ALTERED ELECTROLYTE METABOLISM FOLLOWING SURGICAL ENCROACHMENT[1-4]

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Knowledge on the electrolyte metabolism in surgical patients has been accumulating in the last decade. A concise monograph on this subject has recently appeared in the United States[5], and in our country the ploblem of the altered pattern of electrolyte metabolism in surgery has been explored for the past several years chiefly by Shibusawa and his associates.[6,7] Nevertheless, it is felt that some points require further exploration, because (1) calcium and magnesium have never so far been studied in spite of the fact that an appreciable distortion of metabolism of these electrolytes is expected to occur after a surgical operation, and (2) disproportionate emphasis seems to have been laid in their reports upon the distorted turnover of sodium and potassium, especially as based on the observation of exceptionally severe cases. We have, therefore, undertaken series of studies on patients with common surgical diseases in order to see if any contribution may be made to the knowledge of metabolism of such electrolytes as calcium and magnesium in addition to sodium and potassium, and to verify if the altered electroyte metabolism following the ordinary surgical operation of mediocre scale might entail a disastrous outcome which is beyond control by the conventional after-treatment.

MATERIALS AND METHODS

Patients with gastric ulcer (6 cases), gastric cancer (1 case), appendicitis (2 case) and other miscellaneous diseases which demanded medium-sized operation (3 cases) were observed. Neither fluid infusion (including blood tranfusion) nor medication was given for a week preceding and for two weeks following the operation. The amount of food and beverage taken by the patient was recorded, and the daily intake of water, sodium, chloride, potassium, magnesium, inorganic phosphorus, calcium and nitrogen was computed from the table of food analysis. The samples of blood were collected under a layer of mineral oil in a centrifuge tube from the antecubital vein of the patients in fasting state immediately before and 0, 1, 2, 3, 7, and 14 days after operation, serums were separated, and quantitatively analysed for sodium, potassium, calcium, magnesium, bicarbonate, chloride, inorganic phoshorus, nonprotein nitrogen and protein.

The procedures employed in this study were as follows.

(1) *Serum*

Sodium: Colorimetric uranyl-zinc-acetate-sulfo-salicylic-acid method of Shibata and Mizuta (Modified Savage-Maginus Procedure)[8, 9]

Potassium: Colorimetric silver-cobaltinitrite-choline-chloride method of Shibata and Mizuta.[10]

Calcium and Magnesim: Colorimetric Plasmo-Corinth B method of Yanagisawa.[11]

Chloride: Titrimetric mercury-nitrate (with diphenyl carbazone as indicator) method of Schales and Schales.[10]

Bicarbonate: Microdiffusion method of Conway.[12]

Inorganic phosphorus: Colorimetric molybdate-amino-naphthol-sulfonic-acid method of Fiske and SubbaRow.[13]

Nonprotein nitrogen: Colorimetric nesslerization method of Shibata, Mizuta and Takahashi (Modified Koch-Hanke Procedure)[14]

(2) *Urine*

Sodium: Colorimetric uranyl-zinc-acetate-sulfosalicylic-acid method of Shibata and Mizuta (Modified Van Loon-Lein Procedure)[9, 15]

Potassium: Colorimetric silver-cobaltinitrite-choline-chloride method of Shibata and Mizuta.[10]

Calcium: Titrimetric oxalate method of Murata (Modified Sohl-Pedley Precedure)[16]

Magnesium: Colorimetric titan-yellow method of Garver, Kunkel and Person.[17, 18, 19]

Chloride: Iodometric silver-nitrate method of Sendroy.[13]

Nitrogen: Colorimetric nesslerization method of Shibata, Mizuta and Takahashi.[14]

Results and Discussion

For the sake of clarity the data obtained in this study will be presented in two separate parts: (1) the serum electrolyte pattern and (2) the electrolyte balance.

