

Is tuberculosis a major public health problem ?

Public hearing of 22 February 2007
organized by Ms. Marie-Christine Blandin, Senator
and Mr. Jean-Pierre Door, Deputy

Tuberculosis kills 1.6 million people every year and is therefore a major concern for WHO. The disease was recently the subject of worrying publications concerning the development of multiresistant tuberculosis, which is fatal in a large number of cases and affects around 450,000 new patients per year, and the more recently identified ultra-resistant tuberculosis, which is fatal in almost all cases. In addition, the example of New York has demonstrated that an epidemic of multiresistant tuberculosis can occur in a major industrialized country. Consequently, Mr. Jean-Pierre Door, Deputy, and Ms. Marie-Christine Blandin, Senator, wanted to supplement the report they had presented in 2005 on "the epidemic risk" with respect to this point, by organising a public hearing.

Summary

I – A contrasting picture

A. Tuberculosis is a major public health problem around the world

Up until around the 1990s, there was a relatively steady decline in this disease, to the extent that scientists began to forget all about tuberculosis towards the end of the 1980s.

And yet the figures for 2005 reveal 1,600,000 deaths, 98% of which occurred in developing countries. 8,800,000 new cases were counted in 2005, with 80% of these occurring in the 22 most affected countries.



Mycobacterium tuberculosis culture

Tuberculosis with multiple resistance to drugs is present in 102 countries. Approximately 2 in 3 tuberculosis cases occur in Asia. Africa accounts for 28% of cases, but the proportion of patients per capita there is the highest in the world.

Africa has seen a significant increase in the disease, which now appears to be stabilising. It is nonetheless necessary to remain cautious, since numerous African countries are in a catastrophic situation. Zimbabwe, Kenya and Tanzania have very high HIV rates; only 50% of existing cases are detected; there are 500,000 deaths per year in these countries, half of which are related to HIV.

The situation in Africa is therefore largely linked to the problem of HIV and the influx of patients requiring care from poor, under-equipped and under-staffed health services. Managing patients has become a genuine headache for some countries.

In Europe, tuberculosis has two faces. In Western Europe, the graph demonstrates a slight decline. Eastern Europe, in contrast, is experiencing a very marked rise in the number of cases, due to numerous factors and, in particular, the chaotic situation of the healthcare system, with a significant amount of multiresistant patients. As a result, the management of patients in these countries is very complex.

Tuberculosis is also a family and social, micro- and macro-economic problem. A 10% increase in tuberculosis cases leads to a fall in growth of 0.2 to 0.4% per year in developing countries. Yet saving one year of life costs less than 2 euros.

Controlling tuberculosis is WHO's 6th objective for the millennium: the aim is to control tuberculosis and begin to reverse its increase by 2015.

The 2006 – 2015 Global Plan lists the actions to be undertaken and quantifies their global cost at 56 billion dollars. Around 26 billion dollars are already available, if funding remains at the same level as in 2006. It will be necessary to further increase state funding efforts, particularly in endemic countries and the richest ones in order to make up this deficit.

B. A problem of limited scope in France

6400 cases were declared in 2001 nationally, leading to around 600 deaths. But, for the time being, tuberculosis mainly affects the Ile-de-

France region (Paris concentrates 20% of all patients) and a large proportion of patients originate from endemic zones.

The national tuberculosis control programme falls within the scope of the Public Health law voted for in 2004. **The objective of the public authorities is to stabilise the overall incidence of tuberculosis, reinforcing the control strategy in high-risk groups and zones.**

II – French tuberculosis control policy

A. The vaccination strategy

The opinions of the *Conseil supérieur d'hygiène publique de France* (CSHPF - French Public Health Council) and the *Comité technique des vaccinations* (Technical Vaccination Committee) of 30 September 2006 relative to BCG vaccinations recommend reinforcing tuberculosis control within the context of a national programme and indicate **the possibility of suspending compulsory vaccination**, but on condition that the system of prevention be reinforced. In addition, changes linked to the exclusive availability of an intradermal vaccine (which is more difficult to administer than the traditional ring and could potentially cause complications) have added a further technical difficulty in the vaccination strategy debate.

The programme proposed by the committee responsible for drawing up the national tuberculosis control programme sets two general objectives: consolidation of the gradual fall in the incidence of tuberculosis disease and reduction in disparities.

