the free fluid had disappeared. Under tonics the anaemia improved, and he was dismissed after six weeks a totally different boy, having received in all 108 grains without showing any tendency to nausea or vomiting.

CASE III.—Lad with Haematuria Cured in Eight Attendances.

Naaman, an apprentice carpenter, aged about 17, complained of passing blood in the urine for the previous month or two. The urine was smoky, and on centrifugalization showed ova of bilharzia. He came every other day for three weeks, receiving doses of 2 grains, 4 grains, 6 grains, etc. The urine cleared after the third injection, and by the time that he had received eight doses, amounting in all to 68 grains, the urine was found to be free of ova. He spent his midday rest hour receiving the injection and lying down, but otherwise was not away from his ordinary work.

CASE IV.—Old Man with Pronounced Haematuria Cured after Four Injections Administered in Five Days.

This old man could give no history of his complaint, but the urine was of a thick port-wine appearance with a sediment of urates. Ova were found easily. The first dose was 5 grains; this was followed two days later by a dose of 8 grains; the urine was then amber in colour without a trace of blood. On the next two days he received successively 10 grains and 12 grains; treatment was then discontinued as the centrifugized specimens of urine examined contained no more ova. He had been given 35 grains in the five days without showing any symptom of intolerance.

The treatment was in all these cases carried out in the following manner: The bowels were caused to move daily in the morning by giving if needed a mild laxative at night. Some three hours afterwards the patient lay down upon his left side, and the dose, made up to about one or two ounces by the addition of warm water, was administered by the hospital orderly by means of a funnel attached to a No. 12 rubber worm catheter, which after being lubricated was passed well up into the rectum; it is advisable to compress it firmly between the finger and thumb as it is being withdrawn so that the whole of the solution be introduced. The patient has been directed to lie down for a couple of hours, but whether this is essential has not been finally settled. In some cases the bowel must be cleared first by a soap and water enema, but this is not the rule by any means.

Conclusions.

1. The results of intrarectal administration of tartarated antimony are in no way inferior to intravenous.
2. It economizes time, and is free from all risk.
3. Nausea and vomiting occur less frequently than when the drug is run into the general circulation.
4. Case IV suggests the possibility of reducing the number of attendances for treatment considerably.

REFERENCE.

¹ Castellani and Chalmers: *Manual Trop. Med.*, second edition, p. 482.

SOME FUNCTIONS OF THE SUPRARENAL GLANDS.

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THE medullary portion of the suprarenal gland (derived, with the cells of the sympathetic ganglia, from the neuroblasts of the central nervous system) is well known to be concerned with the elaboration of an internal secretion which contains as one of its active principles the substance known as adrenaline; but the part played in the animal economy by the cortex (developed from the mesothelium of the genital ridge) is still obscure. In view of the vital importance of this organ some experimental results recently obtained in rats seem to be worth recording. Even though there is no evidence that the suprarenal gland of rats is functionally homologous with that of man, yet there is no evidence to the contrary, and some of the findings are most suggestive.

The experiments consisted of feeding or inoculating white rats of varying ages with different preparations of suprarenal cortex for varying periods, and then killing, and examining various organs histologically. The preparations used were as follows, and I am much indebted to these firms for their courtesy and assistance in obtaining these preparations:

1. Adcortogen (by Carnrick Co.), which was dried cortex, and contained some adrenaline.
2. Cortex lipoids (by British Organotherapy Co.), which was a liquid extract containing only the lipoids.
3. Cortex extract B (by Carnrick Co.), which was a watery extract of cortex, containing no lipoids but some adrenaline.

4. Cortex extract C (by Carnrick Co.), which was the same as B, but free from adrenaline.

5. Adrenaline (by Parke, Davis). This was used to obtain control animals for those treated with cortical preparations which were found to contain adrenaline.

In all, 118 animals were used, and the following are the most striking of the results obtained. It is not proposed to give here all the details of the experiments, as it is hoped that the work will be published in full elsewhere.

The general health of the animals was not affected, except rarely when using adrenaline-containing extracts. But an extraordinary formation and deposition of fat was obtained in most of the animals, thus confirming the observations of others that the suprarenal cortex plays a part in controlling the fat metabolism of the body, which may thus become perverted in hyperactivity of the gland. In addition, nearly all the rats developed a curious condition of the coat; the fur was thick, fine and glossy (as it should be in health), but came out very freely on handling; the hair follicles microscopically showed degeneration. This condition was not due to the adrenaline, and points to a connexion between suprarenal cortex and calcium metabolism, as perversion of the latter is known to give rise to nutritional disturbances of the skin.