1. *Serum Electrolyte Pattern*

Figure 1 represents a graphical representation of the serum electrolyte

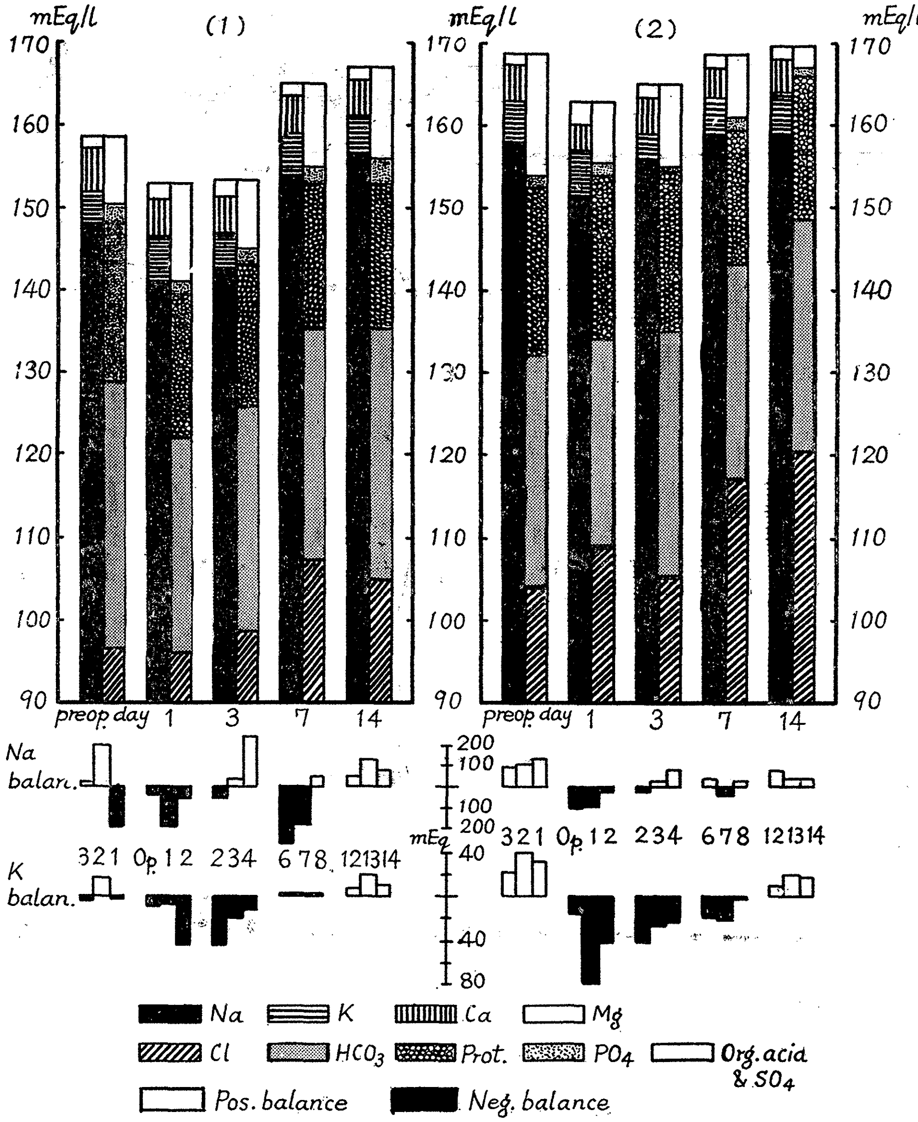

Fig. 1. Alteration of serum electrolyte concentration and metabolic balance of sodium and potassium in surgical encroachment.

pattern in two cases which gave typical responses to the surgical encroachment. Similar response was also observed in the remaining eight cases which came under our study. Inspection of this figure will reveal that surgical operation entailed an appreciable alteration in the serum electrolyte pattern, although the concentration of the individual electrolytes has not deviated markedly from the limits of normal range. Total serum electrolyte was 310 to 330 mEq/l in concentration preoperatively, fell almost as much as 10 mEq/l on the day following the operation, about 3 mEq/l below the preoperative level on the third postoperative day, and almost restored its preoperative concentration by the 7th day. Two weeks however required for the complete restoration. Theree groups listed below were found in the patterns of the alteration of the individual serum electrolytes.

1) Group 1: Sodium, chloride and bicarbonate.

