The role of international research institutes in the control of animal virus diseases

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Summary: The animal virus disease research institutes which justify being classed as "international" in the context of this review are described under five categories, namely, (1) institutes established by a group of countries, (2) national institutes selected to accept an international responsibility, (3) national institutes recognised for a competence in diagnosis of a specific disease, (4) national institutes which have competence in the diagnosis of diseases exotic to their country and provide a service to many other countries on an international scale, (5) national institutes within a region which share a specific competence with neighbouring countries. Examples illustrative of each of these categories are described, with more detailed attention being given to the programme of the Pan American Foot-and-Mouth Disease Center, which covers much more than the provision of a diagnostic service. In this respect, this Center probably has the most comprehensive programme of any in these categories of International Institutes dedicated to improving the measures for the control, eradication and prevention of one of the major virus diseases of animals in the Americas.

KEYWORDS: Americas - Aphthovirus - Cattle diseases - Disease control - International organisations - Laboratory diagnosis - Publications - Research - Research institutes - Veterinary education - Viral diseases.

INTRODUCTION

This paper is one of some thirty given during the 60th Anniversary celebrations of the establishment of the Animal Virus Research Institute, Pirbright. The objective of these contributions was to review the progress made in the understanding and control of the economically important animal virus diseases exotic to the United Kingdom. In discussing the role of international institutes it is convenient to divide them into categories but one essential attribute which they all have is a competence in diagnosis. Today, in most cases, the laboratory confirmation of the field diagnosis is rapid, accurate, precise and detailed. Until the complement-fixation test was developed during the 1940's for routine use in the diagnosis of foot-and-mouth disease (1), it took at least two to three weeks to determine the immunological type of the virus isolated from field outbreaks. With this time lag, it was no diagnosis of the disease for any immediate practical purposes but the information was one factor in attempting to study its epizootiology.

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The animal virus disease institutes which justify being classed as "international" in the context of this review are considered under five categories.

1. Institutes established by a group of countries to serve the needs of a region with funding by member States, directly or indirectly, through an international agency; for example, the Pan American Foot-and-Mouth Disease Center, Rio de Janeiro, Brazil.

2. National institutes which have accepted an international responsibility, usually as a reference centre, from an international agency; for example, the Animal Virus Research Institute, Pirbright, England, designated by the Food and Agriculture Organization as the World Reference Laboratory for Foot-and-Mouth Disease.

3. National institutes which, because of a competence in the diagnosis of specific diseases, are recognised (without necessarily the sponsorship of an international agency) as one of the best places for the submission of biological material for laboratory confirmation of the diagnosis; for example, the Veterinary Research Institute, Onderstepoort, South Africa.

4. National institutes which, as a component in their country's defence against exotic diseases, have acquired a competence in diagnosis and provide a service to countries in their region; for example, the Plum Island Animal Disease Center of the United States Department of Agriculture, Greenport, New York.

5. National institutes within a region such as that of the European Economic Community which share a competence with neighbouring countries and, to a certain extent, much more widely. Examples are provided by the well-known institutes at Lindholm, Denmark; Tübingen, German Federal Republic; Lelystad, Netherlands; and Weybridge, United Kingdom.

**CATEGORY I**

**The Pan American Foot-and-Mouth Disease Center**

The Center was established in 1951 in Rio de Janeiro, Brazil, at the instigation of a number of countries of the Organization of American States. Originally, it was funded by this Organization and administered by the Pan American Sanitary Bureau, now the Pan American Health Organization. For the last twenty years the funding has been by member countries through the Pan American Health Organization.

The Center provides a comprehensive example of the various functions appropriate to an International Institute. These are now briefly described.

