Special Article

"THE CLASSIFICATION OF VIRUSES;
WHY, WHEN, AND HOW"*

by FRANK FENNER

(Lately Professor of Microbiology and Director of the John Curtin School of Medical Research, Australian National University, Canberra City, A.C.T.)

INTRODUCTION.

I am greatly honoured by the invitation of the Sydney Rubbo Memorial Trust and the Australian Society for Microbiology to give this, the Fourth Sydney Rubbo Memorial Oration. Syd Rubbo and I were contemporaries, although he was born a few years earlier than I and obtained his scientific training earlier, culminating in a Ph.D. at the University of London in 1936. He subsequently graduated in medicine while holding the post of Senior Lecturer in Bacteriology in the University of Melbourne. Rubbo was appointed Professor of Bacteriology in that University in 1945, at the age of 33; I was appointed Professor of Microbiology in the Australian National University in 1948, at the age of 34. Thus, we both faced the task of building up departments of Microbiology over about the same period, essentially the decade between 1950 and 1960. Our responsibilities were different. What under Rubbo's leadership became the School of Microbiology at the University of Melbourne eventually embraced some thirteen teaching courses in a wide variety of subjects and in four different faculties: medicine, dentistry, science and agriculture. In the John Curtin School of Medical Research I was faced with the narrower task of building up a department that had no teaching responsibilities except for Ph.D. students, but was given the opportunity and obligation of becoming a major research centre in some branch of Microbiology. Just how well Syd Rubbo succeeded in attracting able microbiologists to his School is demonstrated by the present distribution in senior positions throughout Australia of those who formed the staff of the School in 1967. No fewer than six of them are now professors; D. F. Gray, J. A. Pittard and D. O. White in Microbiology at the University of Melbourne, G. N. Cooper in Medical Microbiology at the University of New South Wales, B. W. Holloway in Genetics at Monash University and F. W. E. Gibson in Biochemistry in the Australian National University.

In those early days of the 1950's, and later, we discussed the differences in our tasks, and we both came to the conclusion that we would not wish to exchange roles. Syd Rubbo carried out much notable research, throughout the

* Fourth Sydney Rubbo Memorial Oration.

whole of his long association with the University of Melbourne, but he enjoyed the wider opportunities of building up a large and diverse teaching department more than the narrower satisfactions of personal research. Relations between our respective departments in Canberra and Melbourne were close. Apart from lecturing there more than I did at any other university in Australia, I was involved in the award of an Australian National University scholarship to allow Frank Gibson, then a young man in Rubbo's department, to do a D.Phil. in Oxford, for in the late 1940's the Australian National University wisely spent some of its statutory grant of £325,000 to provide overseas scholarships for bright young Australians. Subsequently, Bruce Holloway came back from Caltech to a Research Fellowship in the John Curtin School of Medical Research in 1953 and began his work on *Pseudomonas* there. He went to the Melbourne School of Microbiology in 1957 to develop the teaching of microbial genetics, and after rising to a Readership was appointed Professor of Genetics in Monash University in 1968. David White went to Rubbo's department immediately after receiving his Ph.D. at the Australian National University under Stephen Fazekas' tutelage, in 1960, and proceeded to develop excellent courses in virology in the Melbourne School. He was appointed a Professor of Virology there in 1968 and succeeded to the Headship of the School on Syd's death in 1969. Two other members of the present staff of the Department, Ian Holmes and Doris Graham, have Australian National University postgraduate degrees.

THE CLASSIFICATION OF VIRUSES.

At one time Syd and I had common interests in tuberculosis, but our scientific interests diverged as I became increasingly concerned with virology, a subject whose development in the Melbourne School devolved upon David White. Since 1967, when I became Director of the John Curtin School of Medical Research, my own activities in virology have been conducted with the pen and the publisher and not at the bench, and just two weeks ago I relinquished both the Directorship of the John Curtin School of Medical Research and the position of Professor of Microbiology. Apart from the laborious chore of seeing the second edition of "The Biology of Animal Viruses" through the press (it is currently at galley proof stage), my only connection with microbiology now (apart from membership of the Australian Society for Microbiology) is as President of the International Committee on Nomenclature of Viruses (ICNV)—a body whose name we hope to change in the future to the "International Committee for the Taxonomy of Viruses". I retain this post, and this interest in virology, until September 1975. It therefore seemed appropriate that I should take as the subject of the Rubbo Oration this year one of the two important activities of this Committee: "The Classification of Viruses: Why, When and How". The other responsibility is, of course, to name viruses.

WHY CLASSIFY VIRUSES?

It should not be necessary to devote much time to answering this question. Considering only those viruses that infect vertebrates, we now have some information about approximately one thousand different viruses. The attention of

animal virologists has been concentrated upon man as a host animal, with somewhat less attention devoted to the common, domesticated animals. However, there is no reason to believe that other animals are less richly endowed with viruses, and the vast bulk of vertebrate animals remain unexplored as viral hosts. There are perhaps a half million known species of insects, to say nothing of all the other invertebrates, hundreds of thousands of species of plants and a like variety of bacteria and fungi. It is not unreasonable to believe that there are probably several viruses that are specific for every species of living organism, so that the probable number of viruses that exist in nature is indeed vast.

The only way to introduce some sort of order into this great array of different things is to classify them into groups of like objects. Having done that, we need to distinguish these groups, as we distinguish individual people, by giving them appropriate names. The goal of biological classification is to group together organisms (or viruses, which most virologists regard as "living", but not as organisms) that present certain affinities. A further aim, achieved with some higher organisms against the background of evolutionary theory, is to bring out phylogenetic relationships.

