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# Improved clarity of meaning from the use of both formal species names and common (vernacular) virus names in virological literature\*

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During the past 40 years, the Subcommittee on InterRelationships Among Catalogued Arboviruses (SIRACA), a subdivision of the American Committee on Arthropod-borne Viruses, has attempted to serve the community of arbovirologists and the general community of virologists in regards to the classification and importance of arboviruses and other viruses. At first, SIRACA evaluated only antigenic (serologic) relationships among arboviruses. During the past two decades we have

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included genetic and genomic comparisons in order to determine what has been done, where viruses belong taxonomically, and what remains to be done. Current taxonomic placements of most arboviruses originated with our deliberations.

For more than 35 years the International Committee on Taxonomy of Viruses (ICTV; a committee of the Virology Division of the International Union of Microbiology Societies; IUMS) has been attempting to "introduce some order into the bewildering variety of viruses" [14]; it has done that [18]. However, for some working virologists, who have taken the ICTV pronouncements out of context, the resulting taxonomy is bewildering. The principal responsibility for taxonomic placement lies with the individual ICTV Study Groups, committees made up of individuals with extensive experience and expertise regarding the viruses in a particular taxon. These Study Groups make recommendations to the Executive Committee of the ICTV who either accept or reject the suggestions, or ask that they be modified and resubmitted. Thus, the primary level of taxonomic authority, quite reasonably, lies with experts.

However, the resulting ordered lists are sometimes confusing to working virologists because of a lack of recognition of the difference between virus identification and virus taxonomic placement. Van Regenmortel and coauthors have shared with us their rigorous philosophical deliberations in many publications, an elegant example of which is Van Regenmortel's summary of the species concept [11, 15].

The International Code of Virus Classification and Nomenclature stipulates that ICTV does not address virus taxonomic and classification issues below the level of species [18]. However, those levels are of critical importance for studies of virus epidemiology and virus identification, decisions regarding public health responses, quarantine issues and biosafety containment levels, justifications for transport permits, categorization of potential bioterrorism agents, and, of paramount importance, propriety of working with deemed select agents. The following is an example of the way that nomenclatural issues may be of practical importance for virologists. In the U.S., these issues may hinder compliance with the Select Agent Rule of 1997 and its updating as described in the proposed federal regulation [10] that will control the possession, use and transfer of "select" viral and microbial agents. The Select Agent Rule is further affected by the U.S.A. PATRIOT (the United and Strengthening America by Providing Appropriate Tools Required to Intercept and Obstruct Terrorism) Act and related legislation. For Select Agents on this list, export from the U.S.A., import into the U.S.A. and elsewhere, and movement of viruses within the U.S.A. and other countries require permits. In addition, lack of understanding as to what defines a virus can change overall research emphasis because funding opportunities often follow (and sometimes lead) current trends.

Furthermore, a dedicated obstructionist could view formal taxonomy as a way to preclude work with, or retention of, certain viruses. For example, the ICTV lists Belterra virus as a subtype, strain or serotype (exactly which cannot be determined from the tables in the 7<sup>th</sup> ICTV Report [18]) of *Rift Valley fever virus*; Hazara virus as a subtype, strain or serotype of *Crimean*-Congo hemorrhagic fever virus; and Tinaroo virus as a subtype, strain or serotype of Akabane virus. Such ambiguity may prevent work with such viruses, which might legitimately be used as surrogates for studying their more dangerous relatives. The ICTV has made it clear that it does not relate taxonomic placement with epidemiological importance, but such hierarchical listings could easily be misunderstood by those who want to do so and by those who have not taken the time to understand their significance. Belterra, Hazara and Tinaroo viruses may have been placed in taxa by the ICTV but these viruses have no known epidemiological significance and unnecessary control of these viruses would inhibit scientific studies of them. Levels of classification below species (i.e., serotype, serogroup, complex, strain, and isolate) have been defined by individuals and various interest groups, but not by ICTV. This further adds to the confusion because the ICTV lists viruses as "subtypes, strains, or serotypes" without defining these entities.

