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METABOLIC CHANGES ASSOCIATED WITH OPERATION*

BY

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That the recovery from injury follows a recognized pattern has been known from very early times. This was clearly appreciated by John Hunter (1794). In 1872 Bauer observed that an increased elimination of nitrogen followed upon haemorrhage, and Hawk and Gies (1904) showed that the actual operation of venesection without withdrawal of blood was enough to cause increased urinary output of nitrogen and sulphur. This increased nitrogen loss was also noticed by Benedict (1915) during prolonged starvation. Since that time many observers have noted this increased nitrogen catabolism as a result of injury, associated with increased phosphorus, sulphur, and potassium loss (Cuthbertson *et al.*, 1939; Cuthbertson, 1942; Wilkinson *et al.*, 1949). The varying nature of the injuries causing this has tended to emphasize that something inherent in the trauma, or some underlying response, might be common to many and various injuries done to the body, and deprivations to which it might be exposed.

Wilson and Stewart (1939) noted that, in burns, sodium was lost from the extracellular fluids into the cells of the damaged tissues, and also into the erythrocytes of the general circulation. The observations of Cuthbertson *et al.* (1939) on the urinary excretion of potassium and nitrogen led them to believe that the increased excretion of these substances was due to muscle catabolism following operative injury, but they noted that potassium was lost in greater proportion than nitrogen when compared with their relative concentrations in muscle protoplasm. Howard *et al.* (1946) have also shown that the nitrogen, potassium, sulphur, and phosphorus loss is not proportional to their content in muscle, and that the greatest potassium loss occurs in the first 24 hours. Blixenkrone-Møller (1949) demonstrated that the maximal potassium loss after operation precedes the maximal nitrogen excretion.

Wilkinson *et al.* (1950) demonstrated that after surgical operation potassium is lost in the urine in high concentration when the potassium intake is low, that the loss is greatest in the first three days after operation, and that it precedes in time the nitrogen loss, which persists throughout the first post-operative week. In a previous paper Wilkinson *et al.* (1949) had drawn attention to the marked retention of sodium and chloride in the early

post-operative period, occurring at the same time as the phase of increased potassium loss. Annersten and Norinder (1946) had previously observed a slight reduction in serum sodium and chloride after operation. They did not believe that these changes were significant. Similarly Wilkinson *et al.* (1951) noted such slight changes, but again did not believe them to be an explanation of the retention of sodium and chloride after operation.

I first became interested in this problem in 1948, when I observed the retention of chloride and of sodium after operation. The effect was thought to be very similar to the results of the administration of 11-deoxycorticosterone acetate (D.C.A.). In view of the observations of Hans Selye, it was believed that these electrolyte changes might well be due to increased adrenocortical function following the stimulus of operation. It was decided to observe these changes again and, at the same time, to measure adrenocortical function.

Results

Electrolyte Changes

Fig. 1 shows the typical features of the electrolyte changes in the plasma and urine before and after operation. In all cases a great reduction in the excretion of sodium and of chloride in the urine was observed immediately following operation; this persisted for about seven days. After this, the sodium and chloride excretion in the urine tended to rise above the pre-operative level. Associated with these changes, a constant but much diminished fall in serum sodium and plasma chloride was detected during the same period. A return to the pre-operative level occurred about the end of the first week.

During the same period the serum potassium concentration appeared to be variable and showed no pronounced change. In general, the concentration of potassium in the

FIG. 1.—Typical examples of electrolyte changes in blood and urine.

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serum was slightly elevated during some part of the post-operative period. Fig. 2, a composite diagram of the potassium excretion of another series of eight cases under the same conditions, demonstrates the continued loss after operation of potassium in the urine during the period of negligible potassium intake. The increased excretion of potassium appears to decline after the third post-operative day.

