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Studies on the chemistry of anaphylaxis.

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Egg albumin, freed from the other proteins of egg white by repeated crystallization, produces typically the anaphylaxis reaction. It sensitizes in doses as small as one twenty-millionth of a gram, fatally in doses of one millionth of a gram. The minimum lethal dose for sensitized pigs is about one half a milligram by intraperitoneal injection, and about one tenth to one twentieth of a milligram when injected into the circulation. The unpurified proteins of egg white are much less active, the minimum sensitizing dose being about one hundred times greater and the minimum lethal dose being five times greater than with purified egg albumin. This suggests that inhibiting substances are possibly present in crude egg white.

The minuteness of the minimum sensitizing and intoxicating dose of pure protein seems to indicate conclusively that both the sensitizing and the intoxicating agent are one and the same kind of protein molecule, or else two different constituents of the same molecule.

Gelatin seems to be devoid of the power of participating in the anaphylaxis reaction, either with itself or with other proteins. This may be due to its poverty in aromatic radicals ; it probably is not due to the heating that is necessary for the conversion of collagen into gelatin. Addition of tyrosin to gelatin (without

chemical combination) does not modify gelatin in respect to the anaphylaxis reaction.

Milk does not lose its sensitizing or intoxicating power when heated to 100° for 30 minutes. If large enough doses of serum heated to the same degree are used they will sensitize guinea pigs to unheated serum. Coagulation with alcohol destroys or reduces greatly the toxicity of proteins which it renders insoluble in water (egg albumin) but not proteins that it does not render insoluble (serum albumin).

Pure zein is actively and specifically toxic to guinea pigs sensitized with zein, although it is devoid of tryptophane and lysine. Gliadin, which contains a less quantity of aromatic radicals than almost any other protein except gelatin, has but slight power to intoxicate pigs previously injected with gliadin.

Iodization of different specimens of serum by a constant method did not yield constant results. The partially saturated serum proteins suffered no modification in specificity analogous to that found by Obermayer and Pick in the case of the precipitin reaction. When most nearly saturated they may lose the power of sensitizing for the unaltered serum, but this is uncertain. Pure crystallized egg albumin may be saturated with iodine quite readily, the iodine saturating the unsaturated carbon atoms of the benzene ring. Such iodized albumin retains its specificity unaltered, but seems to lose much of its toxicity for sensitized guinea pigs, nor does it sensitize well to egg albumin.

Tryptic digestion of serum furnishes further evidence of the protein nature of the substances concerned in the anaphylaxis reaction. Both sensitizing and intoxicating principles are attacked, and slowly decrease in strength as the coagulable protein disappears. After 59 days' digestion of a sample of serum so that but 4.7 per cent. of the nitrogen was in a coagulable form, the sensitizing dose had been changed from one one-thousandth of a cubic centimeter to one fiftieth of a cubic centimeter, while 5 cubic centimeters intraperitoneally did not intoxicate pigs previously sensitized to bovine serum. Digestion of serum does not affect its specificity for species, but the digested serum sensitizes much better to itself than to bovine serum, and conversely.