The Classification of Viruses

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Recent discussions have centred rather on the nomenclature than on the classification of viruses. This is due in no small part to the reaction to Dr Holmes's 'Virus Supplement' in *Bergey's Manual*. His names were interesting, challenging ones which provoked controversy; and since they were beginning, if only in a small way, to creep into the literature it was necessary for virologists generally to decide whether to bless or to curse: neutrality was impossible. Holmes's classification of animal viruses, on the other hand, seemed to animal virologists to bear hardly any relation to the facts of life. At this point I shall apologize to our distinguished visitor for being repeatedly very critical of his writings. He and I have argued in public before and he knows, I hope, that however rude I may be, it is with the best will in the world. If he knows his Gilbert and Sullivan he will recall what King Hildebrand said to King Gama in *Princess Ida*: 'We will hang you, never fear, most politely, most politely.' Dr Holmes's is the credit for stimulating great interest in virus taxonomy and nomenclature: his action has also been invaluable—and here I am still trying to be polite—as a glaring example of how not to classify viruses. His family and generic divisions, at any rate amongst animal viruses, are based mainly on the symptoms and pathological lesions produced in infected hosts—barely at all on the properties of the viruses themselves. Now signs and symptoms, together with host and tissue specificity, are amongst the most labile properties of viruses, most easily modified experimentally. Further, very similar symptoms and lesions may be caused by viruses widely differing in all their fundamental properties. Thus Holmes places in one genus, *Molitor*, the utterly dissimilar viruses of warts, fowl-tumours and myxomatosis, having in common the one property of causing striking cell proliferation.

You may have gathered that I do not care for Dr Holmes's classification. I have just seen a copy of that of Zhdanov, which is very similar to Holmes's and is, I feel sure, based on it, as it repeats most of Holmes's most glaring errors and adds new ones of its own. Thus it not only includes the Rous sarcoma, warts and myxoma in one genus (*Tumefaciens*) but throws in, for good measure, the Bittner milk factor, an epithelioma of fish, and molluscum contagiosum. Like Holmes, Zhdanov widely separates dog distemper from so-called ferret distemper, Newcastle disease from fowl plague and cat distemper from cat leucopenia. Nearly all Holmes's names have been changed, presumably because Zhdanov was worried by the absence of an adequately confused synonymy.

Viruses are labile, variable agents and we need to rely on characters which are as stable as possible. At Rio de Janeiro in 1950 the Virus Subcommittee

of the International Nomenclature Committee suggested eight criteria to be used in classifying viruses:

- (i) Morphology and methods of reproduction.
- (ii) Chemical composition and physical properties.
- (iii) Immunological properties.
- (iv) Susceptibility to physical and chemical agents.
- (v) Natural methods of transmission.
- (vi) Host, tissue and cell tropisms.
- (vii) Pathology, including inclusion-body formation.
- (viii) Symptomatology.

The more important characters come early on this list; symptomatology, which Dr Holmes stresses even in his generic descriptions, comes last. Emphasis may be rather different for plant and bacterial viruses and will also vary somewhat as between one group of animal viruses and another.

Following decisions taken at Rio and in subsequent meetings, study groups have been trying to apply these criteria to certain better-known viruses such as those of the pox group and the influenza group; and it is hoped to publish shortly descriptions of viruses of these groups from the point of view of taxonomy. The eight criteria are proving very useful in this attempt.

It was felt at the Rome discussion a year ago that the whole essence of the Linnaean binomial system was that its names were closely linked with taxonomic concepts, from the species level upwards. But some idea of taxonomic relations needs nowadays to precede a Linnaean christening. There was an almost unanimous feeling that some internationally agreed orderly nomenclature for viruses was desirable but that our ideas of virus taxonomy were only embryonic; christening at the embryonic stage of development is usually considered premature. It was suggested, therefore, that interim names, non-Linnaean binomials, should be bestowed on certain groups of viruses; the group-names should carry the suffix '-virus'—for example *Poliovirus*—so that all should know them as something apart from the Linnaean system.

I should like to discuss in a little more detail one of the eight criteria—the immunological one. How important are antigenic differences and similarities as indicators of specific or generic relationships? Three groups of viruses suitably illustrate the point.

