
FRANCE

Working paper

NEW CONFIDENCE-BUILDING MEASURES: EXAMPLES OF APPLICATION

Addendum

In document BWC/CONF.III/12, France proposed a number of new confidence-building measures. Firstly, it was felt useful that provision should be made for exchanges of information on national biological defence programmes and that States parties should organize visits to each other's relevant facilities in order to increase openness and transparency. Second, it was proposed, with a view to improving the exchange of information on abnormal epidemics, that States parties should describe their means of collecting epidemiological data and cooperate in improving their epidemiological surveillance systems.

The present document sets out the objectives of, and summarizes the research and development activity under way in, the French biological defence programme, and then describes the French system for the collection and transmission of normal and abnormal epidemiological data.

1. NATIONAL BIOLOGICAL DEFENCE RESEARCH AND DEVELOPMENT PROGRAMME

1.1. Organization

(a) The facilities concerned

The means of defence against agents of biological origin (ABOs) are studied by the Ministry of Defence in three research centres:

- The Centre de Recherches du Service de Santé des Armées (Armed Forces Health Service Research Centre, CRSSA) at Grenoble;

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The Centre de Recherches de Médecine Tropicale du Service de Santé des Armées (Armed Forces Health Service Tropical Medicine Research Centre, CRMTSSA) at Marseille; and
The Centre d'Études du Bouchet (Le Bouchet Study Centre, CEB) at Vert-le-Petit, which is part of the Délégation Générale pour l'Armement (General Department for Armaments, DGA).
In addition, the Service de Recherches de la Direction des Recherches, Études, Technique (Research Service of the Directorate for Research, Studies and Technology, DGA-DRET) finances upstream studies in university or private research institutes.

The Armed Forces Health Service, which comes under the Joint Staff, is responsible for verifying the preparation and use of ABOs in the quantities required for defence research.

(b) Physical protection studies
Such studies are mainly carried out by the CEB. They concern:
Detection of ABOs for the purposes of early warning and monitoring;
Development of methods and means of protection, and evaluation of the efficacy of the equipment currently issued to the armed forces (clothing, respiratory protection devices);
Means of collecting samples and of packaging them for subsequent identification.

The CRSSA carries out research into methods of disinfection that are effective against pathogenic bacteria and viruses. It also does work concerning the collection of samples in the air and on surfaces.

(c) Biological protection studies (epidemiological and prophylactic studies)
Such studies are largely carried out by the Armed Forces Health Service. They concern:
The mechanisms of the virulence and pathogenicity of micro-organisms;
The epidemiology and prophylaxis of the viral diseases of greatest significance for armed forces in the field;
Non-specific immunomodulation and the immunomodulatory effects of bacterial toxins.
CEB deals with local immunotherapy in the protection of the respiratory tract against bacterial or viral infections.
1.2. Summary of research and development work

With a view to keeping knowledge up to date so as to be able to deal with any new threat, including threats arising from the growth in the potential of biotechnology, close coordination exists between the Ministry of Defence's research centres. The Armed Forces Health Service is the coordinator for the subcommission on medical defence against the effects of biological weapons, which meets at regular intervals.

The studies carried out can be classified in four groups:

- Developments in the biological risk in general, natural risks for exposed military personnel (rapid action forces, peace-keeping forces, etc.), risks of use by an adversary of a weapon with a classic or advanced biological constituent;
- Rapid detection and diagnosis of infectious diseases and their agents, efficacy of passive protection;
- Prevention and treatment of infectious diseases, disinfection;
- Progress in fundamental biological sciences.

