MINUTES OF AN INFORMAL MEETING ON NEWLY-RECOGNIZED GROUPS OF VENUSES (ADENOVIRUS, COXACKIE VIRUS, ECHO VIRUS)\(^1\) 26 MAY 1956

Participants:

Dr. John H. Dingle
Western Reserve University
Cleveland, Ohio

Dr. John F. Enders
The Children's Medical Center
Boston, Massachusetts

Dr. Maurice R. Hilleman
Walter Reed Army Institute of Research
Washington, D.C.

Dr. Robert J. Huebner
The National Institutes of Health
Bethesda, Maryland

Dr. Joseph L. Melnick
Yale University School of Medicine
New Haven, CT, Connecticut

Dr. A. J. Rhodes
University of Toronto
Toronto, Canada

Dr. Albert Sabin
The Children's Hospital
Cincinnati, Ohio

Dr. Morris Schaeffer
Communicable Disease Center
Montgomery, Alabama

Dr. Joseph Snedell
Walter Reed Army Medical Center
Washington, D.C.

Secretariat:

Dr. A. M.-H. Payne
Division of Communicable Disease Services
World Health Organization
Geneva

Dr. A. C. Sanaa
World Health Organization
Regional Office for Americas

\(^1\) Enteric Cytotoxic Human Orphan virus
Provisional Agenda

1. Definition of need for international action in this field
   1.1 Epidemiological. Public health importance as cause of
disease. Confusion with disease of public health
importance of other etiology. Distribution. Incidence.
   1.2 Clinical. Definition of clinical syndromes. Identification
of clinical syndrome.
   1.3 Laboratory. Group identification, type identification
and nomenclature. Simplification of methods. Reagents
required.

2. Methodology
   2.1 Dissemination of information
   2.2 Preparation and distribution of reagents
   2.3 Techniques for general application (routine)
   2.4 Techniques for special centres (reference)
   2.5 Need for and functions of special centres
   2.6 Possible location of special centres
   2.7 Integration with existing WHO programmes.

3. Preparation for future Expert Committee
   3.1 Epidemiological studies
   3.2 Laboratory studies
   3.3 Problems of control
   3.4 Workers outside USA interested in the field.

Dr PAYNE opened the meeting by stating that he believed the meeting
should be completely informal, and that no formal report was required.
Minutes would be prepared by the Secretariat. The purpose of the meeting
was to guide WHO in planning its future efforts to assist in the solution
of the many problems associated with the isolation of new viruses now being
isolated.
The meeting should be considered as supplementary to the Symposium of the New York Academy of Sciences (24, 25 May 1956) at which a mass of fresh data was made available. He suggested that it should therefore confine itself to those aspects of the problem which had reached a stage where international action would be likely to be of benefit.

Dr Payne then briefly reviewed the provisional agenda. He felt that little could be said about item 1.1 at the present time other than the data made available at the New York Academy of Sciences meeting. It might be more profitable to consider how fresh information might be obtained. He suggested that the Expert Committee on Influenza, planned to meet in 1958 be nominated the Expert Committee on Respiratory Virus Diseases and deal with the adenoviruses. Dr SMADEN agreed with Dr Payne's suggestion that the Influenza Committee take charge of the Adenovirus Group and proposed that the Poliomyelitis Expert Committee take charge of the Coxsackie and ECHO groups.

Dr HUBBEE pointed out that assignment of one group of viruses to one Committee and the other two groups to the other Committee would complicate the problem. He therefore proposed that one Expert Committee take charge of the three groups of viruses.

After general discussion of the subject by all the participants, it was agreed that it would be administratively convenient to assign the study of these viruses to the two Expert Committees as originally proposed.

Dr EMDES suggested the name of the Expert Committee on Enteroviruses for the Expert Committee on Poliomyelitis.

Item 1.2 of the agenda was then discussed. The following diseases or syndromes were listed as etiologically associated with the Adenovirus group:

- Febrile catarrh (ARD)
- Follicular-conjunctivitis
- Pharyngitis (due to)
- Kerato-conjunctivitis
- Pharyngo-conjunctival fever
- Pneumonitis (due to)

As etiologically associated with Coxsackie viruses:

- Herpangina (due to)
- Pleurodynia, Epidemic myalgia, Bovahola disease
- Aseptic meningitis syndrome (due to)
- Association with myocarditis in infants

As etiologically associated with ECHO viruses:
In process of investigation, data accumulated shows strong evidence indicating the association of type 6 with outbreaks of aseptic meningitis.

Item 1.3 of the agenda (Laboratory) was discussed next.

In regard to the Adenovirus, the Group agreed that complement fixation is a good and easy technique. Antigens are commercially available. This technique could be used by any field laboratory. For typing, the material would have to be referred to a highly developed laboratory.

Dr HINDEES pointed out that a presumptive diagnosis might be made on the basis of cytopathogenic changes in tissue culture and that this would give a more rapid (1 day) answer than CF (2 weeks).