*Technical assistance*

The basic responsibility is to provide technical assistance to the countries of the Region on the prevention, control and eradication of foot-and-mouth disease. This task falls into two parts: (a) the service to the countries free of the disease and (b) the service of the countries in which the disease is present.
(a) Countries free of foot-and-mouth disease

The service here includes assistance with regard to compiling and enforcing importation regulations to act as a barrier against the introduction of foot-and-mouth disease, to seek to reach inter-country uniformity in this respect within an epizootiological region and to collaborate with national and international organisations with similar objectives; to encourage vigilance and the reporting of all outbreaks of vesicular disease, with submission of samples for laboratory confirmation of diagnosis or for differential diagnosis from areas in which vesicular stomatitis occurs; to assist with the preparation of contingency plans for immediate implementation in the case of an outbreak of foot-and-mouth disease; to reinforce these efforts by holding training courses in countries of the region or, occasionally, in a country where there is adequate containment for the housing of infected farm livestock for demonstration of cases of foot-and-mouth disease and other vesicular diseases. In the case of Panama and Central America, enzootic areas of vesicular stomatitis, the Center's laboratories in Rio de Janeiro were always available on a high priority basis for the receipt of samples for differential diagnosis.

(b) Countries in which foot-and-mouth disease exists

The service in this case has changed in emphasis over the years, although the principal subjects continue to be important. An early and high priority was to assist in the planning of control programmes, assisting with their establishment and implementation, providing advice and technical training on vaccine production and quality control, on vaccine storage and distribution, assistance with the identification of virus strain variation and selection of strains for vaccine production. An important task was to stimulate co-operation and collaboration between countries so that success in one country would not be unduly prejudiced by less effective action in a neighbouring country. As national services began to become more effective, the next task was to assist in exploiting this by the preparation of projects for submission to International Credit Agencies for additional, long-term funding. This point was reached only after an initial phase of convincing these Agencies that there were favourable cash-benefits based on socio-economic considerations; the greatest support in this connection was received from the Inter-American Development Bank. This exercise produced new tasks as, for example, developing evaluation techniques to assess the progress of nationally and internationally funded control programmes. All these endeavours were concurrent to organising frequent training courses, to which reference is made later.

The activities in both groups of countries can best be summarised as taking the lead in all matters related to combating foot-and-mouth disease in the countries of the region.

International co-ordination

When dealing with foot-and-mouth disease on a continental basis, it has to be attacked not haphazardly by individual countries but by groups of countries within epizootiological areas. In this context, this means an area circumscribed by geographical barriers which, by their nature, hinder the passage of livestock. This definition has to be qualified as such barriers become penetrated by improvements in communications. The most notable example in the Americas in this respect, and the cause of some concern, is the planned linking of sections of the Pan American Highway through Darien, thus providing land communication between Central America/Panama and South America. The contrast between physical boundaries
and political boundaries is best illustrated, unfavourably, by citing the ease of pas-
\[\text{age (say) between Rio Grande do Sul, Brazil, and Uruguay and also between}
\text{Colombia and Venezuela in the area of their contiguous plains.}
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The action to be taken to obtain effective international co-ordination can range
from area conferences to the establishment of inter-country organisations. A rela-
tively recently established example of such an organisation is COSALFA, the Spa-
\[\text{nish acronym for the South American Commission for the campaign against foot-and-mouth disease.}
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**Research**

From its inception, the Center has had a research programme strictly related to
the improvement of the methods available for diagnosis, epizootiological studies
and the preparation of vaccines.

High priorities included the development of modified live virus vaccines and
their use in field trials in a number of countries, the detection of carrier animals,
the survival of virus in the tissues of vaccinated cattle exposed to infection, and
the formulation and use of oil adjuvant vaccines. There are two aspects of this research
capability that are very advantageous: the opportunities for conducting field trials
of vaccines are excellent and it is a great asset to be able to take a country’s pro-
\[\text{blem straight back to one’s own laboratory.}
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With regard to this last point, there have been many examples of collaborative
research with scientists in other countries. Perhaps the most notable instance was
following meetings between the Presidents of the Republic of Argentina and the
United States of America in 1961 to discuss, among other things, improving the
trade in meat products from Argentina to the USA against the background of the
presence of foot-and-mouth disease in Argentina. Several programmes of study and
research were initiated under the supervision of three Programme Leaders (Argen-
tina, H.G. Aramburu; Pan American Foot-and-Mouth Disease Center, W.M.
Henderson; United States of America, M.S. Shahan). The results of two major col-
laborative studies, (a) on survival of the virus of foot-and-mouth disease in cured
beef from vaccinated and from unvaccinated cattle and (b) an epizootiological sur-
\[\text{vey of the Island of Tierra del Fuego, were published by the US National Academy}
\text{of Sciences National Research Council (5).}
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**Laboratory diagnosis**

