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## USSR VIEWS ON THE NATURE OF VIRUSES AND THEIR ORIGIN

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[According to the Russian editor's note, the article from which the following information was extracted was published as a part of a discussion on noncellular forms of life being conducted by Mikrobiologiya.]

K. Sukhov (1, 2) has made attempts to defend the idea that catalysis plays a role in the multiplication of viruses. He suggested that if the precursors of viruses are low-molecular products of protein synthesis that are devoid of antigenic properties, the objections against W. Stanley's and J. Northrop's hypothesis of the autocatalytic multiplication of viruses become invalid. Sukhov endows viruses with the properties of enzymes which are able to synthesize proteins. The corrections made by Sukhov do not support Stanley and Northrop's hypothesis to a great extent, however. The low-molecular products also must have some sort of specificity; if this were not the case, any virus would propagate in any plant

Contrary to the assumption made by Stanley and Northrop, the propagation of a virus does not correspond to the process occurring in connection with the activation of a proteolytic enzyme. When swine pepsin is added to chicken pepsinogen, chicken pepsin rather than swine pepsin is formed. In other words, the specificity of the final product is determined by the precursor rather than the activator. If viruses were to act like enzymes in activating precursors present in the cell, a mixture of viruses or at least a mixture of varieties of a virus would form. This does not happen: only one virus is formed. Furthermore the theory of autocatalysis does not explain the absence of propagation of a related virus in a plant already infected with a virus. If the virus activates precursors, there is no apparent reason why the process of activation should not be initiated, notwithstanding the existence of a primary infection, by the second virus after the plant has been infected with it.



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Recent observations by V. Ryzhkov indicate that propagation of viruses depends to a considerable extent on the amino-acid composition of the medium and that analogs of natural amino acids suppress this propagation (3).

Lately Sukhov has abandoned the theory of catalysis and now inclines to the view that viruses, including those which have been obtained in the form of crystalline proteins, are living organisms (4, 5, 6). Strangely enough, he assumes that viruses are alive only during the period of their active propagation, and that they become lifeless when they are in a desiccated state.

Data obtained in Ryzhkov's laboratory showed that the virus of tobacco mosaic disease is to some extent independent in its metabolism and that it continues to accumulate even when the synthesis of normal proteins stops (7). For instance, the process of accumulation continues during nitrogen or phosphorus starvation of the plants, i. e., under conditions when the total quantity of protein diminishes considerably in a healthy plant. In diseased plants, the lowering of the total protein content is insignificant: the titer of the virus increases even when the quantity of normal protein drops considerably.

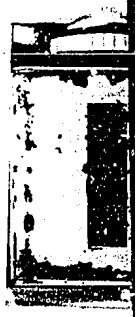
Proponents of the chemical nature of viruses attempted to justify their theory by citing data obtained in the morphological investigation of viruses. Such attempts met with little success, however.

Investigation of the virus of tobacco mosaic disease with the electron microscope showed that the particles of this virus are rods approximately 280 mμ long, with a diameter of 15 mμ. However, the length of the rods is not uniform: although 65-70% of them have a length of 280-320 mμ, there are always smaller rods whose dimensions lie within the range of 40-280 mμ. Stereoscopic examination proved that the images of particles smaller than the average are not due to inclination toward the plane of observation, but actually to the presence of shorter particles.

When exposed to the action of ultrasound, the long rods break up into short rods. If rods of 320 mμ have been prevalent before treatment with ultrasound waves, lengths of 80 mμ, and later of 40 mμ, prevail after the treatment. Unfortunately, precise data on the connection between the process of breaking of the rods by ultrasound and inactivation of the virus are not available. Of great interest is the finding of C. Kausche to the effect that in solutions of the virus of tobacco mosaic disease, the original rod length is restored subsequently to irradiation with ultrasound (8). One may remark in this connection that the effects of ultrasound on cells are also reversible to a certain extent: the cells occasionally restore their life activity even after intense irradiation with ultrasound waves.

The variation in the size of the rods of tobacco mosaic disease virus are not in agreement with the assumption that these rods are macromolecules. If they were macromolecules, more uniform dimensions and sizes which are multiples of unit molecules composing the macromolecules would be expected. If the particles that are visible under the electron microscope were individual molecules of the virus, they would hardly retain the shape of rods after disintegration by ultrasound waves and would not be restored to their original shape after the action of ultrasound waves has been terminated. All these data contradict the assumption that the rods of the virus are individual molecules of a chemical substance.

Sukhov (4, 5, 6) inclines toward the hypothesis of spontaneous generation of viruses in the body of the host, which hypothesis has been defended by P. Remlinger and J. Bailly as applied to rabies. However, the proponents of this hypothesis have not been able to advance in its favor a single argument based on the results of scientific experiments or facts. Furthermore, medical data prove that virus diseases are infectious.



Everything said above supports the theory in regard to the living nature of viruses, a theory to which many Russian and Soviet investigators have adhered to for a long time (cf. D. Ivanovskiy, N. Gamaleya, L. A. Zil'ber). This theory is at present accepted by most Soviet investigators. Ryzhkov has recently adhered to it, and Sukhov now stands close to recognizing its validity.