From the previous work discussed above, and as a result of observations made in the present study, it seems that after operation a reduced excretion of sodium and chloride is to be expected, associated with an increased excretion of potassium. The changes in the blood, however, are not so well established. As has been stated, the decrease in plasma chloride and serum sodium immediately after operation observed by Annersten and Norinder (1946) and by Wilkinson *et al.* (1951) was not considered by them to be significant. The changes in serum sodium of the nine cases of the present series are typically represented by those shown in Fig. 1. The majority are greater than the experimental error of the method used, and, though small, seem to be none the less real. This applies also to the plasma chloride changes detected in ten patients. Since the potassium lost must, in the end-result, be derived from cell potassium, it was thought that the small apparent loss of sodium and chloride in the body fluid after operation, at a time when the body is retaining sodium and chloride, might be due to a replacement of cell potassium by sodium and to an increase in cell chloride. Fig. 3 shows the results of the study of erythrocyte sodium and plasma sodium in another series of six patients. In four of the cases the estimations were made on the day before and after operation. The results show that the decrease in plasma sodium after operation equalled almost exactly the increase in cell sodium (Fig. 3, A and B). In two of the cases the estimations were performed on the day of operation, and on the fourth post-operative day (Fig. 3, C and D). By this time the changes had been reversed; the cell sodium content was now below the pre-operative level and the plasma sodium was above the pre-operative level.

Similar estimations of cellular and plasma potassium were undertaken on these patients, but no constant and appreciable changes were detected. Though no conclusion can be deduced from this small experiment, it does suggest that the slight decrease in serum or plasma sodium after operation is due to that amount of sodium entering the tissue cells.

Body Water Changes
Blood Volume.—(a) *Haemoglobin and haematocrit estimations.*—At the same time as the observations were made on electrolyte changes, some estimations of any

changes to be detected in the body water were also made. Fig. 4 shows the pre- and post-operative haemoglobin and haematocrit levels in the original nine patients of the series. There seem to be two distinct reactions in this series. As would be expected following any haemorrhage, five patients show evidence of haemodilution. The second group of four patients, under the same circumstances, show evidence of haemoconcentration.

(b) *Plasma volume:* In only two patients of this series was the plasma volume determined by the dye method. No significant reduction in plasma volume was detected. (c) *Plasma proteins:* Estimations were undertaken in five patients before and after operation. In four the total plasma protein content was reduced, and in one the increase was not significant. As will be seen from the Table, there was a general reduction in both the albumin and the globulin fraction after operation. (d) *Blood pressure:* These recordings were made in five patients in whom any degree of post-operative shock could be definitely excluded. No significant alteration in blood pressure, except on the day of operation, was noted in any case.

Plasma Protein Content Before and After Operation

Day:	-2		-1		0		+1		+2		+3	
Case	Alb.	Glob.	Alb.	Glob.	Alb.	Glob.	Alb.	Glob.	Alb.	Glob.	Alb.	Glob.
27	3.9	3.2			4.5	2.1	4.8	2.3	4.7	1.5		
28			5.0	2.3					4.8	2.3		
29					4.6	2.4					4.6	2.2
30			5.0	2.7					4.2	2.0		
31												

Extracellular Fluid-space Volume.—This was estimated in only two patients, using sodium thiocyanate. As only relative changes were to be considered, the inaccuracy of the "thiocyanate space" as a measure of the extracellular fluid space was not important. No significant change was observed after operation.

Total Body Water.

—Because more elaborate methods, such as the use of deuterium oxide, were not available, changes in total body water were estimated by means of changes in body weight. Fig. 5 shows a typical example of the changes in body weight, measured in pounds, following operation in patients weighed at the same time each day, in the same clothing, on the same machine, and after a 12-hours fast. A weight loss is noted in three of the cases, a gain in three, and no change in one case. The daily weight loss for the average

FIG. 2.—A composite diagram of the urinary potassium excretion during the early post-operative phase in eight cases.

considered by them to be significant. The changes in serum sodium of the nine cases of the present series are typically represented by those shown in Fig. 1. The majority are greater than the experimental error of the method used, and, though small, seem to be none the less real. This applies also to the plasma chloride changes detected in ten patients. Since the potassium lost must, in the end-result, be derived from cell potassium, it was thought that the small apparent loss of sodium and chloride in the body fluid after operation, at a time when the body is retaining sodium and chloride, might be due to a replacement of cell potassium by sodium and to an increase in cell chloride. Fig. 3 shows the results of the study of erythrocyte sodium and plasma sodium in another series of six patients. In four of the cases the estimations were made on the day before and after operation. The results show that the decrease in plasma sodium after operation equalled almost exactly the increase in cell sodium (Fig. 3, A and B). In two of the cases the estimations were performed on the day of operation, and on the fourth post-operative day (Fig. 3, C and D). By this time the changes had been reversed; the cell sodium content was now below the pre-operative level and the plasma sodium was above the pre-operative level.