The original concept of the member countries of the Organization of American
States that called for the creation of the Center was that it should be a diagnostic
and virus typing laboratory. In this capacity it has acted as a Reference Centre at
regional level in relation to the World Reference Laboratory for Foot-and-Mouth
Disease, Pirbright. Mention has been made of the important function of providing
differential diagnosis when vesicular stomatitis is of concern. Because of this fami-
\[\text{liarity with the disease and the virus, an unusual outbreak in the mid-1960’s of a}
\text{vesicular disease in the State of Alagoas, Brazil, affecting oxen, mules and man was}
\text{quickly identified as having been caused by an Indiana type vesicular stomatitis}
\text{virus. Subsequent investigations in collaboration with the Animal Virus Research}
\text{Institute, Pirbright, added to the information about variation within strains of the}
\text{Indiana type (2).}
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Training courses

The holding of training courses is an arduous but most important activity. Since the first course was held in 1953, about two a year have been organised, either at the Center in Brazil or in another country of Latin America. In the great majority of cases, the courses are international, with participants from a number of countries, usually from an area where the problems and interests are similar. The theme of these courses is predominantly the teaching of techniques: for example, diagnosis, analysis of strain variation, antibody assay, mammalian cell culture, vaccine preparation and quality control, epidemiology, and planning of field campaigns and their evaluation. In countries free of the disease, the topics are policies and actions for the prevention of the introduction of infection, emphasising the need for vigilance and ways of educating the public in awareness of the hazard. Training may also be provided, to a lesser extent, on an individual basis by a trainee spending some months studying and practising a specific technique such as vaccine production.

There were at least two significant consequences to these training courses: namely, all laboratory diagnoses throughout South America are now done by one uniform method, using standard reagents, and an international community of specialists was created by the ever-increasing number of the Center’s “alumni”.

Publications

The Center had to establish itself as a centre of communication. Apart from day-to-day contacts, a continuing flow of information was essential. This was achieved through publications in Spanish and English. One of the first publications, in Spanish and English, was Plan of action in the case of an outbreak of foot-and-mouth disease. This, with a companion film, was widely distributed throughout Panama, Central America, the Caribbean, Guyana, Surinam and French Guyana. Shortly afterwards, a monthly bibliographical and abstracting publication was issued which was replaced in 1971 by the Center’s Bulletin of similar content but with the inclusion of directly contributed papers. The monthly epidemiological report from 1969 must be known in many countries. A number of monographs, technical manuals and bibliographies have been distributed over the years.

The Pan-American Zoonoses Center

The Pan-American Zoonoses Center in Buenos Aires, Argentina, is administered by the Pan American Health Organization and provides, in the field of the zoonoses, a similar type of service to that of the Pan American Foot-and-Mouth Disease Center. Of note, as far as this review is concerned, is that rabies is included in its programme, although most emphasis is on the principal regional problems of the diseases of animals communicable to man, namely, tuberculosis, brucellosis, hydatidosis and leptospirosis, and food microbiology.

