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Isolation of Histamine from the Pyloric Mucosa.

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Although histamine has been isolated from the intestinal mucosa,[1] and from the combined gastric and intestinal mucosa,[2] its isolation from the gastric mucosa alone has not been reported. This report deals with the isolation of the substance in crystalline form, from the pyloric mucosa of the hog, under conditions which preclude the possibility that it is present as a result of putrefaction.

The material was obtained at the slaughter house within 30 minutes after the animal was killed. The mucosa was washed with water and immediately subjected to extraction by 1% sulfuric acid in 80% alcohol. Activated charcoal was added to the extract in sufficient quantity to remove all pigment, the extract filtered from the charcoal, and the histamine adsorbed on Lloyd's Reagent (hydrous aluminum silicate). The Lloyd's Reagent was then extracted with dilute aqueous ammonia, which liberated the histamine. The ammoniacal solution was evaporated to a small volume and mixed with 1½ times its weight of anhydrous sodium carbonate. On standing overnight in a dessicator, this formed a dry cake. This was powdered and extracted with chloroform in a continuous extraction device, until fresh chloroform extracts no longer gave a Pauly reaction. The combined chloroform extracts were filtered from some gummy substance and extracted with a small amount of water. The aqueous extract was boiled to remove chloroform and volatile bases, and then submitted to fractional precipitation with silver nitrate and barium hydroxide, according to the method of Kutscher.[3] The histamine was found in the fraction precipitated by silver in alkaline solution.

The silver precipitate was decomposed with dilute hydrochloric acid and the solution evaporated to a small volume. On standing, a crystalline material separated. This was removed by filtration and the filtrate concentrated to a thin syrup. To this, 20 volumes of alcohol were added, then concentrated sulfuric acid was added,

[1] Barger and Dale, *J. Physiol.*, 1911, **41**, 499.

[2] Abel and Kuboda, *J. Pharm. Exp. Therap.*, 1919, **13**, 243.

[3] Kutscher, quoted by Barger, "The Simpler Natural Bases," London, 1914, 120.

drop by drop, to maximum precipitation. The crystalline precipitate of histamine sulfate was separated by filtration and washed with alcohol and ether.

For identification, the histamine was converted into the dipicrate. The rhombic yellow leaflets obtained melted at 230-232°C. The melting point was unchanged when the material was mixed with dipicrate from known histamine.

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Experimental Low Colonic Obstruction.

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The evidence has been accumulating that one of the major factors in death from high intestinal obstruction is loss of fluid and chlorides. This does not signify that a toxemia of unknown nature is not important in such cases. For this reason we have studied a series of dogs with low colonic obstruction. Eleven dogs survived the operation and at autopsy showed no cause of death other than simple obstruction; in 5 of these, obstruction was produced by a band of gauze tied tightly about the rectum; in the remaining 6 the colon was severed about 8 inches above the anus and both ends closed with sutures. The average length of life in these 12 animals was 8½ days, maximum 20 and minimum 5 days. Autopsies showed the large bowel much dilated, discolored, and filled with gas and fluid fecal material. The small bowel was also markedly distended for some distance above the ileo-cecal sphincter, and showed hemorrhagic areas in the lower portion. The gall bladder was usually dilated; peritoneal cavity clear and containing little or no free fluid.

Food and fluid were allowed ad lib. Some of the animals ate well up to a few days before death, others refused food from the time of operation until death occurred. The 2 showing longest survival periods (19 and 20 days) ate almost like normal animals. All of the animals vomited slightly, the amount depending upon the intake and increasing in the 48 hours prior to death. In no case was the vomiting abundant, as seen in high obstruction.