The course of events is on retrospect fairly clear: the jugular bulb was probably infected through the floor of the middle ear, the disease sparing the mastoid antrum and process. The result was a case very obscure right down to the discovery of the perisinous abscess, which did not exceed a pea in volume. I was not free from anxiety for some days after the second operation. The case well illustrates the necessity for operating sometimes on very slight local indications in the absence of other explanation of a severe infection.

For permission to publish these notes my thanks are due to Mr. J. P. I. Hart, F.R.C.S., who has recorded a somewhat similar case (*Bristol Med.-Chir. Journ.*, 143, September, 1921, p. 78).

ADRENALINE AS A POTENTIAL FACTOR IN HYPERTHYROIDISM.

BY

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In a former article (*BRITISH MEDICAL JOURNAL*, March 31st, 1923) I considered the relationship of the putrefactive group of intestinal organisms to the production of thyroxin. My present purpose is to consider the activity of the same group among the intestinal flora as a potential causative factor in regulating the supply of adrenaline. Berthelot isolated from the intestine a bacillus (*B. phenologenus*) which converts a solution of tyrosin into phenol. This represents a considerable advance in our knowledge of the intestinal flora, for although it had been known for many years that there existed in the intestine bacteria capable of converting the aromatic products of digestion into phenol, no specific function had been attributed to any specific and isolated species among these organisms. This observation suggests a concept which may be found to account for the production of adrenaline either from tyrosin, or else (more probably) from some hitherto unidentified aromatic body closely allied to tyrosin, and, like tyrosin, a product of digestion. Can we in the light of our present knowledge conceive of adrenaline as being produced from tyrosin?

The Amine Producers.

These organisms have the power of removing COO from the COOH group of an amino-acid, converting it into an amine containing one carbon group less than the amino-acid from which it was produced. Apply this to tyrosin. If we limit the function of the amine producers to effecting the change just mentioned, tyrosin becomes, not a body of the adrenaline group, but tyramin, a lower member of the series.

Adrenaline is represented by the formula—

that is, it differs from tyrosin in containing an extra carbon group. If we still regard it as being a derivative of tyrosin, we must attribute an additional function to the amine producers—that of elevating the series by the addition of another carbon group; or else we must postulate a similar synthetic process as being carried out by some other agency, such as the cells of the adrenal glands. Now, as far as the amine producers are concerned, such a view of the question presupposes a type of activity which is, generally speaking, exceptional rather than characteristic among the metabolic processes brought about by micro-organisms. Their function is mainly katabolic; they split up complex into simpler bodies, the building up of complex from simpler bodies being relegated to various types of living body cells. If, then, we are to regard adrenaline as being produced from tyrosin, we

must assume the elaborative activity of some body cell (for example, the cells of the adrenal medulla) to be a factor in its production. On the other hand, if we are to regard adrenaline as being more directly a product of bacterial activity in the intestine, we must postulate the existence of some precursor other than tyrosin. We must seek for its source in some unidentified amino-acid which is, like tyrosin, a product of digestion, and structurally allied to tyrosin (so closely allied to tyrosin as to escape detection by the analytical processes hitherto employed), but which is higher placed in the series than tyrosin. Such a substance will be represented by the corresponding amino-butyric acid, with the formula—

or, better still,

Both the above could be direct precursors of adrenaline, needing only the intervention of the amine producers to effect the change; but as regards the catechol derivative it is important to note that Ebstein and Müller have demonstrated the presence of catechol sulphate in the urine. Such a concept of the origin of adrenaline traces it to a common source with the other endocrine secretion, thyroxin. As explained in my former article, thyroxin is regarded as being derived from tryptophane. Let us consider what happens if this common source (that is, the products of digestion) is interfered with. Such an interference arises when the putrefactive organisms disappear from the intestine. This state of affairs makes itself manifest biochemically, by the diminution or disappearance of indican and all other organic sulphates from the urine, and, clinically, by the development of the familiar syndrome of hyperthyroidism. But what is significant from the point of view of the present investigation is that hyperthyroidism implies not merely changes attributable to thyroxin, but equally important changes attributable to adrenaline, a state of affairs which we should expect if adrenaline and thyroxin are traceable to a common source—the end products of digestion. The absence of all the organic sulphates shows, in fact, that tryptophane and all the aromatic amino-acids are regulated by bacterial action. We should expect, therefore, a part of the syndrome of hyperthyroidism to be really hyperadrenalism. How far is this the case?

