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Filtration through collodion sacs.

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Toxins, ferments, and protein solutions have been filtered through collodion membranes by many investigators but the results have varied to a considerable degree. The following experiments may explain this variation.

Collodion sacs were made and mounted on glass tubes, according to the Novy technique. Before filtration, the empty sacs were immersed in water and submitted to air pressure (three inches of mercury); if perfect, they were then used. The filtration was done under a 2-inch vacuum. After the filtration the sacs were again retested by air pressure. If still perfect, the filtrate was then used for experimentation.

In this manner diphtheria toxin was filtered. One hundredth of a cubic centimeter of this toxin killed a guinea-pig in 39 hours. Three cubic centimeters of the undiluted toxin were filtered through a collodion sac, and one hundredth of a cubic centimeter of this filtrate killed in 38 hours, none of the toxin having been held back by the filter. However, if the toxin was diluted, 1 to 100 before filtration, one cubic centimeter of the filtrate failed to kill, causing only slight induration.

When dilute cobra venom was filtered, all toxicity was lost. On filtering successive quantities of this venom through the same collodion sac, the filtrate gradually became toxic, until the fourth filtrate was practically of the same strength as the control.

This result is in accord with the work of Marbé (*Compt. rend. Soc. de biol.*, 1909, lxvii, 809) on the filtration of agglutinins through collodion sacs, and also with the passage of complement through a Berkefeld filter, as shown by me (*Jour. Med. Research*, 1904, xiii, 409), and later found by Muir and Browning (*Jour. of Path. and Bact.*, 1909, xiii, 232) working on the same subject. Evidently filtration through collodion sacs, as through the Berkefeld filter, is a phenomenon of adsorption, the substances in solution passing through when adsorption has reached a certain degree.

By altering the concentration, the quantity to be filtered, and

the thickness of the sac, results may be obtained varying from total retention to complete passage of the active substance.

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The activation of pancreatic extract.

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Many years ago Heidenhain demonstrated that the pancreas does not contain trypsin in an active form, but that it exists in the pancreatic tissue as a proferment or zymogen. Heidenhain was able to convert pancreatic zymogen into active trypsin by treating pancreas with weak acids. This fact was later confirmed by other investigators. Hekma, who used pancreatic juice obtained from a fistula, observed that the trypsinogen of the juice cannot be activated by treatment with acid. In 1899, Pawlow and Schepowalnikow discovered, in the mucosa of the small intestine, a specific substance which converts trypsinogen into active trypsin, and which activates both pancreatic extract and pancreatic juice. Vernon, in a series of papers published in 1901 and 1902 studied the activation of trypsinogen. His observations were largely upon pancreatic extract, although in some instances he used pancreatic juice. His conclusions are as follows: fresh pancreas shows no enzymotic activity; upon standing a few days extracts suddenly develop nearly their maximal tryptic activity; the addition of small quantities of active pancreatic extract increases enormously the rate of conversion of zymogen into active enzyme; fresh pancreas treated for twenty hours with 0.2 per cent. acetic acid develops active trypsin. Using dog's pancreatic juice, Vernon claims that one per cent. active pancreatic extract liberates three times more trypsin than one per cent. succus entericus. The same result is obtained with glycerine extract of fresh pancreas. Bayliss and Starling, who worked with large quantities of exceptionally pure pancreatic juice, contradict Vernon's results upon the activation of pancreatic juice by any other agent than the enterokinase of succus entericus. They were not able to activate the trypsinogen of the juice with active trypsin, or by means of any simple chemical