Metabolic Changes Associated with Mitral Valvuloplasty

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Patients with chronic congestive heart failure operated upon for the surgical correction of mitral stenosis have been observed repeatedly to have low plasma sodium concentrations and elevated plasma potassium concentrations after operation. This study was primarily directed at an understanding of these abnormalities. The authors have shown that the preoperative patient has a characteristic disorder of body composition noteworthy for a high total body water, a high total body sodium, a low total exchangeable potassium and a low plasma sodium concentration. The effects of surgery on this abnormal body composition, and the therapeutic implications are discussed.

During recent years increasing attention has been paid to the metabolic response to a wide variety of surgical operations. It has been shown that many factors influence this response. Of these, the previous health and nutritional state of the patient, and the severity of the inflicted trauma, are probably the most important. Coincidentally with these studies, techniques have been developed for investigating the total amounts of water, sodium and potassium in the body available for exchange with suitable isotopes. Already some knowledge of the amounts of these substances present in normal individuals has been gained and is available for comparison with the measurements made in patients before and after surgical operations.

By combining the balance and isotope dilution techniques a detailed study may be made of some of the biochemical changes arising after major surgery. It is important to emphasize the dynamic character of these changes; isolated observations reveal only a static disorder, while sequential observations by these methods reveal the rapidly changing picture as each day passes. These methods are particularly valuable in investigating the complex problems that are seen after operations on the mitral valve.

In patients with mitral stenosis of such severity as to warrant surgical intervention, abnormalities in the metabolism of water and electrolytes are already present and the nutritional state has frequently considerably deteriorated as the result of longstanding heart failure. The stress of operation is then superimposed, and it is not surprising that in the postoperative period gross biochemical disturbances may become apparent. The present study is an attempt to elucidate the nature and mechanisms of some of these disturbances.

Methods and Material

The metabolic balance studies were carried out following the principles described by Moore and Ball. The intake of sodium, potassium and nitrogen in the diet has been calculated from food analyses carried out in this laboratory. The intravenous intake given therapeutically or for the performance of various investigations has also been measured. In the case of blood transfusions, which were frequently large, only the readily available nitrogen, sodium and potassium in the plasma have been entered in the balance chart. Similarly only the plasma fractions of these constituents in the operative blood loss have been entered. The total amount of whole blood transfusions and blood loss have been indicated, however, in the legends of the charts. In calculating the total excretion, account has been taken of loss in the urine, feces, wound exudate and fluid drained from the chest.

The method of charting the metabolic balance is essentially that described by Moore and Ball.

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The intake is charted upwards from the zero line and the output downwards from the top of the intake line. A positive balance is indicated by a shaded area above the zero line, a negative balance by an area below the zero line and enclosed by heavy lines.

The body content of water, sodium and potassium has been measured by dilution of deuterium oxide, sodium\(^{23}\) (Na\(^{23}\)) and potassium\(^{39}\) (K\(^{39}\)). The details, accuracy and reproducibility of these technics have been described previously.\(^{2,4\text{-}8}\) The measurements of total exchangeable sodium and potassium have, for the most part, been carried out simultaneously.\(^9\)

The chemical methods used in the metabolic balance studies have been previously described.\(^1\) Urinary excretion of 17-ketosteroids was measured by the method of Talbot\(^{19}\) and of 17-hydroxycorticoids by the method of Reddy, Jenkins, and Thorn.\(^{11}\)

**Clinical Details**

The study is based essentially on the investigations of three patients by metabolic balances (cases 1, 2, and 3) and on isotope dilution measurements made at intervals on these and nine other patients (cases 4 through 12). In case 12 only preoperative measurements were available as the patient died shortly after operation from cerebral embolism. The clinical details are mentioned in the text where applicable. In addition, studies of water metabolism and changes in blood chemistry as a result of operation have been carried out in an additional 81 patients. All were relatively severe cases of mitral stenosis falling into groups III and IV.\(^{12}\) Mitral stenosis was the predominant lesion in all. In some, minor degrees of aortic and mitral incompetence were also present. Except for one of the balance patients (case 1) all have been studied during the relatively cool period of the year from October to March. The patients were brought into the best possible condition for surgery by medical treatment with digitalis, mercurial diuretics and low salt diets before the preliminary preoperative measurements were made. Blood transfusions were given liberally in an attempt to cover the loss at operation and later. The volume of these transfusions and of the other fluids given to the patients immediately after operation was changed at definite intervals. The nature and effects of these alterations in treatment policy will be described later. During the immediate pre- and postoperative periods the dietary sodium intake was restricted to approximately 9 mEq. a day except in cases 1 and 2 where the intake was larger, as described in the metabolic balance studies.

**General Metabolic Changes**

The general metabolic course of patients undergoing mitral valvuloplasty is best illustrated by the balance studies. Cases 1, 2, and 3 are accordingly described briefly in this section; certain aspects are discussed later in greater detail in the next sections along with the findings in the larger groups.

**Case 1** (fig. 1 A, B, C). The patient, a woman 45 years of age, underwent operation May 19, 1952. She had rheumatic fever at the age of 12; at the age of 35 she suffered a right hemiplegia, apparently embolic in origin. In the ensuing 10 years her course was one of gradual deterioration; digitalis, diuretics and sodium restriction were employed. Dyspnea, orthopnea and ankle edema followed; she was fibrillating on admission and showed marked enlargement of liver and spleen, with wasting of the body. Her peripheral edema had disappeared when the study was begun. Clinical and radiologic signs of mitral stenosis were typical. Operation was technically satisfactory and convalescence uneventful save for a small pulmonary embolus on the sixteenth postoperative day. She was readmitted for follow-up study four months later (Sept. 23, 1952) at which time her exercise tolerance was vastly improved; there was no further orthopnea. She was still fibrillating; liver and spleen were still enlarged.