It enunciates no new theory to state that hyperactivity of the thyroid gland is accompanied by a corresponding activity of the adrenals. Hitherto this has been explained on the ground of an interaction between the thyroid and the adrenals, the so-called balancing of endocrine activities. From the foregoing paragraphs, however, the phenomenon is more rationally explained, not by some recondite interaction, but by a simple increase in the source of their particular secretions. To emphasize this I would quote the following pregnant paragraph from Professor Swale Vincent's *Internal Secretion and the Ductless Glands*:

"It is doubtful whether a condition strongly resembling Graves's disease has ever been produced by the administration of thyroid substance to animals. But there can be little doubt that definite toxic effects can be produced by thyroid feeding. These are loss of body weight, gastro-enteritis, and diarrhoea, rather than tachycardia, nervousness, and exophthalmos."

A further important question to be considered in relation to hyperthyroidism is that of the increase in the basal metabolic rate, which is now so generally recognized to be an outstanding feature of the condition. There are two main factors affecting this increase. In the first place, it is due to the greater amount of amino-acids rendered available for absorption by the disappearance, or lessened activity, of the putrefactive group of intestinal organisms. In the ordinary course of events a part of the amino-acids would be converted into phenol, indol, and skatol, and would be excreted in the urine as aromatic sulphates. By being

absorbed, instead of being thus excreted, they exercise the typical effect of protein bodies on metabolism—that is, they stimulate metabolism to a degree considerably in excess of their mere calorific value. The same fate also overtakes the fatty amino-acids. The second factor to be noted is this: that if we can assume that the source of adrenaline is to be found among the amino-acids in the intestine produced by the digestive ferments, the failure of the putrefactive organisms still further to split up this precursor into an excretable substance again has a specific bearing upon the increase in the basal metabolic rate, for it is now generally conceded that adrenaline is the sensitizer of the sympathetic nervous system, “the katabolic nerve of the body.”

A CASE OF TORSION OF THE GALL BLADDER.

BY

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SINCE torsion of the gall bladder is, and from the nature of the case must always be, an extremely rare accident, every case is worth recording.

A woman, aged 67, under the care of Dr. Seal, of South Molton, was taken suddenly ill at 10 p.m. with acute pain, distributed over the abdomen generally. She vomited and was collapsed, but not with the intensity seen in a case of perforation; there was a slight action of the bowels during the night or the early morning. The pain was not relieved, and from about 8 a.m. she was unable to pass flatus. The vomiting increased, and became green with bile; it was never stercoraceous, and never offensive. Dr. Seal could feel a tumour on the right side of the abdomen on the following morning. There was no rise of temperature.

She was seen in consultation with Dr. Seal at 6.30 p.m., when her expression was anxious but not intensely so; the pulse was just under 100, of fairly good volume and regular. The general condition was such as to give any prospective surgeon a reasonable hope of a favourable result of surgical interference.

The abdomen moved badly with respiration, but still it did move. There was a distinctly visible swelling on the right of the middle line. There was no distension, and no visible peristalsis. The mass on the right side was sausage-shaped, with the lower end blunter and more pronounced than the upper. Its long axis was tilted so that the lower end was slightly to the right of the vertical and the upper to the left. It did not appear to move with respiration, and was freely movable in all directions; the hand could be got between it and the liver above the tumour. Auscultatory percussion gave no indications of any connexion with the liver.

It was obvious that some acute abdominal condition was present, and the history pointed more to an intestinal obstruction than either a perforation or an inflammatory process, and it was thought probable that it was a case of growth in the colon, although the fact that the lower end was the more defined and the upper the less mobile was rather against this.

The physical signs connected with the very obvious tumour were distinctly puzzling. The swelling was exactly in the position of the gall bladder, but it was movable, seemingly in all directions. The liver could be felt moving with respiration and the tumour seemed not to move with it. Auscultatory percussion failed to show any connexion between it and the liver. There was no history of any previous trouble in the gall bladder, and there was no temperature to suggest a cholecystitis. The question of torsion or volvulus was never considered.

Operation.