FIG. 3.—A composite diagram of erythrocyte and plasma sodium, in four cases on the day before and after operation, and in two cases on the day of operation and the fourth post-operative day.

potassium were undertaken on these patients, but no constant and appreciable changes were detected. Though no conclusion can be deduced from this small experiment, it does suggest that the slight decrease in serum or plasma sodium after operation is due to that amount of sodium entering the tissue cells.

Body Water Changes

Blood Volume.—(a) *Haemoglobin and haematocrit estimations.*—At the same time as the observations were made on electrolyte changes, some estimations of any

FIG. 4.—Composite diagrams of haematocrit and haemoglobin levels, showing the two different types of reaction.

FIG. 5.—Composite diagrams showing changes in body weight.

male during starvation and without water depletion has been estimated as about 260 g., or 9 oz. (Wright, 1940). If after operation the nitrogen loss is even greater than in starvation alone, a still greater weight loss might be expected. Any weight gain or maintenance of previous weight must therefore be a measure of water retention within the body. Four of the seven cases appear, therefore, to show a water retention after operation.

Urine Volume.—In this paragraph only urinary volume studies are under review. Fig. 6 is a composite diagram of

Fig. 6.—Composite diagram of the average fluid intake and urine output of the nine cases.

the average daily fluid intake and urine output of the nine patients. Except for the day of operation, the urine output in the first six days after operation appeared to remain remarkably constant in these adequately hydrated patients. During the next four days the urine output increased, and approximated to the fluid intake.

Evidence of Increased "Glucocorticoid" Activity

The tests used here to measure increased secretion of corticoids are not necessarily the best for the purpose, but simply those most suitable for performing as routine estimations in a teaching hospital.

Fig. 7.—Composite diagram of circulatory eosinophil counts in six of the nine cases.

Fig. 8.—Composite diagram of blood-sugar changes in four of the seven cases in which sugar determinations were made.

Fig. 9.—Composite diagram of urinary 17-ketosteroid excretion a day in seven of the nine cases.

were made in seven of the nine patients. Fig. 8 shows the blood-sugar levels in four of the seven patients. These four patients showed a considerable rise in blood sugar in the immediate post-operative phase. The remaining three patients had no change in the blood-sugar levels after operation.

It is interesting to observe that, of the three patients in whom there was no evidence of decreased eosinophil counts after operation, one showed increased blood-sugar concentration after operation. Further, of the three patients who showed no evidence of an increase in blood sugar after operation, all showed a considerable fall in eosinophil counts. Thus, applying both tests, only two patients did not give any evidence of increased "glucocorticoid" activity after operation.

Evidence of Increased Androgen Formation

17-Ketosteroid Excretion.—Fig. 9 is a composite diagram of the excretion of 17-ketosteroids a day in the urine following operation. Seven of the nine cases showed evidence of increased 17-ketosteroid excretion on the first or second day. The increased ketosteroid excretion in these cases tended to fall below the pre-operative level by about the sixth day. Of the two cases which did not show an increase in ketosteroid excretion after operation, one was excreting 17-ketosteroids at the upper limit of normal in the pre-operative phase. This was followed in the early post-operative period by a marked fall, followed by a sharp rise again on the fourth day.

Discussion

The Electrolyte Changes

The reduction in the excretion of sodium and chloride in the first week after operation, and the increased excretion of potassium previously noted by Blixenkrone-Møller (1949) and by Wilkinson *et al.* (1949, 1950, 1951), are confirmed in the present series. This study also indicates that these features are common to relatively minor surgical procedures, where no intravenous electrolyte or blood replacement therapy has been undertaken either at the time of operation or thereafter. Gamble (1942) has shown that the intravenous infusion of saline is sufficient, by itself, to cause an increased excretion of potassium in the urine. This factor can be excluded in the present series.

It would seem that the increased excretion of potassium after such operations is a phenomenon similar to the increased potassium excretion following operative fracture of the long bones, as demonstrated by Cuthbertson *et al.* (1939). Cuthbertson (1942) considered this to be part of an intimate response of the organism to trauma. His findings, and those of Wilkinson *et al.* (1950), indicate that the potassium loss after operation occurs to a degree greater in proportion than the nitrogen loss, that it precedes the nitrogen loss, and that it terminates before the phase of negative nitrogen metabolism has ceased. Blixenkrone-Møller has detected an increased potassium excretion within six hours of operation. Benedict (1915) and Howard *et al.* (1946) have shown that the potassium loss during starvation and in progressively diminishing diets is directly proportional to the nitrogen loss when compared with the concentration of both substances in muscle.