WHEN SHOULD VIRUSES BE CLASSIFIED?

Historical perspectives.

"When" involves time, so let us get some historical perspectives. Virology began as a branch of pathology, the study of disease. At the end of the nineteenth century, when the microbial etiology of many infectious diseases had been established, pathologists recognized that there were still a number of common infectious diseases of man and his domesticated animals for which neither a bacterium nor a protozoan could be incriminated as the causal agent. In 1898 Loeffler and Frosch demonstrated that the economically important disease of cattle, foot-and-mouth disease, could be transferred from one animal to another by material which could pass through a filter that retained the smallest bacteria. Following this discovery, diseases transferable by this method were ascribed to what were first called "ultramicroscopic filterable viruses", then "ultrafilterable viruses", and ultimately just "viruses". So that without anyone thinking about it, classification and nomenclature had already begun.

Independently, and at about the same time, the plant pathologist Beijerinck recognized that an important disease of tobacco plants, tobacco mosaic disease, was not caused by a conventional microorganism, but by what he called a "contagium vivum fluidum", i.e., a "contagious living fluid". Nearly twenty years later, at the time of the first World War, the bacteriologists Twort in England and d'Hérelle in France recognized that bacteria could be infected by viruses, for which d'Hérelle coined the name "bacteriophages". Insect viruses were not recognized as such until the 1940's, although Pasteur had made important observations on viral diseases of silkworms many years earlier. Much more recently viruses have been recovered from fungi, algae and free-living mycoplasmas, and only last year two kinds of virus were recognized in an amoeba.

The nature of viruses.

Historically, viruses were defined as infectious agents that could not be cultivated *in vitro* and that passed through filters that retained bacteria. From the practical viewpoint of the plant pathologist and the public health worker, it is convenient to regard the viruses that cause disease as pathogenic microorganisms, and in support of this view Burnet's Dunham Lectures of 1944 were entitled "Virus as Organism". However, other biologists began to wonder whether viruses, whatever their host, might have common properties that distinguished them from microorganisms. André Lwoff was the most articulate of these critics, and argued cogently, in his Marjorie Stephenson Memorial Lecture in 1957, that "viruses are viruses", i.e., that all viruses show some properties that distinguish them from any microorganism. The essential differences between viruses and bacteria are shown in Table 1; in their essential features mycoplasmas, rickettsiae and chlamydiae all resemble bacteria rather than viruses. Exceptions to several of Lwoff's early generalizations have since been discovered, but three are still valid: (a) unlike even the smallest microorganisms (the Chlamydiae), viruses contain no functional ribosomes or other cellular organelles, although some enveloped viruses, notably in the genus *Arenavirus*, contain a few ribosomes derived from the host cell, (b) in RNA viruses the whole of the genetic information is encoded in ribonucleic acid and not deoxyribonucleic acid, a situation unique in biology, and (c) viruses of most genera contain either no virus-coded enzymes, or one or two enzymes that belong to a few particular classes (neuraminidases, nucleases and RNA polymerases); viruses lack enzymes for energy metabolism and they lack genetic information to code for such enzymes. Other distinctions apply to some but not all viruses, e.g., the isolated nucleic acid of viruses of several genera is infectious, so that complete virus particles can be generated intracellularly from a single molecule of the viral nucleic acid.

At a meeting in London last month a group of distinguished virologists drawn from many fields and countries agreed that it was currently impossible to define viruses satisfactorily in a sentence or even a paragraph, bearing in mind both their intracellular states and the extracellular particles or virions. Virions, as virus particles are called, consist of a genome of either DNA or RNA

TABLE 1.

The essential differences between viruses and bacteria.

Character	Virus	Bacterium
Types of nucleic acid	DNA or RNA, never both	DNA and several species of RNA
Infectious nucleic acid	some viruses, +	0
Growth	0	+
Division	0	+
Enzymes of the energetic metabolism	0	+
Genetic information for these enzymes	0	+
Ribosomes	0	+
Genetic information for ribosomal RNA	0	+

enclosed within a protective coat of protein molecules, some of which may be associated with carbohydrates or lipids of cellular origin. In the vegetative state and as "provirus", viruses may be reduced to their constituent genomes, and the simplest "viruses", what some plant virologists are now calling "viroids", may be transmitted from one host to another as naked molecules of ribonucleic acid, possibly associated with certain cellular components. Bacterial episomes pose another kind of problem; should one draw a distinction between bacterial "transfer factors" and viruses? At the other extreme, in terms of organizational complexity, are such large and complex DNA viruses as the poxviruses, containing over thirty structural proteins in the virion and at least four enzymes, and the large tailed bacteriophages with their complex tail and baseplate structure designed for injecting their DNA into bacteria.

Linnaean classification of organisms.