The electrolytes belonging to this group showed the following fluctuation of concentration: a fall on the first to third postoperative days and reversion to or rise over the preoperative level in a week or two after the operation. Serum sodium which remained within the limits of normal range (145–151 mEq/l) before the operation underwent decreases of 5 to 8 mEq/l and 2 to 5 mEq/l on the first and the third day, respectively, and either returned to or rose to the level of as high as 1 to 5 mEq/l above the original with the seventh day. In a few instances the rise persisted until the fourteenth day. A similar but somewhat slighter fluctuathion was also observed on the serum chloride concentration. It exhibited a fall of 1 to 5 mEq/l on the first day, and usually returned to the preoperative level on the third day, but, on occasions, it ascended to the concentration which was as much as 1 to 10 mEq/l above the original. The serum bicarbonate dropped conspicuously (3.0-6.8 mEq/l) shortly after the operation from the preoperative level which ranged from 29 to 33 mEq/l and remained markedly low at least for four hours and reverted to the preoperative level on the third day.

2) Group 2: Potassium, magnesium and phosphate.

The electrolyte concentration of this group displayed a peculiar fluctuation, there occurring a rise on the first postoperative day, followed by a fall below the preoperative level on the third day, and returned to the original level within two weeks after the operation.

Serum potassium concentration, being 4.1 to 5.6 mEq/l preoperatively, rose as much as 0.5 to 1.0 mEq/l on the first day, fell 1.0 to 2.0 mEq/l below the preoperative level on the third day, and returned to the original concentration within the period between the seventh and the fourteenth day.

Magnesium also gave similar alteration. Before the operation its concentration in serum was within the range of 1 to 2 mEq/l. It ascended as much as 0.2 to 1.0 mEq/l on the first day, descended 0.1 to 0.2 mEq/l below the preoperative level, to which it reverted in a week or two.

Phosphate concentration in serum displayed a rise of 0.5 to 1.0 mEq/l on the first day, and then a drop of about 0.5 mEq/l on the third day. It restored its preoperative value, about 3 mEq/l, between the seventh and the fourteenth day aftter the operation.

3) Group 3: Calcium

Serum calcium was quite different in attitude from the other electrolytes, displaying an irregular postoperative fluctuation. This electrolyte remained within the limits of 4.5 to 5.7 mEq/l before the operation and in the majority of cases fell as much as 1.0 to 1.5 mEq/l below the original level after the operation, but individual variation was so evident that it was almost impossible to derive such a regular pattern of the post operative fluctuation as to be comparable with that observed in the group 1 and 2.*

2. *Electrolyte balance*
(*Urine, diet and beverage*)

An appreciable change in the electrolyte metabolism was usually encountered after surgical operation. The data accumulated in this study will be presented in conjunction with metabolism of water and nitrogen for comparison.

The intake of electrolytes was practically zero for a day or two following the operation, because the patient was ordered to fast during this period.

It gradually increased in amount for the next two weeks until it reached the preoperative level. The daily output of urine was similarly extremely small in volume for the several days subsequent to the operation. This was followed by a sudden rise in urine volume which lasted three or four days (postoperative diuresis), and the preoperative urine output was roughly reestablished on the fourteenth postoperative day. There was constipation for a number of days after the operation (postoperative constipation).

The theree groups of electrolytes, namely group 1, 2 and 3, which were identical with those described with reference to the observation of serum electrolyte pattern, were again affirmed by the study of metablic balance.

1) Group 1. Sodium, chloride and water.

Figure 2 represents the average variation of the balance (the output

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* Serum protein dropped to the lowest level on the third postoperative day, showing a decrease of as much as 0.5 to 1.0 g/dl, rose later over the preoperative level in most cases, and returned to the level of original concentration after two weeks or more.

Nonprotein nitrogen exhibited a rise of 5 to 15 mg/dl, and then either recovered its original concentration or fell as far as 5 to 10 mg/dl below the preoperative level. It restored Its original range on the fourteenth postoperative day.

and intake) of sodium chloride and water as well as of the urinary volume and of the concentration of nitrogen and chloride in urine as observed on 4 cases. These electrolytes showed a diminished excretion until the 5th to 7th day following the operation, when they abruptly increased for the next three to five days.