It would appear, therefore, that factors over and above rest in bed and starvation are effective in causing the sodium and chloride retention and increased potassium excretion associated with operation. Selye (1950) believes that these electrolyte changes are a part of the "stress" response, and partly due to an adrenocortical response to injury. Similar retention of water and salt with increased excretion of potassium is observed after the injection of 11-deoxycorticosterone acetate (D.C.A.) in animals (Ferrebee *et al.*, 1941), and in man (Ingle and Thorn, 1941), and also after the administration of A.C.T.H. (Forsham *et al.*, 1948; Mason *et al.*, 1948; Elkinton *et al.*, 1949).

The Cellular Electrolyte Changes

The older concepts that the cell membrane offered an impermeable barrier to the passage of sodium and potassium is now known to be incorrect. Maizels (1949) has shown that in blood-stored at 37° C. an active expulsion of sodium from the cell takes place, accompanied by an uptake of potassium. Mullins *et al.* (1941) have shown the rapid penetration of the erythrocyte by radioactive potassium, and to a less extent by sodium, in three hours. During anaerobic metabolism, in the absence of glucose, the potassium concentration of the serum (Danowski, 1941), or the brain-tissue fluid (Dixon, 1949), has been shown to rise, owing to a loss of potassium from the cells of the respective tissue. Ferrebee *et al.* (1941) have shown clearly that, in dogs, symptoms of cellular depletion of potassium may arise after the administration of D.C.A. It has also been shown that in animals fed on a low-potassium and high-sodium diet partial replacement of deficient cellular potassium can be induced by increase in cell sodium (Heppel, 1939; Miller and Darrow, 1940). Fenn and Cobb (1936) found that after prolonged indirect stimulation of muscles in anaesthetized rats, potassium was lost from the muscle cells and replaced by sodium. After two hours' rest these changes were reversed, indicating that no permanent damage had been done to the muscle.

From all these observations there is strong experimental and clinical evidence to show that potassium and sodium, under certain circumstances, may be interchangeable across the cell membranes. Such an interchange would account for the increased potassium excretion following operation. It would also account for the relatively slight fall in the serum sodium and chloride observed here, and considered not significant by Annersten and Norinder (1946) and by Wilkinson *et al.* (1951). The short study of intracellular electrolyte in the present series confirms this conclusion—an increased erythrocyte sodium content being observed in the immediate post-operative period, and the plasma sodium being reduced by the corresponding amount. No change was noted in the erythrocyte potassium content. This does not invalidate the assumption that the potassium has been derived from tissue cells, as demonstrated by the workers already cited.

The question why potassium should leave the cell under a variety of circumstances seems to be open to two interpretations. Gamble (1942) believes that, in conditions of clinical dehydration, water and potassium pass out from the cell, depending upon the changes in extracellular fluid and electrolyte. In the present series of cases no question of extracellular dehydration arises. Indeed, it has been shown that water and electrolyte, probably in equal relative proportion, are retained within the body.

Another concept, which seems to fit the facts in a more extensive range of conditions leading to the same end-result, has been suggested by Maizels (1949). It is indeed curious that the normal cell-to-tissue cation equilibrium should remain established at any time. As Maizels has indicated, this accumulation of potassium in the cell against the concentration gradient has long been a cause for speculation. Maizels, from his own observations, does not believe that an active excretion of sodium from the cell requires an active absorption of potassium. He believes that potassium passes into the cell passively, and secondarily to the active expulsion of sodium.

It would therefore seem that, following operation or trauma, the relative permeability of the cell-membrane is altered, potassium is liberated, and any tendency to a marked rise in extracellular potassium is prevented by the rapid excretion of that ion in the urine. Either, to replace this cell base, sodium appears to enter the cell from the surrounding extracellular fluid, or else, if Maizels's view is accepted, the "pumping" mechanism breaks down, sodium is not sufficiently expelled from the cell, and perhaps, to maintain the correct osmotic tension, potassium leaks out into the tissue fluids.