## Viral taxonomy is a systematic, hierarchical construction meant to arrange viruses in an orderly fashion (for the benefit of virologists)

Although the ICTV denies that officially promulgated viral taxonomic placement is intended to indicate natural or evolutionary relationships, it is obvious that taxonomy, to some degree, reflects our current view of phylogenetic relationships. At one time, characterization of viruses was accomplished using biological methods, phenotypic characteristics being expressions of genotypes and these expressions serving as useful indicators. Now that methods are available to identify all nucleotides in virus sequences, virus taxonomy has been placed on a genetic foundation, in parallel, but not in exact concordance, with the taxonomies of other biological life forms.

As the taxa devised by ICTV are recognized by the wider virological community, and as the acceptance of them suffuses the thoughts and writings of virologists around the world, it is imperative that the difference between taxonomy and common (vernacular, colloquial) usage be made clear. In slight but significant contrast to taxonomy, common usage is the arrangement of assigning names to the kinds and groups of organisms listed in a taxonomic classification. It is how we speak and write when we mention viruses to others, and we make the assumption that others will know what we are talking about. Thus, whereas taxonomy is the legitimate form of expression regarding the genetics of an organism (or virus), common usage provides the names we use in day-to-day communications. Virus taxonomy is only one aspect of virology; it should not be taken as the tail that wags the dog.

In such daily communication, how do non-taxonomists refer to a virus if the ICTV has not declared it a species? Absurdly, some individuals may even experience personal distress when they believe, erroneously, their favourite virus is not a species, but a subtype of another virus. Other expert viral taxonomists have pointed out the limits and fluidity of rules governing viral taxonomy. Gibbs [4] and Bos [2] have criticized the ICTV pronouncements. Their principal grievances boil down to whether or not the virological community has been given ample opportunities to affect ICTV decisions and whether or not ICTV-engendered typographical conventions for virus names are appropriate, correct, or even useful in virology. We do not intend to insert SIRACA into such arguments. Our intent simply is to clarify that which has already been accepted at the highest level of the ICTV.

As previously conceptualized by Van Regenmortel [15], Van Regenmortel, Maniloff and Calisher, writing for ICTV, defined a species as "a polythetic class of viruses that constitutes a replicating lineage and occupies a particular ecologic niche"... [16], polythetic indicating that no character property is necessary or sufficient to define the class. This simple definition, however, was soon found to be more complex than had been anticipated. For example, the ICTV classifies the three epidemiologically significant, clinically relevant, and easily differentiatable polioviruses (formerly known as poliovirus type 1, poliovirus type 2, and poliovirus type 3) as three serotypes of Poliovirus: Human poliovirus 1, Human poliovirus 2, Human poliovirus 3 [6]. This is taxonomically reasonable, because the three serotypes are genetically similar. That is, the sequence differences are considered so relatively trivial as to be taxonomically irrelevant. These three serotypes constitute replicating lineages (otherwise they would not have remained distinct) but they occupy a particular ecologic niche, the intestinal tracts of humans. That these three viruses differ slightly one from another does not detract from their being a polythetic entity. Indeed, they embody the word polythetic. As Van Regenmortel et al. have unambiguously stated, "The use of a single discriminating character for distinguishing species contradicts the inherent variability of the members of a species and the fact that species are not so-called universal classes definable by a single property" [17].

Nonetheless, as is well recognized, Human poliovirus 1, Human poliovirus 2, and Human poliovirus 3 do not cross-protect against each another. For viral geneticists, the immunological properties of the three viruses are accepted as a single attribute, one that remains within the parameters of "polythetic". But, for viral epidemiologists, this is unacceptable. No matter what

names they are given, no matter how closely these viruses are related genetically, the fact remains that these are three clinically relevant entities. This could be mistaken for an apparent quandary of logic (taxonomy) vs. necessity (day-to-day usage).

