(*Reprinted from Nature, Vol.* 227, *No.* 5265, *pp.* 1346–1347,
September 26, 1970)

Evolutionary Significance of Virus Infection

VIRUS infection is widespread throughout the animal and plant kingdoms, and produces most human illness[1], possibly including certain types of cancer[2]. Particles with viral morphology are easily isolated from sea[3] or river water suggesting that they are ubiquitous. In this communication we have assembled evidence to support the view that viral transduction is a key mechanism for transporting segments of DNA across species and phylum barriers, and that evolution depends largely on this transfer. The evidence may be summarized as follows.

First, if virus infection served no useful function, evolution of effective means for its elimination might be expected. "Natural" resistance is often due to lack of specific virus attachment sites[4]. One may ask why these persist if their sole function is to assist in acquiring illness. Interferon gives protection[5] demonstrating that protection is possible. But it is made normally only after infection and is transient[6]. Similarly, humoral and cellular immunity, though apparently under genetic control[7], appear late in infection. We conclude that total prevention of infection should be possible: the fact that it does not occur suggests that susceptibility to infection confers some advantages on the infected organism.

Second, many viruses cross species barriers with ease, and are often transmitted in nature directly from members of one phylum to another. If the extent of this crossing were known and fully mapped, pathways of infection would probably be found which interconnect each cell, through other cells, to all other cells—both plant and animal. Although some viruses exhibit surprising cell specificity, others, as, for example, arboviruses, are naturally transmitted from insects to vertebrates and back[1].

Third, incorporation of segments of host DNA into infective virions and subsequent transfer to other cells is well known[8]. The transferred DNA has been shown to be incorporated into chromosomal DNA of bacterial cells[8,9]. In animal cells, DNA from two different viruses has been found incorporated in the same virion[10], while host DNA has been shown to be incorporated in polyoma[11] and SV40[12] capsids. As Trilling and Axelrod noted, the presence of SV40 pseudovirions containing sufficient host nucleic acid for the coding of four or five host proteins suggests an efficient mechanism for gene transfer from one cell to another[12]. There are often barriers to adoption of larger segments[13], but these may not affect shorter strands.

Fourth, whole virus genomes may be incorporated into germ cells and transmitted from one generation to the next[1,14]. Whether DNA, fortuitously attached during a previous sojourn of the virus in another species, is also carried along does not seem to have been settled as far as higher animals are concerned.

The fifth point concerns parallel evolution, as observed repeatedly in different species presented with the same problems of environmental stress. While squid and vertebrate eyes differ in many details, they solve the same basic problems and each would benefit enormously from bits and pieces of plans interchanged. A continuous flow and interchange of gene parts "on approval" would both explain and facilitate parallel evolution.

The sixth argument concerns the universality of the genetic code. A long history of evolutionary changes obviously lies behind it[15]. Why is only one version left? If information from the entire biome was read and is to be read by any and all organisms, only one code could (and would) survive.

The seventh and most convincing argument concerns the difficulty of an evolution based on many small changes which are often inconsequential[16], but with choice dictated by survival. The problem is illustrated by this analogy. A parliament governs by passing or rejecting laws. If the laws considered are always the same, changed one word at a time, can this deciding body function effectively? How much more convenient it would be to consider, occasionally, whole laws or sections of them from foreign sources. These new statutes may be in direct conflict with existing order and may confuse administration in a malignant fashion; or, with small alterations, they may improve governance.

The greatest objection to the concepts presented here is that they undermine the foundations of a favourite pastime—the reconstruction of evolutionary relationships by comparing amino-acid sequences[17–19]. The differences observed may as well indicate the number of different virus transductions or transcapsidations required to pass from one animal to a distantly related one. The available data concern homologous proteins of well established importance and do not yield much insight on how new proteins may originate which bear little resemblance to old ones. A corollary of those ideas is that plants or animals which are free of virus infection would evolve very slowly if at all.

Stability of external form during long periods of time may merely reflect the fact that a form more suitable cannot be evolved. Internal biochemistry, however, may have evolved and may be continually evolving in all organisms in parallel. Palaeontology may therefore not accurately reflect either the rate or course of much of molecular evolution.

The essence of the idea described here is that the evolution of one organism depends on contributions and new ideas from all.

The Molecular Anatomy Program is supported by the National Cancer Institute, the National Institute of General Medical Sciences, the National Institute of Allergy and Infectious Diseases, and the US Atomic Energy Commission. Oak Ridge National Laboratory is operated by Union Carbide Corporation Nuclear Division for the US Atomic Energy Commission.

NORMAN G. ANDERSON

Molecular Anatomy Program,
Oak Ridge National Laboratory,
Oak Ridge, Tennessee 37830.

Received May 17, 1970.

[1] *Viral and Rickettsial Infections of Man* (edit. by Horsfall, F. L., and Tamm, I.) (Lippincott, Philadelphia, 1965).

[2] Gross, L., *Oncogenic Viruses* (Pergamon, New York, 1961).

[3] Anderson, N. G., Cline, G. B., Harris, W. W., and Green, J. G., in *Transmission of Viruses by the Water Route* (edit. by Berg, G.), 75 (Interscience, New York, 1967).

[4] Phillipson, L., Lonberg-Holm, K., and Pettersson, H., *J. Virol.*, **2**, 1064 (1968).

[5] Isaacs, A., *Adv. Virus Res.*, **4**, 111 (1967).

[6] Solovier, V. D., in *The Interferons* (edit. by Rita, G.), 233 (Academic Press, New York, 1968).

[7] Hood, L., and Talmadge, D. W., *Science*, **168**, 325 (1970).

[8] Scaife, J., *Ann. Rev. Microbiol.*, **21**, 601 (1967).

[9] Anderson, E. S., *Ann. Rev. Microbiol.*, **22**, 131 (1968).

[10] Baum, S. G., Reich, P. R., Hubner, C. J., Rowe, W. P., and Weissman, S. M., *Proc. US Nat. Acad. Sci.*, **56**, 1509 (1966).

[11] Kaye, A. M., and Winocour, E., *J. Mol. Biol.*, **24**, 475 (1967).

[12] Trilling, D. M., and Axelrod, D., *Science*, **168**, 268 (1970).

[13] Arber, W., and Linn, S., *Ann. Rev. Biochem.*, **38**, 467 (1969).

[14] Huebner, R. J., and Todaro, G. J., *Proc. US Nat. Acad. Sci.*, **64**, 1087 (1969).

[15] Woese, C. R., *Bioscience*, **20**, 471 (1970).

[16] Richmond, R. C., *Nature*, **225**, 1025 (1970).

[17] Anfinson, C. B., *The Molecular Biology of Evolution* (Wiley, New York, 1959).

[18] Joshi, J. G., and Handler, P., *J. Biol. Chem.*, **239**, 2741 (1964).

[19] Margoliash, E., and Smith, E., in *Evolving Genes and Proteins* (edit. by Bryson, V., and Vogel, H. J.), 221 (Academic Press, New York, 1965).