Alterations in Body Water

Plasma Volume.—Wilkinson *et al.* (1951), in a series of 10 cases, demonstrated a decrease in plasma volume immediately after operation—directly by the dye method (T 1824) and indirectly by changes in haemoglobin and haematocrit readings. Studies of plasma-protein fractions indicated that this was due to a reduction in plasma albumin and an increase in plasma globulin. These results, in association with some of the electrolyte changes considered above, led them to suggest a transudation of water, albumin, sodium, and chloride into the tissues at the site of injury. Their cases all received blood transfusion at the time of operation, and were undergoing major surgery. In the present investigation the direct plasma-volume studies were not extended sufficiently to be of any value. So far as indirect mensuration may be of value, five of the patients showed evidence of haemodilution in the immediate post-operative phase and four showed evidence of haemoconcentration. No confirmation of a relative reduction in plasma albumin with an increase in globulin was obtained.

Extracellular Space Volume.—Wilkinson and his associates, in their study of the total extracellular space volume in the same cases, did not observe any regular change in the post-operative period. The studies in the present paper are too few to be of value, but they do tend to confirm this finding.

Total Body Water.—As has been shown in the present series, evidence has been obtained of an increase in total body water in some of the cases. Whether this is due to an increase in the extracellular extravascular space as determined directly by Wilkinson and his associates, or whether it is due to an increase in cellular water, has not been determined here. As Darrow has shown (Gamble, 1942), the excretion of potassium in infantile diarrhoea is associated with cellular dehydration. On the other hand Fenn and Cobb (1936), in their experiments on continued muscle stimulation, showed that the passage of sodium and chloride into the cells was associated with an increase in the intracellular water space.

Urine Volume.—The gradual approximation of the urine excretion to the fluid intake late in the post-operative period would tend to suggest that a water retention had occurred at an earlier stage. The relative diuresis for each patient seems to occur on a different day after the first post-operative week. For this reason the combined chart masks this relative diuretic effect.

Evidence of 11-Oxysteroid Activity

Eosinophil Counts.—Forsham *et al.* (1948) and Carlisle (1950) have indicated that both A.C.T.H. and cortisone depress the circulating eosinophil count. Cope *et al.* (1951) point out that it is specifically cortisone and 17-hydroxycorticosterone which exert this influence in the adrenalectomized animal. The depression of the eosinophil count, provided the reduction is at least by 50%, has often been used in clinical medicine as a measure of adrenocortical activity (Roche *et al.*, 1950). Unfortunately, accurate eosinophil counting is difficult, and Godlowski (1951) has demonstrated that heparin in large doses may produce an eosinophilia in spite of injected cortisone or A.C.T.H.

In the present series six of the nine patients who showed the electrolyte and water disturbances described above also showed a reduction of the eosinophil count by 50% in the immediate post-operative period.

Annersten (1949), in measuring the post-operative rise in blood-adrenaline concentration, has observed an immediate post-operative rise in blood sugar. In an earlier paper (Annersten and Norinder, 1946), a raised blood sugar was also observed on the first and second days after operation. In view of the observations of Annersten (1949) and the work of Cannon (1929), this early hyperglycaemia is undoubtedly due to the liberation of excess adrenaline. Although not commented upon, the results of Annersten

(1949) show that the blood adrenaline is falling by the second post-operative day, whereas the high blood-sugar level is maintained. In the present series a considerable rise in blood sugar occurred in four of the seven patients studied, little or no change being observed in the three others.

Urinary 17-Ketosteroid Excretion

The whole 17-ketosteroid excretion in women, and a part of it in men, is derived from cortical androgens (Forbes *et al.*, 1947). The remainder in men, about 4–6 mg. a day, is derived from testicular tissue.