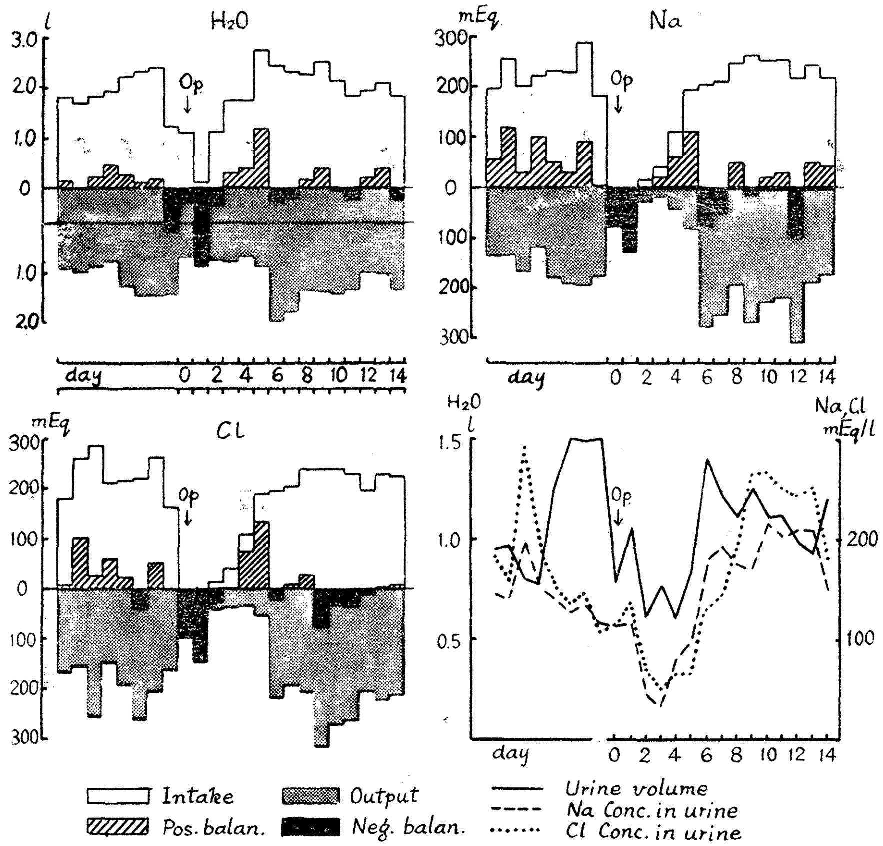

Fig. 2. Alteration of the balance of sodium, chloride and water as well as of their urinary concentration in surgical encroachment.

The balance was therefore negative for two or three days after the operation, positive for the subsequent three or four days, and then restored the approximate epuilibrium. There was a marked decrease in urinary output without any lowering in the concentration of sodium and chloride on the day of operation and for the subsequent two days. Then an oliguria of three to five day duration accompanied by conspicuous reduction in electrolyte concentration appeared, to be succeeded by a marked diuresis accompanied by a rise in the urinary electrolyte concentration. Preoperative level of urinary volume and urinary electrolyte concenration was roughly re-established ot the 7th to 10th postoperative day.

2) Group 2. Potassium, magnesium, phoshate and nitrogen.

