it follows that the reformed polysomes are functionally competent.

The mechanism whereby the decrease in the concentration of ATP induces the redistribution of ribosomes from polysomes to monomers is in doubt. There are three known roles of ATP in protein synthesis in acellular systems: (i) in the activation of amino acids for binding to transfer RNA, (ii) in the synthesis of GTP, and (iii) as a substrate for the synthesis of mRNA. Our study has virtually eliminated the third role as a probable basis for the disaggregation of polysomes and inhibition of protein synthesis induced by low concentrations of ATP. Previous studies in vitro with microsomes (*8*) or ribosomes (*9*) from female rats treated with ethionine failed to show any reversal of the inhibition of protein synthesis by optimum concentrations of ATP, guanosine triphosphate and an ATP-generating system. Therefore, we tentatively conclude that ATP plays some additional but unknown role in the function or stabilization of the polysome and in protein synthesis in the liver. This could conceivably be through an effect on amounts of cofactors necessary for chain initiation (*17*). Reported studies with reticulocytes (*18*) or with sea-urchin eggs (*19*) suggest the possibility that low concentrations of ATP may have similar effects on polysomes in other cells.

Our results offer new possibilities for the study of the metabolism of mRNA in the cells of higher animals under reasonably well controlled experimental conditions. It has frequently been suggested that the mRNA molecules may be very susceptible to degradation when they are not stabilized by attached ribosomes. Our results suggest that this may not be the case in the liver cell, unless ethionine also inhibits the mechanism or mechanisms for mRNA degradation. Is the mRNA in the disaggregated form attached to the endoplasmic reticulum or is it free in the cytoplasm? Does the reformation of polysomes after their breakdown mimic the suggested pathway of their initial formation from mRNA attached to a 40 to 45*S* particle (*20*)? Hopefully, the animal treated with ethionine in which the ATP deficiency and its consequences may be turned on and off at will, may offer a novel system for the study of such questions in the intact cells of a higher organism.

GLORIA A. STEWART
EMMANUEL FARBER
Department of Pathology, University of Pittsburgh, Pittsburgh, Pennsylvania

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Adenovirus Endocarditis in Mice

Abstract. *Viral endocarditis developed in 24 percent of 50 newborn mice 6 to 8 days after intraperitoneal inoculation with murine adenovirus. Typical adenovirus intranuclear inclusions were seen in heart-valve lesions, and high titers of virus were recovered from heart tissue. Furthermore, adenovirions were directly visualized by electron microscopy within endothelial cells and fibroblasts of the heart valves.*

The occurrence of viral endocarditis in man is uncertain, but chronic valvular disease appears in many patients having no history of rheumatic fever (*1*). This fact has led to the suspicion that other agents (*2*), including viruses (*3*), may cause endocarditis and subsequent valvular scarring in man. Burch *et al.* (*4*) recently reported endocarditis in mice infected with coxsackie virus B4. Moreover, others have noted endocarditis in experimental animals infected with virus III (*5*) or encephalomyocarditis virus (*6*). We now describe significant incidence of endocarditis in mice infected with murine adenovirus (*7*). Furthermore, direct visualization by electron microscopy revealed viral invasion and replication within cells of cardiac valve tissue.

Approximately 200 newborn white mice were inoculated intraperitoneally each with 0.1 ml of a suspension containing 0.3×10^4 plaque-forming units (PFU) of murine adenovirus. The animals either died or were killed at intervals between 2 and 21 days after inoculation. Virus was first recovered from heart, kidneys, and blood on day 6. Highest titers (greater than 10^5 PFU per gram of tissue) occurred in the heart on days 9 and 11; concurrently they were high in kidney (8.5×10^4 PFU/g) and blood (1.7×10^4 PFU/ml).

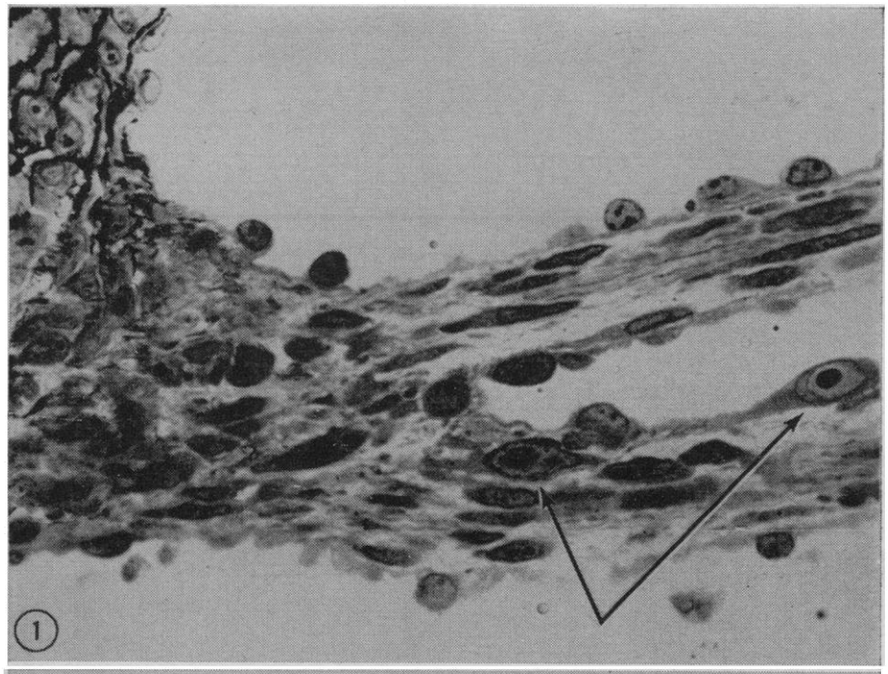
Heart valves of 50 mice that either died or were killed between days 8 and 12 were examined by light microscopy. The heart was bisected along its long axis and fixed in 10-percent neutral buffered formalin; several sections were cut and stained with hematoxylin and eosin. In 12 of these 50 animals foci of necrosis were seen in the valves; the foci contained intranuclear inclusion bodies, characteristic of adenovirus, in endothelial cells and in fibroblasts (Fig. 1). In these areas subendothelial edema and a scanty cellular infiltrate were present. Usually the infiltrate was of mononuclear cells, but in one instance there was necrosis in the valve leaflets with a polymorphonuclear leukocytic infiltrate. Extensive myocarditis accompanied the valve lesions. The lesions will be described in detail later (*8*).

