

## 186 (2709)

**Metabolism of some heterocyclic compounds.**

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Imidazol was fed to rabbits and found to be partly oxidized, thereby increasing the output of uric acid. There was no increase in sulphate or glycuronic acid output. About one-third of the substance was excreted the same as fed.

Pyridine was fed to rabbits and dogs. The methyl derivative was isolated from the dog urine, but no conjugated product found in the urine of rabbits. The nitrogen and sulphur partition was studied after the work on rabbits.

Pyrrole was fed and injected into rabbits and dogs. The nitrogen and sulphur partition was studied, but no definite detoxication isolated from the urine of rabbits.

Picric acid was fed to rabbits, and picramic acid isolated from the urine.

The relation of nitro indols to acetyl picramic acid was studied.

## 187 (2710)

**Studies on adrenal insufficiency.**

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*Duration of survival after adrenalectomy.*—The adrenals were removed in 36 dogs, an interval being left between the removal of the right and left. In 7 of these animals intravenous injections of Ringer's solution with dextrose added were given, usually once in the 24 hours.

Of the 29 animals which received no injection, one suffered from respiratory difficulties from the time of the second opera-

tion till its death after  $3\frac{1}{2}$  days. The lungs were found congested. One dog died on the fourth day, a stitch abscess breaking into the peritoneal cavity. One dog died 26 hours after the second operation with extensive consolidation and œdema of the lungs. The remaining 26 dogs showed at autopsy no pathological changes sufficient to account for death, apart from those which are described below as associated with adrenal insufficiency. One of these animals survived the second operation for 15 days; another (in advanced pregnancy) died on the 16th day. Two died on the 10th day; 2 lived 8 days; 4 lived 7 days; 5 lived 6 days; 2 lived 5 days; 6 lived 4 days. Two died on the third day, and one lived 2 days. As our results are so different from those emphasized in the literature, it must be stated distinctly that the removal of the adrenals was complete in all our dogs as verified both at operation and *post mortem*. No accessory adrenals were found by careful macroscopic search in any of our dogs.

Of the 7 injected dogs, one is alive on the 28th day after removal of the second adrenal (having given birth to 6 pups on the 16th day, two of which are alive and being excellently nursed by the mother).<sup>1</sup> One of the injected dogs died on the 34th day; two died on the 21st day; one on the 16th day. The remaining two animals were shown at autopsy to be suffering from pulmonary complications; one of them died 12 days after removal of the second adrenal with œdema and congestion of the lungs; the other died on the 6th day with severe pulmonary congestion and a subcutaneous hematoma at the site of the last operation, probably due to slipping of a ligature.

In general the injections were begun the day after the removal of the second adrenal and before symptoms of adrenal insufficiency had appeared. When the injection was not begun until the animal was moribund, it was sometimes of great temporary benefit but did not seem to prolong life nearly to the same extent.

*Symptoms.*—The most characteristic are those pointing to a profound disorganization of the digestive mechanism. The animal usually recovers completely from the second operation in a few hours or even less. Then follows a period of apparently normal health. The appetite is good, the individual peculiarities

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<sup>1</sup> She died near the end of the 33rd day after removal of the second adrenal. The pups are in excellent condition more than 3 weeks after birth.

in the behavior of the animal are unchanged. This period of good health is longer or shorter according to the length of time the animal survives, no notable change occurring, as a rule, until a relatively short time before death. The great symptom which announces a serious change is the refusal of food. The anorexia is usually total, and comes on rather abruptly, often accompanied or followed, occasionally preceded, by vomiting and diarrhea. Sooner or later in most cases bile appears in the vomit, and the stools are not infrequently heavily charged with bile. Blood may be seen sometimes in the vomit or the stools or in both. Once the typical anorexia has appeared it is practically always permanent till death with the exception that the animal may be tempted once or twice by some delicacy. The picture is essentially that of a severe and permanent gastro-intestinal upset. In this the symptomatology agrees with the pathological changes found *post mortem*.

Weakness is not necessarily a prominent symptom until near the end. It is especially evident in the hind legs when the animal tries to walk or stand. The legs are widely separated so as to widen the base of support, they wobble, move stiffly and the movements are poorly coordinated. Convulsions, with or without coma, and apparent hallucinations accompanied by a peculiar cry, are occasionally observed. Exaggerated reflex excitability, with twitching of the limbs, etc., is more common.

Symptoms of circulatory disturbance (slow and often irregular pulse, but sometimes a very rapid pulse) are frequently found shortly before death. The rectal temperature may be subnormal, but is often normal up to the time of death.

In the animals treated by injections, the same general symptoms ultimately come on, but their onset is postponed, roughly speaking, in proportion to the lengthening of the survival period. In not a few instances it has been observed that some of these symptoms, even when quite pronounced (including the asthenia, the nervous, circulatory and perhaps less often the digestive symptoms), disappeared under the treatment, and that more than once in the same animal.

*Autopsy findings.*—Almost in every case more or less blood or blood pigment is found in the contents of one or more portions of the gastro-intestinal tract. Not infrequently the hemorrhage is considerable. Blood is not seldom found in smaller or larger

amount during life in the feces or vomit. It is not found in the esophagus unless the animal has recently vomited. Bile is generally abundantly present in the alimentary canal, usually in the stomach as well as in the intestine. The bile in the gall bladder does not contain blood or blood pigment when the autopsy is performed immediately after death, as was the case in the great majority of our animals.

Marked congestion and extensive hemorrhages are frequently encountered *post mortem* in the mucosa of one part or another of the gastro-intestinal tract (stomach, pyloric end of duodenum, small intestine, especially the upper end, and colon, never in the esophagus). Some congestion is the rule. Marked congestion of the pancreas is frequent.

The beneficial effect of the injections is of course compatible with the idea that in the absence of the adrenals toxic substances accumulate which are responsible for the pathological changes and the symptoms. If these are being eliminated by way of the gastro-intestinal mucosa, it is not difficult to see that the injection of solutions which are known to be in part excreted into the intestine, at least in the first instance, might aid in washing out the toxic substances and in diluting them, so that the concentration necessary to produce symptoms and to cause damage to the gastro-intestinal mucosa or other tissues would not be so easily reached. This is not the only way in which such injections might act. The one thing clear is that they cannot supply the missing cortical hormone if there is one, the absence of which might be specially associated with the disorganization of the digestive mechanism.

## 188 (2711)

Reaction to Gram's stain by certain spore-forming bacteria.

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It has been customary to consider that the greater number of the spore-forming bacteria are positive in their reaction to Gram's stain. The positive correlation of these two properties has been