immediately cooled and reacidified, it was found at P_H 5.1 to 4.9 (natural acidity less than half neutralized) the destruction during one hour's boiling was increased to 58 per cent. Neutralization of a larger proportion of the natural acidity regularly increased the rate of destruction of the vitamine at 100°. When alkali was added to an initial P_H of 11, which fell to about 9 during the hour of heating, the destruction found by feeding of the juice thus treated but immediately cooled and reacidified, was about 65 per cent. On repetition of the last mentioned experiments but with reacidification omitted, and the treated juice stored up to five days in the refrigerator before feeding, the destruction found was 90 to 95 per cent. Whether the difference between the juices which were, and those which were not, reacidified is attributable wholly to the prolonged action of the hydroxyl ions at a temperature of 10° C., and P_H only 9, or whether there are here involved other factors possibly including a tendency toward reversal of the destructive process upon reacidification, remains to be determined.

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The tuberculin reaction and anaphylaxis as studied by the Dale method.

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It is natural that the various tuberculin reactions, as well as other specific phenomena of hypersensitiveness in bacterial disease, such as the mallein and typhoidin reactions should have been thought of from the beginning as probably anaphylactic in nature.

We do not think it suitable in this preliminary communication to go into the details of the controversial literature that has been waged for some time concerning this problem. Our studies are not completed, but as far as they go, they show sharp results in that we have checked up skin sensitiveness in tuberculous and experimentally sensitized animals with the state of general anaphylaxis as indicated by the uterine reaction observed by the Dale method.

The uterine method used in this way gives more conclusive results than any other because it avoids the uncertainties that always attend general anaphylactic experiments carried out on guinea pigs with bacterial extracts.

Our results so far may be summarized as follows:

Tuberculous animals, unless inoculated with overwhelming doses, always become anaphylactic to tuberculo-protein. Positive uterine reaction is never obtained, however, before the end of the third week, and sometimes not until the sixth week at a time when the disease has made considerable progress.

Skin reactiveness may develop in such pigs, however, as early as the ninth day, long before the uterus gives any signs of general anaphylaxis.

There may, thus, exist in the tuberculous animal marked skin reactivity without any uterine hypersensitiveness.

Both skin reactiveness and general anaphylactic hypersensitiveness may fade together in the prelethal stages when the pigs are very sick.

Normal guinea pigs are easily rendered anaphylactic to extracts of tubercle bacilli by injecting them intraperitoneally on successive or alternate days, for ten injections, and testing them on and after the eighteenth day after the last injection.

Such anaphylactic pigs tested from the time of the last few injections until the time of the fully developed hypersensitiveness have never, except in two instances, given typical skin reactions, and in one of these two the reaction was not as marked as in the typical tuberculous animal, and in the other the possible absence of tubercles could not be excluded.

Guinea pigs sensitized experimentally with tuberculo-protein, therefore, may be very highly anaphylactic as evidenced by the uterus, and show absolutely no typical skin reaction.

There are two types of skin reaction, one which resembles the skin reaction obtained in human beings sensitive to horse serum, etc., which develops within a few minutes or within one half hour, appears to be chiefly a vascular reaction with edema, etc., and which fades without subsequent inflammation within a few hours. This has, occasionally, been observed in the anaphylactic pigs on intracutaneous injection, and is, we believe, probably a

true anaphylactic skin reaction in all that this term implies. It should be noted, however, that as far as we know no careful analysis has ever been made to prove experimentally that such skin reactions run entirely parallel with general anaphylaxis.

The other type of skin reaction is the typical tuberculin, typhoidin, etc., reaction which begins gradually, within three, four or five hours, reaches its maximum after 24 or 48 hours, and does not fade for four or five days. It is marked by definite inflammatory reactions with perhaps some hemorrhage and a little necrosis. It is distinctly a cell-injury reaction.

Since this last reaction and general anaphylaxis plainly are shown not to go hand in hand, the question arises, are they of fundamentally different nature or are they perhaps reactions to two different substances in the tuberculin preparations. It has been suggested that the true tuberculin reaction is rather analogous to toxin hypersusceptibility than to true anaphylaxis, and is incited by hypersusceptibility to a toxic constituent of the tuberculin rather than to the tuberculo-protein.

Loewenstein and Pick have studied tuberculin chemically and believe that the substance which induces the typical tuberculin reactions belongs to the class of polypeptides and is dialyzable.

Working with fish bladder membranes we have been able to show, so far, that the substance in O. T. and in the alkalin extracts of ground tubercle bacilli which causes the skin reactions diffuses through such membranes.

Whether or not this dialyzate produces or fails to produce reaction with the sensitized uterus we have not yet been able conclusively to determine.

The general trend of our work, however, together with studies to be reported in another place, lead us to make the following preliminary suggestion:

Substances like whole proteins, cannot establish chemical or physical relationship with the body cells to any degree without the intervention of antibodies, because they are not diffusible. In the case of such substances, therefore, the antibody mechanism is necessary to establish such relationship.

The instantaneous nature in which the anaphylactic reactions which take place through the intervention of antibodies occur, suggests that these are cell surface phenomena.

Substances which have a smaller molecular structure than the whole proteins and are more diffusible, can react with cells without the intervention of antibodies. The determining criterion, therefore, upon which it depends whether a substance is antigenic or, in other words, an antibody former, is, therefore, its ability or inability to diffuse.

In the case of substances which can pass through membranes to some degree, antibody formation is not necessary, and hypersusceptibility may depend upon changes which cannot be measured as we can measure antibodies.

Also, because of the diffusible nature of these substances, the reactions may be intracellular and this would account for the later inflammatory reactions due to definite cell injury.

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A modification of Folin's uric acid method.

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In an effort to improve Folin's uric acid reagent it was found that by dialyzing under special conditions Folin's solution and evaporating the solution so dialyzed a superior reagent was obtained. A similar, though not identical, reagent was prepared by boiling down Folin's solution and filtering off the precipitate. When mixed in the proper proportions these two substances yield a reagent superior to Folin's in the following respects.

1. There is no precipitate such as is frequently encountered with Folin's solution.

2. The color developed with a given quantity of uric acid is about four and a half times as intense as that developed in Folin's method.

3. The color does not fade over a period of many hours.

Since this work was done we have learned of Wu's isolation of the pure ammonium phospho-18-tungstate.[1] This substance was prepared by his method and its chromogenic powers were found to be the same as those of our salt. Like the latter the

[1] H. Wu, Jour. Biol. Chem. 1920, xliv, 189.