Improving public health preparedness for and response to the threat of epidemics: tularaemia network

Report of a WHO meeting

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14–15 SEPTEMBER 2003
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1. Introduction

A meeting on Improving public health preparedness for and response to the threat of epidemics: tularaemia network was held in Bath, United Kingdom, from 14 to 15 September 2003, just prior to the 4th International Conference on Tularemia (15–18 September 2003). The list of participants and details of the agenda are given in Annex 1 and Annex 2 respectively.

Professor Arne Tärnvik (Division of Infectious Diseases, Umea University, Sweden) chaired the meeting.

2. Meeting objectives

The main objectives of the meeting were to outline WHO's activities on other biological agents and develop a workplan for tularaemia.

3. Tularaemia: present state of knowledge and gaps

Professor Arne Tärnvik presented a summary and led discussions on the current state of knowledge and gaps in five fields related to tularaemia:

a. Clinical management
b. Epidemiology and surveillance
c. Diagnostics
d. Outbreak/emergency response
e. Research.

a. Clinical management
The signs and symptoms of ulceroglandular, glandular, oropharyngeal, and respiratory forms are well described. However, aberrant clinical expression (urinary tract infection, secondary wound infections, etc.) remains to be fully described. Treatment regimens for severe tularaemia rely on old antibiotics, such as streptomycin and chloramphenicol, which are no longer generally used.

b. Epidemiology and surveillance
The general geographical distribution of tularaemia disease, as well as that of the mammalian hosts and vectors, is well described. The sequencing of the genome of several strains of *Francisella tularensis* is close to completion. In addition, assays for molecular differentiation among subspecies will allow isolates within a given subspecies...
to be differentiated. Less well understood are the natural reservoirs and distribution of *F. tularensis* in and between outbreaks.

c. **Diagnostics**

The following are well described: sampling methods from ulcers and blood; culture and identification of the agent; serological assays; and polymerase chain reaction (PCR) from secretions in human wounds. Less well developed are PCR and culture from clinical specimens other than wound secretions. The infrastructure needed for laboratory diagnostics, as well as molecular methods for identification of gene-manipulated strains also need to be developed. A network of diagnostic laboratories with defined tularemia capabilities could be established.

In the long term, it would be important to standardize reagents and have the possibility to exchange them (e.g. antigen standards, DNA standards, primers). To do this, it would be necessary to identify regional laboratories that could produce and distribute the reagents. It was thought that, in the future, standardization would be carried out in collaboration with the Lyon office of Communicable Disease Surveillance and Response (CSR), WHO.

d. **Outbreak/emergency response**

Methods for culture and rapid PCR-based identification, including subspecies differentiation, are well described. So too are ELISA-based methods for *F. tularensis* detection in environmental samples. Less well developed are the infrastructure needed for sampling, transport, and laboratory diagnostics; and molecular methods for identification of gene-manipulated strains, as mentioned in section 3d. Strategies for the clinical management of outbreaks, including the issue of antibiotic resistance, and dealing with public information need to be developed. There is also a need for response teams, for assessment and rapid diagnosis.

e. **Research**

It was agreed that research was needed on issues related to the protection of laboratory workers handling *F. tularensis*. For example, studies of the host response to *F. tularensis* in experimental models and humans are necessary.

Strategies for protecting workers handling *F. tularensis* (e.g. fever watch, vaccination, and administration of antibiotics) need to be examined.

Issues related to vaccine development and duration of immunity also need to be considered.
4. WHO’s activities to assist countries to manage biological threats

Dr Williamina Wilson (WHO, Geneva, Switzerland) presented WHO’s activities to assist countries to manage biological threats, in the context of WHO’s strategy for global health security. This strategy, founded on a global partnership, is supported by three pillars: contain known risks, respond to the unexpected, and improve national preparedness. The International Health Regulations, which are currently being revised, provide the overarching mandate to guide countries towards global health security. WHO’s activities on anthrax were outlined: (i) establishing a global network of anthrax experts and diagnostic laboratories with defined anthrax capabilities; (ii) establishing standard procedures relating to anthrax and disseminating information; and (iii) setting up and implementing training and quality control/quality assurance. The approach being followed for anthrax was discussed as a possible model for future WHO activities on tularaemia.