The balance of nitrogen demonstrated a transient negative phase with high excretion on one day and a rapid return to positive balance as her intake improved with resumption of calorie intake. Potassium followed a similar pattern. Sodium intake was restricted throughout, but the balance was consistently positive except for the first day after operation. Body weight showed an increase for three days postoperatively, then a sharp reduction followed by a later rise. Eosinophile count was near zero for two days after operation, then returned sharply to normal or above normal values save for two days immediately preceding her pulmonary embolus. Urinary steroid analyses showed elevation of the 17-ketosteroids on the first postoperative day; there was an increase in 17-hydroxycorticoids persisting three days and then falling slowly to the subnormal starting values.

Intake-output fluid balance (fig. 1C) was not remarkable; the initial total body water and total exchangeable sodium were elevated; the total exchangeable potassium was slightly low. Following operation, body water and sodium further increased as potassium decreased. On late follow-up (128 days), a return of total body water to the lowest recorded fraction of body weight (55.4 per cent) was accompanied by a fall in total exchangeable sodium and a rise in total exchangeable potassium.

The serum concentrations of sodium and potassium showed changes in opposite directions, the sodium falling and potassium rising postoperatively, and later returning towards normal. Both were normal initially.
Case 2 (fig. 2A, B, C). The patient, a 40 year old woman, was operated upon Oct. 31, 1951. With no previous history of rheumatic fever, this patient was first told that she had a cardiac murmur in 1948. Within a year she noted increasing dyspnea and palpitation, and was digitalized. In 1950 she had a cerebral embolus, with left hemiplegia and gradual recovery. Disability increased although she maintained her occupation as a typist; digitalis, ammonium chloride and diuretics were used. She was thin and emaciated with a residual left-sided weakness. Typical signs of mitral stenosis were present with hepatomegaly, and cardiac enlargement. Operation was technically satisfactory; convalescence was uneventful. Her first readmission for follow-up was on Feb. 10, 1952, 105 days after operation. There was no edema. Exercise tolerance was greatly improved. Cardiac signs were unchanged. She was again studied on Oct. 31, 1952 (365 days after operation). There was still further conspicuous improvement. She was leading a normal life, symptom-free on digitalis.

Balance of nitrogen was consistently positive; there was no increase in excretion rate after operation. Potassium balance was close to zero save for a considerable period after surgery. Sodium balance showed a positive trend save for a spontaneous diuresis beginning on the fifth postoperative day,
METABOLIC CHANGES IN MITRAL VALVULOPLASTY

Fig. 2. (A) Case 2. Metabolic balance chart. The operative blood loss was 225 ml. and the blood transfusion at operation 500 ml. Further details are described in the text. (B) Case 2. Cumulative balances and serum electrolyte changes. (C) Case 2. Changes in fluid balance, body composition and serum electrolytes.

lasting four days, accounting for 500 mEq. of sodium, and towards the end of which Mercuhydrin was administered. Following this episode excretion rates again became very small. There had previously been (five days before operation) a one-day sodium diuresis (100 mEq.) on Mercuhydrin. Body weight changes followed the sodium balance; there was again in this case a postoperative weight gain, dropping abruptly during diuresis, and then rising slowly during the ensuing year. Eosinophil count was moderately low (75 to 125 cu. mm.) until operation when it dropped to near zero for three days, and then rose to values higher than those seen preoperatively. Caloric intake was never seriously impaired. Urinary steroids were not measured.

Intake-output fluid balance showed the postoperative water loading with large fluid intakes,
and later diuresis. The starting total body water and total exchangeable sodium were elevated; the total exchangeable potassium was low. These measurements were not repeated until after her diuresis and from that time a gradual and consistent approach of all these measurements toward normal was seen.

The serum concentration of sodium was initially near normal and fell abruptly to 125 mEq. per liter during the postoperative period of water and salt loading; there was then a rise and later a small dip at the very end of diuresis; only at this later time did potassium rise. These values were later normal.

Case 3 (figs. 3, 4 and 5). This patient, a woman aged 50 years, was operated upon Nov. 29, 1952. She recalled having had chorea in childhood; at the age of 15 she noticed dyspnea and palpitation on exertion; these symptoms gradually progressed. At the ages of 22 and 24 she had two normal pregnancies, and was adjusted well to her disease until the age of 42 when orthopnea and paroxysmal nocturnal dyspnea began. During the 18 months prior to admission there was rapid deterioration so that walking on the level was difficult despite digitalis and a low salt diet. She was a thin, slightly wasted woman, without edema. Auricular fibrillation, enlarged heart and liver and murmurs both systolic and diastolic were present. Operation was technically satisfactory. There was a six-day febrile period after operation during which the patient was anorexic; thereafter improvement was uninterrupted although her appetite remained poor. She was readmitted June 19, 1953 (156 days later), for

![Fig. 3. Case 3. Metabolic balance chart. The operative blood loss was 334 ml. and the blood transfusion at operation 2500 ml. Further details are described in the text.](image)

![Fig. 4. Case 3. Cumulative balances and serum electrolyte changes.](image)

![Fig. 5. Case 3. Changes in fluid balances, body composition and serum electrolytes.](image)
Exercise tolerance was tremendously improved and she was leading a normal life. She had not regained her preoperative weight and was anorexic, possibly because of digitalis overdosage; cardiac signs were unchanged.

