

of growth, and this though the one was squamous in type, the other adenomatous. So perfect was the apposition of cells that but for the sharp transition from one tissue to another, an observer in ignorance of the conditions of experiment could well believe that here had occurred a metaplasia. The fact thus experimentally proven that cancerous and normal epithelium can secondarily unite must not be forgotten in judging instances of apparent metaplasia at the edge of tumors.

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**Vaughan's split products and unbroken proteins. A comparative study of their effects.**

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The following is a brief summary of our results :

*Comparing the Action of Vaughan's Egg-white Poison to  
Unbroken Protein.*

1. Inoculations of the unneutralized acid poison into normal guinea pigs gave the same picture as that of the unbroken protein when inoculated into sensitized guinea pigs, whether the poison was given intraperitoneally or intracerebrally. The filtrate from the neutralized poison injected intracardiacally also gave typical symptoms.

2. *Effect of Heat.*—The egg-white poison was not affected when heated to 100° C. for 15 minutes; heated to 120° C. for 15 minutes it was reduced, but its toxic action not completely destroyed.

3. *Chloral Hydrate.*—Normal guinea pigs under the influence of chloral were completely protected against one and a quarter fatal doses of the poison. If two or more fatal doses are given death results. Chloral mixed with the poison, and then given, caused irregular results which was interpreted as meaning that there is no chemical union of the chloral and poison *in vitro*. We assume that the chloral protects by union with certain vital cells.

4. *Lecithin (Egg) Effect on Serum Anaphylaxis.*—Emulsified with the serum and the resulting emulsion injected into serum

sensitized guinea pigs, no protection resulted. Lecithin given, in doses from 250 to 500 milligrams or more, to serum sensitized guinea pigs protects them from a second injection of 5 c.c. horse serum given twenty hours later.

*Lecithin (Egg) Effect on the Poison.*

Neither when emulsified with the poison ; nor given as a preliminary injection, followed by the egg-white poison, twenty hours later, was there any protection afforded. The difference in the protective action of preliminary doses with the serum and with the poison, we think, is due to the absorption by the lecithin of the ferment in the sensitized guinea pig which causes the splitting of the whole protein, thus preventing the cleavage and liberation of the poison.

In the case of the poison, this cleavage has been done in the retort, and as the lecithin does not protect against the poison itself, death occurs as in control animals. Apparently this supposed absorption of ferment by the lecithin takes place slowly for if the lecithin and serum are injected simultaneously death occurs typically.

Eighteen to one hundred hours after the inoculation of 500 milligrams of lecithin the serum sensitized animals were protected from the second injection of 5 c.c. horse serum. Thus far these are the time limits, after the injection of lecithin, that we have allowed before giving the second injection.

We assume, with Banzhaf and Famulener, that chloral allows the ferment or zymogen in a sensitized guinea pig to split the protein, but protects the animal's vital cells from the action of the poison, and similarly protects the normal guinea pig from Vaughan's split poison.

*The Residue.*

1. The sensitizing action of Vaughan's residue (egg-white) differs with different products. Two out of three were inactive. This inactivity may be due to the heat used in the Vaughan method. In fact the loss of the toxic properties of the residue can be fully explained through the action of the heat alone, irrespective of any cleavage of the molecule due to the alcohol and sodium hydroxide used.

2. All vaccinating properties of the active egg-white residue appears to be completely absent. This, also, would be expected from the prolonged heating to which it has been subjected, which is in complete accord with the effect of heat on whole protein.

The toxic and vaccinating properties are first lost and, later, the sensitizing properties. The finding of the residues incapable of sensitizing completes the parallel of the effect of heat on unbroken proteins.

If the vaccinating properties of the typhoid residue are lost, as might be inferred from the loss of those of the egg-white, the use of large doses of the typhoid residue to absorb the bacteriolytic ferment in typhoid fever showing severe toxic symptoms, as suggested by Vaughan, would probably not be successful. Experiments now being carried out on the typhoid residue, will, we hope, soon permit us to make a definite statement on this point.

3. *Besredka's Antianaphylactic Vaccination.*—Following the method of Besredka, precipitating serum protein with alcohol and extracting the precipitate with physiological salt solution, a filtrate was obtained, called by him "petit serum." According to his article this "petit serum" was never toxic to a serum sensitized guinea pig, and yet it vaccinated, but did not sensitize. Proceeding on the theory that Besredka's results were due to the dilution of this protein, not to a separation of the substances, we concentrated the filtrate of his "petit serum." On intracardiac injection five out of seven serum sensitized guinea pigs gave typical anaphylactic symptoms, followed by death. This proves that the lack of toxicity in his work had been due to dilution and not to freedom from the substance producing toxic substances.

The sensitizing action was tested out, and in certain doses we were able to sensitize animals, not as regularly as with whole serum, but sufficiently to show the presence of sensitizing properties in the "petit serum."

4. *Absence of Antianaphylaxis in Rabbits*—In conclusion we wish to confirm the results of Arthus, Lesué, and Dreyfus, that antianaphylaxis is not produced in the rabbit by the methods that ordinarily so readily and rapidly produce it in the guinea pig.

The present attitude of comparing man's sensibility to serum with that of the guinea pig is possibly an error. Man, perhaps,

should rather be compared to the rabbit. The rabbit does not show the explosive anaphylaxis of the guinea pig, unless the inoculation is given intravenously. The occurrence of this in man is rare and under conditions not yet understood and not explainable by the guinea pig. This occurrence is occasionally shown after the first injection of serum.

The ordinary serum sickness in man is not grave, nor need the Arthus phenomenon in the rabbit be grave. Therefore, any attempts at finding a method of antianaphylaxis which does not resensitize, for practical purposes, in man should be tried out in the rabbit as well as the guinea pig.

We wish to thank Dr. Vaughan for his generosity and kindness in sending us his split products, and for his courtesy in permitting one of us to finish our work in his own laboratory.

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**Notes on sensitization with tuberculin to tubercular rabbit-serum.<sup>1</sup>**

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These notes are some of the results of our study of sera, toxins and related substances. We have noted by means of the kymograph the changes in pressure and respiration produced when we injected into normal dogs, treated with tuberculin or other toxic substances, the sera of normal and diseased animals. A number of interesting facts were found in this way, regarding substances in the serum of animals having tuberculosis, which we think worth reporting.

The tubercular rabbit serum with which these results were obtained, was drawn from rabbits which had been infected 35 days previously with a virulent culture of bovine tuberculosis injected intravenously. The serum was defibrinated and separated centrifugally.

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<sup>1</sup>This paper was presented by title at the meeting of the American Association for the Advancement of Science, Dec. 27, 1909.