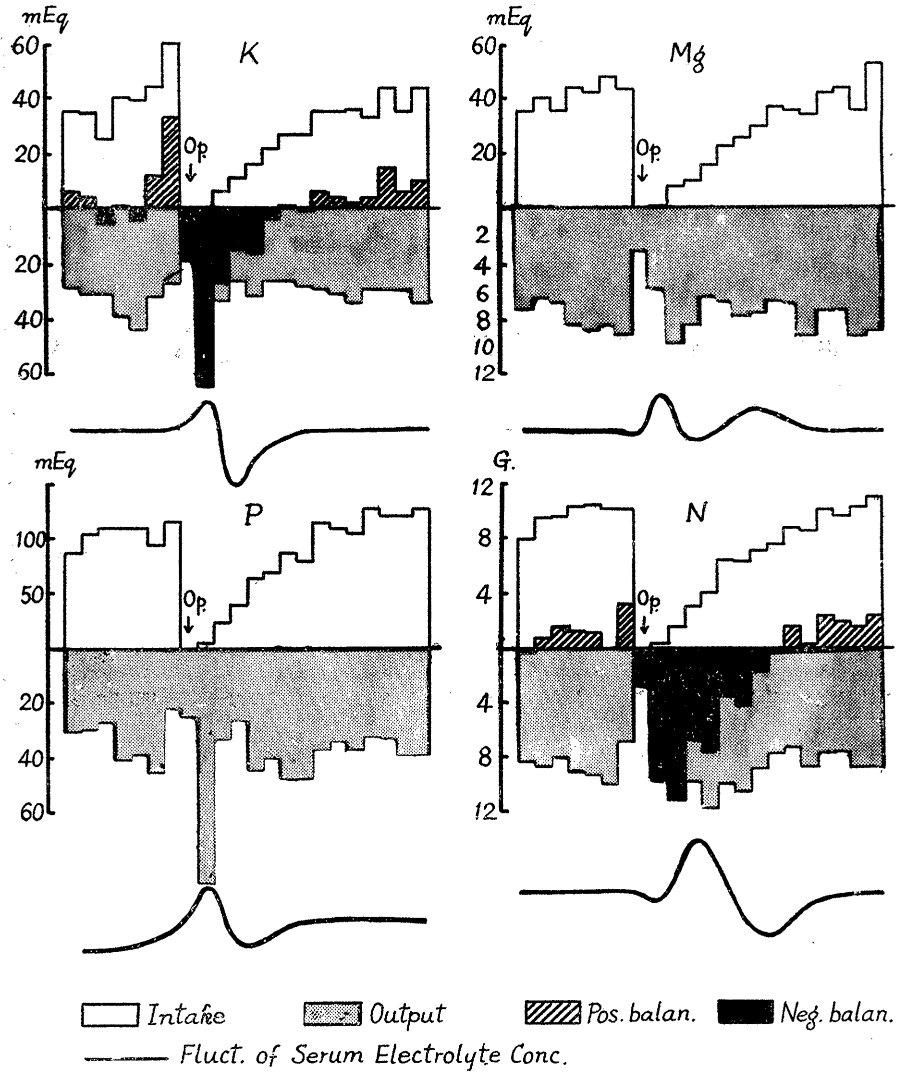

Fig. 3. Alteration of the balance of potasium, phosphate, magnesium and nitrogen as well as of their concentration in serum in surgical encroachment.

Figure 3 is graphical representation of the mean pre- and postoperative flutuation of the metabolic balance and the serum concentration of potassium, phosphate and nitrogen, which were studied on 9 cases.

On the day of operation the excretion of these electrolytes, of potassium and phosphate in particular, underwent diminution in association with the decrease in urinary volume, whereas on the following day it exhibited a transitory but marked rise in spite of the meager intake of electrolytes and the reduced urinary output as a result of postoperative fasting, and then again it fell below the preoperative level for four or five days. Similar fluctuation was also observed with magnesium, although negative balance was less marked and shorter in duration (for 2 or 3 days).

Urinary nitrogen excretion rose for five to seven days following an operation, resulting in negative nitrogen balace for four or five days. It is thus apparent that the postoperative loss in these electrolytes and nitrogen takes its own course quite independently of the amount of intake, although there is some individual variation. Furthermore, this negative balance in the phosphate and magnesium metabolism after the operation must be more marked and prolonged than several days which was period of negative balance as actually observed, since the loss of these electrolytes in the feces must be considerable and yet had to be completely ignored in this study. Of course an attempt to measure the fecal loss of electrolytes and nitrogen was made, but its result was not satisfactory, as the postoperative constipation hindered their exact estimation.

3) Group 3. Calcium.

Figure 4 illustrates the average variation of the metabolic balance of calcium and its concentration in the serum as was studied on eleven cases. It shows also the mean variation of the elimination of this electrolyte in the feces which was computed from the observation made on two cases for the sake of better understanding. It will be inferred from this figure that the discharge of calcium (into the urine as well as into the feces) varied roughly in proportion to the rise and fall of its intake, there being no indication of alteration of pattern of matabolism directly traceable to the surgical encroachment.

Discussion

In the preceding section three groups of electrolytes were assorted on the basis of the specificity and similarity of the altered metabolism induced by the surgical encroachment. They are characterized by the following attitude in the balance and the concentration in the serum.