Adoption of a system of classification also involves consideration of the nomenclature of the objects to be classified; "taxonomy" implies both classification and nomenclature. Two hundred years ago Linnaeus introduced a latinized binomial nomenclature into biology, and phylogenetic classifications of animals and plants based upon the theory of evolution have since been introduced. International Codes of Nomenclature with rigid sets of rules, and Judicial Commissions to pass judgement on proposed names, have been set up for the naming of plants and of animals, and in 1947 an International Code of Nomenclature of Bacteria and Viruses was approved, and has been revised since then, first in 1958, and a new revision of the International Code of Nomenclature of Bacteria is now being processed. Although they are primarily concerned with nomenclature, all these Codes involve agreement upon a system of classification. A distinguished bacterial taxonomist, Dr. S. T. Cowan, has pointed out that these Codes are based on "acceptances", i.e., beliefs we would like to justify but are unable to prove. The principal "acceptance" is that we are able to arrange living things in an orderly system that is indicative of both rank in a hierarchy and phylogenetic relationships. Classifications of animals and plants attempt to be scientific by deriving their taxa from a consideration of phylogenetic relatedness. Very recently this approach has been reinforced by tests for genetic relatedness, i.e. the information content of the genetic material of the agents concerned. This has been tested by homology experiments with DNAs extracted from the cells of a variety of animals, and a comparison of the amino acid sequences of certain key proteins. It is to be expected that the phylogenetic and the molecular biological approaches will eventually be combined further to strengthen the scientific basis for classifications of organisms.

According to some competent bacterial taxonomists, the classification of bacteria into the same hierarchical pattern as that used for plants and animals; phyla, subphyla, classes, orders, suborders, families, genera and species, has led to a chaotic situation. Numerical methods, readily exploited with the aid of electronic computers, may offer a solution and are now being extensively exploited, not least by Professor V. D. Skerman of Brisbane, a former member of Rubbo's department in Melbourne; but purely numerical methods have the

disadvantages that the weighting of characters is involuntary rather than deliberate, and that pleiotropism may lead to some characters being scored several times. Virologists believe that all characters are not equal and that weighting is important; for example, they consider that the type, amount and conformation of the viral nucleic acid are taxonomically much more important characters than host range or pathogenic potential, and they are therefore reluctant to use purely numerical methods based on a large assemblage of characters. Indeed, there is a good deal to be said for the notion that viruses should be classified solely on the basis of the molecular properties of their genomes. Of all living things, viruses are the best suited for the developing science of molecular taxonomy (Table 2).

TABLE 2.

Molecular taxonomy as applied to viruses.

Properties of the viral nucleic acid
Type, amount, conformation, number of molecules
If single-stranded, 'sense' of strand (messenger or complementary)
Base composition
Oligonucleotide maps
Base sequence
Properties of viral proteins directly reflecting base sequence of nucleic acids
Amino acid composition
Peptide maps
Amino acid sequence
(Antigenic relationships, reflecting sequences of antigenic determinant sites)
Experimental tests: Molecular hybridization
Different viral nucleic acids
mRNA with viral DNAs
mRNA with viral RNAs (if double-stranded or complementary single-stranded)

Early classifications of viruses.

Until about 1950 little was known about viruses other than their pathogenic behaviour. Most early proposals for viral classification were restricted to viruses of plants and vertebrates and were based upon the symptomatology of diseases rather than the nature of the viruses; in essence, they classified host responses rather than the etiological agent. Some attempts to encompass all viruses into a Linnaean latinized binomial scheme, e.g. that proposed by Holmes in the 1948 edition of Bergey's Manual, were clearly premature and led to ridiculous groupings, for they were based solely on pathogenic behaviour—thus, for example, among the viruses of vertebrates myxoma virus, Rous sarcoma virus and papilloma viruses were grouped together as "tumor viruses" and given the same "generic" name: *Molitor* (Table 3); and there were similar confusing proposals for bacteriophages and plant viruses. Indeed, some of the suspicion that some plant virologists now exhibit for a latinized binomial nomenclature may stem from this misplaced enthusiasm of one of their number. On the other hand, the distinguished British plant virologist Sir Frederick Bawden made the pioneering suggestion in 1941 that viral classification should be based upon the properties of the virus particle.

In the early 1950's Bawden's approach was exploited by animal virologists, among whom Sir Christopher Andrewes was the leading figure. Over the next

TABLE 3.

Classification of viruses by the type of disease they cause (some examples from F. O. Holmes in "Bergey's Manual of Determinative Bacteriology" Sixth Edition (1948), Williams & Wilkins, Baltimore)

Genus	<i>Hostis</i> : diseases mainly characterized by vesicular lesions <i>pectoris</i> : foot-and-mouth disease virus (<i>Enterovirus</i> ^a) <i>equinus</i> : vesicular stomatitis virus (<i>Rhabdovirus</i>)
Genus	<i>Molitor</i> : diseases mainly characterized by tissue proliferation without vesicle or pustule formation <i>verrucae</i> human wart virus (<i>Papillomavirus</i>) <i>hominis</i> molluscum contagiosum (<i>Poxvirus</i>) <i>bovis</i> cattle wart virus (<i>Papillomavirus</i>) <i>buccalis</i> canine oral-papillomatosis virus (<i>Papillomavirus</i>) <i>tumoris</i> Rous sarcoma virus (<i>Leukovirus</i>) <i>gingivalis</i> rabbit oral-papillomatosis virus (<i>Papillomavirus</i>) <i>sylvilagi</i> rabbit papilloma virus (<i>Papillomavirus</i>) <i>myxomae</i> myxoma virus (<i>Poxviridae</i> , <i>Leporipoxvirus</i>)

^a Names in brackets indicate genus, according to current classification.

fifteen years many viruses of medical interest were allocated to what were called "groups", and these groups were given names constructed from a chosen prefix plus the word "virus", a notion first proposed by Burnet in 1953. Descriptions were published in the virological literature of seven such groups of viruses of vertebrates: Myxovirus, Poxvirus, Herpesvirus, Reovirus, Papovavirus, Picornavirus and Adenovirus. Definitions of these groups were published by experts in the field, acting either as individuals or sometimes as small international groups, and names were proposed according to the inspiration of the authors of the papers that described the group. Two methods predominated; what could be called "latinized"—a chosen latin prefix plus "virus", e.g. myxovirus and adenovirus—and the use of acronyms and sigla, like "reovirus" from "respiratory enteric orphan" and "picornavirus" from "pico (= little) RNA virus".