The organs to which attention was directed more particularly were those of internal secretion, and the following are the most conspicuous of the results obtained.

Thymus.—The gland was obviously affected by the treatment. There was most marked increase of invading mast cells; some of these cells are apparently always present in this animal, but the significance of this great increase is not clear. The gland was apparently responding to stimulation in the direction of involution, as indicated by an increase in the Hassall's corpuscles and chromophobe complexes, normally so scanty in the rat. In many cases, also, there were present large clear eosinophil cells of endothelial type invading the gland by the lymph channels, and sometimes completely destroying the normal structure. The appearance of these cells, both here and in the haemolymph glands, can hardly be a specific effect of the treatment, but probably indicates some degree of lowered resistance, the lymph glands being the organs first attacked.

Pancreas.—The gland appeared normal, but two points of interest may be mentioned. First, in the series where adrenaline was being given, a definite thickening of blood vessel walls, both here and in the spleen, was frequently found; secondly, lymphocytes were usually present in the islets. This lymphocyte increase was not confined to the pancreas, but was found in many organs, and is interesting in view of the increase commonly found in Addison's disease. The suprarenal gland, as a whole, appears to stimulate the appearance of lymphocytes in the tissues (no blood counts were made); perhaps there may be some connexion between the sexual immaturity of status lymphaticus and the influence exerted by the suprarenal cortex on the gonads.

Spleen.—Generalized lymphocytic increase was well shown, and the vascularity and blood pigments were very constantly increased. Adrenaline appears to affect the organ adversely; the capillaries were found engorged with blood, lymphocytes were frequently found below the endothelium of the blood vessels, and the typical structure was lost. Increase of giant cells was frequently observed, but no evidence of tuberculous infection.

Male Gonads.—The treatment at first hastened the genital development, but, when continued for some time, in every case degeneration of the seminiferous tubules occurred. The breakdown was very marked, but after a long interval some repair was usually found. The interstitial tissue was also affected, the lipoid constituent causing a cellular decrease and the non-lipoid constituents an increase; in this way a balance may be kept by the full action of the gland. The interstitial tissue contained a large quantity of eosinophil exudate in nearly every case.

Female Gonads.—Sexual precocity in the female rat is difficult to determine experimentally. Degeneration of the older follicles was always found; the younger follicles appeared normal, and therefore were either more resistant to treatment or had undergone repair. The interstitial cells were constantly increased.

Suprarenals.—Evidence was obtained that normally tells atrophy at the medullary border, and that regeneration occurs from the zona glomerulosa; this change was found to be accelerated in pregnancy, and could be stimulated by treatment with cortical preparations more easily in the female.

than in the male. Acute degeneration of the whole gland followed inoculation with the non-lipoid cortical constituents, together with adrenaline.

Thyroid.—The gland was apparently stimulated by the cortex, but adrenaline over-stimulated it to the point of exhaustion.

Haemolymph Glands.—The most striking change observed was in the pigment. Three types could be distinguished. First, the yellow-brown amorphous pigment due to breakdown of haemoglobin; this was always increased, showing that the suprarenal stimulates blood destruction. Secondly, bright yellow pigment in fatty droplets, probably representing some of the inoculated lipid material laid down in altered form in these glands. Thirdly, brown pigment found in special cells of varying size and shape in varying amounts; these are melanoblast cells, and were found most frequently in the haemolymph glands, occasionally in the true lymph glands, and rarely in almost any situation, distributed by the lymph channels. The suggestive point about these cells is that they were only found when the preparation contained adrenaline, and never under any other conditions. Excessive or perverted activity of the suprarenal medulla, therefore, may be directly responsible for the pigment formation of Addison's disease and may also play a part in the formation of pigmented tumours.

Conclusions.

Although it is not possible to apply results obtained with certain animals to another species, nor possible always to distinguish between glandular hyperactivity and perverted activity, nor between purely structural hyperplasia and functional hyperplasia, yet the following conclusions seem worthy of record:

1. The suprarenal cortex plays a part in fat metabolism and in calcium metabolism.
2. The suprarenal cortex stimulates the thymus to involution.
3. The suprarenal cortex controls the gonads in both male and female with respect to both reproductive and interstitial cells.
4. The suprarenal gland acts as a whole in controlling general health, in controlling haemoglobin breakdown, in regulating the production of lymphocytes, in regulating the production of mast cells, and in stimulating the thyroid.
5. The suprarenal medulla is connected with the formation of melanoblast cells.
6. Inoculation with various suprarenal extracts appears to lower the resistance of experimental animals, as is indicated by the condition of the lymph and haemolymph glands.

