

Tuberculosis Update



March 2008

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A World TB Day update on the national and global tuberculosis situation and current UK initiatives contributing to the control of tuberculosis.

Introduction from the Chief Medical Officer (CMO)



This World TB Day newsletter focuses on current initiatives by the Health Protection Agency (HPA) and others supporting the implementation of my Action

Plan "Stopping Tuberculosis in England", including the UK's international commitment to fight tuberculosis. The theme for 2008, "I am stopping TB", highlights the contributions of individuals who are involved in the prevention and control of tuberculosis such as nurses, doctors, allied professionals and researchers, as well as those who have formerly received treatment for the disease. TB continues to be a considerable international public health challenge with nearly 9 million new cases being reported globally and more than a million and a half dying of a preventable and curable disease each year.

In this country, TB remains an important public health issue, most particularly in large cities

amongst certain population groups. Provisional data from the Health Protection Agency for 2007 show that the number of reported cases has remained stable since the 11% increase reported in 2005. This emphasises the need to continue implementing the Action Plan and further strengthen tuberculosis control in the UK.

World TB Day provides the opportunity to recognise the importance that individuals involved at the forefront of tuberculosis activities in the UK can make in reducing the burden of tuberculosis at local, regional, national and international level. There is more need than ever for greater commitment and research to provide new drugs, diagnostics and vaccines, as well as high quality service provision that meets local needs. The HPA continues to contribute to research dedicated to tuberculosis vaccine development and evaluation and implement measures to improve and maintain surveillance, while also supporting high quality clinical care by providing reference microbiological services to the NHS. In addition, the Department of Health has provided direct financial support for specific project initiatives and service development such as the workshops for commissioners following the launch of the TB Toolkit, the introduction

of static X-ray units in key feeder prisons, and London's Find & Treat project, which works with local TB services to improve active case-finding and completion of treatment in hard to reach groups.

This newsletter provides up to date information on scientific developments in vaccine and drug research, new project initiatives, and current activities at local and regional level. The prevention and control of tuberculosis requires the sustained commitment and collaboration of individuals and groups if the disease is to be effectively tackled. The contributions in this newsletter reflect the country's continuing commitment to fight the disease at home and overseas. I hope you find the contents of use.

Please feed back your comments to:

tbsection@hpa.org.uk

Further information on tuberculosis can be found on the Department of Health website: <http://www.dh.gov.uk/en/PublicHealth/CommunicableDiseases/Tuberculosis/index.htm>

Sir Liam Donaldson

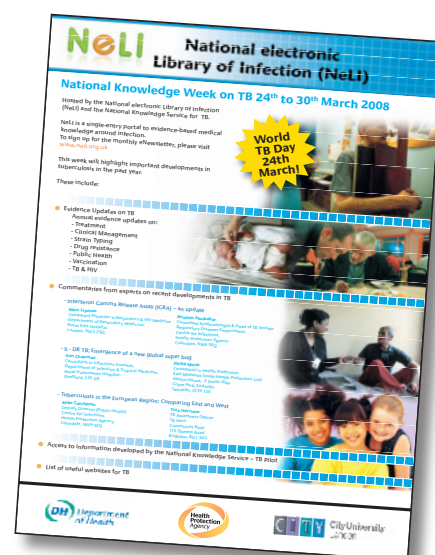
Chief Medical Officer, Department of Health

National Knowledge Week on TB

The National Knowledge Service - TB Pilot (NKS - TBP), along with the National electronic Library for Infection (NeLI), will be hosting the National Knowledge Week on TB from March 24th - March 30th 2008.

The National Knowledge Week on TB is a National Library for Health initiative designed to provide busy health professionals with an annual evidence update on TB.