In the meantime, a classification using quite different criteria had been established by epidemiologists. Since they were concerned primarily with the transmission of infection from one host to another, epidemiologists developed a classification based on the mode of transmission; they grouped viruses together as "respiratory viruses", "enteric viruses" or "arthropod-borne (arbo-) viruses". The last term in particular continues to be widely used, but, as Table 4 indicates, this epidemiological classification, although useful for the purposes for which it was devised, is in no sense taxonomic.

The next notable advance in classification was contained in a paper by one of the members of the Australian Society for Microbiology, Dr. P. D. Cooper, whose proposal in 1962 for a chemical classification of viruses stimulated Professor André Lwoff, who was then President-elect of the International Association of Microbiological Societies, to take action to separate viruses from the provisions of the Bacteriological Code of Nomenclature. Subsequently, Lwoff called together a Provisional Committee on the Nomenclature of Viruses, which met in 1965 and paved the way for official action. At the Ninth International Congress for Microbiology in Moscow in 1966 the recommendations of the Provisional Committee were considered and in part adopted, and an official international committee was established, called the International Committee on Nomenclature

TABLE 4.

Epidemiological classification: taxonomic classes transmitted by respiratory, enteric or arthropod-borne routes.

Respiratory, with respiratory-tract symptoms

Adenovirus, Herpesvirus, Rhinovirus, Enterovirus, Orthomyxovirus, Paramyxovirus, Coronavirus

Respiratory, leading to generalized disease

Polyomavirus, Iridovirus, Herpesvirus, Poxvirus, Togaviridae (rubella), Paramyxovirus, Arenavirus

Enteric, sometimes leading to generalized disease

Parvovirus, Adenovirus, Enterovirus, Coronavirus

Arthropod-borne (Arbovirus)

Alphavirus, Flavivirus, Rhabdovirus, Orbivirus, Bunyamwera supergroup

of Viruses (ICNV). A number of "Rules" were adopted and others added in 1970 (Table 5). Some of these rules have produced, especially among plant virologists, a degree of suspicion that they were being imposed upon by medically trained virologists that has almost broken the Committee apart. Some plant virologists were indignant that medical virologists should accept sigla like "reovirus" (which is a perfectly good name—we have now forgotten what it means), but forbid the use of sigla by others.

Because I had an interest in general virology and was an Australian (international committees like to have some representatives from south of the equator), I was among the eight virologists elected to membership of the Executive of this new committee, and at the Tenth International Congress for Microbiology in Mexico City in 1970 I was elected its President, with a five-year term of office. One of my tasks during my term as President is to heal the breach between plant and animal virologists without sacrificing any important principles.

TABLE 5.

Summary of the rules approved by ICNV (from P. Wildy "The Classification and Nomenclature of Viruses" 1971, Karger, Basle)

1. The code of bacterial nomenclature shall not be applied to viruses.
 2. Nomenclature shall be international.
 3. Nomenclature shall be universally applied to all viruses.
 4. An effort will be made towards a latinized binomial nomenclature.
 5. Existing latinized names shall be retained whenever feasible.
 6. The law of priority shall not be observed.
 7. New sigla shall not be introduced.
 8. No person's name shall be used.
 9. No nonsense names shall be used.
 10. For pragmatic purposes the species is considered to be collections of viruses with like characters.
 11. The genus is a group of species sharing certain common characters.
 12. The rules of orthography of names and epithets are listed in Chapter 3, section 6 of the proposed international code of nomenclature of names (C).
 13. The ending of the name of a viral genus is *-virus*.
 14. To avoid changing accepted usage, numbers, letters or combinations may be accepted for names of species.
 15. These symbols may be preceded by an agreed abbreviation of the latinized name of a selected host genus or, if necessary, by the full name.
 16. Should families be required, a specific termination to the name of the family will be recommended.
 17. Any family name will end in *-idae*.
 18. A family is a group of genera with common characters.
-

Membership of ICNV and its Executive Committee.

The original membership of ICNV comprised five national members for each country, who were proposed by the national Societies for Microbiology of the different countries of the world, plus the members of the Executive Committee and its subcommittees. This arrangement led to the presence on the committee of many persons who had no interest whatever in viral classification or nomenclature, and who, because of their positions in their local national scientific hierarchies, were often present at the International Congresses where vital decisions were taken. Therefore, at the second International Congress of Virology in Budapest in 1971 it was agreed to reduce the national membership of ICNV, which is now constituted as shown in Table 6. This arrangement provides that while national representation is ensured, the majority of members of ICNV are virologists who are genuinely interested in its activities.

The affairs of ICNV are run by the Executive Committee, which has the composition shown in Table 7.

HOW SHOULD VIRUSES BE CLASSIFIED?

Those involved in trying to frame proposals that will win international acceptance have to steer a careful course between the Scylla of centralized dictation of irrevocable rules, which is likely to result in proposals that scientific

TABLE 6.

