days before tolerance was uniformly induced from the same parabiotic union.

Whatever the final explanation, it seems clear that immunological tolerance can be induced in adult animals. It also seems clear that the required antigenic dosage for development of tolerance is very critical and thus the length of time during which homologous parabiosis need be maintained to induce tolerance may be a function of this dosage, which in turn is at least partially consequent to degree of histocompatibility difference between strains. At any rate, length of time during which parabiosis must be maintained to induce immunological tolerance depends upon the strains of mice joined in parabiosis. This observation is strikingly similar to previous observations indicating differences among strains of mice as to capacity of developing classical immunological tolerance when splenic cells are injected intravenously during the neonatal period as well as differences in capacity of donor cells from various strains to induce this phenomenon(5).

Summary. 1. Parabiosis between Z animals and AZ F_1 hybrid animals results in immunological tolerance of the former strain to the latter. 2. When parabiotic union between Z and AZ F_1 animals is maintained less than 30 days a tolerant state is not regularly produced, but when maintained 30 days or more, tolerance of Z for AZ F_1 hybrid skin grafts is the rule. 3. Tolerance between Z and Ce strain mice may be produced in adult life by maintenance of a parabiotic union between members of these 2 strains. 4. Under these circumstances Z mice more readily become tolerant to the strain of the parabiotic partner than do Ce strain mice. 5. Implications of these findings to the theory of immunological tolerance are discussed.

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Received April 7, 1960. P.S.E.B.M., 1960, v104.

Penetration of Radioactive Phosphorus into Normal and Shocked Rats' Brain.* (25799)

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Traumatic shock is accompanied by changes in enzyme activities of liver, heart and brain. Strawitz and Hift(1) and Packer, Michaelis and Martin(2) have demonstrated uncoupling of oxidative phosphorylation, as well as shifts in concentrations of phosphate, sodium, potassium and calcium, accompanied by swelling of mitochondria in shock. The intracellular changes suggested that the permeability of some tissues might change in shock, and that in particular the blood brain barrier might be affected. This possibility was tested with an autoradiographic method. When the Masson trichrome stain, as modified by Goldner, was used on brains of normal and shocked rats‡ no significant differences could be found.

Method. Young adult Wistar rats weighing 200-300 g were injected intraperitoneally with P^{32} inorganic phosphate, approximately 35 μc per 100 g body weight. Shock was induced within 10 minutes after injection with the drumming method(3) in an apparatus consisting of 4 drums driven by one motor.

* This work supported by grants from U.S.P.H.S. and Abbott and Wallace Labs.

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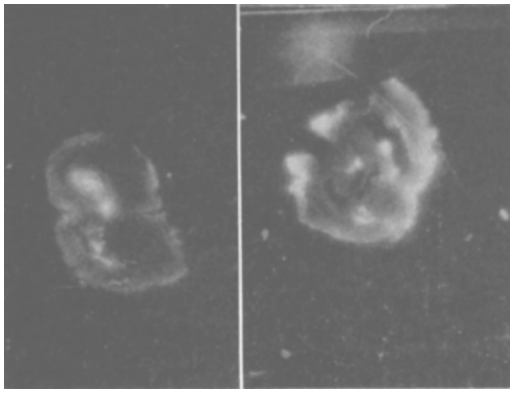
‡ We wish to thank Dr. John A. Wagner for these tests.



Control Shock

FIG. 1. Autoradiographs of sagittal sections of rats' brain after intraper. inj. of P^{32} phosphate.

The inner diameter of the drums was 37.4 cm. Each drum was fitted with 2 prisms with bases fixed peripherally facing each other, on the same radius. Fore and hind limbs of the animals were tied with adhesive tape. The rats were tumbled for 500 turns during 12.5 minutes. They were then unfettered and held in individual cages for 2 hours. During this period shock developed, with prostration, shallow breathing and, in most cases, cyanosis. Both experimental and control animals were decapitated having been exposed to the radioactive phosphate for the same length of time. Their brains were excised and fixed in 10% formalin. Sagittal sections, 50 μ thick, were made and exposed on Kodak No Screen X-Ray film for 4 weeks, in a refrigerator. The films were developed and radioactivity was examined. Eight experiments were done with 13 controls and 26 tumbled rats.

Result. The photographs (Fig. 1) show typical samples of autoradiographs of normal and tumbled rats' brains. In normal brains radioactivity was noted with clear outlines around the regions which were bathed by cerebrospinal fluid, such as walls of the ventricles and surface of the cerebral cortex. In tumbled rats, diffuse penetration of P^{32} into the brain tissues was found.

Discussion. Borell and Örström(4) reported that after intraperitoneal injection of radioactive phosphate into rats and rabbits, the choroid plexus took up the isotope 10 to 80 times more rapidly than did nervous tissue. Bakay(5) observed that after intracisternal injection of P^{32} the brain took up large amounts quite rapidly. These reports indicate that the brain has an inherently rapid phosphate metabolism, but that penetration of phosphate from the blood stream into it is normally severely delayed. Bakay (6) suggested that radioactive phosphate enters the brain *via* the cerebrospinal fluid after it has passed the blood-cerebrospinal fluid barrier during initial phase of absorption. The feature of this phase is a large deposition of phosphorus in the surface area, and presumably because of a direct passage of the phosphate through the blood brain barrier by transcapillary exchange, the latter phase of absorption shows a very gradual increase of P^{32} in the whole brain.

Summary. The clear outline in our controls around regions bathed by cerebrospinal fluid may be due to P^{32} after it had passed through the blood cerebrospinal fluid barrier. The diffuse and widespread penetration of P^{32} into brains of tumbled rats indicates alteration of permeability caused by damage at the blood brain barrier. This penetration can not be seen with usual stain technics nor is it due to dispersion following extensive petechial hemorrhage within the brain substance.

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