In regard to Coxsackie A viruses, Dr DICKLE said that the same principle stated in relation to the use of complement fixation for adenoviruses could be applied here with the important difference that there are no commercially available antigens.

Dr SARAH pointed out that when herpangina is suspected it is highly advisable to inoculate baby mice and that this technique is simple enough to be used by laboratories not highly developed.

Dr HUEHNER recommended the inoculation of 1-3 day-old mice with material from anal swabs. When the mice come down, the material from one of them can be used as antigen for CF.

Dr SANNELL pointed out that the lesions produced in baby mice by this type of virus are specific enough to be used for diagnostic purposes without resorting to serology.

Dr HUEHNER raised the question of the respective advantages of anal or throat swabs.

Dr HUEHNER recommended anal swabs although he agreed that it would be advisable to do both. When doing throat swabs, care must be taken to break vesicles in the throat.

Dr HINDEES expressed his preference for throat swabs. Drs Sannell and Meindert both expressed their opinion as to the limited advantage of doing serology in this group of viruses without doing isolation. Dr Sannell stressed the importance of all laboratories having baby mice available which would be useful for isolation of other viruses as well.
The Group came to an agreement that in relation to this group of viruses it would be best for a laboratory to obtain specimens for virus isolation and at the same time paired sera for serology.

**Coxsackie B Viruses.** The Group agreed that the specimens of choice in cases of pleurodynia are stools and nasal swabs. The material obtained from these sources may be inoculated into tissue cultures and into baby mice less than 24 hours old. Dr. Sabin said that for isolation purposes, tissue cultures of human amnion cells and monkey kidney cells are of choice. HeLa cells are not satisfactory. Dr. Hennessy pointed out that viruses isolated in tissue culture must be typed to be identified, but this was not essential when isolated in baby mice.

Dr. McKee stated that in his experience, tissue cultures are preferable to mice. In reference to CFS he proposed that the availability of this technique be mentioned while recognizing its limitations.

Dr. Snedell considered that we are not at the stage in which this technique may be recommended as a diagnostic method.

Dr. Hennessy stressed that although group B was most commonly isolated from sick persons it was also isolated from normal persons. It was agreed that in an outbreak, normal persons—not family contacts—should also be studied to determine the relative prevalence of the virus in sick and well persons.

In regard to aseptic meningitis, the Group agreed that the same recommendations be made as in the case of pleurodynia. Isolation of virus should also be attempted from CFS. The etiological association of this syndrome with the five types of Coxsackie B virus and type 2 of Coxsackie A virus was stressed.

**ECHO Viruses.** Specimens of choice are stools and nasal swabs. Tissue cultures from monkey kidney cells and human amnion cells are of choice for the isolation of viruses of this group. Most ECHO viruses will not grow in HeLa cells. When identifying an unknown poliovirus, Coxsackie group B and A9 should first be excluded.

Sera for ECHO types 2 to 6 and 14 are available and may be used as a pool. If a virus does not fall into these groups it must be sent to a reference laboratory. No CFS test is yet available.

Point 2.1 of the agenda was then taken up. It was considered advisable to make available to the largest possible number of interested people the proceedings of the meeting of the New York Academy of Sciences on this subject.
The possibility was raised of the World Health Organization helping to finance the publication of the proceedings of the meeting in greater numbers - Dr. MATTEN promised to investigate this but was not hopeful. The question of making a summary of the New York meeting in order to expedite information was also discussed, but it was agreed that it will not be practical in view of the rapid changes being introduced in the field which would make any summary outdated on appearance.

Point 2.2 of the agenda on "preparation and distribution of reagents" was discussed. It was emphasized that the current practice of each laboratory preparing and testing its own sera was uneconomical and often crippling in the time consumed. A "commercial" approach producing and testing big batches was the logical solution.

The National Foundation for Infantile Paralysis is financing the production of typing sera for viruses of the Convulsive and Pneumococcal groups. It is expected that the Foundation will consider requests for typing sera in limited quantities for reference laboratories.

In regard to typing sera for the Adenovirus group, Dr. SCHWARTZ stated that the Virus and Bacterial Unit of the Communicable Disease Center is planning to produce these sera in the near future at least for the more commonly found types and will be glad to provide the World Health Organization with small amounts of sera for reference laboratories.

Item 2.5. It was the feeling of the Group that it would be advisable for the World Health Organization to designate a limited group of reference laboratories round the world, not to exceed 8 or 10 in number.

These laboratories would be responsible for the typing and classification of viruses isolated in the respective zones of influence. They should be provided with the necessary typing sera.

It was agreed that only material collected during outbreaks should be accepted by reference laboratories for classification and typing.

In relation to point 2.6 of the agenda, possible location of special centres, a list was made up of the outstanding laboratories and research workers in points outside the United States of America, which could be considered for possible reference laboratories.

The Group strongly stressed the advisability of the World Health Organization stimulating epidemiological studies on diseases associated with these groups of viruses in areas outside the United States.

Item 3 was then considered and it was felt that this had already been adequately covered in discussions of the other items and at the New York Academy of Sciences meeting.

The meeting was then adjourned.