Balance of nitrogen demonstrated a marked increase in excretion rate, low intake, relative caloric starvation and marked negative balance for eight days after operation. Thereafter, excretion was less marked but balance was still negative up to discharge; daily caloric intake rarely exceeded 1000. Potassium balance was essentially zero for the duration of study. Sodium balance was a spectacular example of conservation with zero intake. Save for the day of operation when blood transfusions increased sodium intake and the following day when some sodium was lost through drainage from the chest there was a remarkable lack of sodium intake or loss. For a period of 16 days there was a total of only 160 mEq. flux with the environment, and net zero balance. Body weight rose in the early postoperative period, then fell suddenly with a large water, nitrogen and potassium loss. Thereafter, it slowly declined during the period of observation. Eosinophile count showed an operative full. It did not at any time thereafter rise to high levels. Urinary steroid analyses showed a slight rise in 17-ketosteroid excretion over the otherwise abnormally low levels. The 17-hydroxycorticoid excretion was greatly increased for six days and intermittently elevated for eight more days.

Intake-output fluid balance (fig. 5) showed water loading for six days after operation, then a diuresis for two days, followed by normal balance. The initial total body water was not elevated, but on the fifth postoperative day it was increased by 2.3 liters, which was later excreted in the urine. At follow-up five months after operation the total body water was within the normal range. Total exchangeable sodium was elevated at the outset, and remained about the same until follow-up when it was reduced to normal. The total exchangeable potassium was low throughout.

The serum concentrations of sodium and potassium showed the conspicuous "diamond-shaped" configuration of inverse changes seen previously. The sodium, initially normal, fell to 122 mEq. per liter. This change was maximal by the second and third postoperative day, later returning to normal values.

In summary it is apparent from the metabolic studies that the response with regard to nitrogen balance, eosinophile counts and urinary steroid excretion is not beyond the range of expectation for surgical operations of similar severity.1 23 On the other hand, there are conspicuous abnormalities in body composition before operation and considerable disturbances in salt and water metabolism in the early postoperative period. The tendency towards lowering of the plasma sodium concentration is truly remarkable; it is often accompanied by an elevation of the plasma potassium concentration.

This disorder has been the source of considerable difficulty in treatment and speculation as to pathogenesis. While a lowering of the plasma sodium concentration during positive sodium balance is a normal feature of post-traumatic metabolism (the "sodium paradox"), it does not usually occur to such a marked extent and is ordinarily not accompanied by such a marked hyperkaliemia. These aspects have accordingly been studied in greater detail in a larger group of patients.

Preoperative Body Composition

The clinical study of body composition has been greatly extended by the development of the isotope dilution methods.7 8 The measurement of total body water,7 8 total exchangeable sodium and potassium7 4 5 9 15 17 permit the observer a remarkable insight into body composition as regards four of its most significant parameters: water, extracellular "mass" (sodium), lean tissue mass (potassium) and fat (by inverse proportion to water content).

Measurements of total body water, exchangeable potassium and exchangeable sodium were made in 12 patients before and at intervals after operation. The results are shown in table 1. In all cases except case 12 there was no peripheral edema at the time of the first measurements. The results in the female patients before operation are compared with those obtained in healthy adults in table 2. The mitral stenosis patients have a definite excess of total water and sodium in their body composition. The total exchangeable potassium is slightly diminished, but this decrease only attains a low degree of significance by statistical comparison. In case 6 no preoperative determination of total potassium was made. Only three male patients with mitral stenosis were studied with isotopes, and in them the changes in body composition were similar to those seen in the females, but the group is too small for detailed statistical analysis. The total exchange-
### Table 1—Isotope Dilution Measurements before and after Mitral Valvuloplasty

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<td>41.25</td>
<td>130</td>
<td>1871 45.4</td>
<td>5.0</td>
<td>1306 33.8</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>+14</td>
<td>41.40</td>
<td>135</td>
<td>1955 47.2</td>
<td>5.0</td>
<td>1468 35.5</td>
</tr>
</tbody>
</table>
able sodium on a milliequivalent per kilogram basis was exceptionally high in cases 11 and 12. No peripheral edema was present in case 11, but this patient was emaciated. In case 12 the high total sodium was associated with slight pitting edema at the ankles, but considerable wasting was also present.

In all those with mitral stenosis the normal ratio between total exchangeable sodium and potassium was lost. In healthy females the ratio of exchangeable sodium to exchangeable potassium is 1.02 while in healthy males it is 0.90. The corresponding ratios in the female and male patients with mitral stenosis were, respectively, 1.25 and 1.33, indicating a relative excess of sodium over potassium in their body composition.

