BCG-vaccinated populations. More secure identification of those with latent TB infection using blood tests based on gamma-interferon release from TB-sensitised lymphocytes may help,³ and there will no doubt be further developments in this field. But might vaccines have a part to play here as well? Experience with other infectious diseases conditions us to think solely in terms of *pre-exposure* vaccines, but with TB a possible approach could be *post-exposure* vaccination aimed—like chemoprophylaxis—at reducing the risk of later progression to active disease.² Certainly, mathematical modelling backs up what seems intuitively likely: that control of TB will not be achieved simply by treating cases of active disease.⁴ Finding and treating active infectious cases as quickly as possible is vital, but this “firefighting” approach will not eradicate TB.

Trials of fluoroquinolones in reducing the duration of TB therapy are under way, but really major steps forward will probably only occur with new classes of drugs, not discovered serendipitously but developed in a targeted way, driven by a deeper understanding of the molecular structure and cellular metabolism of the TB bacterium.^{5–6} In particular, we must unravel the mechanisms which enable TB to remain viable for long periods in an actual or near non-replicative state, and to largely camouflage its presence from the host's immune system while it does so. Nitroimidazole derivatives are beginning to show promise in dealing with these dormant organisms, and developments in this area are crucial to reducing overall treatment times for TB. A very promising diarylquinoline⁷ with early and late bactericidal activity, no cross-resistance with existing TB drugs and activity against multidrug-resistant (MDR) TB is moving

towards clinical trials. We must hope that, at last, wholly new drugs for TB really are on the horizon.

In terms of diagnosing active disease, problems with the sensitivity of nucleic acid assays when applied to primary specimens mean they have not been the hoped-for breakthrough in terms of timing, and they remain relatively expensive and demanding technically. There have, though, been drops in culture times, and there are developments in rapid identification of organisms using techniques that may be applicable in relatively resource-poor settings.^{8–9} Will we achieve the goal, predicted for decades but so far elusive, of a serodiagnostic method for active disease that is both highly sensitive and highly specific? Some innovative approaches may lead us in the right direction.¹⁰

A few years ago a conference on MDR TB at the Royal Society of Medicine in London was subtitled “From molecules to macroeconomics”. The future management of TB will depend on developments in both of these areas and at every level in between. At a strategic national and international level there are perhaps grounds for (very) cautious optimism which were not present even 5 years ago. Progress in vaccine development, improved diagnosis of latent TB infection and faster identification of active disease, the prospect of strengthened national TB programmes and the emergence of global goals backed up by expressions of political will (and a little money) are encouraging signs. They might achieve little, though, without an AIDS vaccine and the widespread availability of antiretroviral drugs, but HIV/AIDS programmes and TB programmes must work together and not divert funding away from each other.¹¹ Further, extensively drug-resistant (XDR) TB is a very serious worry indeed, and could well sweep aside the slightly encouraging developments outlined above.^{12–15}

At the level of the individual patient, and specifically in resource-rich countries, there will be a powerful drive towards management of each case on a multidisciplinary basis, as with cancer.¹⁶ Indeed, given that (unlike cancer) the physical health and even the mortality of other people depend on the effective management of the initial patient, the case for wide professional involvement is a very strong one. Reliable identification of latent TB infection will be accompanied by a personalised assessment of the risk of progression to disease. Strain typing will improve techniques of contact tracing/active case finding, but probably only after a few years chasing red herrings, when molecular studies imply a clustering of cases where in fact there is no recent association. There will be yet faster diagnosis and drug susceptibility testing

of active disease, and treatment regimens really will be shorter and less potentially toxic. I'm less optimistic about stigma. Twenty years ago, HIV/AIDS could reasonably be regarded as "the new leprosy" in terms of the public reaction to those with the condition. TB has now moved into that role and, unlike HIV/AIDS, it has too few articulate, high profile and powerful sufferers to alter public perceptions. If we are to do better in the next 25 years than we have done in the last 25, there must be social and political changes, not just scientific ones.¹⁷

Thorax 2007;**62**:1019–1021.
doi: 10.1136/thx.2007.090936

Correspondence to: Dr John C Moore-Gillon, Department of Respiratory Medicine, St Bartholomew's and Royal London Hospitals, London EC1A 7BE, UK; john.moore-gillon@bartsandthelondon.nhs.uk

Competing interests: None.