The National Knowledge Week on TB will provide a comprehensive collection of peer reviewed primary research articles and systematic reviews summarising the best evidence and highlighting advances in the last year to showcase the best current knowledge and issues in TB. Latest resources will include those related to treatment, clinical management and diagnosis, strain typing, public health, vaccination, and drug resistance in TB. Specialists will also be providing commentaries on some topical issues in TB, including short pieces on interferon gamma release assay (IGRA), status of TB in Europe, and extensively drug resistant TB (XDR-TB). The resources produced for the knowledge week can be accessed from <http://www.neli.org.uk/IntegratedCRD.nsf/TBNKW?OpenForm>



Tuberculosis Surveillance Update: Provisional 2007 Data

Provisional enhanced tuberculosis surveillance data for the United Kingdom¹ show that 8496 cases were reported in 2007, a rate of 14 cases per 100,000 population². This represents a small decrease (0.7%) from the provisional number of cases reported in 2006. Fifty two percent (4403/8496) of patients were reported to have pulmonary tuberculosis in 2007, a similar proportion to that reported in the provisional 2006 data (53%, 4553/8555).

London accounted for the highest proportion (39%) of provisionally reported cases in 2007, followed by the West Midlands (11%). The lowest proportion was reported in Northern Ireland (1%). There was a decrease in the provisional number of cases reported in 2007 compared to 2006 in half of the UK regions/countries (Figure 1). The East of England had

the biggest fall (20%) in cases compared to 2006; London showed a decrease of 3%. In those regions not showing a decline, the number of cases increased between 3% (Yorkshire and the Humber) and 37% (North East). In Scotland, the provisional number of cases increased by 4% but remains within the range seen over the last 8 years.

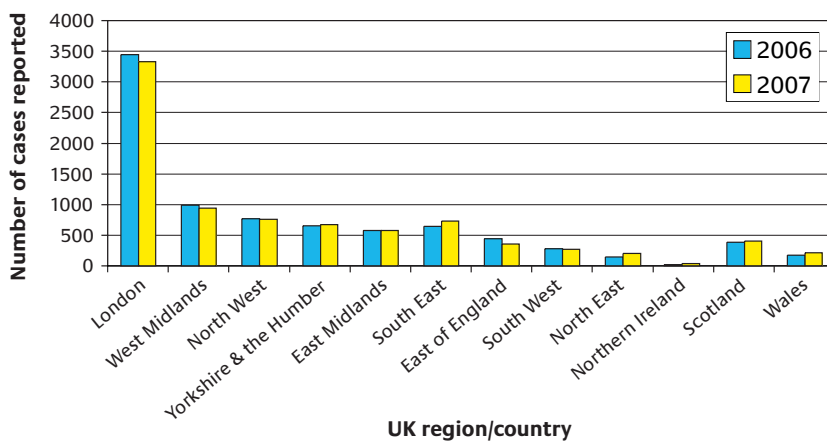
The provisional data for 2007 suggest that the annual number of cases of tuberculosis in the UK has remained stable but high. These data should be interpreted with caution, as some tuberculosis cases diagnosed in 2007 are still being reported. Some provisionally reported cases may also be de-notified and finalisation of the dataset involves a process of cleaning and the removal of duplicate reports. The final number of cases will

therefore be different from the provisional figures reported here.

The finalised dataset will also be linked with information on isolates reported through the UK Mycobacterial Surveillance Network (MycobNet) to provide additional clinical and microbiological information on cases, including drug susceptibility testing results. Finalised 2007 data with more detailed demographic, clinical and microbiological information will be made available on the HPA website this autumn at: http://www.hpa.org.uk/infections/topics_az/tb/menu.htm

- 1 Enhanced Tuberculosis Surveillance in England, Wales and Northern Ireland; Enhanced Surveillance of Mycobacterial Infections in Scotland.
- 2 Rate calculated using the Office for National Statistics 2006 mid-year population estimate.

Figure 1. Provisional number of tuberculosis cases reported for 2006 and 2007 by UK region/country



TB Toolkit

We reported in the March 2007 Tuberculosis Update, the imminent launch of the TB Toolkit by the Department of Health, designed to help commissioners of TB services secure high quality services to best suit local needs. The Toolkit was launched in June last year (available at the following website: http://www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/DH_075621at). Since then, the Department has funded TB Toolkit workshops facilitated by NHS colleagues with expert knowledge of commissioning to provide practical help in locally implementing the Toolkit recommendations. By the time this newsletter is published, every Strategic Health Authority will have held a Toolkit workshop. These workshops have been well received and well attended by NHS commissioners and service providers, and the Department hopes that this work will aid development of sustainable local TB services. The Toolkit has already been used to support service developments, and it will be interesting to review progress over the next twelve months.