In the comparisons shown in table 2 the only figures available for healthy adult females refer for the most part to a group with a mean age younger than that of the mitral stenosis patients. However, in the case of total body water there is probably a slight decrease with advancing years, which renders the differences more striking. Little is known about the alterations in total exchangeable sodium and potassium with increasing age, but the available evidence does not suggest that there is any definite change between the third and fifth decades. For ease of reference the normal body composition of a healthy adult of similar weight to the patient with mitral stenosis has been calculated and is shown on the chart for comparison with the preoperative and later results (figs. 1C, 2C, 5 to 8, 11 and 12). The values shown in table 2 have been used for this purpose in females. The corresponding values for healthy young adult males are: total body water 62.0 per cent of body weight, exchangeable sodium 41.4 mEq. per kilogram, exchangeable potassium 46.8 mEq. per kilogram.2

Postoperative Changes

Changes in Body Weight and Total Body Water. In the first six cases in which total body water was measured (cases 1 to 6 in table 1) the fluid intake in the immediate postoperative period was unrestricted. In these circumstances there was regularly an increase in weight after operation in spite of the negative nitrogen balance. Normally patients lose weight after surgery as a result of a number of factors.1,21 It is an outstanding abnormality of surgical metabolism for body weight to increase after operation. This was clearly due to water retention as was confirmed by the observations with deuterium oxide (figs. 1C, 5, 6, 9, and table 1). In cases 1, 3, 4, 5, and 6 measurements made within six days of operation all showed an increase in the total body water over the preoperative value. In
TABLE 2.—Body Composition of Female Mitral Stenosis Patients before and after Operation in Comparison with Healthy Adult Females

<table>
<thead>
<tr>
<th></th>
<th>Body Water</th>
<th>Exchangeable Sodium</th>
<th>Exchangeable Potassium</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No.</td>
<td>Age</td>
<td>% Body Weight ± s.d.</td>
</tr>
<tr>
<td>Healthy females*</td>
<td>24</td>
<td>29.7</td>
<td>50.5 ± 4.7</td>
</tr>
<tr>
<td>Mitral stenosis before oper-</td>
<td>9</td>
<td>43.2</td>
<td>54.5 ± 5.1</td>
</tr>
<tr>
<td>ation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mitral stenosis</td>
<td>7</td>
<td>41.0</td>
<td>52.0 ± 5.4</td>
</tr>
<tr>
<td>3-6 mos. after operation</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* The figures for total body water and for exchangeable potassium in healthy females are taken from previously published results obtained in this laboratory.† The figures for exchangeable sodium are a combination of the results in seven females reported by Forbes and Perley and in five females studied in this laboratory; there was close agreement between these two series.

case 2 the measurement was made eight days after operation following a large water diuresis and an increase was not seen (fig. 2C). It is thus clear that in patients allowed unrestricted access to fluids, water retention readily occurred after operation even though the sodium intake was severely restricted. For example in case 3 there was a gain in total body water of 2.3 liters as measured on the fifth postoperative day, but the isotope studies showed an increase in exchangeable sodium of only 22 mEq and by cumulative balance an increase of 55 mEq. Similarly, in all the other cases studied water was retained in considerable excess of sodium. The water retention persisted in these cases for the first week after operation but thereafter subsided. The measurements had all fallen to about the preoperative value by the time of discharge from the hospital which was usually between two and three weeks after operation.

In cases 7 through 11 the fluid intake was restricted to 1500 ml. a day for the day of operation and the early postoperative days. This figure does not include restoration of the operative blood loss and chest drainage fluid which were approximately covered by blood transfusions. In these cases with a strictly regulated fluid intake there was a steady loss of weight after operation and the total body water measurements no longer showed any definite increase but remained either approximately un-

![Fig. 6. Case 5. Charted as in figure 1C. The postoperative water loading, later excreted, with associated weight change is shown. The inverse sodium-potassium relationship in the serum is characteristic. The initial body composition shows an elevation in body sodium and a lowering of body potassium. In late convalescence (167 days after operation) body weight has increased significantly with a fall in total exchangeable sodium, and a rise in total exchangeable potassium. Although the absolute body water content has increased, the relative fraction (52.5 per cent of body weight) is at its lowest observed value, suggesting that body fat has been deposited.

Water Excretion in Relation to Total Body Water. The changes in total body water occur-
ring shortly after operation can be correlated with water retention as shown by plotting the fluid intake and the urine output as a "balance." This clearly takes no account of extrarenal fluid loss, but nevertheless it shows that in those cases with considerable increases in total body water after operation there was a great excess of fluid intake over urine output (figs. 5 and 6). This was most noticeable during the day of operation and the first postoperative day when the urine output was always low even though the intake was extremely large. On the other hand the patients with a restricted fluid intake still maintained in this immediate postoperative period a urine volume similar to that seen in the unrestricted patients. In consequence there was no gross excess of fluid intake over output and no rise in total body water (figs. 7, 8, 9).

The ability of the kidney to excrete water during the first few days after a mitral valvuloplasty was studied more extensively by comparing three groups (30 cases each) in whom varying policies were followed with regard to fluid administration (table 3). All were investigated during the winter months when large cutaneous losses of water due to hot weather may be excluded. In one group of cases studied during this period (January to March, 1953), the mean total fluid intake exclusive of blood
transfusion for the day of operation and the two succeeding days was 4400 ml., and the urine output 1750 ml. In the other two groups the patients were allowed to drink freely; intravenous infusions of 5 per cent dextrose solution were frequently given and the fluid intakes were consequently much larger. In the period October 1952 to January 1953, the mean intake of 30 cases was 7610 ml. over the same three days while the urine output was 2340 ml. Thus an increase of 3210 ml. in intake was only associated with a gain of 850 ml. in urine volume. Similar results were obtained in a group of 30 cases with unrestricted fluid intake studied a year earlier in the months January to March, 1952. In comparison with the restricted cases in the first group the intake in this third group was greater by 3460 ml. but the urine output only by 810 ml. The individual figures in these 90 cases are shown in figure 9, where it is apparent that in the majority of cases the kidneys were not able to respond proportionately to a large water load in the immediate postoperative period.