By electron microscopy, adenovirions were directly visualized in nuclei of endothelial cells (Fig. 2) and fibroblasts of the valves; in some of these nuclei, virus particles were sparsely scattered, while in others there were large masses of adenovirions in crystalline arrays.

Also in these foci of necrosis were degenerating cells from which large masses of virions were being spilled into the interstitium of the lamina propria.

The reparative process in mice infected with murine adenovirus remains to be investigated. Presumably, acute lesions, such as we observed in the valves, may be expected to heal, with resultant scar formation and dystrophic calcification. Such chronic lesions were seen in the myocardium in this same experimental model.

Viruses are capable of invading and damaging cardiovascular tissues in man (*9*). The extent and incidence of such lesions, especially viral endocarditis, are not well defined. Our study and that of Burch *et al.* (*4*) make it appear that more than one virus may multiply in and destroy cells of cardiac valve tissue in experimental animals. Whether a similar phenomenon occurs in man is unknown. However, from changes in electrocardiogram it is well known that many generalized viral infections in man may be associated with myocardial involvement. This point raises the possibility that in at least some of these cases valvular involvement may occur, with subsequent scarring and resultant chronic valvular disease.



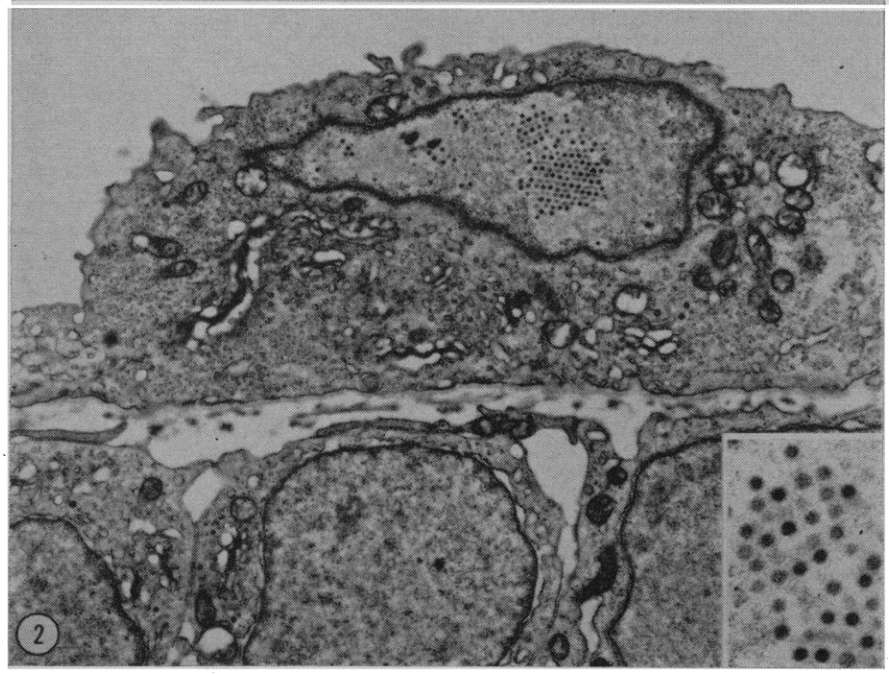


Fig. 1 (top). Commisure and leaflets of aortic valve from a mouse infected with adenovirus, showing inclusion bodies (arrows) within nuclei of endothelial cells and fibroblasts. One-micron section of araldite-embedded material; Paragon multiple stain; about × 600. Fig. 2 (bottom). Electron micrograph of valve lesion (Fig. 1); the nucleus of the endothelial cell contains adenovirions in crystalline arrays; about × 8300. Inset is a view of virions in detail; × 34,600.

Z. R. BLAILOCK
E. R. RABIN
J. L. MELNICK

Department of Pathology and *Virology and Epidemiology, Baylor University College of Medicine, Houston, Texas 77025*

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Cell Aggregation: Its Enhancement by a Supernatant from Cultures of Homologous Cells

Abstract. *A supernatant medium has been prepared from living embryonic neural retina cells which specifically promotes their histogenetic aggregation. Its function is dependent upon at least two experimentally separable steps: selective uptake and functional utilization.*

The mechanisms that mediate and control mutual attachment and histogenetic aggregation of embryonic cells are a major factor in considerations of differentiation and multicellular organization (*1*). Much information on this