November 27, 1957

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Dear Audre:

I read yesterday your Marjorie Stephens on lecture, which I enjoyed greatly. I have long felt bad that <u>General Virology</u> should have been written in 1952, just as the relation of DNA to the replicating material was being understood. You have elegantly solved some semantic difficulties, while creating a few others (such as "foreign entities"). I also feel a little reluctant to define a "virus" as possessing only one type of nucleic acid; in this case, you are really identifying <u>vKuØs</u> with <u>virus particle</u> since the replicating virus may involve two specific nucleic acids in the usual (unknown) relation to one another, only one of the two being incorporated into the particles.

I am sending you today two MS's, one to appear in "Protoplasmatologia," the other in "The Viruses" by Burnet and Stanley. I wish I had read your lecture in time to adopt your clarifying definition of "infection" and to use the word "transmissible" rather than "infective" throughout.

As you will see (if you read at least the shorter article and the last section of the longer one). I have recently centered my thinking about viruses on the process of maturation as a specific cytomorphogenetic process controlled by the viral genome (not by itself, of course, but within the cellular genome). Adopting the view that the essence of a virus is a specific, replicating genetic material capable of transmission to other cells by a specific apparatus acquired at maturation, I would today define a virus as "an element of genetic material capable of assuming a transmissible form by incorporation into a transmission apparatus synthesized under the virus' own control." The wording is still clumsy, but will be refined. The general, pagsive transmissibility of bacterial DNA (and probably other cellular nucleic acids) is shown by transformation and transduction, but my definition would make transmissibility an insufficient criterion for virus. What I like in my definition is that it places a defective prophage where it belongs, as a nonvirus that can again become a virus (by mutation), and which exemplifies the natural transition between viral and nonviral genetic elements.

Incidentally, I notice you agree with me (General Virology, Chapter 18) and with Lederberg as to the historical solution to the dilemma between regressive evolution and transmissible cellular fragment.

With kindest regards, also to Mme Lwoff,

Sincerely yours,