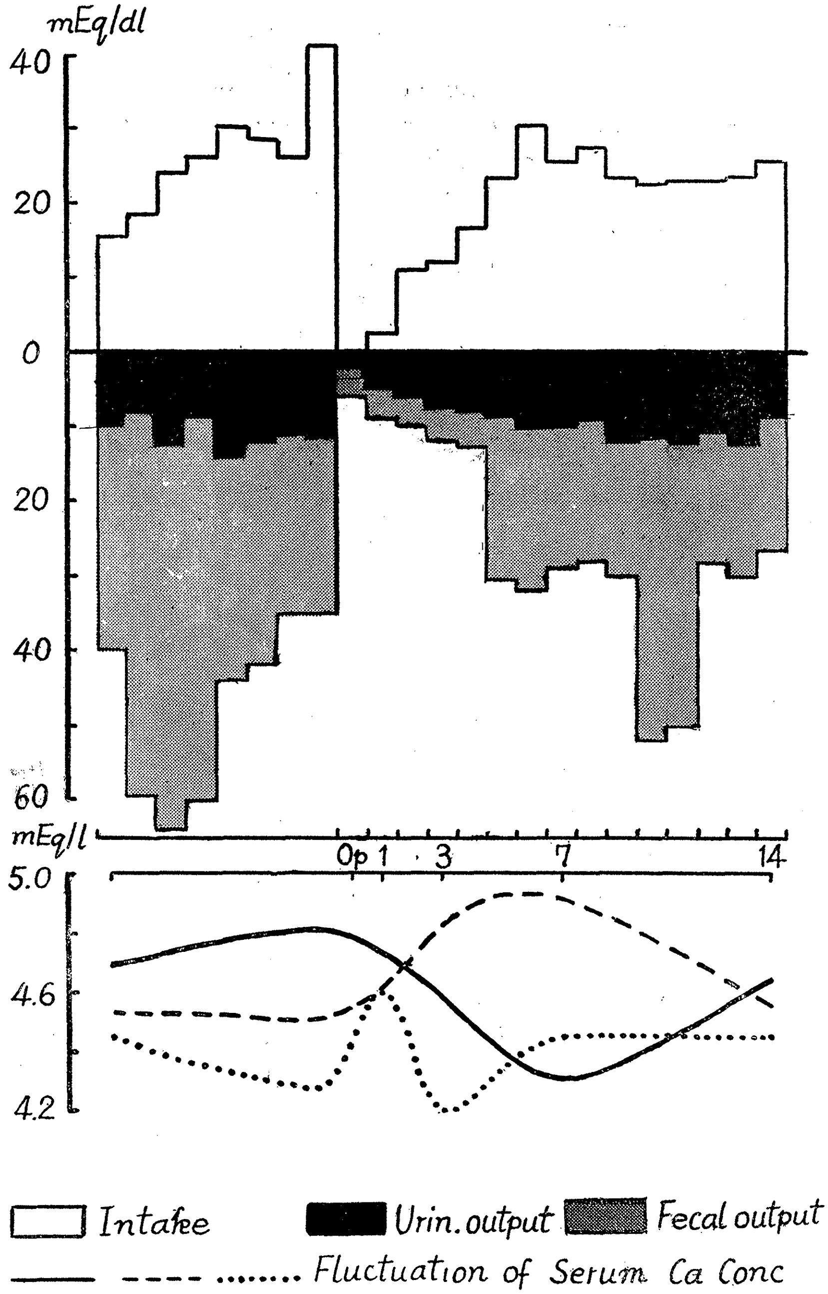

Fig. 4. Metabolic balance of calcium and its concentration in serum in surgical encroachment.