Other examples can be provided, among them the classification of La Crosse and related viruses. At present, the California serogroup orthobunyaviruses are placed as follows [3]:

### family Bunyaviridae

genus Orthobunyavirus

species California encephalitis virus

serotypes CEV BFS 283, AG83 497 virus, Inkoo virus, Jamestown Canyon virus, Keystone virus, La Crosse virus, Lumbo virus, Melao virus, San Angelo virus, Serra do Navio virus, Snowshoe hare virus, South River virus, Tahyna virus, and Trivitattus virus

The fact that the ICTV does not consider La Crosse virus a species, could be taken to indicate that it is no more or less distinct from California encephalitis virus (CEV BFS 283) snowshoe hare virus, or others listed, than are any of these closely related orthobunyaviruses. Note again that because the ICTV has not vet defined taxa below the level of species, it has not defined "serotype" (or "strain", "isolate" or "variant"), which has led to a confounding feature: certain viruses are considered serotypes but "serotype" is not defined. Irrespective of all this, socalled slight differences between viruses may have the aforementioned considerable epidemiologic significance. The mosquito vectors of these California serogroup viruses are taken as being the particular ecologic niche of these viruses and the relatively few nucleotide sequence differences between these viruses is consistent with the use of the term "polythetic". These viruses may not fit a more narrow definition of "species" but, correctly or not, connotation as a species gives the impression that differences between these viruses do not warrant much consideration. We would not accept such a generalization and we are certain this was not the intent of the ICTV. Indeed, Mayo et al. [7] recently attempted to define "type species" in virus taxonomy. They stated that "The Type Species does not represent any sort of "typical" member of the taxon, and (sic) nor need it be the member of a taxon about which most is known." [7]. If a type species "is an abstraction and not a virus culture", there is no need for working virologists to italicize the common names of viruses, and certainly no need to agonize over such typography, because italicization in such instances would be incorrect. The most direct solution would be to not italicize anything, unless you are making a taxonomic statement. This has the twin advantages of allowing an individual to mention a virus with whatever name is commonly used and is appropriate, while making life a bit easier at the same time. If you wanted to call one of your children home for dinner would you go into the street and shout "Homo sapiens"?

#### Taxonomic placement vs. virus identification

It is evident that *California encephalitis virus* has been elevated to the level of species for historical reasons, since California encephalitis virus (CEV BFS 283) was the first member of this complex of viruses to be recognized [5]. It is not, however, the most "important" member of this serogroup. La Crosse virus is the chief cause of pediatric arboviral encephalitis in the U.S., whereas *California encephalitis virus* has been known to cause only a handful of human illnesses. Furthermore, a great deal more is known about the molecular genetics, epidemiology, transmission, and general biology of La Crosse virus than about any other orthobunyavirus. Clearly, taxonomic consideration was not given to these important features or to the geographic distribution of La Crosse virus, all quite logical.

We have no doubts that La Crosse virus is a distinct entity, as different from snowshoe hare virus (different vector, different geographic distribution, different pathogenicity for humans) as

Human poliovirus 1 is from Human poliovirus 2, perhaps even more so. Whether La Crosse virus is considered a species or is not, is irrelevant to the day-to-day operations of epidemiologists, virus laboratory workers, and medical entomologists.

The ICTV has made many efforts to clarify the terms and definitions it has established [summarized in 8, 19]. This might be a reflection of the confusion that continues to surround virus nomenclature. A recent paper attempted to review the genetic relationships between and among hantaviruses (family Bunyaviridae, genus Hantavirus), while also taking into consideration certain biological features of these viruses [9]. That publication is a good example of the confusion that exists within the virological community as to what is of taxonomic importance and what is of biological importance. The literature contains many such instances of investigators clearly wanting to rely on genetic attributes for both virus identification and classification, but such papers usually contain an indication of hesitation in relying completely on such data. In fact, as Van Regenmortel et al. [17] have clearly stated, "classifying viral genomes should not be confused with classifying viruses. Although correlation of the results of the two activities may be high in some cases (e.g., picornaviruses, geminiviruses, potyviruses), genome comparisons expressed as the degree of similarity (homologous analysis) cannot by themselves amount to formal taxonomic species demarcation" [17]. Given that a viral nucleic acid sequence is not a virus, it is illogical to consider such sequences as representing a "species". We have discussed the implications of sole reliance on molecular techniques for virus characterization in a previous publication [1].

