

small. When K is large the high electrical resistance of the protoplasm in *Nitella* and *Valonia* suggests that either D_P or P_P is small (*i. e.*, when a substance is present largely as ions there is very little penetration).

If the external concentration remains constant while the pH value changes so as to decrease the concentration of undissociated molecules the rate of penetration will diminish even when the protoplasm is permeable to ion pairs only.

These conclusions apply qualitatively when the time curve of penetration is not of the first order.

In case of an exchange of ions the rate will be proportional to the product of the exchanging ions on opposite sides.

The fact that certain weak electrolytes enter rapidly and that the electrical resistance of the protoplasm in contact with strong electrolytes is very high suggests that strong electrolytes may enter largely as undissociated molecules formed at the surface by collision of ions.

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Investigations of Methods in the Study of Anaphylaxis.*

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Comparisons were made of the intraperitoneal, respiratory and Dale methods with the intravenous route to determine which method of inducing anaphylactic shock was most reliable in the evaluation of a given state of hypersensitiveness. To make such a determination, we deviated somewhat from the regular method of a single shock dose and employed what might be termed the double shock method, that is we compared 2 criteria in the same animal.

In the first group we gave intraperitoneal injections to 46 sensitized animals. From one to several hours later these same animals received an intravenous injection of the same material in considerably smaller amounts.

Of these 46 animals, 21 were negative by both methods. Of the remaining, after the intraperitoneal injection 12 were negative, 3 gave a \pm reaction,¹ 5 gave a + reaction and 5 gave a +++ reac-

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¹ — no anaphylactic reaction. \pm doubtful reaction. + showing dyspnea and

tion. After the intravenous injection 2 gave a + reaction, 5 gave a ++ reaction, 4 gave a +++ reaction and 14 died. Comparing our results, the reactions following the intravenous injection were more severe than those following the intraperitoneal injection.

In the next group we exposed 29 nasally sensitized animals to the same antigenic dust after a suitable incubation period. As in the first group, these animals were later given an intravenous injection of an extract of this antigenic dust.

Of these 29 animals, after the inhalation exposures 7 were negative, 5 gave a ± reaction, 8 gave a + reaction and 9 gave a +++ reaction. After the intravenous injection 4 were negative, 2 gave a ± reaction, 3 gave a + reaction, 3 gave a +++ reaction and 17 died. Here again after the intravenous injection more pronounced reactions were obtained than after the inhalation.

In a third group of studies we have compared the uterine horn reaction and the intravenous method in the same animal. Departing from the original method of Dale wherein he killed the animal by a blow over the head and then removed the uterine horn, we first completely anesthetized a virgin guinea pig, performed a laparotomy, and removed the uterine horn which was immediately set up in oxygenated Locke's solution and attached to a recording drum. The abdominal wound was then sewed and the animal allowed to recover completely from her anesthesia. She was then given an intravenous injection of the specific antigen to which she was sensitized. We have thus a graphic tracing of a sensitized uterus as well as a reaction after intravenous injection in the same animal.

In this group of 23 animals the Dale was positive in 11 cases, doubtful in 1, and negative in 11, whereas with the intravenous method 18 died and only 5 were negative. The 5 which were negative after the intravenous injection also showed a negative Dale reaction.

From our results we believe there is evidence that the intravenous route shows a greater reliability as a shock inducing method in comparison with the intraperitoneal, respiratory and Dale methods as a final criterion for the determination of a state of hypersensitiveness.

scratching. ++ marked dyspnea, convulsive movements. +++ severe dyspnea, convulsions, collapse but final recovery. Death—typical anaphylactic death with completely ballooned lungs, this death occurring usually within a few minutes after injection.