Group 1: Serum sodium exhibits the greatest alteration following the surgical operation. It drops for about a week after the operation and then rises slightly over the preoperative level for a while. Inasmuch as the sodium constitutes practically the entire serum cations, its fluctuation inevitably results in change in concentration of chloride and bicarbonate in the serum, two major anions which are in epuilibrium with the cations. The rise and fall of sodium concentration cause the parallel increase and decrease in chloride and bicarbonate concentration. The alteration in the latter electrolytes is less pronounced than in the former, beause the change in sodium concentration is divided and counterbalanced by the responses in chloride and bicarnonate separately. The marked diminution in bicarbonate concectration shortly after the operation is well attributable mainly to hyperpnea during the course of operation and to the increased production of organic acids, of lactic acid in particular. Changes in the urinary excretion of sodium, chloride and water and of their metabolic balance may be divided into four stages. (1) negative balance which continues for the first two days after the operation (the first stage), (2) positive balance which occurs for the period of the third to the fifth day (the second stage), (3) negative balance during the sixth to the eighth day (the third stage), and (4) phase of restoration which is characterized by alternation of the slightly positive and the slightly negative balance (the fourth stage).

Extreme oliguria and diminution in the urinary excretion of electrolytes without marked decrease in their concentration is characteristic of the first stage. Fasting in conjunction with decrease in the urinary volume rather than the selective inhibition of excretion of individual electrolyte from the kidneys is supposed to be responsible for the negative balance in this stage, since electrolyte concentration in urine does not differ from that of the preoperative state.

Oliguria persists in the second stage, but daily output is not quite so small as in the first stage. The oliguria in this stage is characterized by conspicuous diminution in the electrolyte concentration, presenting a sharp contrast to the oliguria in the first stage. Increase in intake (food and beverage) together with the decrease in output due to decreased loss of electrolyte and water brought about by the diminution in the urinary excretion constitutes the causative factor of the positive balance. The serum sodium concentration is low throughout the first and the second stages, as was stated in the preceding section. Sodium retention in the tissue is presumably responsible for the hyponatremia.

A considerable increase in the urinary excretion of electrolytes occurs when the postoperative electrolyte balance passes into the third stage, where a remarkable diureses with high electrolyte content is found concomitantly with the approximate re-establishment of the preoperative intake of food and beverage.

The fourth stage refers to the phase of recovery in which the balance is gradually restored to the normal epuilibrium.

Sodium concentration in the serum stays either slightly above or within the normal range, inferentially connoting the release of electrolytes into the blood, which have accumulated in the tissue during the preceding stages (sodium diuresis).

Contemplation of the current conception of renal function and endocrinology (mechanism of stress advocated by Selyé)[20] will offer an explanation of the results described above. The oliguria unaccompanied by decreased urinary concentration of electrolytes in the first stage is considered to be brought about by diminished renal blood flow which is a direct effect of the surgical encroachment, a condition which causes a uniform decrease of all the urinary constituents including water and electrolytes. Excessive liberation of adrenalin from the adrenal medulla and the stimulated sympathetic nervous system will for the most part be responsible for the diminished renal blood flow, because the fall of serum bicarbonate concentration (acidosis due to the increased production of lactic acid by adrenalin) and drop of the blood eosinophile count (destruction of the eosinophilic cells by the increased amount of glucocorticoids released from the adrenal cortex by ACTH which is secreted by the anterior pituitary by the indirect stimulation of adrenalin through the hypothalamus) are simultaneously observed in this stage.

Oliguria of the second stage is attended by the marked fall of the urinary concentration of sodium and chloride. The quantitative reduction of these electrolytes in urine is so evident that even the diminution in daily urinary volume, one of the most salient feature of the altered metabolism, may recede a little into the background. No doubt, reabsorption of sodium and chloride from the kidneys as well as their retention in tissues is playing a major role in this phenomenon, being enhanced by the increased secretion of mineralocorticoids from the adrenal cortex, which is precipitated by the stress of surgical encroachment. Exaggerated adrenocortical response constitutes, therefore, the essential part of the mobilization of endocrine system in this stage.

As soon as the endocrine function is restored approximately to the preoperative status in the third stage, both the electrolytes (sodium and chloride) and the water are released from the sites of their accumulation, i.e. from the tissues, to be discharged into the urine.[5,6,21-27]

It will be worth while to mention that sodium and chloride are the same electrolytes which constitute the key portion of the extracellular fluids.

