

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.

5372

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

CHARLES M. GRUBER, WILLIAM T. K. BRYAN AND
LYMAN K. RICHARDSON.

From the Department of Pharmacology, Washington University School of Medicine.

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. Podwysotszki¹ administered subcutaneously an extract of podophyllin and observed that catharsis resulted. His results were confirmed by Neuberger² and Dixon.³ Dixon also reported catharsis by subcutaneous injections of podophyllotoxin. Craig⁴ reported catharsis from extract of aloe. His results were later contradicted

¹ Podwysotszki, *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.

by Cohn⁵ but confirmed by Hiller,⁶ Meyer⁷ and Kohlstock.⁸ The latter experimenters used aloin in aqueous solution subcutaneously. That the extract of colocynth caused catharsis when injected subcutaneously was demonstrated by Radziejewski⁹ and confirmed by Hiller,⁶ Cascara sagrada was administered subcutaneously by MacCallum¹⁰ and he observed a cathartic action. His results were confirmed by Ott and Scott¹¹ who used extract of cascara and by Brauer¹² and Pietch¹³ who used the water soluble glucoside of cascara sagrada "peristaltin". Both Chistoni¹⁴ and Walther¹⁵ were unable to produce catharsis by the subcutaneous injection of the aqueous extract of this drug. The fact that phenolphthalein causes catharsis when administered either subcutaneously or intravenously was shown by Ott and Scott,¹¹ and Abel and Rowntree.¹⁶ Ott and Scott¹¹ were the only investigators to study the effect of these drugs on the contractions of the intestine. They observed the fact that both phenolphthalein and cascara sagrada increased the height of the contractions with a loss of the general tonus.

This investigation was undertaken to shed some light upon the mode of action of these drugs on the intestine in producing purgation.

Non-anesthetized dogs with Thiry-Vella fistulae were employed. Only the ileum was studied. A rubber balloon, connected to recording Brodie Bellows, was inserted in the lumen of the gut to write the changes in general tonus and the contractions. Phenolphthalein, bitter and bitterless glucosides of cascara sagrada (P-D and Co.), extract of rhubarb, extract of podophyllin and the extract of aloe were employed. In some instances, the effects of atropine sulphate in 3 to 5 mg. doses and morphine sulphate in 1 to 10 mg. doses, upon the changes produced by the cathartic drugs were also studied. The drugs were administered either intravenously, or injected into the lumen of the fistula. Morphine also was given by mouth in small doses.

⁵ Cohn, *Berlin. Klin. Wochenschr.*, 1882, **68**.

⁶ Hiller, *Z. f. Klin. Med.*, 1882, **4**, 481.

⁷ Meyer, *Schmiedeberg's Arch.*, 1891, **28**, 186.

⁸ Kohlstock, *Chorité Annalen*, 1892, **17**, 283.

⁹ Radziejewski, *Arch. Anat. u. Physiol.*, 1870, **1**.

¹⁰ MacCallum, *Univ. Calif. Publications Physiol.*, 1903-04, **1**, 163.

¹¹ Ott and Scott, *Med. Bull. Phila.*, 1908, **30**, 90. *Ott's Contribution to Physiol.*, 1909, Nos. 7 and 18.

¹² Brauer, *Munch. Med. Wochenschr.*, 1910, 1812.

¹³ Pietch, *Therap. Monatsheft.*, 1910, **24**, 35.

¹⁴ Christoni, *Arch. Farm.*, 1914, **17**, 97.

¹⁵ Walther, *Munch. Med. Wochenschr.*, 1910, 1812.

¹⁶ Abel and Rowntree, *J. Pharm. Exp. Therap.*, 1919, **1**, 231.

The usual reaction of the intestinal loop to the cathartic drug when injected intravenously was a sudden decrease in the general tonus and a decrease in the height of the rhythmical contractions. If peristaltic contractions were present these were temporarily inhibited. Peristaltic contractions usually began, without changing the decreased general tonus, 2 to 10 minutes after injection of the drug. The amplitude of these contractions increased gradually until in many instances their severity caused such pain that the animal became restless and whined during each contraction. Borborygmi were always heard. When the cathartic was placed in the lumen of the gut the first response was a rise in general tonus. This was followed by a decrease in general tonus to a point below the control level and by the introduction of peristaltic contractions.

Atropine when injected at the height of the cathartic action always temporarily produced a decrease in general tone and a disappearance of the peristaltic contractions. Although the rhythmical contractions continued they were always decreased in amplitude. Following this sudden change in tonus and activity of the gut the peristaltic contractions reappeared, but were less extensive and of longer duration than before, more nearly the type normally seen in the unmedicated gut.

Morphine sulphate when injected intravenously, when injected into the lumen of the gut, or when given by mouth invariably caused a sudden increase in the general tonus of the gut and a temporary disappearance of the peristaltic contractions.

5373

Utilization of Carbon Compounds by *Mycobacteria* in a Synthetic Medium.

MALCOLM H. MERRILL. (Introduced by M. S. Fleisher.)

From the Department of Bacteriology and Hygiene, St. Louis University School of Medicine.

The utilization of a number of carbohydrates, when added to plain broth as the basic medium, by organisms of the genus *Mycobacterium* was reported previously.¹ The method employed was limited to determinations of utilization of reducing sugars only. In order to determine the extent to which other carbon compounds were

¹ Merrill, Malcolm H., *J. Bact.*, 1930, **20**, 235.