CATEGORY 2

The Animal Virus Research Institute

The Animal Virus Research Institute, Pirbright, was designated the World Reference Laboratory for Foot-and-Mouth Disease in 1958. The work that led to this recognition began in the 1940’s, when it became apparent, with the increasing use
of foot-and-mouth disease vaccines, that antigenic variation occurred to a significant extent, in that a vaccine prepared from a virus strain isolated from a past series of outbreaks might not protect adequately against the current field strains of the same immunological type (3, 4). The collection of variants or sub-types (as they were then named) that subsequently grew in size in each laboratory came to be identified by numerical suffixes but without co-ordination. The first task of the World Reference Laboratory was to introduce order into this chaos and then to become the sole authority for the acceptance of a new variant and the assignment of its identifying numerical suffix. It was not anticipated at that time that today's high precision would be introduced into strain identification, thus adding greater validity to the results of tracing the origin of outbreaks. The importance of this work needs no emphasis.

CATEGORY 3

The Veterinary Research Institute, Onderstepoort

The example of a national institute with a special competence which would appear to be most appropriate is the Veterinary Research Institute of the South African Ministry of Agriculture. This institute is internationally recognised for its authority in the identification of the virus of African horse sickness and its numerous serotypes. It also held this authority in the earlier history of bluetongue of sheep, lumpy skin disease and Wesselsbron disease. With the dissemination of a number of virus diseases of animals from Africa, there are now other national institutes with competence in the diagnosis of various formerly exotic viral infections but without the same historical recognition of Onderstepoort with regard to African horse sickness.

CATEGORY 4

National institutes with a competence to diagnose animal virus diseases exotic to their country with a service available to other countries.

Great Britain

The policy of the Ministry of Agriculture, Fisheries and Food, implemented through the State Veterinary Service, with regard to the identification of diseases of animals is that there must be a national capability for the diagnosis of all diseases cited in the various Acts and Orders for which the Ministry is responsible. This capability is provided by two national institutes, namely, the Animal Virus Research Institute, grant-aided by the Agricultural and Food Research Council, and the Central Veterinary Laboratory, Weybridge, of the Ministry of Agriculture, Fisheries and Food. The Pirbright Institute is responsible for the diagnostic service covering most of the virus diseases of animals exotic to the country. The Weybridge Institute is responsible for the diagnosis of rabies, the virus diseases of poultry and of certain virus diseases of animals which were previously enzootic — for example, classical swine fever. In both cases, a service is provided to any other country seeking assistance.

United States of America

The current policy of the United States Department of Agriculture is best ascertained by reference to a report issued in 1983 by the US National Research Council
on Agriculture entitled Long-term Planning for Research and Diagnosis to Protect US Agriculture from Foreign Animal Diseases and Ectoparasites (6). There are two locations of interest — the Plum Island Animal Disease Center, Greenport, New York, and the National Animal Disease Center, Ames, Iowa.

The Plum Island Animal Disease Center

The Center, inaugurated in 1956, is the diagnostic and research institute directed towards preventing foreign diseases of animals from endangering the livestock population of the United States. In addition to providing a comprehensive diagnostic service, semen and other specimens from live animals are tested for the presence of infectious agents prior to importation. The microbiological hazards of products of animal origin are assessed prior to importation. These services are available to others and the Plum Island Center is regarded by the countries of the Americas and by the Pan American Foot-and-Mouth Disease Center as their reference laboratory for diagnosis of diseases exotic to the hemisphere. Another activity is the training of US veterinarians and, to a rather limited extent, the training of foreign veterinarians.

The National Animal Disease Center

The responsibility of this institute is for research and diagnosis of the diseases of livestock and poultry present in the country. It has other activities covering diseases of doubtful classification — for example, some that have been eradicated and are therefore foreign or exotic. These are Venezuelan equine encephalomyelitis, malignant catarrhal fever, vesicular stomatitis, and exotic Newcastle disease.