(a) Risk evaluation, threat evaluation

The research has largely to do with health risks (epidemics and infectious, unusual, hostile environments). The areas of study are:

- The epidemiology and prophylaxis of yellow fever, dengue and malaria;
- Food- and water-borne infections and poisoning;
- Hepatitis A and E, cholera, salmonella and shigella infections and botulism;
- Factors of virulence, access to the pathogenicity of bacteria, role of iron;
- Immunosuppressive viral diseases (AIDS) and slow viruses;
- Immunosuppressants of bacterial origin (Pseudomonas toxins) and burn complications;

The risks of new threats from single-celled micro-organisms and eukaryotes that after cloning express exogenous toxins or substances (example: erabutoxin A of Laticauda semifasciata expressed by E. coli).

CRMTSSA carries out epidemiological and prophylactic studies on menigococcic meningitis (it is a WHO reference centre for such infections). It is engaged in fundamental research on flaviviruses (antigenic structure and genome mapping).
(b) Rapid detection and diagnosis, passive protection

This has been the focus of effort in recent years:

Application of flux cytometry to the detection of aerosolized bacteria
(the work in progress has shown that with this technique, which is readily
automated, some 100 living micro-organisms can be detected using apparatus of
a size and cost compatible with large-scale distribution);

Application of antibodies to the detection of bacteria, viruses and
toxins (a method derived from the ELISA and ELIFA methods can detect
quantities of toxins of less than 5 mg (staphylococcal enterotoxins); this
novel technology can be combined with automation and adapted for use with
portable equipment);

Application of immunosensors and biosensors to the detection of ABOs
(these techniques are still the subject of very advanced fundamental research);

Use of nucleic acid probes and gene amplification techniques capable of
detecting traces of genes coding for viruses, toxins or factors of virulence
or resistance; use for genetically modified micro-organisms (the models under
study being the hepatitis A virus and the toxin of Clostridium botulinum);

Evaluation of the performance of the armed forces' new mask and its
components on exposure to ABOs (bench measurements using various
micro-organisms and viruses);

(c) Prevention and treatment, disinfection

The research into ABO-specific vaccination has gradually given ground to
studies of immunomodulation. The latter area is of more interest, since
precise identification of the ABOs with military potential is difficult,
making vaccination against every risk impossible. As regards natural risks,
in-depth study is in progress of:

The antigens and the mechanisms of their expression in the malaria agent;

The antigens and the genomes of flaviviruses (yellow fever, dengue), with
a view to identifying immunizing structures free from side effects;

The antigens of the viruses of hepatitis A and E, the resistance of these
viruses to disinfectants, and the relevant antiviral therapy;

Vaccination against viruses of acquired immunodeficiencies;

Non-specific immunostimulation with the help of natural substances;

Local immunotherapy using human immunoglobulins in the prevention and
treatment of respiratory infections in cases of immunodepression;
The survival of micro-organisms and viruses in the environment, and ways and means of disinfecting the air and surfaces.

(d) Fundamental research

Protection against ABOs and the use of ever more sophisticated technology means that the laboratories working for the Ministry of Defence must maintain substantial technological potential and know-how. To this end, there are many collaborative arrangements with university and private laboratories. Among more than 25 projects supported by DRET, there is research on:

- The cloning of antibodies and paratopic mutagenesis;
- The cellular receptors of viruses and toxins;
- Hepatotropic and neurotropic viruses (genetics and expression in hosts);
- The mechanisms of bacterial infection;
- The mechanism of antigen stimulation of lymphocytes, interleukins in the activation and repression of cellular cycles;
- Genetic polymorphism.

Current research in France on protection against ABOs is being conducted in scrupulous compliance with the 1972 Convention.

This research is directed by the Ministry of Defence and carried out in laboratories that come under that Ministry or by public or private institutes working under contract.

The research carried out under the auspices of the Ministry of Defence in the sphere of protection against ABOs is mostly published in the scientific literature or is the subject of open-access communications.

2. SURVEILLANCE OF COMMUNICABLE DISEASES IN FRANCE

Where communicable diseases are concerned, the objectives of surveillance are:

1. To determine the incidence and the characteristics of an infectious disease and to develop early-warning systems and signs for epidemics;
2. To make possible action to break the chain of transmission in the event of an epidemic;
3. To identify the factors of risk of an infection so as to be able to propose the most suitable preventive measures and recommendations;
4. To evaluate preventive measures.