Some Soviet investigators recognize the living nature of viruses, but regard them as filterable forms of bacteria. Certain virus diseases are complicated by bacterial infections; in cases of influenza, Hemophilus influenzae can be isolated; in cases of swine cholera, Bacillus suipestiferus. Before the discovery of viruses, these bacteria were regarded as causative factors of the above diseases. When it had been established that filterable viruses are actually the causative factors, attempts were made to prove that the viruses are filterable phases of bacteria. This point of view was developed by V. A. Krestovnikova et al. with reference to typhus; they assumed that typhus is produced by a filterable form of B. proteus $X_{19}$ (9).

This hypothesis received its most general expression in the writings of G. Bosh'yan (10). Other investigators thought that a virus is the filterable phase or stage of a definite microbe; Bosh'yan assumes that a virus is the filterable phase of several different microbes. Thus, Bosh'yan describes the following phases of the virus of equine infectious anemia: gram-positive bipolar bacilli, gram-negative bacilli, sarcinae, yeast, and forms resembling mycelia. Bosh'yan also reports that he obtained microbial forms of the viruses of foot-and-mouth disease, equine encephalomyelitis, rabies, Japanese encephalitis, and swine influenza. However, he does not give any data on the properties of the microbial cultures he obtained.

In connection with the hypothesis that viruses are filterable forms of bacteria, one might mention the following. In the course of investigations on the etiology of virus diseases, microbes capable of producing these diseases were isolated in many cases. Ivanovskiy isolated from the unfiltrated juice of a plant having the tobacco mosaic disease a bacterium capable of producing this disease. Subsequently microbes, the early generations of which produce smallpox, measles, yellow fever, hog cholera, typhus, and other diseases, were isolated on many occasions. These facts received a rational explanation when the symbiosis of viruses and microbes was discovered. It was established that the viruses of smallpox, infectious ectromelia, and poliomyelitis are adsorbed by some yeast, bacterial, and protozoal cultures and that they retain their virulence in the adsorbed state.

Such adsorption also takes place under natural conditions. The symbiotic relationship between viruses and microbes is not limited to adsorption. Some viruses which are adsorbed on bacteria and particularly on yeasts are capable of propagating in symbiotic cultures. Cultures of this type were originally obtained by L. Zil'ber and Ye. Vostrukhova in the case of vaccinia virus (11). Symbiotic cultures were also obtained with other viruses, e.g., those of measles, foot-and-mouth disease, and herpes. In some cases (rabies, for instance), it proved impossible to develop a symbiotic culture. In the light of the published data on the subject (12), it may be stated with certainty that microbes carry viruses under natural conditions and that the phenomenon of symbiosis involved here may be reproduced in the test tube. The data explain the reason why bacteria which exhibit specific pathogenicity could be isolated from virus material. These bacteria are carriers of the corresponding viruses.

Under the circumstances, investigators who try to uphold the theory to the effect that viruses are filterable forms of bacteria should have carried out control experiments to check whether the bacteria they isolated did not contain an adsorbed virus. They did not conduct such control experiments, however. The instability of the specific virulence of microbial cultures isolated from virus material has already been mentioned by Ivanovskiy. During the more

than 40 years of existence of the theory in regard to filterable forms of bacteria, none of the adherents of that theory had ever discovered a new microbe which possesses the specific pathogenicity of a virus. In all cases the microbes that had been described turned out to be known microbes which carried viruses. At present, it is obvious that the theory under discussion is not based on any reliable facts or experimental data.

In regard to the origin of viruses, it may be assumed that they are descended from primary precellular organisms whose nourishment consisted of amino acids and simple polypeptides available in the environment. When cellular organisms developed, the primary organisms became adapted to an intracellular mode of existence. This was due to the fact that the primeval ocean at this stage lacked organic matter. The objection that viruses cannot be of precellular origin, because there were no cells on which they could prey at that stage of the evolution of living matter, is refuted by the considerations outlined above. These considerations were presented by Svet-Moldavskiy in 1948 at a conference of our institute /not identified/.

Another objection to the hypothesis under discussion is connected with the absence of data on saprophytic viruses. If viruses are descendants of precellular forms of life which at one time existed independently, it may be assumed that not all of them have changed into parasites. However, the concept of saprophitism should be applied to viruses in a different sense as compared with bacteria. Saprophytic viruses do not vegetate in the external medium, but exist in the organism of an animal without producing any ill effects. For instance, the virus present in the submaxillary glands of 84% of adult guinea pigs does not produce any pathogenic symptoms, unless it had been injected into the brain of young guinea pigs. Then it causes subacute meningitis. Adult guinea pigs with infected glands are immune to meningitis produced by the virus. The properties of the virus found in the submaxillary glands of guinea pigs are similar to those of typical saprophytic bacteria, for instance, B. coli. These bacteria also cause meningitis when injected into the brain.

There is a large group of viruses which produce diseases only under certain conditions. The virus of herpes is one of them; it may develop in the human body for years without producing any pathogenic symptoms. Among viruses that affect animals, there are gradations of pathogenicity, starting with the viruses of measles and smallpox, which invariably produce the disease in a susceptible organism, and ending with the virus from the submaxillary glands of guinea pigs that has been described above. It is difficult to establish the presence of saprophytic viruses, because there are no direct methods for detecting them. Perhaps electron-optical methods will help. In any case, lack of information on saprophytic viruses cannot be used as an argument against the hypothesis to the effect that viruses are descended from precellular forms of life.

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