There is, nonetheless, a door leading from this confusion. The ICTV itself has taken the lead by indicating "taxonomic names are not appropriate when referring to physical entities like the virions found in a preparation seen in an electron micrograph" [12]. Van Regenmortel [13] pointed out that one cannot centrifuge a species, one can only centrifuge virions of a member of that species and that "Some virologists may (incorrectly) write that they have inoculated the species *Nicotiana tabacum* with one or another viral species, instead of saying that they inoculated a tobacco plant (a member of the species *Nicotiana tabacum*) with a member of a viral species. Precision in a scientific publication is indeed desirable and can be achieved by referring once, for instance in the Materials and methods section of a manuscript, to the taxonomic placement of the virus under study (species X, genus Y, family Z). **Thereafter, vernacular names can be used throughout the publication**." (emphasis ours). When referring to a particular mammal species, mammalogists state the species name, then the common name or vice versa, i.e., deer mouse (*Peromyscus maniculatus*); so should virologists. Thus there is an open door.

If we desire a more user-friendly nomenclature, then we will need the terms to express it. Those terms have been available for decades and have been used by animal virologists, but now seem to have gone out of favor. We find this remarkable because previous classifications, based on virion morphology, antigenicity, and cross-protectivity assays served as the basis for initial virus classifications; these techniques are still relevant and, with only slight modifications, necessary. Given that pathogenesis, antigenicity, morphology and replication strategy are all expressions of viral genomes, this is not surprising.

We agree with the ICTV that taxa are not entities and that viruses are entities. Taxonomic names are useful for categorizing, for understanding genetic relationships and for expressing an ideal in general terms. Thus, it would be sensible if virologists would simply cite the taxonomy of a virus at the beginning of a paper and use the common name thereafter. For example, the introductory sentence of a paper regarding La Crosse virus could be worded, "La Crosse virus (family *Bunyaviridae, genus Orthobunyavirus*) is the most common cause of pediatric encephalitis caused by an arbovirus in North America."; the virus family and genus names would not be mentioned again in the paper.

The introductory sentence of a paper regarding Sin Nombre virus might be worded, "Sin Nombre virus (family *Bunyaviridae*, genus *Hantavirus*, species *Sin Nombre virus*) is an etiologic agent of hantavirus pulmonary syndrome, a potentially fatal illness of humans." and the virus family, genus, and species names never again mentioned in the paper. Certainly, the names of these viruses need not be italicized, because they are the names of viruses, not the names of species.

Another relevant example is the use of the words "West Nile virus" in a manuscript. This virus has been placed in the family *Flaviviridae*, genus *Flavivirus*, species *Japanese encephalitis virus*, as have other important human pathogens, including Murray Valley encephalitis virus and St. Louis encephalitis virus. This has only taxonomic meaning. The sentence might be written "West Nile virus, (family *Flaviviridae*, genus *Flavivirus*, species *Japanese encephalitis virus*) is an etiologic agent of human disease." Likewise, description of the isolation of one of the four dengue viruses could be begun "We isolated dengue 2 virus (family *Flaviviridae*, genus *Flavivirus*, species *Dengue virus*) from the blood of a febrile human in ...". The name of the taxon and the name of the virus are distinct.

Taxonomy is of little interest to most people and scientific journals do not seem eager to understand or employ modern taxonomy. Even Archives of Virology, the voice of the Virology Division of the IUMS, often publishes articles with taxonomic errors. Therefore, we suggest that when mentioning a virus in a publication, the family, genus and species names should be given, all italicized, simply to orientate the reader. Thereafter, the virus would be referred to as any other organism, by its common name, leaving species names to taxonomy texts.

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