Membership of the International Committee on Nomenclature of Viruses (ICNV)

National members. Consisting of one representative of each national society affiliated with the International Association of Microbiological Societies.
 Life members, elected by ICNV.
 Members of Executive Committee of ICNV (ECICNV)^a
 Members of subcommittees of ECICNV^b.

^a elected by ICNV from among all virologists, not only those that are national or life members of ICNV.

^b proposed by Chairmen of Subcommittees and elected by ECICNV.

TABLE 7.

Membership of Executive Committee of ICNV (ECICNV)

<i>Officers</i>	President	} Elected at General Meeting of ICNV (may be re-elected)	
	Vice-President		
	Two secretaries		Permanent
<i>Elected members</i>	Eight members. Elected at General Meeting ^a of ICNV. Half to retire at each General Meeting; not available for immediate re-election.		
<i>Ex-officio members</i>	Chairmen of Subcommittees of ECICNV:		
	Vertebrate Virus:	H. G. Pereira (United Kingdom) ^b	
	Invertebrate Virus:	C. Vago (France)	
	Plant Virus:	R. J. Shepherd (USA)	
	Bacterial Virus:	A. Eisenstark (USA)	
	Code & Data:	A. J. Gibbs (Australia)	
	Coordination:	P. Wildy (United Kingdom)	

^a General meetings held at each International Congress of Virology (now held at intervals of 4 years). ICNV may conduct postal votes between general meetings.

^b Present incumbents

workers won't use, and the Charybdis of allowing any independent group of scientists to erect its own classification and nomenclature, without concern for internationally-agreed "rules", a course that will lead to chaos.

I hope that the International Committee on Nomenclature of Viruses has now settled down to an effective working arrangement that should enable it to steer that course. Importantly, there is general agreement on many of the "Rules", notably those that refer to an international nomenclature and universal classification that embraces all viruses. There was also a unanimous decision at the 1973 meeting of the ECICNV that the "Rules" should be subjected to careful scrutiny before the next International Congress of Virology in 1975, and that proposals for alteration should be debated at length by the general meeting of ICNV that will be convened at that time.

Operational Subcommittees of ICNV.

Concerning the criteria for classification, there is general acceptance among virologists and on the ICNV that the classification of viruses should be based primarily on the physicochemical properties of viral particles; primarily morphology and the amount and nature of the viral nucleic acid. However, while agreeing to the notion of a universal classification of viruses, ICNV had to accept the fact that most working virologists are familiar with only a small number of viruses, and rare is a man whose research interests encompass viruses that parasitize hosts belonging to more than one Kingdom. Several subcommittees were therefore established (Table 7), the first four of which are concerned respectively with viruses of the major subdivisions of organisms: vertebrates, invertebrates, plants and bacteria. The Coordination Committee, chaired by the first President of ICNV, Professor P. Wildy, has the task of relating the findings of these four subcommittees when they refer to groups of viruses of which representatives appear to be found in more than one of the major subdivisions, e.g., viruses resembling the reoviruses of vertebrates are also found in plants and insects. Finally, since it is clear that our present knowledge of the variety of viruses that must exist is at a very elementary stage, a Code and Data Subcommittee was established, with the responsibility of working out ways in which basic data on viruses could be collected, stored, retrieved and compared. Most subcommittees operate through a number of Study Groups that consist of leading scientists who are personally working on viruses of particular groups, and proposals pass back and forth between the Executive Committee and the Study Groups, via the appropriate subcommittees, before being presented to the ICNV itself.

At this stage I shall depart from the "universal" viewpoint that I have followed so far, and, in order to illustrate the principles of viral taxonomy, I will consider in some detail the viruses of vertebrates, which are the ones that I know best, and in which the practice of classification and nomenclature is most advanced. As I said a moment ago, virologists are agreed that the primary criteria for viral classification are the nature of the viral genome and the morphology of the viral particle. Since electron microscopy often allows us to study morphology relatively easily, I shall discuss that first.

The structure of viruses of vertebrates.

Three structural classes of viruses of vertebrates can be distinguished: isometric particles, which are usually "naked" but in some groups are enclosed within a lipoprotein envelope; long tubular nucleoprotein structures, which are always enclosed within a lipoprotein envelope (Fig. 1); and not illustrated in the Figure are a few groups of viruses that have a more complex structure, in which the detailed symmetry of the nucleocapsid has not yet been worked out. It is not possible to consider structural details here; suffice it to say that isometric particles are usually icosahedral and the known icosahedral viruses of vertebrates can be defined structurally by the number of subunits in the outer shell (Table 10). Tubular nucleocapsids appear to consist of a single repeating polypeptide, arranged with helical symmetry around the viral nucleic acid. Electron micrographs have now been published that illustrate the structure of most known viruses of vertebrates.

Fig. 1. *Structural types of viruses of vertebrates.* Schematic diagrams of the structure of (A) a simple non-enveloped virion with an isometric capsid that has cubic symmetry; and (B) an enveloped virion with a tubular nucleocapsid that has helical symmetry. The capsids consist of morphological subunits called capsomers, which are in turn composed of structural subunits that consist of one or more chemical subunits (polypeptide chains). The larger icosahedral viruses have a "core" (not illustrated) inside the isometric capsid, which consists of protein subunits directly associated with the nucleic acid.