Over the past few years, the surveillance of communicable diseases in France has developed appreciably. There are several reasons for this:
Recognition of the inadequacy of surveillance based almost exclusively on the compulsory notification of certain diseases;
Growing need for the evaluation of health policies;
Emergence of new pathologies, particularly AIDS;
Need for action against certain diseases connected with the consumption of contaminated foodstuffs.

This increased need for action has resulted in the diversification of surveillance instruments, the use of new means of communication (videotex), the preparation of protocols for action in the event of epidemics, and better dissemination of information.

2.1 General principles governing surveillance

Surveillance has been developed on the basis of a variety of factors:
Clinical/or biological information;
Exhaustive or sample-based collection of information on:
  Serious and/or infrequent diseases (exhaustive collection of the "compulsory notification" type);
  Frequent and minor diseases (sample-based collection using networks of doctors and/or laboratories);
Frequency of collection (continuous or periodic);
Possible coverage of several geographical levels (national, regional, departmental or communal).

It is important, where possible, to have at least two independent and complementary surveillance systems for each disease. Comparison of the data obtained using these different surveillance systems makes it possible to verify the exhaustiveness and representativeness of the information collected.

2.2 Surveillance systems

In France, surveillance of communicable diseases at the national level is based on a number of information systems:
Collection of information on notifiable diseases;
The National Reference Centres;
Networks of microbiological laboratories;
Networks of general practitioners or medical specialists;
Ad hoc surveys or surveys of specific groups within the population.
(a) **System based on compulsory notification**

As a tool of epidemiological surveillance, compulsory notification for certain communicable diseases is governed by a decree of 10 June 1986, which laid down a two-part list of diseases:

The first part relates to diseases to which national or international measures may apply. These diseases must be confirmed by the appropriate National Reference Centre (cholera, plague, smallpox, yellow fever, rabies, exanthematic typhus and African viral haemorrhagic fevers);

The second lists diseases subject to measures to be taken at the local level, or diseases for which notification is an evaluation tool (typhoid, tuberculosis, tetanus, poliomyelitis, diphtheria, meningococcal infections, mass food poisoning, botulism, indigenous and imported malaria in overseas departments, AIDS, brucellosis and legionnaire's disease).

Most notifiable diseases are sufficiently serious to lead to hospitalization: notification is then effected by the hospital doctor responsible for the disease after the diagnosis is confirmed. Only three out-patient notifiable diseases are liable to be diagnosed: tuberculosis, brucellosis and mass food poisoning.

Notification is effected at the departmental level: each Departmental Directorate for Health and Social Assistance ensures that notification criteria are observed and that the information requested is exhaustive. All the notification forms are sent once a week to the Infectious Diseases Bureau in the General Health Directorate; a national return is drawn up each year and published.

Like any passive surveillance system, notification does not enable all the cases of a disease to be recorded; hence it is important to evaluate the notification rate and especially the representativeness of the information. This evaluation can be carried out only if other independent surveillance systems exist for a given disease. The notification rate varies from one disease to another: it is good for very rare or very serious diseases (100 per cent for poliomyelitis, 85 per cent for AIDS and 75 per cent for meningococcal infections), but markedly less so for diseases usually confirmed by serological examination (brucellosis and legionnaire's disease). However, qualitative evaluation shows that the representativeness of the data is good.
Additionally, and independently of the notification system, doctors are invited to notify the Departmental Directorate of Health and Social Assistance as soon as possible by telephone, videotex or letter of:
- Any infectious disease occurring in the form of multiple outbreaks;
- Cases with an unusual clinical expression or course.

(b) National Reference Centres

The National Reference Centres are designated every three years by the Minister responsible for health. At present there are 40 such centres, 17 of them located at the Pasteur Institute in Paris.