Tuberculosis Vaccine Developments

One of the targets of the Global Plan to Stop TB (2006-2015), in support of the United Nations TB-related Millennium Development Goals, is to develop an effective, affordable, licensed TB vaccine that could be used to reduce the global incidence of tuberculosis. A number of international organisations are collaborating in an attempt to achieve this ambitious target, and the HPA is making an important contribution to this area.

The tuberculosis group at the HPA Centre for Emergency Preparedness and Response (CEPR) has a major programme of research devoted to vaccine development. CEPR is a partner in two large EU-funded consortia, TB-VAC and MUVAPRED (Mucosal Vaccines against Poverty Related Diseases), and one part of CEPR's research programme is focussed on independently evaluating lead vaccine candidates that have been developed by groups across Europe. TB-VAC is an integrated project for the design and testing of new

vaccine candidates against TB and has a large element dedicated to the identification of novel candidates. In contrast, MUVAPRED has focussed on existing candidates, but is investigating whether protective immunity can be obtained following vaccination by the mucosal route (i.e. needle-free delivery).

Lead candidates include improved BCG vaccines (e.g. BCG strains expressing additional antigens), BCG being delivered by the oral route, viral vectors expressing subunit antigens, and other novel expression systems designed to induce a protective cell mediated host response. The sub-unit vaccines will probably be used in developing countries to boost immunity generated by BCG given shortly after birth.

The pre-clinical studies performed at CEPR are playing an important role in the selection of the most promising candidates to be taken forward to clinical trials being conducted both in Europe and Africa. Several candidates have already been

through phase I trials. Ongoing collaborations across the HPA will ensure that CEPR is able to evaluate the ability of any lead vaccine candidate to protect against challenge by *M. tuberculosis* strains that are prevalent within the UK.

Although the development of an improved tuberculosis vaccine is a lengthy and challenging process, there is a strong commitment from numerous international organisations to ensure that novel vaccines will be fully evaluated over the next 5-8 years in order to achieve this particular target within the Millennium Goal.

IGRA Q & As

Following a period of consultation, the Health Protection Agency has published a position statement and Questions and Answers (Q & As) for health care workers and members of the public on the use of interferon gamma release assay tests (IGRA). The Q & As build on guidelines published by the National Institute for Health and Clinical Excellence (NICE) in 2006 and provide further information especially in areas where new evidence has accumulated in recent years. Information is provided on a wide variety of subjects ranging from when to use the test, to where and how it might be used.

The Q & As and position statement are available at <http://www.hpa.org.uk/consultations/2007/IGRA.htm>

Static Digital X-Ray Machines in Prisons

In prisons, people with risk factors for TB are over-represented. Because of this, prisons represent an opportunity to engage with groups at higher risk of TB. One third of cases in the outbreak of isoniazid resistant TB in north London had been prisoners.

At the HPA annual conference last September, Offender Health announced a new Department of Health initiative - five London prisons (HMPs Belmarsh, Brixton, Pentonville, Wandsworth and Wormwood Scrubs) have been selected for installation

of static digital X-ray machines in this financial year. These are to be used as part of a wider programme by prison/PCT partnerships to improve the detection & management of cases among offenders. This decision follows a successful evaluation of a 2-year Mobile X-ray Unit (MXU) project, which has proved the utility of X-ray technology in diagnosing potentially infectious pulmonary disease among hard to reach populations, including prisoners. A further three to four units will soon be introduced outside London - the eventual siting of these will be influenced by local TB prevalence, technical reports on the suitability of individual establishments, and proposals by prison/PCT partnerships on their use in wider TB prevention and management programmes, to maximise the impact of this limited resource.

