SCIENTIFIC PROCEEDINGS

ABSTRACTS OF COMMUNICATIONS

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98 (2058)

Some relations between hydrogen-ion concentration and antigenic properties of proteins.[1]

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The recent work of J. Loeb[2] and others has indicated the important rôle which the hydrogen-ion concentration plays in affecting the physical and chemical properties of proteins. Our studies were designed to determine whether certain biological properties of the proteins were also affected by hydrogen and hydroxyl-ions over the range of concentration which markedly affects such properties as osmotic pressure, swelling power, viscosity, power to combine with ions, electrical charge, etc.

Our first studies upon the anaphylactogenic properties of proteins were made with gelatin. We failed to produce anaphylaxis in guinea pigs with this protein when it was introduced intravenously or intraperitoneally in solutions at its isoelectric point

[1] These studies were aided by a grant from the Loomis Research Fund of the Yale School of Medicine.

[2] Loeb, J., Proteins and the Theory of Colloidal Behavior, New York, 292 pp.

($P_H = 4.7$) and in more acid and in more alkaline solutions. With pure, crystallized hen ovalbumin (isoelectric point, $P_H = 4.8$) we obtained anaphylaxis in the guinea pig readily and consistently. When this protein is introduced into the animal in solutions more acid than those in which it is isoelectric, it is a distinctly more potent antigen than when introduced in the solution with which it is isoelectric or in more alkaline solutions. Sensitization with 5 and intoxication with 50 milligrams of ovalbumin gives acute and usually fatal anaphylaxis when the sensitization is obtained with the protein at P_H 2.0-2.5 regardless of the acidity of the intoxication dose. Sensitization with the same dose of the protein at P_H 4.7-4.8 or at 9.0-10.0, regardless of the form of the intoxicating dose, gives reactions which range from only barely perceptible anaphylaxis to shock which is evidenced by the usual paralysis but which is usually lacking in the respiratory syndrome, the "air hunger," and which is practically never fatal. With larger sensitizing doses of protein (50 milligrams) acute anaphylaxis (including the respiratory as well as the paralytic reaction) can be produced by the protein at any of the three hydrogen-ion concentrations studied. We have obtained entirely similar results in guinea pigs which were passively sensitized with equal doses of the sera of rabbits, themselves actively sensitized with the acid, isoelectric and alkaline solutions of ovalbumin. Further, we have obtained similar results by the method of passive sensitization with a plant protein, the crystalline globulin edestin (isoelectric point, $P_H = 6.9$). Here again the protein in acid solution is a more effective sensitizing agent than in approximately isoelectric or in alkaline solution. Its intoxicating potency apparently is not affected by the P_H of the solutions at the points tested (2.0-2.5; 6.2-7.0; 9.0-10.0).

It is the tendency in immunological literature to stress the parallelism between anaphylactic and precipitating antibodies in immune sera. Indeed some workers incline to the view that the two are identical (Coca,[3] 1920). We have conducted some titrations of precipitins in the rabbit sera which were used for the passive sensitization of guinea pigs. With ovalbumin, the precipitin titrations were highest in the serum (anti-"acid antigen")

[3] Coca, A. F., "Hypersensitiveness," Tice's Practice of Medicine, pp. 107-198.

which conferred the most intense passive hypersensitiveness in guinea pigs, and lowest in the serum (anti-"alkaline antigen") which conferred the lowest hypersensitiveness. With edestin the precipitin titrations were reversed. The rabbit serum prepared with "acid antigen," although more effective in sensitizing guinea pigs, gave lower precipitin titrations than either of the sera prepared against "unadjusted" or "alkaline antigen." The indications from these experiments are that modifications in the hydrogen-ion concentration may simultaneously affect anaphylactogenic and precipitinogenic potencies of different proteins differently. Some of the questions raised by these observations are being studied further.

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Experiments on vitamin A.

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These experiments relate chiefly to questions concerning the storage of vitamin A in the body and the bearing of this upon methods of examining foods to determine their relative richness in vitamin A.

Even at weaning time young animals may already have a considerable store of vitamin A in the body and thus be able to continue to grow for some time upon a diet carefully freed from vitamin A but adequate in all other respects. Young rats separated from their mothers at a uniform "weaning" age of four weeks show very different growth curves and survival periods on the same experimental diet free from vitamin A, according to the vitamin A content of the mother's diet. The differing stores of vitamin A in the bodies of experimental animals, even at early ages, has undoubtedly been a very large factor, not fully appreciated, in previous experiments dealing with this vitamin