It was early noticed (Fraser *et al.*, 1941) that there was a diminished excretion of 17-ketosteroids in the urine following trauma and surgical operations. However, the same workers (Forbes *et al.*, 1947) demonstrated later that they had missed an early rise in 17-ketosteroid excretion in the first 24 hours after operation. After this, ketosteroid excretion fell to its lowest point about the fourth or fifth day, and by the tenth day regained normal levels. Control patients showed that starvation alone did not cause this rise, and then fall, in excretion. Landau *et al.* (1948) also showed that starvation by itself decreases the total 17-ketosteroid excretion. A sharp rise in the excretion of 17-ketosteroids followed by a fall to below normal levels in 30 patients suffering from haemorrhage, fractures, burns, infection, and operation was shown by Stevenson *et al.* (1944). A similarly elevated 17-ketosteroid excretion was noted by Freeman *et al.* (1944) after severe muscular fatigue. Talbot *et al.* (1945) found evidence of increased urinary excretion of 11-oxysteroid-like substances in active Cushing's syndrome, in adrenal cortical virilism, after burns, and in post-operative patients. Cope *et al.* (1951) observed increased excretion of 11-oxysteroids in acute medical conditions such as diabetic ketosis, congestive cardiac failure, bronchopneumonia, coronary infarction, and status asthmaticus. Forsham *et al.* (1948) demonstrated an increase of both 17-ketosteroids and 11-oxysteroids in the urine after A.C.T.H. therapy. This finding has been confirmed by Sprague *et al.* (1950) in a large series of cases.

In the present series seven of the nine patients showed a large increase in ketosteroid excretion in the first two days after operation, followed by a fall reaching a minimum at the sixth post-operative day. Of the two patients who did not show increased ketosteroid excretion, one showed a slight fall. The other case, excreting 17-ketosteroids before operation at the upper limit of normal, had at that time a very low eosinophil count. After operation 17-ketosteroid excretion fell dramatically, associated with a marked rise in the eosinophil count.

Conclusions

Some evidence has been produced of increased 11-oxysteroid secretion and 17-ketosteroid excretion as a measure of increased adrenocortical activity after operation. This has often been shown in recent years in association with trauma, burns, acute medical conditions, and operation itself. The present study has shown that these changes are also associated with alterations in electrolyte and water balance. Changes of sodium, chloride, and water retention, associated with increased potassium excretion and with exchanges of sodium for potassium within the cells, are very similar to the effects of 11-deoxycorticosterone. Though they may be accounted for by other means, such as local accumulation of fluid and electrolyte in damaged tissues, the fact that they are associated with other evidence of adrenocortical activity suggests that they are themselves linked with such activity. Prunty (1949) has recognized a similar phase of decreased plasma sodium and chloride in acute porphyria. The study of eosinophil counts, uric acid excretion, and neutral reducing steroid excretion indicated an increased adrenal activity during the acute phase of the disease. As Selye has suggested, such a response may occur in a variety of conditions, all in themselves a reflection of injury to the organism.

The retention of sodium chloride and water in the body after operation, in amounts greater than apparent needs, has now become recognized. The diminished urinary excretion of chloride in the first weeks after operation vitiates the urinary chloride estimation as a measure of body chloride requirements. This has been accepted by Marriott (1951). Attempts to replace the apparent chloride deficiency will only lead to water and salt overload. I believe that plasma chloride estimations in the post-operative period are of greater value in estimating body chloride deficiency. Even these determinations, as has been demonstrated in this paper, will give a false low reading.

The importance of potassium in the serum and extra-cellular fluids has been well recognized ever since the work of Ringer (1883). In recent years great interest has been focused on the loss of potassium in various acute medical and surgical conditions. Brown *et al.* (1944) described low levels of serum potassium in chronic nephritis, associated with muscular weakness and paralysis. Holler (1946) drew attention to a similar low potassium level during the treatment of diabetic coma. It is, however, largely due to the work of Darrow and his associates that clinical potassium deficiency has become widely recognized (Govan and Darrow, 1946; Darrow, 1948; Darrow and Pratt, 1950). As shown by these and other workers, potassium can be lost to the body in gastro-intestinal disorders such as diarrhoea (in children), sprue, intestinal fistulae, prolonged vomiting, and in certain types of diet, such as the Borst diet (Kolff, 1950).

Tarail and Elkinton (1949) have demonstrated that in both normal and potassium-depleted patients the kidney has a limited minimal excretion of potassium, below which minimal level the excretion does not appear to fall. This continued potassium loss, even in the presence of cellular potassium deficiency, they believe to be an important factor in producing further depletion. If, in addition to these other sources of potassium deficiency, the incident of a surgical operation increases the urinary potassium loss, cellular potassium depletion is further increased, and the production of a state of clinical potassium deficiency is hastened. The fact that the rapid mobilization of cellular potassium after an operation is often associated with a rise in serum potassium concentration makes the recognition of cellular depletion all the more difficult. I have seen several patients with a cellular potassium deficiency in which the serum potassium, though falling from a concentration greater than normal, was still within the normal range when electrocardiographic evidence of cellular potassium deficiency was detectable.