Improving local prevention and control: Standards for TB services

In England, the Health Protection Agency's Local and Regional Services Division (LaRS) plays an important role in the prevention and control of TB. LaRS is currently undertaking a project to develop and implement service standards which will ensure that all areas of the country have the same high quality service provision.

When the HPA was established in 2004, the specialist expertise and resources available at local level varied considerably, often dependent on whether or not TB was a local health issue. Recently, with the changing nature and extent of the burden of TB disease in England, districts which hardly ever saw TB cases are experiencing complex public health problems, which require expert public health interventions.

In response to this situation, LaRS has developed a set of standards for all aspects of its TB specialist services. Following a review of the literature, a draft set of standards for TB prevention and control was proposed. Using the Delphi method, a multidisciplinary group of TB experts both from the HPA and the NHS worked to refine the standards and a document was produced and consulted on.

The standards have now been converted into a self-assessment tool so that each Health Protection Unit (HPU) can measure their current compliance. The methodology is based on that used by the Healthcare Commission, to assess the performance of healthcare providers.

The self-assessment tool is intended to identify areas where practice is good or satisfactory (green light) and areas of practice where units assess themselves as amber or red. This will help local units identify service elements which require further development. Training packages

will be developed to meet identified training needs, and training delivered as required across the country.

The self-assessment will be repeated later in the year, and any HPU which still does not comply will be supported further, until the standards are met across the country.

Find & Treat - Strengthening tuberculosis control in London among hard to reach groups

Research in London has demonstrated that rates of tuberculosis are highest among hard to reach populations, especially homeless people, drug and alcohol users and prisoners. Tuberculosis control in these populations is complicated by delayed diagnosis, high levels of infectivity and drug resistance, immunosuppression, overcrowded living and poor treatment adherence leading to onward transmission and outbreaks. The recent Mobile X-ray Unit (MXU) screening pilot demonstrated that the MXU was able to reach vulnerable populations and identify cases of active disease early, but a high proportion of cases referred to local tuberculosis services for confirmation of diagnosis and treatment were rapidly lost to follow up care. In response, the Department of Health established 'Find & Treat', a two year pan-London health and social care project that works alongside the MXU and frontline services to improve the care of hard to reach groups.

Find & Treat are a small multidisciplinary team of tuberculosis nurse specialists, social and outreach workers. Since October 2007, the project has received information from services across London about more than 130 complex and challenging tuberculosis patients. In the majority of these cases, local TB services have asked for support from the Find & Treat team. Support could include: locating and re-engaging patients who have been lost to follow-up care; providing a link between prison health, the MXU and tuberculosis services; organising case conferences and directly observed therapy (DOT) partnerships and sign-posting relevant allied support services in the community.

Through a series of pan-London workshops the project aims to share good practice and learn from established case management models used by street outreach and other allied services working with hard to reach groups. Find & Treat also involves homeless people who have had tuberculosis as peer educators for other service users and professionals. The peer educators assist with training, awareness raising and screening events and support hard to reach patients to access services and complete treatment.

The project works closely with the Department of Health, NHS London, Department of Communities and Local Government and the National Treatment Agency to inform policy makers on the importance of tackling tuberculosis among hard to reach groups. Find & Treat is an opportunity for tuberculosis service providers to profile their work and communicate ideas directly with allied professionals and policy makers. For more information please contact: f&t@1greekstreet.org.uk

Challenges for TB awareness



Awareness is the key to reducing stigma and misconceptions about TB but alongside this comes a challenge – how can we stop TB by raising knowledge about the disease without adding further stigma?

In the UK, TB is concentrated in certain population groups such as the homeless, prisoners, substance

mis-users and communities linked to high-TB incidence countries. TB Alert can provide small grants to patients to assist them through treatment, the majority of which come from these groups. However, over a dozen people have approached TB Alert over the past eighteen months to volunteer as media advocates. All have been treated for TB recently yet not one fits the epidemiological picture and the majority experienced a delay in diagnosis. Although a small number and a self-selecting group, there are probably more individuals in similar circumstances.

