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RESTRICTED

MINUTES OF AN INFORMAL MEETING ON NEWLY-RECOGNIZED GROUPS OF  
VIRUSES (ADENOVIRUS, COXSACKIE VIRUS, ECHO VIRUS)<sup>1</sup> 26 MAY 1956

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<sup>1</sup> Enteric Cytopathogenic 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 syndromes.
  - 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 numbers 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 SMADEL agreed with Dr Payne's suggestion that the Influenza Committee take charge of the Adenovirus group and proposed that the Poliomyelitis Expert Committee takes charge of the Coxsackie and ECHO groups.

Dr HUEBNER 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 ENDERS 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:<sup>1</sup>

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<sup>1</sup> Note: The nomenclature adopted here was for convenience only and should not be regarded as expressing the Group's preference for any particular clinical classification.

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)  
Pleurodymia, epidemic myalgia, Bornholm 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 ENDERS 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 (four days) answer than CF (two weeks).

In regard to Coxsackie A viruses, Dr DINGLE 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 SABIN 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 HUEBNER 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 SMADEL pointed out that the lesions produced in baby mice by this type of virus are specific enough to be used for diagnostic purposes and group identification without resorting to serology which is, however, necessary for type identification.

Dr MELNICK raised the question of the respective advantages of anal or throat swabs. He also mentioned that in poliomyelitis comparative tests have shown that virus is recovered more regularly from a faecal specimen than from a rectal swab.

Dr HUEBNER recommended anal swabs although he agreed that it would be advisable to do both anal and throat swabs.

Dr ENDERS expressed his preference for throat swabs. Drs SMADEL and MELNICK both expressed their opinion as to the limited advantage of doing serology in this group of viruses without doing isolation. Dr SMADEL 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 anal 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 amniotic cells and monkey kidney cells are of choice. HeLa cells are not satisfactory. Dr RHODES pointed out that viruses isolated in tissue culture must be typed to be identified as a Coxsackie virus, but this was not essential when isolated in baby mice.

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

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

Dr ENDERS 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 the community.

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 CSF. The etiological association of this syndrome with the five types of Coxsackie B virus and type nine of Coxsackie A virus was stressed.

ECHO Viruses. Specimens of choice are stools and anal swabs. Tissue cultures from monkey kidney cells and human amniotic cells are of choice for the isolation of viruses of this group. Most ECHO viruses do not produce high cyto-pathogenic titres in HeLa cells. When identifying an unknown poliovirus, Coxsackie group B and A9 should first be excluded.

Sera for ECHO types 1 to 14 are available and may be used as pools. If a virus does not fall into these groups it must be sent to a reference laboratory. CF tests for the ECHO viruses and antibodies are known but have not yet been applied diagnostically.

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 PAYNE 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 uneconomic 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 Coxsackie and ECHO 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 SCHAEFFER stated that the Virus and Rickettsial Unit of the Communicable Diseases 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 eight or ten 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 material collected during outbreaks should be given highest priority 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 outside the United States of America, which could be considered as 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.