**Sodium Metabolism.** This was investigated by balance studies, by frequent measurements of serum sodium concentrations and by determinations of total exchangeable sodium at approximately weekly intervals. The sodium intake in all the cases was restricted, though to a variable degree. In cases 1 and 2, studied by both balance and isotope dilution technics, the sodium intake was approximately 40 mEq. a day (figs. 1A, and 2A). In case 3, also studied by both methods, the intake was only 9 mEq. a day (fig. 3) and a similar restriction was applied to cases 4 to 11 in whom isotope studies only were carried out.

In case 1 the patient was steadily retaining sodium both before and after operation as is shown in the cumulative balance chart (fig. 1B). This sodium retention continued up to the time of discharge from the hospital. In case 2 there was similarly preoperative retention of sodium, interrupted transiently by an injection of Mercuhydrin (fig. 2B). After operation sodium retention continued at approximately the same rate, but on the fifth day after operation a spontaneous sodium diuresis began and 500 mEq. were excreted in five days. Towards the end of the sodium diuresis an injection of Mercuhydrin was given, but this was clearly only responsible for a small part of the sodium excretion. Subsequently up to the time of discharge from the hospital there was a further period of steady sodium retention. In both these cases the isotope measurements confirmed the increase of sodium in the body (table 1). The initial preoperative measurements of total exchangeable sodium were in the upper part of the normal range and the further sodium retention accordingly led to unduly high values. In spite of this evidence of a growing excess of sodium in the body, the serum sodium concentration fell significantly after operation (figs. 1B, 2B). In case 1 this fall was from 138 mEq. per liter to 125 mEq. per liter, and in case 2 from 140 mEq. per liter to 125

---

**Table 3.** Changes in Urine Output and in Blood Chemistry Compared with Different Fluid Intakes. The Fluid Intakes and Urine Outputs Represent the Totals for the Day of Operation and the Two Succeeding Days

| Period of Study | No. of cases | Fluid intake for 3 days ml. | Blood transfusion ml. | Blood and Serum Chemistry
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>F</td>
<td>M</td>
<td>Total</td>
<td>Age Yrs.</td>
</tr>
<tr>
<td>Gr. 1. 1/53 to 3/53</td>
<td>Mean s.d.</td>
<td>24</td>
<td>6</td>
<td>30</td>
</tr>
<tr>
<td>Gr. 2. 10/52 to 1/53</td>
<td>Mean s.d.</td>
<td>25</td>
<td>5</td>
<td>30</td>
</tr>
<tr>
<td>Gr. 3. 1/52 to 3/52</td>
<td>Mean s.d.</td>
<td>20</td>
<td>10</td>
<td>30</td>
</tr>
</tbody>
</table>
TABLE 4.—Comparison of Decreases in Serum Sodium and Chloride Concentrations on Second Postoperative Day in Three Groups of Patients Receiving Different Fluid Intakes
(See table 3 for details)

<table>
<thead>
<tr>
<th>Changes in Serum Sodium</th>
<th>Changes in Serum Chloride</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean decrease in serum sodium</td>
</tr>
<tr>
<td></td>
<td>± s.d. mEq./L.</td>
</tr>
<tr>
<td>Group 1. Restricted fluids</td>
<td>6.3 ± 4.4</td>
</tr>
<tr>
<td>Group 2. Unrestricted fluids</td>
<td>9.6 ± 3.4</td>
</tr>
<tr>
<td>Group 3. Unrestricted fluids</td>
<td>10.4 ± 6.3</td>
</tr>
</tbody>
</table>

![Graph](image)

Fig. 10. Relationship between serum sodium change (abscissa, in mEq. per liter) and excess of fluid intake over output (ordinate, in liters) based on the same three-day periods, indicated in figure 13. Data are based on the same 90 patients shown in figure 13. It will be noted that as fluid intake exceeds output by greater volumes, there is a tendency to lower the serum sodium more markedly. However in the lower intake ranges (excess over output being 2.5 liters or less) considerable drops may still be seen and correlation is less clear cut.

mEq. per liter. The levels were restored slowly after operation. In case 2 it is of considerable interest that the rise in serum sodium concentration began immediately before and continued during the large sodium diuresis (fig. 2B).

In the other cases with the more severely restricted sodium intake there was no opportunity for any significant degree of sodium retention. In case 3 the cumulative balance (fig. 4) and the isotope dilution studies (table 1) showed no sodium depletion. Nevertheless, after operation the serum sodium concentration fell sharply from 141 mEq. per liter to 122 mEq. per liter (fig. 5). Thereafter it rose slowly and was finally restored to the preoperative level. The large changes in serum sodium concentration observed in this case clearly occurred without any significant changes in the amount of sodium in the body. Similar observations were made in cases 4, 5 and 6 in whom definite postoperative decreases in serum sodium developed with, at the same time, slight increases in the total exchangeable sodium (table 1 and fig. 6).