REFERENCES

- 1 **Stop TB Partnership.** *The global plan to stop TB, 2006–2015.* Geneva: WHO, 2006 (WHO/HTM/STB/2006, 35). <http://www.stopTB.org/globalplan> (accessed 24 September 2007).
- 2 **Kaufmann SHE,** Baumann S, Nasser Eddine A. Exploiting immunology and molecular genetics for rational vaccine design against tuberculosis. *Int J Tuberc Lung Dis* 2006;**10**:1068–79.
- 3 **Lalvani A.** Diagnosing tuberculosis infection in the 21st century: new tools to tackle an old enemy. *Chest* 2007;**131**:1898–906.
- 4 **Dye C,** Williams BG. Eliminating human tuberculosis in the 21st century. *J R Soc Interface* (Epub ahead of print 9 August 2007).
- 5 **Ginsberg M,** Spigelman M. Challenges in tuberculosis drug research and development. *Nat Med* 2007;**13**:290–4.
- 6 **Williams KJ,** Duncan K. Current strategies for identifying and validating targets for new treatment-shortening drugs for TB. *Curr Mol Med* 2007;**7**:297–307.
- 7 **Andries K,** Verhasselt P, Guillemont J, et al. A diarylquinoline drug active on the ATP synthase of *Mycobacterium tuberculosis*. *Science* 2005;**307**:223–7.
- 8 **Moore D,** Evans C, Gilman R, et al. Microscopic-observation drug-susceptibility assay for the diagnosis of TB. *N Engl J Med* 2006;**355**:1539–50.
- 9 **Hilleman D,** Rusch-Gerdes S, Richter E. Application of the Capilia TB assay for culture confirmation of *Mycobacterium tuberculosis* complex isolates. *Int J Tuberc Lung Dis* 2005;**9**:1409–11.
- 10 **Agranoff D,** Fernandez-Reyes D, Papadopoulos A, et al. Identification of diagnostic markers for tuberculosis by proteomic fingerprinting of serum. *Lancet* 2006;**368**:1012–21.
- 11 **Moll T.** TB on the back burner, losing curable status. *Int J Tuberc Lung Dis* 2007;**11**:355.
- 12 **Ghandi N,** Moll A, Sturm AW, et al. Extensively drug resistant tuberculosis as a cause of death in patients co-infected with tuberculosis and HIV in a rural area of South Africa. *Lancet* 2006;**368**:1575–80.
- 13 **Raviglione M.** XDR-TB: entering the post-antibiotic era? *Int J Tuberc Lung Dis* 2006;**10**:1185–7.
- 14 **Blower S,** Supervie V. Predicting the future of XDR tuberculosis. *Lancet Infect Dis* 2007;**7**:443.
- 15 **Dorman SE,** Chaisson RE. From magic bullets back to the Magic Mountain: the rise of extensively drug-resistant tuberculosis. *Nat Med* 2007;**13**:295–8.
- 16 **Department of Health.** *Tuberculosis prevention and treatment: a toolkit for planning, commissioning and delivering high-quality services in England.* London: Department of Health, June 2007. http://www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/DH_075621 (accessed 9 October 2007).
- 17 **Maher D,** Dye C, Floyd K, et al. Planning to improve global health: the next decade of tuberculosis control. *Bull WHO* 2007;**85**:341–7.

Lung disease in children

The future for lung disease in children

Warren Lenney

Chest physicians and respiratory paediatricians must work closely together to prioritise areas of respiratory research

The textbook space dedicated to specific diseases usually reflects the importance of the disease at the time of publication. In Sir Wilfred Sheldon's "Diseases of Infancy and Childhood" published in 1951, the top five respiratory disorders were tuberculosis (36), suppurative lung disease (22), pneumonia (20), croup, diphtheria and bronchitis (12) and asthma (10), where the figures in parentheses reflect the relative percentage page space of the five disorders. In 1990 in "Respiratory Illness in Children" by Phelan, Landau and Olinsky the top five were acute respiratory infection (30), asthma (27), cystic fibrosis (19), congenital abnormalities (16) and tuberculosis (8). By the time textbooks are published they are already out of date because of the rapidly changing clinical picture, but what is clear over the past half century is that paediatric respiratory disease has remained common and is a significant burden in childhood for families and for the health economy. In the UK, approximately 25% of all paediatric outpatient attendances, 30% of paediatric inpatient events and 35% of paediatric primary care

consultations are because of significant respiratory morbidity. Much adult respiratory disease has its origins in childhood (or even at conception in diseases with strong genetic influences). Sixty percent of asthma in adults today originates in early childhood, and it is interesting to speculate what the broad respiratory picture will look like in children in 20 years' time.

With regard to acute respiratory infections, it is highly probable that viruses will remain the principal culprits and, in the winter months, acute viral bronchiolitis will continue to dominate our hospital wards and be the cause of recurrent cough and wheeze.¹ Respiratory syncytial viral (RSV) bronchiolitis is characterised by Th2 cytokine release² and, through the upregulation of neutrophil growth factor, causes persisting increased vascular permeability and airway hyperresponsiveness.³ Despite understanding the underlying mechanisms of the acute infection and the subsequent respiratory symptoms, prevention and treatment remain elusive. The monoclonal antibody palivizumab

has become the preventive treatment of choice in a very small number of high-risk infants, but its high cost and the local variability in the virulence of RSV has led to much debate about when to use it.^{4–5} Despite much research, the complex immunopathology of RSV has prevented the development of a safe and effective vaccine,⁶ although current studies are evaluating subunit vaccines⁷ and medicines which can block its replication.⁸ Treatment for severe acute viral bronchiolitis has advanced little over the last 30 years, and there is no medicine on the horizon that is likely to be of significant benefit other than additional oxygen for hypoxaemia.

It seems that the rhinovirus (RV) is more likely to induce allergic sensitisation than RSV, but strategies to prevent RV infections are not close at hand. Although the prevalence of childhood asthma in the UK is now lower than previously, recurrent wheeze and allergic asthma in childhood will continue to be major health issues. It seems most unlikely that any new pharmacological agents will become available in the next 20 years, so improvement in management needs to be directed at environmental issues which influence wheezing and better delivery of care in the community, targeting those individuals who need it most. At present the "inverse care law" applies in that, despite guidelines, care pathways, effective medication and improved understanding of the pathophysiology of the disease, control of asthma symptoms remains poor with patients failing to get access to the level of care they need.