We must achieve a fine balance in raising awareness about TB. It is vital that frontline health professionals are aware of the disease and its symptoms and are ready to consider it as a possible diagnosis regardless of patient background. The public and vulnerable groups

also need to have advice made available to them to enhance their understanding of the disease. Equally we need to send out a message of reassurance to avoid adding further to the fear surrounding TB: whilst anyone can get TB, the risk to most people in the UK is still very low indeed.

This year for World TB Day and beyond, TB Alert is stopping TB by producing awareness materials aimed at health professionals, the public and vulnerable groups. For more information go to: <http://www.tbalert.org/resources/awareness.php>



New Drugs – New Tools

To tackle the global tuberculosis emergency we need new tools to gain control and first among these would be a better treatment regimen. Although the current internationally approved regimens are effective under clinical trial conditions and in well managed directly observed treatment short-course (DOTS) programmes, their long duration means that many patients default. The combination is potentially toxic and many patients are unable to tolerate them. Improved outcomes would be achieved if treatment duration was reduced to four months but to date there are no effective four month regimens.

Moxifloxacin is an 8-methoxyquinolone used widely for the treatment of respiratory tract infections. A series of animal studies indicated that moxifloxacin might shorten tuberculosis treatment in regimens where it was substituted for isoniazid or ethambutol and these data have been confirmed in recently reported phase IIb trials. To take these data forward into clinical practice, the University College London - Medical Research Council (UCL-MRC) tuberculosis clinical trials group are performing a randomised placebo-controlled double blind trial comparing two treatment shortening regimens with the standard six month regimen for the treatment of adults with pulmonary tuberculosis. The two treatment shortening regimens to be trialed are i) two months moxifloxacin, isoniazid, rifampicin and pyrazinamide followed by two months moxifloxacin, isoniazid and rifampicin or ii) two

months ethambutol, moxifloxacin, rifampicin and pyrazinamide followed by two months moxifloxacin and rifampicin. The short title REMoxTB has been given to the project (Rapid Evaluation of Moxifloxacin in tuberculosis).

The study is being sponsored by UCL and funding comes from the European Developing Country Clinical Trials Partnership, the Global Alliance for TB Drug Development and the British MRC. We aim to recruit 2400 patients from sites across Africa in Kenya, Tanzania, Zambia and South Africa over the next eighteen months. This is the first tuberculosis clinical trial performed to international regulatory standards and the methods created in the study could be generalised to other future studies for novel drugs in the development pipeline. It is hoped that data will be presented to regulatory authorities to permit a reduction in tuberculosis treatment duration to four months, the first improvement for almost thirty years. The first patient was recruited just a few weeks ago and the data should be complete in three years time. If successful, agreements are in place to make the drugs available at an affordable price in low income countries.

For many years there has been little progress in improving tuberculosis therapy - at last there is a prospect that, through the efforts of academics, funders, pharmaceutical companies, clinicians and patients, this may be about to change.

London TB Metrics

In 2005, in response to the CMO's Action Plan, the pan London TB group reformed as the Stopping TB in London group. Key work streams were identified based on the recommendations of the Action Plan and in 2006, London TB Metrics were developed by the group which define and set standards for TB services in London. The metrics have since been reviewed and updated. The new Strategic Health Authority for London agreed to make TB a London local priority for 2007/08 and in 2008/09 for all Primary Care Trusts (PCTs). Locally, PCTs and TB services in London can use the TB Metrics to measure and monitor the complete care pathway, which contributes to treatment completion rates. The target is for 85% of all TB patients to complete treatment and PCTs will be performance managed by treatment completion rates. The Stopping TB in London group is currently reviewing its membership and function to better reflect the working relationships between PCTs, TB services and NHS London.

Produced by the Tuberculosis Section, Health Protection Agency Centre for Infections

We gratefully acknowledge the contribution of colleagues across the Health Protection Agency and the continuing collaboration of colleagues at the Department of Health, Communicable Disease Surveillance Centre Northern Ireland, National Public Health Service for Wales, Health Protection Scotland, TB Alert and others who contributed to the production of this newsletter.