In cases 1 to 6 fluid was given freely, but even when the fluid intake was restricted so that there was a progressive fall in body weight and no increase in total body water after operation the serum sodium concentration still fell (fig. 7). Further evidence was sought by comparing measurements made preoperatively and on the second postoperative day in the three groups of cases, 90 in all, described above (table 3). In the two groups with unrestricted fluid intakes the decreases in serum sodium were greater than in the group with restricted fluid intake. Specifically, the unrestricted groups showed mean postoperative serum sodiums of 127 and 128 mEq. per liter while the restricted group was 131 mEq. per liter. These are averages of three groups of 30 cases each. Statistical analysis shows that these differences are significant (table 4), and in both instances the comparisons contrast unrestricted fluid regimens with the restricted group. There is thus some relation between the excess of fluid intake over urine output and the extent of the decrease in serum sodium concentration. The larger falls in serum sodium were usually seen in those patients showing considerable fluid retention (fig. 10). It is, how-
ever, quite clear that decreases in serum sodium concentration still occurred even in the presence of a low fluid intake and adequate urine volume.

**Persistent Low Serum Sodium Concentrations.** It is to be emphasized that in the majority of cases the transient fall in serum sodium characteristically observed after operation was not associated with any loss of sodium from the body and occurred in patients having adequate amounts of total exchangeable sodium. Usually the serum sodium began to rise on the fourth or fifth postoperative day and thereafter steadily climbed to the normal range. However, in a certain number of cases the serum sodium level either before or after operation was persistently low. This condition was particularly seen in severely disabled patients kept strictly on a low sodium diet and treated vigorously with mercurial diuretics. In them the measurements of total exchangeable sodium often showed some evidence of salt depletion. The following case is illustrative of those few which showed sodium depletion prior to operation.

**Case 8** was that of a female with severe mitral stenosis and auricular fibrillation who had been treated with a low salt diet for six months prior to operation. On admission to the hospital there was no peripheral edema but there was hepatomegaly and considerable pulmonary congestion. She was accordingly given several injections of Mercuhydrin before operation (fig. 11). On the day before operation the serum sodium was only 133 mEq. per liter and the total exchangeable sodium was 1575 mEq. or 33.5 mEq. per kilogram, a low figure for a person of her slim build. After operation the fluid intake was restricted to 1500 ml. a day; there was a slow loss of weight and a slight gain in total body water. The serum sodium fell to 125 mEq. per liter in which region it remained for nine days in spite of a highly successful valvuloplasty. A total exchangeable sodium measurement on the seventh postoperative day showed an increase of 78 mEq., confirming that the losses of sodium from hemorrhage at operation and in chest drainage fluid had been adequately restored. During this period she was clearly not making good progress. She could only think and speak slowly though there was no evidence of any definite paralysis. She was largely indifferent to her surroundings and was frequently incontinent of urine.

On the tenth postoperative day she was given an infusion of 3 per cent sodium chloride yielding 240 mEq. of sodium. During the 24 hours from the beginning of this infusion the total fluid intake was 1250 ml., and the urine output of 650 ml. contained a total of 7 mEq. of sodium. Thus 237 mEq. of sodium was retained in the body after 24 hours; at the same time the serum sodium had risen from 125 mEq. per liter to 131 mEq. per liter. Thereafter there was a great improvement in her general condition and a slow steady rise in the serum sodium concentration to 142 mEq. per liter even though the sodium intake was kept at 9 mEq. a day. The total exchangeable sodium, measured five days after the infusion, when the serum sodium had reached 138 mEq. per liter, was 1855 mEq., an increase of 202 mEq. over the reading before the infusion. At the same time the total body water had increased by 0.9 liters. Further measurements were made 118 days after operation, when she was
METABOLIC CHANGES IN MITRAL VALVULOPLASTY

in excellent health, had gained 12.5 Kg. in weight and had an enormously improved exercise tolerance. The results at this time are shown in table 1, and, using these figures for comparison, there is evidence that there was a deficiency of sodium in the body when she came to operation. At that time she had 1575 mEq. of exchangeable sodium in contrast to 1915 mEq. when she was in good health. Normal serum sodium concentrations were only attained when this deficiency was restored.

Similar features were seen in case 9, a female with a tight mitral stenosis, minimal aortic regurgitation and auricular fibrillation. On admission the serum sodium concentration was 140 mEq. per liter and the total exchangeable sodium 2210 mEq. or 49.6 mEq. per kilogram. She was treated preoperatively on a 9 mEq. a day sodium diet, mercurial diuretics and ammonium chloride. On this regime the total body water did not change but the serum sodium concentration fell to 133 mEq. per liter before operation (fig. 8). The estimated loss of sodium through hemorrhage and chest drainage was about 150 mEq, but she only received about 90 mEq. in the transfusions given at operation. The postoperative measurement of total exchangeable sodium was only 1871 mEq., a decrease of 348 mEq. The serum sodium concentration fell to 125 mEq. and was unduly slow in returning to the normal range, reaching only 135 mEq per liter on the fourteenth postoperative day; at this time the sodium deficiency was still 264 mEq. in comparison with the preoperative reading. In this case the large sodium loss resulting from the mercurial diuretics and operation apparently impeded the restoration of the serum sodium concentration.

In the two cases described above fluid intake was restricted to 1500 ml. a day, and there was no evidence of water retention when the serum sodium concentration was persistently low. Retention of water without sodium may, however, occur preoperatively as is illustrated in the following case.