In viruses of type B the envelope is a complex structure consisting of an inner virus-specified protein shell (membrane protein, made up of structural subunits), a lipid bilayer derived from cellular lipids, and one or more morphological subunits (peplomers), each of which consists of one or more virus-specified glycoproteins. (From Fenner, McAuslan, Mims, Sambrook and White (1973): "The Biology of Animal Viruses", 2nd edition, Academic Press, New York.)

The chemical composition of the virion.

As I have already pointed out, ICNV classification is based primarily on the physicochemical characteristics of the virus particle. The simpler viral particles consist of nucleic acid and a few polypeptides specified by it. More complex virions usually contain lipids and carbohydrates as well, which in most viral genera are specified by the genome of the cell and not that of the virus. In exceptional situations cellular nucleic acids or polypeptides may be incorporated into viral particles.

Nucleic acids. Viruses differ from all organisms in that they contain only a single species of nucleic acid, which may be either DNA or RNA. Some viral nucleic acids can be readily visualized on the electron microscope, and this is the best way of determining their size. The viral nucleic acid may be single-stranded or double-stranded, the total viral genome may consist of one or of several molecules of nucleic acid, and, if the genome consists of a single molecule, this may be linear or it may have a circular configuration (Table 8). As yet no nucleic acid of a vertebrate virus has been found to be methylated, or to contain novel bases of the type encountered in bacterial viruses or mammalian transfer RNAs, but some virions contain oligonucleotides rich in adenylate. The base composition of DNAs from viruses of vertebrates covers a far wider range than that of the vertebrates themselves, for the guanine plus cytosine content of different viruses varies from 35% to 74%, compared with 40% to 44% for all chordates. Indeed, the guanine plus cytosine content of the DNA of viruses of one large genus (*Herpesvirus*) ranges from 46% to 74%.

The molecular weights of the DNAs of different viruses of vertebrates varies from just over 1 million to about 200 million daltons (Table 8), always occurring as a single molecule that may be linear or cyclic, single-stranded or double-stranded. Because of the way they become integrated and excised from cellular DNA, some papovaviruses may contain cellular DNA, either as the exclusive nucleic acid of a "pseudovirion" or covalently linked to a segment of viral nucleic acid. Or else the particles may be "empty" and lack any nucleic acid at all.

The range of molecular weights of viral RNAs is much less than that of viral DNAs, from just over 2 million to about 12 million daltons of single-stranded RNA, and there are two genera with a genome totalling 15 million daltons of double-stranded RNA. The genomes of several RNA viruses consist of several different molecules, which are probably loosely linked together in the virion (Table 8).

Viral nucleic acid can be extracted from virions by treatment with detergents or phenol. The released molecules are subject to digestion by nucleases, but if this is prevented the isolated nucleic acid of viruses belonging to certain families and genera (Papovaviridae, *Adenovirus*, Picornaviridae, Togaviridae) is infectious. Among RNA viruses this means that the viral RNA functions as messenger RNA. Many isolated viral RNAs are not infectious even though they contain all the needed genetic information, for the nucleic acid in the virion, that contains all the genetic information for the virus, is the complementary strand (c in Table 8) from which messenger RNA must be transcribed by a virion-associated transcriptase (T in Table 8) before multiplication can proceed.

RNA VIRUSES

Fig. 2. Diagram illustrating the shapes and relative sizes of vertebrate viruses of the major taxonomic groups (bar = 100 nm). (From Fenner *et al.* (1973): "The Biology of Animal Viruses", 2nd edition, Academic Press, New York.)

Proteins. The major constituent by weight of the virion is protein, and, because of the limited amount of genetic information carried by viruses, the protein shells of all viruses consist of a relatively small number of repeating protein subunits (Table 9). Among viruses of vertebrates the protein of isometric viruses usually consists of two or three different polypeptides; more are found in

TABLE 8.
The nucleic acids of viruses of vertebrates.
DNA

Single-stranded linear	Double-stranded	
	Linear	Cyclic
<i>Parvovirus</i> (1.8) ^a	<i>Adenovirus</i> (23) <i>Herpesvirus</i> (100) <i>Iridovirus</i> (130)? ^T <i>Poxvirus</i> (160), T ^b	<i>Polyomavirus</i> (3) <i>Papillomavirus</i> (5)

RNA		
Single-stranded		Double-stranded, Several molecules
One molecule	Several molecules	
<i>Picornaviridae</i> (2.6,m) ^c <i>Togaviridae</i> (4,m) <i>Rhabdovirus</i> (4,c ^c ,T) <i>Paramyxovirus</i> (7,c,T)	<i>Orthomyxovirus</i> (4,c,T,7p) ^c <i>Leukovirus</i> (10-12,m,R.T.,4p)	<i>Reovirus</i> (15,T,10p) <i>Orbivirus</i> (15,T,10p)

^a Figures in brackets indicate molecular weights in million daltons.

^b T = Transcriptase; R.T. = Reverse transcriptase.

^c m = messenger; c = complementary; p = pieces.

TABLE 9.
The numbers of proteins in the virions of viruses of vertebrates and their location and function.

