9234 P

## Localization of Foreign Proteins and Dyes in Neoplastic Growth.

F. DURAN-REYNALS.

*From the Rockefeller Institute for Medical Research.*

The permeability of the stroma of malignant tumors of mice, both transplanted and spontaneous, has been investigated by the intravenous injection of a variety of foreign sera and dyes. The relative amount of the sera localized in the tumor was determined by the use of immunological methods and the dyes could be easily detected by direct examination under water.

After the intravenous injection of 0.25 cc. sera from the horse, rabbit, or chicken, precipitation tests on the extracts of the tumor, various organs, and the blood showed that, in the early period after injection (24 to 48 hours), a larger amount of the foreign sera was in the blood and tumor than in any of the organs.

After 3 to 5 days the sera from chicken and rabbit had disappeared from the blood and were found only or mostly in the tumor. Horse serum persisted in the blood for at least 10 days, but the tumor tissue always contained more of it than the blood.

The dyes which were tested are T. 1824, Pontamine Sky blue, Brilliant Vital red, Vital New red, Dianil blue, and others, diluted at 1:1,000. These were injected intravenously at the amount of 0.25 to 0.50 cc. and were all found to localize selectively in cancer tissue with comparatively little localization in organs such as the liver and lymph nodes, where they might be expected to accumulate. The localization in the tumor takes place rapidly, the dye being clearly detected in the growth within one half hour after the intravenous injection. The maximum accumulation is accomplished in 12 to 20 hours. A broad zone of skin around the tumor is also deeply stained. The first 2 of the above series seem to give the most clear-cut results. T. 1824, a dye allied to Trypan blue, was selected for more extensive investigation. During the first few days after the intravenous injection of 0.25 mg., this dye is found localized in the healthy part of the tumor, the necrotic tissue remaining unstained. Ten days or more later, in the rapidly growing, transplantable tumors, the dye has disappeared from the healthy part of the tumor and is found accumulated in the necrotic part. Pontamine Sky blue and Dianil blue behave like T. 1824 in this respect; but a variety of other dyes localize in both the healthy and necrotic parts, and still others were found to stain only the necrotic parts.

All mouse tumors so far studied, spontaneous or transplanted, primary or metastatic, are deeply stained after injection of T. 1824, and even pin-point metastases in the lung and liver may be readily detected by their blue color. The results are equally definite with the Brown-Pearce epithelioma of the rabbit and a sarcoma of the chicken. Five or 10 cc. of the 1:1,000 solution was injected in these cases.

Examination of the fresh, stained tumor with the naked eye or with a magnifying glass reveals that, although the whole tumor appears blue, the dye is mostly fixed in the stroma of the growth. Microscopic observations have not been extensively carried out as yet. However, the preliminary work so far done seems to indicate that T. 1824 behaves like Trypan blue, according to the careful studies of Ludford.[1] The cancer cell would be surrounded rather than penetrated by the dye.

The dye itself is without effect on the growth rate of the tumor. As it is known to combine readily with protein materials, an attempt was made to combine it with a toxic substance. Both rattlesnake venom and *Bacillus paratyphosus B.* toxin rapidly lose their toxicity in combination with the dye, but in this combination the dye still localizes in the tumors. In spite of the gross loss of toxicity, there appears to be an effect on the growth rate of the tumor following the intravenous injection of the dye in combination with a toxin.

## 9235 P

## Active Immunity to Experimental Poliomyelitis by Intranasal Route in *Macacus rhesus.**

S. D. KRAMER, L. H. GROSSMAN AND G. C. PARKER.

*From the Laboratories of the Infantile Paralysis Commission of the Long Island College of Medicine.*

We wish to report protection against intranasal infection with subsequent development of immunity in monkeys that had received instillations of pituitrin S and adrephine,† followed by intranasal instillations of potent virus suspensions.

[1] Ludford, R. J., *Proc. Royal Society London*, B, 1929, **104**, 493.

* This work was supported by a grant from the Friedsam Foundation, and the President's Birthday Ball Commission for Infantile Paralysis Research.

† The pituitrin S and adrephine was in part supplied to us through the kindness of Parke, Davis & Company, Detroit, Michigan.