SESSION I

THE ARENAVIRUSES: PHYSICOCHEMICAL PROPERTIES, MORPHOLOGY, AND ANTIGENICITY

Arenavirus taxonomy: a review

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Despite a late beginning, the construction of the arenavirus taxon and its placement in the scheme of the International Committee on Taxonomy of Viruses has now been completed. The bringing together of the member viruses has already provided valuable indications of promising laboratory and field study approaches; in the future this classification will contribute further to our understanding of the natural history and disease processes of the human pathogens of the group.

Lymphocytic choriomeningitis (LCM) virus was one of the first pathogens of the human central nervous system to be isolated and propagated in the laboratory. In 1933 the virus was discovered by Armstrong & Lillie (1) when autopsy material from a fatal case thought to be St Louis encephalitis was passaged intracerebrally in monkeys. At about the same time, Rivers & Scott (14) isolated the virus from 5 people with aseptic meningitis and Traub (18) found the virus in the mouse colony of the Rockefeller Institute at Princeton, New Jersey. Traub continued working with the virus and made valuable contributions to the concept of self-tolerance advanced by Burnet & Fenner in 1949 (4). From that time, the complex interrelationship between LCM virus and the immunologic response of the rodent host has been explored in detail, but viral characterization and classification have received little attention until recently.

In 1964, Johnson (7) and Webb (19) called attention to the similarities in chronic infection patterns between LCM virus in mice and Machupo virus in hamsters and in its natural host *Calomys callosus*. By this time, Machupo virus had been serologically linked with other New World viruses to the Tacaribe complex (8), and in the following years attempts to demonstrate a relationship between LCM virus and members of the complex were continued. Webb and Johnson collaborated unsuccessfully with Rowe and his colleagues in searching for serological ties, and with Bergold in searching for ultrastructural ties. Bergold et al. (2) found that Tacaribe virus particles, concentrated from cell cultures and examined by negative contrast electron microscopy, were spherical, 85 nm in diameter, and had surface projections.

In late 1968, collaborative studies were undertaken in the Middle America Research Unit and in our laboratory at the Center for Disease Control (9). We carried out thin-section electron microscopy of lymphoid tissues of *Calomys callosus* and lymphoblastoid cell lines infected with Machupo virus, Vero cells infected with Tacaribe virus, and mouse macrophages infected with LCM virus (the last from unpublished work of M. S. Hirsch, A. K. Harrison, and F. A. Murphy). Our observations were in complete agreement with the initial publication on LCM virus morphology by Dalton and his colleagues (6) several months previously. The morphological similarities, later expanded to all other serologically related viruses (10, 11), prompted us to propose a new taxonomic group to include LCM virus, Machupo virus, and the other members of the Tacaribe serocomplex. These similarities also prompted Rowe and his colleagues to re-examine the serological interrelationships; using indirect immunofluorescence, they soon showed one-way cross-reactions between LCM virus antigen and antisera to Tacaribe complex viruses (15). Taken together, the morphological, physicochemical, and serological data became the basis for a formal proposal and definition of the *arenavirus* group (from the Latin *arena*, sand). This name reflects the characteristic fine granules seen within virions by thin-section electron microscopy; it was chosen by a group of interested virologists after being suggested by Ernest Borden in this laboratory (16). The taxon was approved and given genus status by the International Committee on Taxonomy of Viruses (20); however,

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in keeping with the elevation of many taxa to family status, a sense of parallelism may yet require that arenaviruses, likewise, be elevated and the family be termed Arenviridae.

The merit of constructing the arenavirus taxon was proven in 1970 when Lassa fever was first described and the causative virus characterized (3, 5, 17). The rapidity of this characterization by Buckley, Casals, Spier, and their colleagues allowed extrapolation from known attributes of other arenaviruses; this contributed to the choice of laboratory methodologies and to the search for the reservoir host.

At present, 10 arenaviruses are known: LCM (the prototype virus; world wide), Junin (Argentina), Machupo (Bolivia), Amapari (Brazil), Pichinde (Columbia), Parana (Paraguay), Tamiami (Florida), Latino (Bolivia), Tacaribe (Trinidad), and Lassa (West Africa) viruses. The definition of the taxon is as follows (12, 13): The viruses contain single-stranded RNA in 4 large pieces (and several smaller pieces) with a total molecular weight of approximately 3.5×10^6. The viruses have 4 major polypeptides (2 of which are glycosylated) and contain lipid and carbohydrates. The virion density is 1.17–1.18 g/ml in sucrose and the virion sedimentation coefficients are 325–500 S. Infectivity is labile to lipid solvents, acids (pH $<$ 5.5), and radiation (ultraviolet and gamma). The virions have a unique morphology in thin section; they are spherical or pleomorphic and range in diameter from 50 to 300 nm (mean 110–130 nm). The particles have a unit-membrane envelope covered with club-shaped projections 10 nm in length and have a varying number of electron-dense granules within an otherwise unstructured interior. These granules, 20–25 nm in diameter, have been shown to be ribosomes. Viral constituent synthesis takes place in the cytoplasm, often with inclusion body formation; maturation occurs via budding, primarily from plasma membranes. The viruses of this group variably cross-react in indirect immunofluorescent tests, and to a lesser extent in complement-fixation tests, but not in neutralization tests. Viral properties that contribute further to this definition are covered in more detail in other papers.

RÉSUMÉ

TAXONOMIE DES ARÉNAVIRUS: BILAN DE LA SITUATION

L'élaboration et la définition du taxon des arénavirus a été terminée et le taxon a été inséré dans le schéma du Comité international de Taxonomie des Virus. L'intérêt de grouper des virus possédant les mêmes propriétés physico-chimiques et biologiques réside dans la possibilité de préciser les méthodologies à adopter au laboratoire, sur le terrain et même dans le cadre clinique. Cet intérêt a été prouvé dans le cas du virus de Lassa, dont la caractérisation rapide a apporté des connaissances précieuses quant à l'histoire naturelle du virus et à la maladie chez l'homme.

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DISCUSSION

PFAU: In 1970, the Vertebrate Virus Subcommittee of the International Committee on Taxonomy of Viruses established an Arenavirus Study Group, the terms of reference of which were to update periodically the virus characterization data sheets given in Wildy's *Classification and Nomenclature of Viruses*, to suggest additional specific names and other matters related to generic composition, and to seek the views of virologists working in the field. A final report has been submitted for publication in *Intervirology* to provide the opportunity for as many virologists as possible to have access to it before its submission to the Vertebrate Virus Subcommittee at the International Congress for Virology in Madrid, September 1975. Comments on this report are invited.