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ANNULAR PANCREAS

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The commonest developmental abnormalities of the pancreas concern the ductal systems. Accessory pancreatic tissue—isolated masses separate from the main gland—occurs not infrequently in the stomach or duodenum, but may be found in most of the abdominal viscera. Other anomalies are pancreas divisum (Hyrtl) consisting of two separately functioning glands; bifid tail of the pancreas; and annular pancreas in which a band of pancreatic tissue encircles the duodenum, usually in its second part. Cysts and fibrocystic disease may occur.

In 1933 McNaught was able to find descriptions of only 40 cases of annular pancreas in the literature, the first three referring to the condition in birds, in which it is apparently a normal finding (Ravitch and Woods, 1950). In June, 1952, the total number of cases recorded was at least 75, and it is significant to note that 20 of these have been recorded since the end of 1949, indicating a higher actual incidence than the statistics show. In the absence of obstruction, cases may easily be overlooked either at operation or at necropsy.

A further case has recently been brought to light during an operation for chronic duodenal ulcer by one of us (N. C. T.).

Case Report

A male clerk aged 30 was admitted on October 13, 1951, with a history of two and a half years' epigastric pain two hours after meals, relieved by food, rest, and alkalis. There had been periods of freedom of up to nine months. He had no vomiting, but had lost 28 lb. (12.7 kg.) in weight since the onset. After investigation elsewhere he was told that a duodenal ulcer was present. The only abnormality

detected was a gastric succussion splash. A gruel fractional test meal showed a high acid curve rising to 65 ml. N/10 free HCl at one hour.

A barium-meal examination disclosed a spastic deformed duodenal cap with folds radiating from an ulcer scar. There was no gross obstructive lesion of the second part of the duodenum. In view of his relapse despite more than one good course of medical treatment, he was operated upon on October 16. The presence of an anterior chronic duodenal ulcer was confirmed. The rest of the viscera appeared normal, except that, about 2–3 cm. below the junction of the first and second parts of the duodenum, the organ was encircled by pancreatic tissue of healthy appearance and texture, the abnormal part being a band about 1–2 cm. in diameter (see illustration). A subhiatal vagotomy and Heineke–Mikulicz pyloroplasty was then carried out. During the pyloroplasty opportunity was taken to feel the duodenum from within its lumen, and there appeared to be no appreciable constriction. The patient made an uncomplicated recovery from this operation, and an insulin test meal 17 days later showed a much lower acidity and no secretory response to the insulin.

Diagram showing band of pancreatic tissue encircling the duodenum.

Nine months after operation the patient was symptom-free, and a further barium-meal examination showed no delay in emptying of the stomach and no evidence of constriction of the duodenum.

Discussion

Aetiology.—The condition affected males in 50 out of the 64 cases in which the sex was recorded. Various theories have been advanced concerning the embryological origin of the ring—for example, persistence of the left half of the ventral anlage of the pancreas which ordinarily atrophies, fixation of the ventral bud of the pancreas to the duodenum before rotation of the gut, or a smooth spread round the duodenum as is said to occur in birds. Other congenital abnormalities have been found associated with the annular pancreas in some 20 cases, the most frequent being malrotation of the abdominal viscera.

Symptomatology.—Patients with annular pancreas may present at any age with symptoms due to the condition, or the condition may be symptomless. The youngest recorded case was in a 16-mm. embryo (Weissberg, 1935), while two cases were operated upon at the age of 74 (Smetana, 1928; Custer and Waugh, 1944). Thirty-seven cases had symptoms due to the annulus. Most of the nine presenting in the first decade appeared shortly after birth, with symptoms of high intestinal obstruction or with jaundice probably due to compression of the common bile duct. If symptoms have not developed by this time it would seem reasonable to suppose that the patient has a good chance of remaining symptom-free throughout life. A study of the literature suggests that this is not the case. Adults usually present with high intestinal obstruction, with symptoms suggesting peptic ulceration, or, less commonly, with acute haemorrhagic pancreatitis. In the first there may be rapidly progressive or recurring episodes of obstruction. This sometimes results from pancreatitis of the annulus, but this is not a constant finding in those specimens which have been sectioned. Those patients with a history suggesting peptic