Case 11 was that of a male who had been severely disabled with mitral stenosis and auricular fibrillation for several years. During the last two years his condition deteriorated rapidly and for some time before study he was confined to bed with extreme respiratory distress even at rest. He had lost a large amount of weight. On admission, he was grossly emaciated, there was some peripheral edema and the serum sodium was 138 mEq. per liter. After treatment with mercurial diuretics and restriction of sodium intake to 9 mEq. per day the peripheral edema disappeared but the serum sodium fell. When the detailed preoperative studies were begun (fig. 12) the serum sodium was 134 mEq. per liter, the total exchangeable sodium 2507 mEq., or 64.9 mEq. per kilogram and the total body water 26.1 liters. His condition began to deteriorate further and he became more breathless, apathetic and disoriented. He slowly gained weight. A week later the serum sodium was 126 mEq. per liter, the total body water 29.4 liters and the total exchangeable sodium 2501 mEq. Thus he had gained 3.3 liters of water without any increase in body sodium. After this measurement his fluid intake was restricted to 1 liter a day, he lost weight and the serum sodium concentration rose slightly. There was some improvement in his general condition and a successful valvuloplasty was carried out under local anesthesia despite the apparently preterminal state of the patient. The fluid restriction was continued, there was no further fall in serum sodium concentration and there was a conspicuous improvement in his condition. The total body water on the third postoperative day was 26.3 liters. Subsequently the serum sodium concentration rose

Fig. 12. Case 11. Charted as in figure 1C. Clinical details are described in the text. Serum electrolytes show change similar to case 8, figure 11; sodium is low preoperatively and goes lower as weight and water are gained; postoperative changes are not marked. The potassium is initially high but postoperatively does not rise further. Starting body composition is remarkable for its large excess of sodium, and the remarkably low body potassium as postoperative changes become apparent. The total body water at 74.7 per cent of body weight is among the highest observed, and was borne out by the remarkable cachexia seen clinically. In late convalescence (114 days) weight gain has been marked (11 Kg.); the water fraction has fallen to 61.6 per cent of body weight. Although the progression of body composition toward normal has been great, the patient at this time still has a relatively high total body water, and his body sodium-potassium ratio is still elevated.

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steadily to normal, and there were small increases in total body water and exchangeable sodium. On the thirtieth postoperative day he was changed to a high calorie diet with a sodium intake of 35 mEq. a day. Thereafter, while in the hospital, he gained weight steadily with only slight further increases in total body water and exchangeable sodium but a considerable rise in total exchangeable potassium. In this case the results suggest that there was a small deficiency of sodium in the body before operation when the serum sodium was low despite the apparently high figure for exchangeable sodium on a body weight basis. The striking feature, however, was the ease with which he retained water at this time, leading to a further depression of the serum sodium.

Potassium Metabolism. This was investigated by the same methods as in the sodium studies. In all cases there was a loss of potassium from the body after operation clearly shown in the balance studies and confirmed by the isotope dilution measurements (figs. 1A, 2A, 7 and table 1). Coincident with this large excretion the serum potassium concentration rose. This was a constant finding in all the cases studied (figs. 1C, 2C, 5–8). The increased potassium excretion was at its greatest on the day of operation despite the oliguria and did not persist after the operation. The extent of the rise in serum potassium concentration could not be correlated with the amount of blood transfused at operation, the fluid intake in the immediate postoperative period or the volume of urine excreted (table 3). There appeared to be a definite inverse relationship to the serum sodium concentration, as the largest falls in the latter were invariably accompanied by considerable increases in the serum potassium concentration. Furthermore in those cases where the serum sodium concentration was persistently low either before or after operation the serum potassium remained consistently high (figs. 8, 11, 12) and only fell when the serum sodium concentration rose.

Correlation of Isotope and Balance Measurements of Sodium and Potassium. In cases 1 to 3 the results of the isotope dilution studies may be checked against the cumulative metabolic balances for sodium and potassium. This comparison is summarized in table 5 where the changes from the preoperative to the last measurement before discharge from the hospital are shown. During this period of three to four weeks there is good agreement between the sodium measurements. In two of the potassium studies the correlation is also reasonably close, but in case 3 there is some discrepancy between the two methods, the isotope measurements showing a greater loss of potassium than can be accounted for in the balance study. The extent of agreement that may be anticipated between the two methods has been more fully reviewed elsewhere.13, 14, 15

Chloride Metabolism. This has been studied only by measurement of serum concentration before and after operation. In general the changes ran parallel to those found in sodium concentrations. After operation there was a considerable fall (table 3), and this was affected in the same way as the sodium by restricting the fluid intake (table 4). The scatter in the chloride determinations was, however, greater and the changes do not attain such a high degree of significance.

Changes in Blood Urea Nitrogen. These were studied in the three groups of cases shown in Table 3. There was invariably a rise in blood urea nitrogen after operation related to at least two factors, namely the size of the blood transfusions given at operation and the fluid intake and urine output after operation. The rise was least in group 3 where the smallest blood transfusions were given and fluid intake was unrestricted; in both groups 1 and 2 the rises were larger and approximately similar, but in the group 2 cases the blood transfusions and fluid intake were greater than in the group 1 cases.