The patient was with considerable difficulty persuaded to submit to operation; it was performed the same evening. Before the peritoneum was opened a dark red mass was seen, exactly like one seen when operating for extrauterine gestation. As soon as the peritoneum was opened a very little serous fluid escaped, and it was found that the tumour was a large gall bladder, quite black and nearly gangrenous from strangulation by two half-turns of the neck just at the edge of the liver. The turns were from left to right. After reducing the twist the gall bladder was removed with the greatest ease, since the point of constriction could be readily brought out of the abdomen, and the ligature could be applied to perfectly healthy tissue. The patient made an uneventful recovery.

The organ when removed was about the size and shape of a large pear. The walls were very much thickened, and it was quite black with extravasated blood. It was tightly distended with blood-stained bile, and it contained ten or twelve moderate-sized gall stones. Three of the larger of these were tightly lodged behind a valve or fold of mucous membrane; from their position and the thickness of the wall, they might easily have been overlooked during the course of an ordinary cholecystotomy.

Irwin in recording a case has collected seven previous ones, in only one of which were gall stones found. He also comments on the difficulty of diagnosis. Judging from the case under consideration, the difficulty would seem to lie chiefly in the fact that the possibility of its

occurrence is not taken into account. In spite of the fact that the tumour did not move with respiration, and that it seemed to be free from the liver, there is no doubt that at the time of examination the lower rounded end of the mass and its position were distinctly suggestive of gall bladder, and if the surgeon had in his mind the possibility of this condition being present it is more than likely that he would arrive at a correct diagnosis.

With regard to success of laparotomy, which Irwin also mentions, if all cases were as easy and straightforward as the one under discussion the surgeon could have nothing to fear, so far as mortality is concerned, beyond the ordinary anaesthetic risk.

ILEO-COLIC INTUSSUSCEPTION CAUSED BY MECKEL'S DIVERTICULUM AND SIMULATING ECTOPIC GESTATION.

BY

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THE two features in the following case which seem to warrant placing it on record are, first, the mimicry of ectopic gestation and the absence of the usual signs and symptoms of an ileo-caecal intussusception, and, secondly, the impossibility of reducing the intussusception by the ordinary methods, on account of the tight grip of the ileo-caecal valve.

A woman, aged 30, who had been married for three years, and during that time, and indeed all her life since puberty, had had no menstrual irregularity, ceased to menstruate three months before she was taken ill. As she was in good health at the time, she concluded that she was pregnant.

On June 16th, 1922, she was seized with acute abdominal pain, definitely located in the right iliac region, and occurring in spasms of variable duration; in the intervals she was not entirely free from pain. On that day she vomited once, but not afterwards. On June 18th she called in Dr. Young, who suspected a tuba-

FIG. 1.—Diagram of abdominal findings; T=tumour, U=uterus.

FIG. 2.—Diagram of removed ileum.

gestation, threatening rupture; when I saw the patient with him later in the day I concurred in the diagnosis and sent her in to Victoria Hospital, Swindon, for operation.

Her condition then was highly suggestive of a tubal gestation; she was in great pain at intervals, the spasms lasting only a few minutes, and her expression was one of “fear of impending catastrophe.” The pulse was not rapid (80), but small and feeble, the temperature 98° F. There was no general distension of the abdomen, and rigidity was confined to the right rectus muscle below the level of the umbilicus.

The bowels had acted normally up to that time; there was no diarrhoea, neither mucus nor blood in the stools, no tenesmus, and no swelling typical of an intussusception. On bimanual examination the uterus, enlarged, but somewhat indefinite in outline, could be felt pushed over to the left by a large elastic swelling which bulged down into the right lateral fornix and was felt to be continuous with a similar swelling in the right iliac fossa. This abdominal swelling reached nearly to the level of the umbilicus, was tender, and did not vary in size. The rigidity of the rectus over it rendered precision of palpation impossible.

Operation.

With the assistance of my colleague Dr. Young, at 9.30 p.m. a paramedian incision was made below the umbilicus, and the uterus, of the size of a three months' pregnancy, together with the appendages were found lying over to the left and physiologically normal. The appendix, presenting nothing abnormal, was drawn out of the wound. There followed the caecum, so mobile that it was easily pulled completely out of the abdominal wound after being dislodged from the pelvis in which it had lain. After packing off the rest of the abdominal contents the caecum was more closely examined; it was found to be very large and soft, and within its lumen could be felt a harder, more elastic, and slightly movable tumour. The entering ileum was also swollen to double its normal