These centres have the following tasks:

(a) Provision of expert opinion: contribution to strain identification at the request of medical and sometimes veterinary analytical laboratories. This work requires the maintenance of prototype strains and/or reference anti sera. Such activities often constitute direct applications of the research work carried out in these centres.

(b) Contributing to epidemiological knowledge by means of the isolates sent for examination. For this contribution to be effective, prerequisites are:

- Knowledge of the representativeness of the strains sent to the Centre as compared with the strains isolated in France;
- Possession of additional information accompanying the isolates, such as the age, sex and clinical indications of the patient, the type of the sample, the presumed origin of the contamination, and so on.

(c) Warning function: it is the task of each Centre to inform the Minister responsible for health immediately of any observation it has been called upon to make during its work which might have serious repercussions for the health situation in the country. This warning is justified in the event of multiple outbreaks (salmonella due to a single serotype, listeria, legionnaire's disease and so on), but also isolated cases of a rare disease (African haemorrhagic fevers, botulism, plague, cholera, polio and so on).

(d) Technical advice to the Government, either on the occasion of technical meetings or in the drawing up of recommendations (malaria prophylaxis for travellers, vaccination timetable, composition of influenza vaccine, monitoring of tuberculosis and so on).
(c) National videotex network for the surveillance of infectious diseases

This network was set up in 1984, in cooperation with the National Institute of Health and Medical Research. It is based on a videotex communication system embracing a number of partners: the Infectious Diseases Bureau, the Unit for Biostatistical and Biomathematical Research, National Reference Centres, the National Health Laboratory, Departmental Directorates for Health and Social Assistance, and "watchdog" doctors and laboratories.

The network draws on 550 "watchdog" general practitioners – 1 per cent of the total number of French general practitioners. Seven communicable diseases are currently subject to continuous surveillance through the network: influenza syndromes, urethritis in males, acute diarrhoea, mumps, measles, chickenpox and hepatitis assumed to be of viral origin. In addition, ad hoc epidemiological surveys are carried out on request (attitudes to vaccination, Lyme disease, and so on). The results of the surveillance are updated each week and broadcast on videotex bulletins indicating the development of the monitored diseases in space and time.

An electronic mail service enables the partners to communicate with one another directly. This allows the "watchdog" doctors to notify any unusual pathology they observe during their duties, and enables the health services to broadcast warning messages.

(d) National Health Laboratory networks

The National Health Laboratory runs a number of networks of private and public medical biology laboratories which supply information on the germs (bacteria or viruses) identified during their activities:

A network of hospital laboratories dealing with bacteria isolated in blood and cerebrospinal fluid;

A network of university hospital virology laboratories dealing with viral infections;

A number of networks dealing with sexually transmitted diseases.

(e) Ad hoc surveys

Ad hoc surveys are carried out:

To evaluate the incidence of diseases which are not covered by routine surveillance: retrospective surveys on listeriosis, toxic shock syndrome, anisakiasis, and so on; surveys of prevalence (nosocomial infections, "point-in-time" surveys); or
To evaluate preventive activities (vaccination coverage, attitude to the prevention of sexually transmitted diseases and AIDS).

(f) Other sources of information

Medical death certificates (a posteriori validation);
Sale of vaccines or medicines;
Screening activities:
  Blood donation (syphilis, hepatitis B, HIV);
  Anti-venereal-disease dispensaries;
  Tuberculosis control;
Health certificates (issued at age 24 months);
Hospital morbidity (based on the medical component of the information systems)

2.3 Dissemination of information - cooperation

The results of the surveillance are all analysed and commented upon in the weekly epidemiological bulletin distributed by the Ministry of Health to more than 5,000 addresses.

The Departmental Directorates for Health and Social Assistance are in a position to issue departmental epidemiological bulletins which are more in keeping with the epidemiological situation locally.

Cooperative arrangements exist with a number of countries, both for the exchange of epidemiological data and as regards the methodologies used by the various components of the infectious disease surveillance system.