I should like to thank Professor Cullis for her continued interest and helpful criticism throughout this work. The expenses of this research are being defrayed by a grant from the Royal Society.

THE VIRULENCE OF DIPHTHERIA-LIKE ORGANISMS.

(Further Note.)

BY

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THE bacteriological diagnosis of diphtheria, though based generally on the morphology and cultural characteristics of the *Bacillus diphtheriae*, must depend ultimately on the animal test, whereby the pathogenicity of the infecting organism can be definitely established. While the animal test is advisable, even in clinical work, as a periodical check on the routine methods of diagnosis, in dealing with the carrier problem and prevention of diphtheria it is indispensable. The time may come when some other test may replace it; this is, however, very improbable.

By the intracutaneous method (Eagleton and Baxter, 1921) a large number of pathogenicity tests can be carried out speedily and economically. Further experience of this method has served to confirm our belief in its reliability, evidence of which is given in the second part of this paper. The first section deals with 161 cultures of diphtheria-like organisms, all of which were tested for pathogenicity, and the majority for fermentative power. Slopes of Loeffler's

serum medium were employed for primary cultures, and plates of the same medium for subsequent purification.

The intracutaneous method was used for testing pathogenicity, checked frequently, especially when the findings were negative, by subcutaneous injections, as will be described later.

I. EXAMINATION OF CULTURES.

The cultures were derived from three sources, and each group will be considered separately.

(a) Thirty-seven cultures from cases of clinical diphtheria gave the following results:

Morphology.	Glucose.	Saccharose.	Virulence.
<i>B. diphtheriae</i>	Acid	Negative	+ 33
<i>B. diphtheriae</i>	Not done	Not done	+ 3
Hoffmann's bacillus ...	Not done	Not done	— 1
			37

Of the 33 virulent cultures of *B. diphtheriae* the "sugar" reactions of which were tested, 2 fermented saccharose as well as glucose. These cultures, after plating, had been maintained on Loeffler medium for over ten weeks, and were seemingly pure, judging by smear preparations and appearance of growth. On replating, however, a very slight contamination was found—in one case a coccus and in the other a Gram-positive bacillus which produced acid in saccharose. When freed from these impurities the two strains failed to ferment saccharose.

(b) A single throat swab was taken from 112 patients who had had diphtheria and had completely recovered at the time of examination. Nineteen strains of *B. diphtheriae* and Hoffmann's bacillus were obtained, and gave the following results:

Morphology.	Glucose.	Saccharose.	Virulence.
<i>B. diphtheriae</i>	Acid	Negative	+ 9
<i>B. diphtheriae</i>	Not done	Not done	+ 1
<i>B. diphtheriae</i>	Acid	Negative	— 1
Hoffmann's bacillus ...	Negative	Negative	— 5
Hoffmann's bacillus ...	Not done	Not done	— 3
			19

Five of the nine virulent strains, when first tested in sugars, produced acid in saccharose; this was, however, due to a very slight degree of contamination. The fermentation of saccharose in these cases was generally slight, and might not take place till after the third day of incubation.

The most difficult contamination to eliminate is a Gram-positive sporing bacillus, which may lie dormant for weeks in a culture on solid medium. This organism ferments glucose and saccharose, and, when abundant or in pure culture, liquefies Loeffler medium.

(c) Comprises 105 cultures from 67 carriers, none of whom had had diphtheria, but most of whom had been in contact with a case. The results found in this group were as follows:

Morphology.	Glucose.	Saccharose.	Virulence.
<i>B. diphtheriae</i>	Acid	Negative	+ 30
<i>B. diphtheriae</i>	Not done	Not done	+ 3
<i>B. diphtheriae</i>	Acid	Negative	— 52
<i>B. diphtheriae</i>	Acid	Acid	— 8
<i>B. diphtheriae</i>	Not done	Not done	— 1
Hoffmann's bacillus ...	Negative	Negative	— 11
			105

Of the 30 virulent cultures, one produced acid in saccharose, but as with similar cases in the other groups, a very slight contamination was found to be responsible.

When we compare these three groups we notice that in Group A only one culture was avirulent and that was Hoffmann's bacillus. All the remainder were virulent, and, except for three not tested, gave typical "sugar" reactions. In Group B we find 10 virulent and one avirulent *B. diphtheriae*, the remainder being Hoffmann's bacillus; whereas in Group C, of 94 bacilli morphologically resembling *B. diphtheriae*, only 33 were virulent; excluding the eight strains which fermented saccharose (*B. xerosis*) and the one avirulent