The group *Myxovirus* (influenza-like viruses) contains, on the recommendation of the international subcommittee, three group-members or species—influenza A, B and C. *M. influenzae*-A and -B are given the equivalent of specific rank because, first, they are quite distinct antigenically; secondly, they show quite a number of other definite though minor biological differences; these concern morphology, susceptibility to inhibitors, range of variation, pathogenicity for ferrets and mice, epidemiological behaviour. On the other hand, it is recommended that *Poliovirus hominis* contains three serotypes, not three species. This is because there is antigenic overlap amongst them and because the biological differences, which mainly concern ease of adaptation to rodents,

are less striking. But at present to classify the arthropod-borne encephalitis viruses is too difficult. By haemagglutination Casals and Brown place them in two groups, cross-reacting within each group but not from one group to another. Neutralization and complement-fixation tests are more specific but indicate some cross-relations—louping-ill having perhaps a relationship to members of each group. Two genera may be coming into focus here, but what of separation of species? The West Nile, Japanese B and St Louis viruses stand very close together—are they only serotypes? No one would propose to make yellow fever conspecific with any of the others; but most might call the two dengue viruses serotypes rather than species. With Uganda S, Ntaya and so forth, differentiation is mainly serological—what are our guiding principles here?

It is, however, one thing to describe and relate together individual viruses which are closely allied—the equivalents of species and genera—but quite another to classify these into families and higher taxa. Some people hold that viruses may be derived from bits of the host-cell; I do not myself regard this view with great favour but admit that it is an arguable proposition. If it should prove true—that herpes simplex is ultimately derived from human material and the Rous virus from that of the fowl, then any classification of viruses on Linnaean principles makes nonsense. But even if things are otherwise, the agents we call viruses may have come to resemble each other as a result of convergent evolution. It would not surprise me to learn that pox-viruses arose as specialized micro-bacteria and the viruses related to yellow fever as specialized micro-protozoa. The ability of the latter to multiply in either insect or vertebrate would fit with such an idea. If their ultimate origins are so much in doubt, it would be foolish to press on too fast with the designation of Suborders, Families and Tribes.

There is one fundamental question which it would be foolish to ignore. More and more recent work indicates that viruses multiply by some method other than by binary fission. It is suggested in the case of some bacterial viruses that they consist of two parts, an inner core of nucleoprotein and carrying the hereditary characters of the 'phage' and an outer envelope together with a tail consisting of phosphorus-free protein and carrying the apparatus necessary to enable the phage to infect a bacterial cell. The phage sheds this coat when it enters its host cell, the nucleoprotein replicates as such and only at quite a late stage in the developmental cycle does it begin to produce the protein of the outer coat. Such a method of reproduction may appear very different from what we conceive of as happening when a bacterium divides. It may, however, prove to be not wholly different from what is going on inside a cell as a preliminary to the large-scale crude process of binary fission.

The bearing of all this on virus classification is this: if virus multiplication should prove to correspond to the secret processes within a cell, are not viruses really very different from any form of cellular life? In 1939 Dr Holmes classified the viruses as Vira, a Kingdom of equal status with animals and plants. In 1948 he had second thoughts and degraded them to an order (Virales) of Bacteria. I am wondering if perhaps his first thoughts were not better than his second. I am not trying to answer this question: I hope you will discuss it.

There is a difficulty in separating viruses from bacteria in that the dividing line between them is not as sharp as might appear from what I have just been saying. The rickettsiae are minute obligate intracellular parasites (most of them at any rate), having many properties in common with viruses; yet they are by common usage classed with bacteria. Between them and the bulk of viruses stands the group of large viruses related to that of psittacosis—the Chlamydozoaceae. These are many of them susceptible to sulphonamides, chloromycetin, aureomycin and other antibiotics which do not affect true viruses. They resemble the rickettsiae in many other ways and at least one, that causing heartwater, has been placed by different workers on different sides of the dividing line. The international study group unanimously decided that they should not be reft from their natural relations, the rickettsiae, but should be included with them and outside the true viruses, taking their places in the mouth-filling genera *Miyagawanella* and *Chlamydozoon* of the Chlamydozoaceae. This view was endorsed by the main Virus Subcommittee. If we accept this view and are logical, we shall stop calling these agents viruses. There would then be no excuse for vendors of certain antibiotics to claim that ‘their spectrum of activity includes the viruses’.

The organizers of this discussion have very sensibly placed me, as representing sound common sense, between the two extremists, Drs Holmes and Bawden. Dr Holmes wants to start classifying and naming viruses on Linnaean lines right away. Dr Bawden is almost certain to advise you to have nothing to do with any such proceeding. Frankly, I do not know whether the Linnaean system will ever be generally applied to viruses or not: it well may be, as a matter of convenience. All such systems are a matter of convenience. I am all in favour of adopting a line which leaves it open to those who follow after us to apply this system or not as seems expedient, with the least possible disturbance of accepted usage. But we need to classify viruses *first* and we retard progress by trying to classify before we have the basic facts which alone would justify our attempt. I am sorry to have to prepare a gallows for Dr Holmes, but I am sure he will meet his end bravely.