these only one huge cyst was present, with small numbers (0-31) of minute dead ones in some cases.

Two lots of rats were experimentally infested on June 6, 1930. Half were again fed onchospheres on October 23 and half on November 7; in each case control rats received equal numbers of onchospheres. Four animals from each lot, and the same number of controls, were autopsied 42 days later, on December 4 and December 18. The remaining animals were reserved for other purposes. The autopsy findings show that the eggs of the second feeding developed in the uninfested control rats and were entirely inhibited in the rats containing 6 months old cysts.

| | CONTROLS | PREVIOUSLY INFESTED RATS | |
|---|---|---|---|
| | Average No. of Cysts | Average No. | |
| | | 6 Month Cysts | Minute Dead Cysts |
| Lot 1 | 113 | 22 | 0.25 |
| Lot 2 | 124 | 24 | 0.75 |

It may be concluded, therefore, that infestation with *Cysticercus fasciolaris,* of from 3 to 6 months' standing, protects the rat host against superinfestation. Experiments are under way to determine whether very large feedings of eggs will override the protection; whether a few very old cysts will furnish as much protection as a large number of younger ones; whether the immunity will disappear, and at what time, after the worms are removed from the huge cysts.

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## Observations on the Formation of Wheals. IV. Influence of Calcium Concentrations upon Histamine Wheals.

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We[1] reported that an unidentified substance could be extracted from the skin of dogs which is capable of augmenting histamine wheals. We have now identified this substance as calcium in a certain zone of dilution and only within this zone, as follows:

The proteins in the water extract were precipitated by alcohol. The alcoholic filtrate was evaporated and the residue extracted with

[1] Weaver, W. K., McConnell, F. H., and Alexander, H. L., PROC. SOC. EXP. BIOL. AND MED., 1930, **27**, 486.

water. The active substance was precipitated from this solution by mercuric acetate. It was redissolved in fresh water when hydrogen sulphide was passed through the mixture. The active principle in solution was further separated from organic impurities, phosphates, etc., by treatment with mercuric sulphate and barium carbonate according to the method of West and others. It was found in the filtrate after this process. When this solution was dialyzed against pure water in a thick collodion sac, the active principle did not pass through, but when redialyzed in a thin collodion sac it was recovered from the dialysate. Advantage was taken of this fact to separate the active principle from practically all remaining impurities. Evaporation of the solution after these steps revealed a few crystals which, although small, were suggestive of calcium sulphate. These resisted ashing temperatures although an earlier ashing of an impure fraction had caused the activity to disappear.

With attention focused upon calcium sulphate, experiments were tried in which this pure salt in very weak concentrations was used in place of skin extract. This, too, was found to have an augmenting effect on histamine wheals. Other calcium salts had a similar effect. An interesting similarity in the behavior of calcium sulphate and skin extract was observed. When skin extract was added to histamine solutions it was noted that the size of the wheals was not in proportion to the concentration of the extract. Often one to 10 dilutions of the skin extract produced a larger augmentation than was obtained with the normal concentration, whereas, concentrated extracts often produced less augmentation.

With the discovery of the augmenting effect of calcium sulphate, it was found that the same peculiar behavior was encountered with this salt. It gave the best augmenting effect in low concentrations; frequently only 2 parts per million. The effect diminished upon concentration and finally disappeared entirely. Calcium determinations upon the skin extract then showed that their calcium content fell within the optimum zone found for calcium salts.

Other similarities between the behavior of skin extract and calcium sulphate were observed. It was found that the augmenting power of skin extract disappeared entirely in the presence of excess calcium sulphate, soap, citrates, and when tested on a dog in which acidosis had been induced by means of ammonium chloride. These same substances were found to have a similar inhibiting effect upon the augmenting power of calcium sulphate.

The difficulties experienced in the isolation and identification of calcium as the substance in skin extracts capable of augmenting

histamine wheals have been increased by the fact that many of the reagents employed have contained calcium impurities. Washed ashless filter papers were finally used instead of the ordinary type which contained considerable calcium. Also, silica dishes were employed for the evaporation and ashing of the material.

Other inorganic substances were investigated in regard to their augmenting effect on histamine wheals. It is suspected that magnesium and phosphates have some augmenting power, although the possibility of the existence of calcium impurities in these substances has not been excluded. Other tissues besides skin were found to give active extracts. Among these was blood which was used as the most common source since it furnished a solution as a starting point.

Control tests were run on all solutions tested in order to make sure that there was not enough histamine or calcium in the extracts to give wheals in the absence of added histamine.

Atropine and codeine, which also are wheal-forming substances, are likewise augmented both by skin extracts and by calcium.

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## Response of Intact Small Intestine in Non-anesthetized Dogs to Cathartic Agents, to Morphine and Atropine.

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Many earlier investigators used cathartic drugs subcutaneously and intravenously, but due to the toxicity of and local irritation caused by these methods of administration they were soon discontinued. Podwyssotzki[1] administered subcutaneously an extract of podophyllin and observed that catharsis resulted. His results were confirmed by Neuberger[2] and Dixon.[3] Dixon also reported catharsis by subcutaneous injections of podophyllotoxin. Craig[4] reported catharsis from extract of aloe. His results were later contradicted

[1] Podwyssotzki, *Schmiedeberg's Arch.*, 1880, **13**, 29.

[2] Neuberger, *Schmiedeberg's Arch.*, 1891, **28**, 32.

[3] Dixon, *Therap. Monatshefte*, 1903, **16**, 102; *Brit. Med. J.*, 1902, **18**, 1244.

[4] Craig, *Verchow-Hirsch. Jahresber.*, 1875, **1**, 493.