5. Recommendations

a. Production of international guidance on tularaemia

It was agreed that there was a need for international guidance on tularaemia, aimed at public health, veterinary, and laboratory personnel. A small working group should be established for each of the five topics discussed at the meeting, to examine the issues in detail. The chair of each working group was agreed upon (see box below). Each chair should identify other experts in their field and invite them to join the working group.

<table>
<thead>
<tr>
<th>Working group</th>
<th>Chair</th>
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<tbody>
<tr>
<td>1. Clinical management</td>
<td>Dr Arne Tärnvik, Sweden</td>
</tr>
<tr>
<td>2. Epidemiology and surveillance</td>
<td>Dr Anders Sjöstedt, Sweden</td>
</tr>
<tr>
<td>3. Diagnostics</td>
<td>Dr May Chu, USA</td>
</tr>
<tr>
<td>4. Outbreak/emergency response</td>
<td>Dr Roland Grunow, Germany</td>
</tr>
<tr>
<td>5. Research</td>
<td>Dr Richard Titball, United Kingdom</td>
</tr>
</tbody>
</table>

Each group would meet once a year, as would the chairs of each group. WHO should coordinate these meetings, perhaps as satellite events to international meetings, and should seek funds to help participants to attend.
Expected output
Each group would be expected to produce a report: the reports would be assembled to produce international guidance on tularaemia. A draft outline is expected from each group within 6 months and a working draft should be produced within 12 months. The final document is expected to be ready within 2 years. Electronic publication on the WHO web site would allow rapid and wide dissemination of the material, and updates could also be easily posted.

b. Establishing a network of diagnostic laboratories with defined capacities for tularaemia
It was agreed that WHO and the meeting participants should focus their activities on the production of international guidance. However, it was felt that it would also be useful to establish a network of diagnostic laboratories with defined capacities for tularaemia, primarily as an information-gathering exercise. This would identify the laboratories which currently work on tularaemia and ascertain their capacities. As the network becomes established, its scope could be expanded, under the direction of the Diagnostics working group.

Dr May Chu (Centers for Disease Control and Prevention, Colorado, USA) led a discussion on the content of a tularaemia questionnaire, based on that for anthrax. Sections to be altered, added, or deleted were identified and discussed.

Members of the group would identify laboratories to which the questionnaire should be sent. WHO would also identify laboratories who have indicated (as part of the survey of anthrax laboratories) that they work on *F. tularensis*.

Expected output
A questionnaire for laboratories should be finalized following input from Dr May Chu and the meeting participants. WHO should distribute and collect the questionnaires, and share the information with the group.

6. Presentation of the outcome of the WHO meeting to the 4th International Conference on Tularemia
A summary of the current knowledge and gaps in tularaemia was prepared by Professor Arne Tärnvik for presentation at the 4th International Conference on Tularemia (15–18 September 2003) in Bath, to draw the attention of the wider tularaemia community to the outcome of the WHO meeting.
Annex 1

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Annex 2

Agenda

14 September 2003
14.00–14.15 Secretariat’s welcome.
       Chairman’s welcome and introduction.
14.15–15.00 WHO’s activities on other biological agents: current activities on
            anthrax as a possible model for tularaemia
15.00–15.30 Outline of meeting objectives and expected deliverables:
            • Identifying a laboratory network for tularaemia
            • Assessing laboratory capacity for tularaemia diagnosis
            • Defining guidelines, training, and resource needs
            • Defining formation and topics of working group
              – Clinical management
              – Epidemiological and surveillance
              – Diagnostics
              – Outbreak/emergency response
              – Research
15.30–16.00 Coffee
16.00–17.30 Continued discussions on topics and aims of working group
19.30 Group dinner

15 September 2003
09.00–09.15 Summary of previous day’s session
09.15–10.00 Discussion on content of tularaemia questionnaire for laboratories
10.00–10.30 Composition and expected output of working groups
10.30–11.00 Coffee
11.00–11.15 Summary of the goals and deliverables, with timelines and
            priorities
11.15–11.30 Closing remarks (Chairman and Secretariat)