	Isometric		Tubular Capsid	Envelope	Enzymes		
	Capsid	Core			Trans- criptase	Neura- minidase	Other
<i>Parvovirus</i>	3			—			
<i>Polyomavirus</i>	3	(3)		—			
<i>Adenovirus</i>	4	2		—			
<i>Herpesvirus</i>	12			12			
<i>Iridovirus</i>	10	5		?	?		+
<i>Poxvirus</i>	13	17		—	+		+
<i>Picornaviridae</i>	4			—			
<i>Togaviridae</i>	1			2			
<i>Orthomyxovirus</i>			1	4		+	
<i>Paramyxovirus</i>			1	3	+	+	
<i>Rhabdovirus</i>			1	2	+		
<i>Leukovirus</i>		6	?	2	+	(reverse)	+
<i>Reovirus</i>	3	4		—	+		+

the large viruses. The peplomers in the envelope of virions likewise comprise a few polypeptide species, although the situation is more complex in *Herpesvirus*. The proteins on the outer surface of the virion of naked viruses, or in the envelope of enveloped viruses, have a special affinity for complementary receptors present on the surface of susceptible cells. They also contain the antigenic

determinants that are responsible for the production of protective antibodies by the infected animals.

As gene products go, some viral polypeptides are small but most are quite large, with molecular weights of up to 150,000 daltons. The smaller polypeptides are usually internal, the larger ones usually on the outside of the virion. The only distinctive feature about the amino acid composition of the structural polypeptides of the virion is that those intimately associated with viral nucleic acid in the "core" of some icosahedral viruses are relatively rich in arginine. All the virus-coded proteins that project from viral envelopes, the peplomers, are glycoproteins; but the membrane protein that is usually found beneath the lipid of the envelope (Fig. 1B) is never a glycoprotein.

Although most virion polypeptides have a structural role, some have enzymatic activity. Many viruses contain a few molecules of an internal protein that functions as a transcriptase, and one of the two kinds of peplomers in the envelope of myxoviruses has neuraminidase activity. A variety of other enzymes are found in the virions of the larger, more complex viruses.

In addition to polypeptides that occur as part of the virion, a large part of the viral genome (most of it with the large DNA viruses) codes for polypeptides that have a functional role during viral multiplication but are not incorporated into viral particles. Few of these "non-structural viral proteins" have been characterized yet.

In most viruses lipid is only found in the envelope and is of cellular origin; likewise, the carbohydrate that occurs as part of the peplomers that project from the envelope is of cellular origin. The poxviruses are exceptional in that they contain virus-specified lipid and carbohydrate.

PRESENT STATUS OF CLASSIFICATION OF VIRUSES OF VERTEBRATES.

During my general introduction I have mentioned as illustrations some terms that are used to define recognizable "groups" of viruses; "groups" that ICNV has agreed to call genera and families. In the concluding part of this talk I will summarize the present state of knowledge about the classification of viruses of vertebrates, going beyond what is currently accepted by ICNV into some areas that are still under active discussion. At its meeting in London last month ECICNV favoured the wide use of family names, but so far has set itself resolutely against any higher taxa that could imply evolutionary relationships between groups of viruses that are now classified as families. Virologists in general, and members of the ECICNV as well, while seeing considerable advantages in bringing together like viruses into families and genera, have so far been reluctant to adopt latinized specific names, and for the time being the vernacular names continue to be used for particular viruses.

The genera and families now widely accepted, and based on the classification of viruses on physicochemical characters, also make sense for many other viral properties, including those of practical importance like pathogenic potential and mode of spread.

DNA viruses.

Table 10 illustrates how the DNA viruses can be classified on physico-chemical criteria and what the properties of each genus are. You can see that they fall into several very well-defined groups and that these are equally well, and similarly, defined either by the amount of DNA the virion contains or by the size and shape of the virion. Table 11 shows how the experts in the field (members of the Study Groups of ICNV) are thinking about classifying and

TABLE 10.

Summary of the properties of viral nucleic acid and morphology of virion among recognized genera of the DNA viruses of vertebrates.

Genus	Genome		Virion	
	Mol. wt. ^a	Nature ^b	shape ^c	size (nm)
<i>Polyomavirus</i>	3	D,C	icosahedral (72)	45
<i>Papillomavirus</i>	5	D,C	icosahedral (72)	55
<i>Adenovirus</i>	20-29	D,L	icosahedral (252)	70-80
<i>Herpesvirus</i>	100	D,L	icosahedral (162), enveloped	capsid 100; envelope 150
<i>Iridovirus</i>	130	D,L	icosahedral (~1500), ? enveloped ^d	capsid 190
<i>Poxvirus</i>	160-200	D,L	brickshaped	300 × 250 × 100
<i>Parvovirus</i>	1·2-1·8	S,L	icosahedral (32)	20

^a in million daltons; in all cases the genome is a single molecule.

^b D, double-stranded; S, single-stranded; C, cyclic; L, linear.

^c number in brackets indicates number of capsomers in the viral capsid of isometric viruses.

^d Iridoviruses of vertebrates but not insects may be enveloped.

TABLE 11.

Accepted or currently proposed family and generic names for DNA viruses of vertebrates.

Papovaviridae	Poxviridae*
<i>Polyomavirus</i>	<i>Orthopoxvirus</i>
<i>Papillomavirus</i>	<i>Parapoxvirus</i>
	<i>Leporipoxvirus</i>
Adenoviridae*	<i>Capripoxvirus</i>
Mammalian	<i>Avipoxvirus</i>
Avian	<i>Entomopoxvirus</i> (insect)
Herpesviridae*	
Several genera	Parvoviridae*
Classification undecided	<i>Parvovirus</i>
	<i>Satellovirus</i> *
Iridoviridae*	<i>Densovirus</i> (insect)
Vertebrate	
Insect	

* Classification agreed, family or generic names not yet accepted by ICNV.

naming these viruses. Many of the taxa and names proposed are still tentative, and will need to be considered by ICNV before they are accepted. When we look in greater detail at this classification we see that the pathogenic behaviour of these viruses accords very closely with the groupings we have made on physicochemical grounds; and virologists who study viral multiplication find that

this feature also shows close resemblances within families and genera and wide divergences between them. All this is very encouraging, for it means that the classification makes sense and provides a shorthand way of recognizing how a particular virus may be expected to behave.