Without reaching any conclusion with respect to compulsory vaccination, the committee proposes 3 measures at this stage:

- vaccination of high-risk infants during the first month of life, irrespective of the context;
- better training in intradermal BCG use and technique;
- monitoring of the vaccine cover of high-risk children.

B. The five components of the policy implemented

1 – Ensure early diagnosis and suitable treatment for all cases of tuberculosis disease

To achieve this, it is necessary to promote access to healthcare and develop confidence in the healthcare system, more specifically for vulnerable people, for example foreign nationals in breach of the regulations, who must be informed of their rights and the screening and healthcare system.

In the context of preventing the emergence of multiresistant strains, it is necessary to reinforce scrupulous compliance with treatments. It is crucial that TB treatments be taken regularly to ensure the full recovery of patients and prevent the emergence of multiresistant strains.



Mycobacterium tuberculosis

This question is particularly pertinent for individuals of no fixed abode.

2 – Improve detection of tuberculosis, in particular by reinforcing detection of its most contagious forms, reducing the time taken to reach a diagnosis and implementing systematic investigations around a given case.

3 – Maintain resistance to antibiotics at a low level

The measures essential for the prevention of multiresistance are early diagnosis, suitable treatments and specific measures concerning the management of multiresistant tuberculosis. It is necessary to:

- diagnose cases as quickly as possible;
- rapidly transfer cultures to national reference centres if multiresistance is suspected;
- define the practical methods for application of molecular tests to detect resistance to Rifampicin;
- consolidate decision-making and the availability of treatments for multiresistant tuberculosis;
- reinforce the role of providing advice and information on multiresistant tuberculosis linked to the national reference centres;
- ensure the continuity of supply of second-line treatments.

4 – Improve epidemiological monitoring and knowledge of the key factors involved in tuberculosis

This involves having the tools required to monitor epidemiological trends and dynamics and to adapt the control policy as a result, in particular:

- improve the exhaustivity of microbiological documentation of compulsory notifications;
- foster the commitment of all the players involved;
- develop the role of health professionals responsible for coordination and monitoring in hospitals;
- ensure the systematic collection of information that is currently lacking, in particular in high-risk

groups.

5 – Adapt the tuberculosis control system to new challenges

The existing disparities warrant adaptation of the way tuberculosis control is currently organised, with intensification of efforts focusing on the most affected populations and zones.

The objective is therefore to organise regional management of tuberculosis control and to adapt national guidelines on a regional level, remembering that tuberculosis control has been “recentralised” since 1 January 2006.

III – Unresolved ethical questions

New data concerning tuberculosis raise a number of questions closely related to ethical aspects, the most important of these being the restriction of compulsory vaccination to the most exposed populations.

A. Opinions in favour of a control policy targeting populations exposed to a risk of contracting the disease

According to the “transmissible diseases” section of the CSHPF, the BCG alone cannot eradicate tuberculosis in France and the plan announced by the government must therefore be up and running before any consideration can be given to stopping the BCG.

The section has pronounced itself in favour of targeting compulsory vaccination, reserving it for migrants, native French people travelling in high-risk countries or those with a history of tuberculosis in the family, along with certain vulnerable individuals.



The Haute Autorité de lutte contre les discriminations (HALDE or French anti-discrimination authority) has also returned a favourable opinion relative to targeting tuberculosis control. It does not consider targeted vaccination

and screening of certain populations – in particular on the basis of their geographic origin – to be discriminatory.

Its opinion is clear: *“We cannot hide behind the fear of being accused of discrimination when it comes to taking a decision with respect to high-risk groups. This is a public health problem, not a prob-*

lem concerning discrimination”.

B. Opinions opposed to a control policy targeting populations exposed to a risk of contracting the disease

The *Comité consultatif national d'éthique* (CCNE or National Ethics Committee) is opposed to this type of targeting. Its negative response to the question: *“Is it ethically acceptable to abolish compulsory BCG vaccination in the general population in France and to reserve it exclusively for those populations deemed to be high-risk?”* was based on several considerations.

The analysis according to which the difference in the risks of contracting tuberculosis to which, firstly, globally defined vulnerable groups and, secondly, the rest of the population, are exposed, justifies targeting of children in the first category only in the context of a vaccination programme, does not take into account one essential fact: these populations are not isolated, they are not what might be termed “ghetto-ised” in non-ethical terms, and the current trend is even towards their integration as part of a process of mutual aid and solidarity. The risk of contamination between different types of populations therefore remains high, as long as a tuberculosis control policy is not applied to the whole population, and this is particularly evident in highly urbanised areas with a high population density.