Australia

The Australian National Animal Health Laboratory

This new laboratory built by the Australian Government at Geelong, Victoria, and commissioned for operation in 1984, is the most advanced high containment laboratory building yet completed for working safely with the most infectious diseases of animals. After years of study and consultation, it was designed to handle exotic agents causing animal disease under conditions as near to perfection as possible, so that the work would be without risk to Australia’s livestock. During the period of planning and construction there were repeated debates about whether work should be permitted with infectious foot-and-mouth disease virus before an outbreak of the disease occurred in Australia. The final decision, taken one year ago, was against the introduction of live virus for the time being but with the qualification of future reviews being made of the situation. Work is proceeding with other viruses and with inactivated foot-and-mouth disease reagents, to enable the staff to initiate research and to acquire a competence in diagnosis.

The justification for including this new institute, conveniently known by its acronym “ANAHL”, is the potential which it has as a reference laboratory for the region of South-East Asia and Australasia. In 1982, the author stated during the Australian National Farmers’ Federation Forum, Geelong, Victoria: “Anyone concerned with the world problem of the major virus diseases of animals must welcome the addition of ANAHL to the company of the Animal Virus Research Institute, UK, and the Plum Island Animal Disease Center, USA, thus forming a well-located triad of high security laboratories. ANAHL is ideally located for participation in any regional programme of animal disease control that might be started in South-East Asia and thereby making a contribution of inestimable value.”
Foot-and-mouth disease is enzootic in Burma and Thailand, which has resulted in periodic spread of the disease into Malaysia with, on occasion, dangerous progress southward. Types O, A and C have progressively been the cause of outbreaks of foot-and-mouth disease in the Philippines, and Indonesia has also had problems, but to a lesser extent. The concept for a regional programme for the prevention, control and eradication of foot-and-mouth disease in South-East Asia could start in the 1980's in a more propitious climate than that in the Americas in the 1950's, when the Pan American Foot-and-Mouth Disease Center was created for this purpose. At that time there was the political will of the Organization of American States, the Pan American Sanitary Bureau and, later, the participation of the Inter-American Development Bank. In South-East Asia there are the Association of South-East Asian Nations (ASEAN), the Animal Production and Health Commission for Asia, the Far East and the South-West Pacific (APHCA), a regional international credit agency (the Asian Development Bank), and a large country with animal production as its primary industry threatened by the proximity of foot-and-mouth disease and now with the most modern high containment laboratories, still under-utilised (Australia).

It is encouraging to know that this concept of a regional animal health programme has been discussed on a number of occasions by the organisations mentioned. The complexity of the political decisions that have to be made in any multinational project is, however, likely to make progress hard and slow.

CATEGOR 5

This category covers the growing number of national institutes with a high scientific reputation, but whose diagnostic services have usually been solely for their own country. The oldest of these institutes are in developed countries, especially in Europe. With the participation of their countries in programmes of aid to developing countries, contacts are established which lead to the provision of advice, technical assistance and training. Mention is made of four such institutes in the description of this arbitrary system of categorisation (p. 514). This selection of a few of the currently best-known institutes may seem to be invidious, but all are excellent examples.

DISCUSSION

An attempt has been made to identify the various components that contribute towards the importance of the role of international virus disease institutes.

A primary role is to provide an international service of diagnosis by the testing in the laboratory of specimens from field outbreaks. The information sought and, whenever possible, provided is not just confirmation of a tentative diagnosis. When positive, the immunological characteristics of the isolated virus are required so that the most suitable vaccine can be recommended, and any information by which a possible origin may be identified is most valuable. It is only an international institute that can provide the comparative information from its data bank. A sequel to confirming the occurrence of disease is to report urgently the result of the examination to the country and, depending upon the agreed procedure, to neighbouring countries, regional organisations and international organisations such as the International Office of Epizootics and the Food and Agriculture Organization. For furthering effective action, the international institute should be able to mount a team
of epizootiologists whose appraisal of the situation will influence subsequent national and international decisions with regard to the imposition of sanitary control measures. In the case of foot-and-mouth disease, up to the end of the 1960’s most of the developed countries free of the disease did not give serious consideration to the use of vaccine following an introduction of infection. A number of factors have contributed towards a change of attitude. These include the increasing size of animal production units, with the daunting problem of a sufficiently rapid elimination of infection by slaughter and disinfection and a greater availability of vaccine of improved potency. A consequence has been the establishment of vaccine banks, an action that was taken in Great Britain following the termination of the prolonged series of outbreaks in 1967/68. These banks were of liquid vaccine of regular production batches, periodically renewed. The replacement of this system by the storage of antigen in liquid nitrogen for subsequent formulation and blending has been under development during the last few years, and seven countries are contributing to the new international vaccine bank which comes into operation at Pirbright in 1986.