RNA viruses.

There are many more individual species of RNA viruses and many more groups, in spite of the fact that the range of genetic information is so much less than among the DNA viruses. Classification is correspondingly more difficult. Table 12 sets out the physicochemical properties of the main genera of RNA viruses, which have proved more difficult to investigate adequately than most of the DNA viruses, mainly because enveloped viruses (as most of them are) are much more difficult to purify in large amounts. We still do not know for certain the amount and nature of the RNA (whether there is one molecule or several) and its arrangement within a nucleocapsid, for the genera *Arenavirus* and *Coronavirus*, nor for several other groups like the Bunyamwera supergroup that have been recognized but not yet named.

TABLE 12.

Summary of the properties of viral nucleic acid and morphology of virion among recognized genera of the RNA viruses of vertebrates.

Genus	Genome		Size and shape		
	Mol.wt. ^a	Nature	Nucleocapsid	Envelope	Virion
<i>Enterovirus</i>	2·6	S,1,m ^b	icosahedral (20–30 nm) ^c	—	
<i>Alphavirus</i>	4	S,1,m	icosahedral (30–40 nm)	+	60–70 nm
<i>Orthomyxovirus</i>	4	S,7,c	helical (9 nm)	+	80–120 nm
<i>Paramyxovirus</i>	7	S,1,c	helical (18 nm)	+	100–300 nm
<i>Arenavirus</i>	3·5	S,?,?	?helical	+	85–120 nm
<i>Rhabdovirus</i>	4	S,1,c	helical (5 nm)	+	180 nm × 70 nm
<i>Leukovirus</i>	10	S,4,"m"	?helical/icosahedral	+	100–120 nm
<i>Reovirus</i>	15	D,10	icosahedral (45 nm)	—	70–80 nm
<i>Orbivirus</i>	15	D,10	icosahedral (45 nm)	—	60–70 nm

^a in million daltons.

^b S, single-stranded; D, double-stranded; 1 etc. indicates number of molecules of nucleic acid in genome; m, viral RNA has messenger function; c, viral RNA is the complementary strand.

^c diameter of capsid.

Looking in more detail at the genera and families of RNA viruses (Table 13), it is again clear that there is a close association between the groupings made on physicochemical criteria and the ways these viruses multiply and the kinds of disease they produce.

SUMMARY.

If it were fully elaborated, discussion of the classification of viruses could be expanded to encompass the whole of virology. I have narrowed the field down to viruses of vertebrates, and concentrated on the physicochemical properties of the virus particle rather than the mechanisms of viral multiplication or

TABLE 13.

Accepted or currently proposed family and generic names for RNA viruses of vertebrates.

Picornaviridae	<i>Coronavirus</i>
<i>Enterovirus</i> (subgenus: <i>Cardiovirus</i> *)	<i>Arenavirus</i>
<i>Rhinovirus</i> (subgenus: <i>Aphthovirus</i> *)	
	Retroviridae*
<i>Calicivirus</i>	<i>Leukovirus</i>
	<i>Mammavirus</i> *
Togaviridae	<i>Lentovirus</i> *
<i>Alphavirus</i>	<i>Spumavirus</i> *
<i>Flavivirus</i>	
<i>Rubivirus</i> *	Rhabdoviridae*
<i>Pestivirus</i> *	Vertebrate
	Plant
Orthomyxoviridae*	Insect
Influenza A	
Influenza B	Reoviridae*
Influenza C	<i>Reovirus</i>
	<i>Orbivirus</i>
Paramyxoviridae*	Plant
<i>Paramyxovirus</i>	Insect
<i>Morbillivirus</i> *	
<i>Syncytiovirus</i> *	

* Classification in general agreed, but family or generic names not yet accepted.

the pathogenic behaviour. The heartening feature of our progress so far is that many other characteristics of viruses fall together with the classification that I have outlined, and, as Dr. A. Bellett showed several years ago, this classification can be derived from a consideration of viral nucleic acid alone, without knowledge of the viral structure. So that the classification makes sense, and it is a great help to anyone who, like me, has got involved in the business of writing books about viruses. I had not the time to elaborate on future possibilities of molecular taxonomy based on nucleic acid hybridization, which offers great promise within defined groups, but is probably not much use in making comparisons of different families. Indeed, from an evolutionary point of view, taxa higher than the families set out in Tables 11 and 13 may be quite irrelevant, for viruses arose from cells and it may well be that each family represents a separate evolutionary process. So that even if we do adopt a Linnaean nomenclature, we shall probably not have any justification for embarking upon the path that has caused bacterial taxonomists so much trouble, namely the higher taxa, that involve implied relationships between families. In spite of the indifference or antagonism of many virologists, I believe that formal classification and nomenclature is here to stay, and my experience of ICNV and ECICNV so far encourages me to say that this important activity is in the hands of dedicated and competent investigators.

This document is a scanned copy of a printed document. No warranty is given about the accuracy of the copy. Users should refer to the original published version of the material.