In this case, it would become paradoxical to “target” the BCG vaccination programme against only those children deemed to be at risk, while their playmates deemed “not to be at risk” but in contact with the same contaminating individuals as the former – unless they were isolated, which is ethically unacceptable – would not benefit from the same treatment.

Abolishing compulsory vaccination does not mean abolishing vaccination itself. But what meaning is given to *reserving it exclusively for high-risk populations?*

For the latter, there would not really be much choice; it would be up to them to understand that accepting vaccination in their targeted group would be in their own interests, that is true, but also in the interests of the rest of the population: vaccination of these populations to protect the population as a whole.

Studies have indeed shown that stopping vaccination within these populations would lead not only to an increase in the incidence amongst them, but also in the rest of the population. How can we then avoid talking about stigmatisation?

The arrival of cases of resistant Mycobacterium tuberculosis disease on our doorstep also

pleads in favour of maintaining compulsory vaccination since the BCG offers identical protection against all types of tuberculosis.

Hence the CCNE advocates the greatest caution when it comes to abolishing widespread compulsory BCG vaccination before the incidence level of 5 per 100,000 recommended by the International Union against Tuberculosis and Lung Diseases (IUATLD) has been reached in France.

It recommends the development of an efficient and evaluated policy of TB screening and control for the whole population, within which particular attention should be paid to vulnerable populations, without targeting: a generalised policy, with targeting this time having an ethical sense, aimed at promoting access to healthcare and tuberculosis screening for the most deprived populations, with the creation of anonymous and free healthcare structures, following the example of what has been done for HIV.

IV – The prospects opened up by research

A. New anti-TB vaccines

The quest to fund new anti-TB vaccines has been very active both internationally and in France, where four vaccine candidates have been identified and tested on laboratory animals, with these nonetheless requiring improvements before clinical trials in humans can be begun.

For the first time, some of these vaccine candidates, obtained in France or in other European countries, have been shown to be more protective than the BCG in laboratory animals: this is a major advance, which must be highlighted.

Research has therefore made enormous progress in the last 10 years and is likely to deliver some genuinely interesting products in the near future.

B. Rapid diagnosis

Thanks to advances in the field of molecular biology, bacilli – even in very small quantities – can now be detected by gene amplification performed *in vitro*. The technologies need to be fine-tuned in order to be able to use them to rapidly detect bacilli.

C. New medicines

The quest to find new medicines concerns, for example, new antibiotics resulting from studies performed on the interaction between tuberculosis bacilli and the host's cells.

At present, several substances are in the process of being tested. The structure of the major components of the bacillus has been resolved and the inhibitor screening stage has begun.

Today, international funding agencies in the research sector are mainly supporting development, without focusing very much on fundamental research. Yet this first stage, which comes before development, is essential and is too often neglected; as a result, the future in terms of the discovery of new, more effective drugs looks less bright.

Conclusion

The public authorities will soon have to make choices, particularly in terms of BCG vaccination.

Although compulsory vaccination is now being questioned, populations exposed to the tuberculosis bacillus will need to continue to be protected, since the vaccine prevents severe forms of the disease in children.

It is true that this change has been precipitated by the halting of production of the vaccine administered by a ring, this having been replaced by a product that needs to be injected intradermally, a tricky injection technique that doctors are not very familiar with.

The subject is a very sensitive one.

Targeting can be viewed as positive discrimination. It may also be seen as stigmatisation. Therefore presentation and education are essential in a debate that cannot be reduced to a dialogue between doctors.

The choice is a complex one. Two eminent French bodies – HALDE and the CCNE – reach different conclusions.

What's more, the choice is incomplete since tuberculosis control cannot be reduced to BCG vaccination.

In contrast, travel, migratory flows, the movements of populations, invite us to remain vigilant, first of all, and, secondly, certain factors play a major role, such as quality of care, rapid diagnostic methods, the existence of effective treatments, the organisation of personalised discussions, for example investigations amongst family and friends.

Whatever the case, the risk of an epidemic is not past and the emergence of multi- and ultraresistant tuberculosis means that we must not lower our guard.



National TB Campaign - 1966