Group 2: Contrary to the electrolytes pertaining to group 1, potassium, magnesium and phosphate, which belong to the group 2, are all alike in being the constituents of the intracellular fluids.[28] Only a minute quantity is contained in the extracellular fluids. They increase in the serum on the day following the operation, then decrease below the preoperative level and return to the original range on the seventh day or so. The concentration of non-protein nitrogen in the serum ascends on the third post operative day, and descends below the preoperative level about a week later. It is restored to the normal range in the second week.

Comparison of this fluctuation of the electrolyte concentration in the serum with the variation of electrolyte discharge in the urine reveals that the increase in the urinary excretion of potassium, phosphate, magnesium and nitrogen, or their negative metabolic balance, is associated in phase with the elevation of their concentration in the serum, while their decrease in the urine, or their positive metabolic balance, is associated with their lowered serum concentration. This will indicate that the stress of surgical operation expels the intracellular substances transitorily into the extracellular fluids (comprising the urine), but the constituents of the cell thus lost are again recovered after the effect of encroachment has passed away.

Shibusawa propounded a theory on the basis of his experimental observations that surgical encroachment provokes the secretion of antidiuretic hormone[27] from the posterior pituitary in conjunction with the release of adrenalin from the adrenal medulla as well as with the liberation of vasodilator materials from the liver. According to Selye[23] a surgical operation produces a stress which results in the increased secretion of adrenocortical glucocorticoids, the hormones accelerating the tissue destruction. Altered metabolism of electrolytes following the operation may be aptly explained from the viewpoint based on this knowledges. Oliguria in the first stage refers to the action of adrenalin and vasodilator materials, while the electrolyte retention in the second stage is related to the secretion of antidiuretic hormone and the negative nitrogen balance is attributed to the enhanced tissue destruction resulting from the release of glucocorticoids. Reparation of the tissues thus destroyed and deranged commences as the activity mobilized endocrine system subsides. Drop of serum electrolyte concentration as well as the diminution in the urinary electrolytes is a profile of the tissue destruction.

Group 3: This group has only one electrolyte, i.e. calcium, as its component. Calcium is discharged into the urine and the feces in amount roughly parallel with that of intake, without displaying any pattern specific for the operation, although its concentration in the serum may occasionally show some response which might be attributed to surgical encroachment. Such a response, if any, has not impressed us as a characteristic feature of calcium metabolism in surgical operation. This fact will be accounted for by the fact that there is a huge bulk of deposit of calcium in the bones, but these are solid architecture and are so inert to the stress that they can hardly be mobilized rapidly. The electrolytes incorporated into the first group and second group, namely sodium, potassium, chloride and bicarbonate, exist in the intra-and extracellular fluid, the liquid milieus which are apparently more sensitive to the injury and mobilizable with more rapidity. In this connection parathyroid gland which has to do with calcium, magnesium and phosphorus may deserve serious considerations.

Summary and Conclusion

Twelve patients with surgical diseases were operated on without any aid of the auxiliary treatment, either preliminary or postoperative, and they were studied for the serum electrolyte concentration as well as for the metabolic balance of electrolytes, including sodium, potassium, calcium, magnsium, chloloride, bicarbonate, phosphate and water, during the whole period of three weeks covering the preoperative (one week) and the postoperative (two weeks) stages.

The results obtained are summarized as follows: —

1) Srugical encroachment entails an orderly fluctuation of serum electrolyte concentration, which is individually specific for the relevant anions and cations, usually within the range of normal limits. Deviation of serum electrolyte concentration is supposed to be extremely rare in the routine surgical cases.

2) Three groups of electrolytes are divided according to their attitude of response to the surgical encroachment, which is presumed to be related to the property of their depot in the tissues. Sodium, chloride, bicarbonate and water are incorporated into the first group and exist in the extracellular fluids. They are deposited in the tissue for a while shortly after the operation (stage of oliguria, with and without the fall of concentration in the urine), and then discharged (stage of diuresis) until normal balance is reestablished (stage of recovery). Potassium, magnesium, and phosphate, belonging to the second group, are contained in the intracellular fluid. They are passed from the tissue into the urine and feces for a relatively short period of time immediately following the operation (stage of tissue destruction) and then they are deposited till the tissue is repaired completely (stage of reconstruction). Calcium which belongs to the third group has its depot in the bones. It exhibits no specific pattern of metabolic response to the

surgical operation.

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