or the hindgut as anterior and posterior station infections. This terminology also permits no consideration for the possible lack of infectivity of such organisms for vertebrate hosts.

JOHN R. ANDERSON
STEPHEN C. AYALA
Department of Entomology and Parasitology, University of California, Berkeley 94720

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Experimental Herpes Encephalitis: Crystalline Arrays in Endoplasmic Reticulum

In an electron microscopic study of herpes simplex encephalitis in rabbits (*1*), we encountered an unusual cytoplasmic crystalline array. Typical herpes simplex virus particles were seen in nuclei of neurons and astrocytes. The virus was not observed in macrophages and endothelial cells; however, in the cytoplasm of these cells, crystalline arrays of round osmiophilic particles were frequently seen. The particles, appearing as spheres with centers of low electron density, measured 22 to 24 nm in diameter. No tubular arrays were observed. They were always enclosed within membranes (Fig. 1, arrow) of the endoplasmic reticulum, and were never seen free in the cytoplasm.

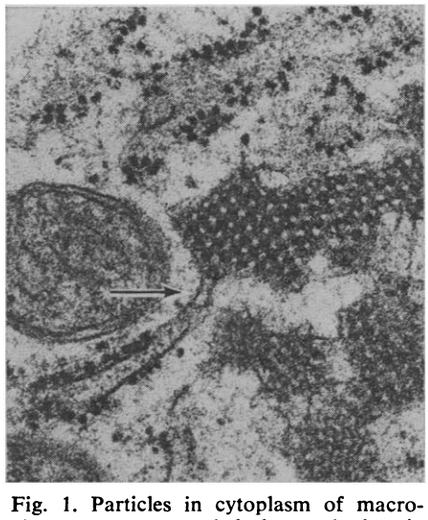

Fig. 1. Particles in cytoplasm of macrophage are surrounded by endoplasmic reticulum membrane (arrow) (× 44,200).

Although described by others (*2–14*), the nature of these unique aggregates has not been satisfactorily elucidated. In a recent report they were considered to represent polio virus within the endoplasmic reticulum on the basis of their size (*12*). However, the same aggregates have been found within the endoplasmic reticulum of experimental herpes simplex and rubella (*4*) infections where the morphology of the infecting viruses is altogether different from that of these particles. Furthermore, such crystals have been found in several virus-associated diseases [porcine polio (*3*), Rous sarcoma virus-induced tumors (*2, 5*), infectious mononucleosis (*8, 10*), Burkitt's lymphoma (*7*), and Aleutian disease of mink (*14*)], in a variety of conditions less clearly associated with viruses [transmissible canine tumors (*6, 11*), leukemia (*7, 10, 13*), reticulum cell sarcoma (*7*), and Dego's disease (*9*)], and in cultured cells from presumably normal human tissue (*7*). While it is possible that these crystals represent a virus common to all these states, their occurrence predominantly in mononuclear, lymphoid, and endothelial cells over such a wide range of conditions makes this unlikely. These data, and the consistent localization within the endoplasmic reticulum of endothelial cells and macrophages suggest that these aggregates represent a host cell response to virus disease or cellular proliferative states.

Note added in proof: Since the submission of this comment, deMartino (*15*) has demonstrated similar structures with occasional tubular profiles in the endothelial endoplasmic reticulum in glomerular capillaries of rhesus monkey and nephritic man. This finding, confirming Chandra's (*7*) observation, makes it unlikely that the structure represents viral particles.

J. RICHARD BARINGER*
JOHN F. GRIFFITH
Massachusetts General Hospital, Boston, Massachusetts 02114

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16. The virus was isolated in the laboratory of Dr. J. Enders and obtained through the courtesy of Dr. S. Kibrick.
17. Supported by special fellowship 2 F 11 NB-1664-03 NSRB (J.R.B.) from the National Institute of Neurological Diseases and Stroke.

* Requests for reprints should be addressed to Dr. Baringer, Veterans Administration Hospital, 42nd Avenue and Clement Street, San Francisco, California 94121.

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In the meantime, the spinal cords of five additional cynomolgus monkeys that had been infected experimentally with type 3 poliovirus were examined by electron microscopy and by a fluorescent antibody technique. It seems remarkable that only in those animals that had become severely paralytic (4 to 5 days after inoculation) could we observe crystalline aggregates of round dense particles within the cytoplasm of endothelial cells and of mononuclear inflammatory cells. Poliovirus antigen was demonstrated once again by immunohistochemical examinations within the same cell types. It should be emphasized that the crystalline arrays were not always enclosed within cisternae of the endoplasmic reticulum but were most frequently seen to be embedded in the ground cytoplasm proper. Furthermore, the individual particles usually did not exhibit an electron-translucent center as did those encountered by Baringer and Griffith in experimental herpes simplex encephalitis and by others in a variety of pathological conditions. We are, therefore, still of the opinion that the crystalline formations recently described by us represent indeed aggregates of newly synthesized poliovirus particles.

K. BLINZINGER
Max Planck Institute for Psychiatry, Munich 23, West Germany

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