globin E being retained as a genetic trait in thalessemic human beings, while it has practically disappeared from the blood of mammals generally, or whether it is the result of similar type of physiological adjustment that occurs in birds and in thalassemic human beings.

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Multiplication of Poliovirus in Reticuloendothelial Cells without Generalized Cytopathogenic Effect

With a technique previously described (*1*), we obtain from the peritoneal exudate, artificially produced in cynocephalus monkeys, living *in vitro* cultures of reticuloendothelial cells. These cultures, prepared in flattened tubes, show after 4 to 5 days a quite homogeneous population of histyocyte-macrophage type of cells established on the surface of standard-size cover slips that are introduced into the flattened part of the tube. The number of cells in 1-week-old cultures is approximately 10^5; this is of the same order of magnitude as that obtained in cultures of trypsinized monkey kidney cells prepared in the usual way in the same kind of tubes (*2*).

One monkey can provide enough exudate to prepare 40 to 50 cultures at one time, and it can be used again as a source of cells after a 7- to 10-day period of rest. Experiments with poliomyelitis virus were performed with the Mahoney type I strain. One thousand $TCID_{50}$ were introduced into each tube in 1 ml of medium, usually on the first or the second day of the culture.

No definite cytopathogenic effect was seen in the infected cultures observed during 8 and, in some cases, during 13 days, after introduction of the virus. Moreover, the acidification of the medium was progressing in these cultures at the same rate as it was in the noninfected controls. In cultures of monkey kidney cells that were infected simultaneously with the same virus concentration, the acidification of the medium was inhibited, and all cells were destroyed in 3 days.

In fixed and stained preparations of the cultures of reticuloendothelial cells 4, 6, 8, and 13 days after introduction of the virus, one can observe a nearly normal population of histiocytic cells, most of them having clear nuclei, distinct nucleoli and numerous cytoplasmic ramifications (Fig. 1). No typical poliomyelitis lesions, as they were described in human fibroblasts (*3*) or in human and monkey epithelial cells (*4*), are present.

Titrations performed with the supernatant fluid of the exudate cell cultures reveal that, despite the apparent lack of cytopathogenic effect, the virus is multiplying and is released in the medium. The virus introduced at the start at a concentration of 10^3 ID_{50} per milliliter is no longer detectable after 48 hours in control tubes without cells, while in the presence of exudate cells, this concentration rises to 10^5 to $10^{5.5}$ ID_{50} per milliliter and remains at a level of 10^5 to 10^6 ID_{50} per milliliter during at least 8 days despite complete renewal of the medium on the third and the sixth days. It is apparent, therefore, that release of virus by the cells is nearly continuous during this period.

It is permissible to conclude from these experiments that a culture of monkey reticuloendothelial cells reacts in a quite different way from a similar monolayer culture of dispersed epithelial or fibroblastic cells when infected with the same concentration of virus. Two possible explanations can be put forward:

1) Only a small proportion (less than 10 percent) of the cells in the reticuloendothelial cultures is available for infection and virus reproduction. If so, the specific destruction of the virus-infected cells would be difficult to observe even if present (*5*). One would then have to admit that, during the culture period, new cells are permanently coming to maturity in the sense of receptivity to virus. The mechanism of this possible maturation is not clear, but a similar phenomenon was noted *in vitro* with other freshly explanted tissues (*6*).

2) The other possibility is that the individual infected reticuloendothelial cells produce and release the virus in a more continuous and less explosive way than the epithelial or fibroblastic cells, and that virus reproduction in these cells is not necessarily associated with cell destruction.

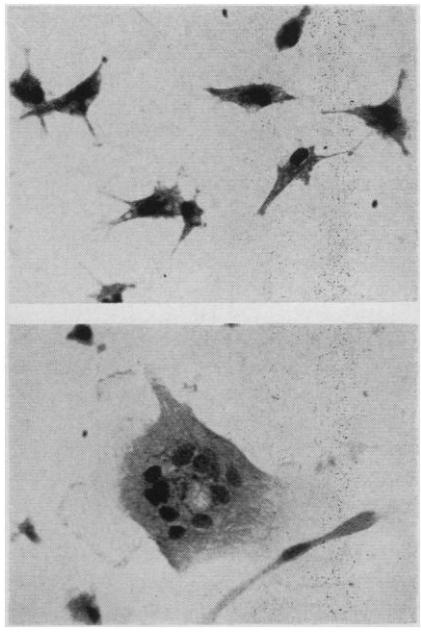

Fig. 1. Eight-day culture of monkey peritoneal exudate cells, 7 days after introduction of 1000 ID of poliovirus. The virus titer of the culture fluid on the day of cell fixation was 10^6 ID_{50} per milliliter. (Top) normal histiocytic cells; (bottom) normal giant cell.

Anyhow, these experiments afford direct proof that polio virus can multiply *in vitro* in a population of reticuloendothelial cells that have been taken from a polio-sensitive species without any generalized cytopathogenic effect. These observations corroborate by an *in vitro* test the numerous data (7) obtained on the living animal concerning the massive poliovirus multiplication localized during the first stage of infection, most probably in the elements of the reticuloendothelial system that are connected with the alimentary tract without evident histological lesions.

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