Uniformity is desirable in the use of measures relevant to disease control; thus, a training programme or at least a guidance manual is an important contribution from an international institute. In emergency, an internationally based voice can exercise strong pressure upon a diffident authority to conform with a regional programme. This emphasises the importance of the constitutional base of the international laboratory so that it may assume leadership in any emergency.

The models provided by the Pan American Centers (Foot-and-Mouth Disease and Zoonoses) might well be followed in other regions which form an appropriate geographical or epizootiological unit and in which the benefits of coordinated multinational activity have not yet been achieved in the control of animal diseases.

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LE RÔLE DES INSTITUTS INTERNATIONAUX DE RECHERCHE DANS LA PROPHYLAXIE DES MALADIES VIRALES ANIMALES. — W.M. Henderson.

Résumé : Les instituts de recherche sur les maladies virales des animaux, qui méritent d’être classés comme instituts « internationaux » dans le cadre de cette étude, peuvent appartenir à l’une des cinq catégories suivantes : 1) instituts mis en place par un groupe de pays ; 2) instituts nationaux à qui est confiée une responsabilité internationale ; 3) instituts nationaux reconnus pour leur compétence dans le diagnostic d’une maladie spécifique ; 4) instituts nationaux dont la compétence en matière de diagnostic des maladies exotiques pour leur propre pays est mise au service de nombreux autres pays au plan international ; 5) instituts nationaux qui, dans une région donnée, partagent une compétence particulière avec des pays voisins. L’auteur décrit des exemples représentatifs de chacune de ces catégories. Le programme du Centre panaméricain de la Fièvre aphteuse, qui assure des services beaucoup plus nombreux que le diagnostic, fait l’objet d’une présentation détaillée. De ce point de vue, ce Centre est probablement, parmi ces catégories d’Instituts internationaux, celui dont le programme est le plus complet de tous, puisqu’il se consacre à améliorer les mesures de prophylaxie, d’éradication et de prévention d’une des principales maladies virales animales dans les Amériques.
COMETIDO DE LOS INSTITUTOS INTERNACIONALES DE INVESTIGACIÓN EN EL CONTROL DE LAS ENFERMEDADES VÍRICAS ANIMALES. — W.M. Henderson.

Resumen: Los institutos de investigación de las enfermedades víricas de animales, que merecen ser clasificados como institutos «internacionales» en el marco de este estudio, pueden pertenecer a una de las cinco siguientes categorías: 1) institutos organizados por un grupo de países; 2) institutos nacionales a quienes se confía una responsabilidad internacional; 3) institutos nacionales reconocidos por su competencia en el diagnóstico de una enfermedad específica; 4) institutos nacionales cuya competencia en materia de diagnóstico de enfermedades exóticas para su propio país es puesta al servicio de otros muchos países a nivel internacional; 5) institutos nacionales que, en una región determinada, comparten una competencia especial con países vecinos. Describe el autor ejemplos representativos de cada una de estas categorías. Se presenta pormenorizadamente el programa del Centro panamericano de la Fiebre aftosa, que efectúa, además del diagnóstico, otros muchos servicios. En esta óptica, probablemente este Centro, es entre estas categorías de Institutos internacionales el que tiene el programa más completo de todos, por cuanto se dedica a mejorar las medidas de control, erradicación y prevención de una de las principales enfermedades víricas animales en las Américas.


REFERENCES


