

control guinea pigs, were given five challenge injections each of 0.2 ml. of encephalitogenic mixture administered every other day. Allergic encephalomyelitis developed in thirteen animals in the experimental group, and in seventeen of the control group.

The existence of acquired resistance to experimental allergic encephalomyelitis demonstrated by these experiments is at variance with the widely accepted opinion that the encephalomyelitis is caused by anticerebral antibodies: and it may be suggested that the experimental allergic encephalomyelitis is a process *sui generis*. Further inquiry is necessary to determine the duration of acquired resistance.

Our evidence may contribute to the comprehension of the complex wave-like course of the demyelinating diseases of the nervous system in man. These experiments suggest that the acquired resistance develops not only in animals surviving experimental allergic encephalomyelitis but may also be induced by the brain substance of embryo and new-born rabbits which lack any encephalitogenic activity.

It seems legitimate, therefore, to test the therapeutic capacity of such brain substances, either with adjuvants or without them, in demyelinating diseases in human beings.

Our assumption is that experimental allergic encephalomyelitis and the resistance acquired against it are elicited by different factors. The adult brain contains two factors, of which one is responsible for the development of the encephalomyelitis and the other for the development of acquired resistance against it. The brain of embryo and of one-day-old rabbits contains only the latter factor.

It is the purpose of the forthcoming studies to produce purified fractions of the brain possessing the capacity to induce acquired resistance against experimental allergic encephalomyelitis and to elucidate the mechanism of this resistance. We suggest a close relationship between the acquired resistance to the experimental allergic encephalomyelitis and enhancing phenomenon in the homo-hetero transplantation of tumours in animals pre-treated with lyophilized tissue.

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<sup>1</sup> Svet-Moldavskaya, I. A., and Svet-Moldavsky, G. J., Abstracts 11th Conf. Iwanovsky Institute for Virology, p. 78 (Moscow, 1958).

<sup>2</sup> Kabat, E. A., Wolf, A., and Bezer, A., *J. Exp. Med.*, **88**, 417 (1948).

### Erythrophagocytosis in Cancer-bearing and Lymphoma-bearing Mice

In addition to the phenomena of agglutination and hæmolysis<sup>1</sup> of red cells in saline extracts of the spontaneous tumours of *C3H* mice, there is a third phenomenon, perhaps related to the first two because it also is evidence of red cell injury, which is observed in *AKR* and *C58* strains of mice (both are usually referred to as leukæmic strains, but the *AKR* strain is better classified as a variety of lymphoma). This third phenomenon is erythrophagocytosis in the enlarged spleens.

In the *C3H* mice the tumours (mammary carcinomas) can be divided into black or red vascular or white non-vascular tumours; sometimes one tumour has areas of each kind. The black colour is the result of hæmolysis and probably capillary

cytolysis; sections show masses of hæmolysed red cells lying in structureless pools. The red colour is extravasation of more or less intact red cells; erythrophagocytosis is usually observed, the phagocyte being either a macrophage or a tumour cell. An agglutinin and a lysin can be extracted with saline from both black and red tumours. In the white tumours there is little evidence of red cells being present, and erythrophagocytosis was not observed; an agglutinin and a lysin, however, can be extracted with saline. In no case was erythrophagocytosis observed in the spleen, regardless of the colour of the tumour and regardless of the enlargement of the spleen (3 to 4 times normal); this also applies to the *DBA<sub>2</sub>* and the *A/Heston* strains. The spleens of the tumour-bearing mice showed hæmosiderosis, the hæmosiderin granules being localized almost exclusively in macrophages, some of which were laden with them. The presence of so much hæmosiderin is presumptive evidence of a hæmolytic process, probably in the tumour. Direct Coombs tests and elution techniques demonstrated antibodies, or substances acting like antibodies in their ability to agglutinate test cells, in many tumour-bearers with moderate-sized tumours, but they were never obtained from the red cells of males or tumour-free females<sup>2</sup>.

*C58* mice showing no signs of leukæmia showed no erythrophagocytosis in the normal-sized spleens. If the mice had leukæmic glands (the peripheral blood of these animals is usually aleukæmic), conspicuous erythrophagocytosis was always found in the enlarged spleens, red cells being ingested by macrophages. In two cases a lysin was obtained from the lymph nodes; elution studies were carried out, but without success.

No erythrophagocytosis was found in the spleens of normal *AKR* mice, but in mice with lymphomatous glands and enlarged spleens there was always erythrophagocytosis in the spleen, and in one case in the liver. No attempts have yet been made to extract an agglutinin or a lysin from the lymph nodes, nor have elution studies yet been done.

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<sup>1</sup> Ponder, E., and Nesmith, J., *Cancer Res.*, **12**, 2, 104 (1952).

<sup>2</sup> Ponder, E., and Ponder, R. V., *Revue d'Hématol.*, **9**, 3, 562 (1954).

### Assay of Erythropoietin in Bone Marrow Suspensions

RECENTLY the presence of a substance capable of stimulating erythropoiesis (erythropoietin) in the peripheral blood of man<sup>1</sup> and anæmic animals<sup>2</sup> has been demonstrated repeatedly by a variety of assay methods<sup>3-4</sup>. Except for the few techniques which utilize the normal animal for assay purposes, all the current methods employ animals altered in such a way as to increase sensitivity to the test substance. Despite theoretical objections raised to the use of non-physiological preparations, such as the hypophysectomized or starved animal, in an assay, the results have been found reliable when iron-59 incorporation into the erythrocyte or reticulocytosis is chosen as the measure of erythropoietic activity<sup>5</sup>.

A recently developed hæmatological study method is the measurement of iron-59 incorporation by human bone marrow cultures (Thorup, A., personal communi-