<table>
<thead>
<tr>
<th>Case</th>
<th>Interval, days</th>
<th>Change in Sodium</th>
<th>Change in Potassium</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>21</td>
<td>+250 mEq.</td>
<td>+208 mEq.</td>
</tr>
<tr>
<td>2</td>
<td>28</td>
<td>+250 mEq.</td>
<td>+198 mEq.</td>
</tr>
<tr>
<td>3</td>
<td>22</td>
<td>+76 mEq.</td>
<td>+189 mEq.</td>
</tr>
</tbody>
</table>

Table 5.—Comparison of Changes in Sodium and Potassium in the Body as Measured by Metabolic Balance and Isotope Dilution
Changes in Late Convalescence

Nine patients returned for further studies between three and six months after discharge from the hospital. In all a good functional result had been obtained. Their exercise tolerances were greatly improved. In the majority (cases 1, 2, 4, 5, 7, 8, and 11) there was a corresponding improvement in nutritional state following the operation. The striking features were the gain in weight and the return of the body composition toward normal (table 1 and figs. 1C, 2C, 5-7, 11, 12). In case 6, however, convalescence had been complicated by the development of two attacks of pneumonia and pleurisy. She had lost weight and her general condition had deteriorated in spite of considerable relief of her dyspnea. Her body composition was still abnormal. In case 3, although the cardiac symptoms had greatly improved so that she was able to lead a practically normal life, there was persistent anorexia after operation, possibly due to high digitalis dosage, and she had failed to gain weight.

The results in seven female patients, three to six months after operation, are shown compared with the healthy adults and the preoperative measurements in table 2. Case 6 has been excluded from this group as she was not fully recovered from the pneumonia when the measurements were made. These patients now show no significant differences as regards body composition in comparison with the healthy adults. In case 1 a further study was possible one year after operation; she continued to gain weight and lose sodium over this period. In the male patient, case 11, who had been greatly emaciated, some restoration of body composition towards normal had occurred after 114 days (fig. 12). Even though he had gained over 10 Kg. in weight the process was still clearly incomplete. With improved cardiac function he was rebuilding muscle mass rapidly and in 114 days had increased his total exchangeable potassium from 1290 mEq. to 2097 mEq., almost double the earlier figure. His water fraction had lowered from its high value of 74.7 per cent to 61.6 per cent, as clear evidence of fat accumulation. At this time his clinical appearance was that of a most dramatic "filling out" of subcutaneous fat, and muscular masses; no longer bedridden, he was active about the house.

His total exchangeable sodium was still elevated as evidence of some further metabolic convalescence yet to be completed.

Discussion

Disordered Biochemistry. The body composition of the patients with mitral stenosis before surgery showed certain abnormal features when contrasted with that of healthy adult women, namely a relative excess of sodium and water. Such features are, of course, commonly seen in edematous patients,16, 17, 18 but in these cases no clinically detectable edema was present at the time of the measurements. These changes may also be seen as a result of undernutrition17, 19 and of various chronic wasting diseases20 which lead to a loss of cell mass and of fat. Chronic cardiac disease undoubtedly falls into this category and the preoperative body composition is probably due to the wasting rather than latent edema. In this respect it is of interest that with the gain in weight seen over the course of several months after a successful valvuloplasty the proportions of water and sodium in the body decrease, as the exchangeable potassium rises. This is clear evidence of an increasing muscle mass, and an increasing store of body fat. Taken together, these indicate a reversal of the "syndrome of depletion" and a rebuilding of those energy-exchanging and energy-storing tissues vital to an active existence.8 Taken together these changes are a most eloquent witness to the effectiveness of the valvuloplasty itself; where cardiac function is slow to return, or fails to return, such restorative changes are not seen. Similar changes are seen in the rehabilitation of those suffering from chronic undernutrition19 and in convalescence from a successful surgical operation.20, 21

Immediately after operation several complex changes develop, which are common to all types of trauma and are in no way peculiar to those undergoing mitral valvuloplasty. These features, which are also regularly seen in patients without cardiac disease, include the increased nitrogen excretion,1- 21 the loss of potassium in excess of nitrogen,1 the fall in eosinophil
count and the rise in urinary excretion of 17-ketosteroids and 17-hydroxycorticoids. In noncardiac patients also, postoperative retention of water, decrease in serum sodium and elevation of serum potassium concentration frequently occur. However, in patients with mitral stenosis undergoing surgery these changes are often extremely conspicuous and merit further consideration.

The mechanism of the changes in serum sodium concentration seen postoperatively is obscure. The results reported here clearly show that the serum sodium concentration falls postoperatively even though there is no loss of sodium from the body and, more strikingly, even where sodium loading is occurring. Retention of water may play a part, but when the fluid intake is restricted so that no apparent increase in total body water occurs a definite decrease in sodium concentration still develops. Figure 10 offers graphic evidence that in general there is a poor correlation between water retention and postoperative hyponatremia. Thus the evidence suggests that "external dilution" is not the only significant factor, if it is assumed that the retained water is evenly distributed over the body. Clearly, if fluid were held preferentially in the extracellular fluid, only a small amount would be required to produce a definite decrease in the sodium concentration. Changes in total body water of under 1 liter cannot be detected with confidence by the deuterium oxide method.

Other factors that may be of importance are movements of electrolytes and water between the intracellular and extracellular compartments. After operation potassium leaves the cells in considerable quantity and is rapidly excreted at a time when there is marked oliguria. It is possible that at the same time water moves out of the cells into the extracellular fluid where it is retained and dilutes the sodium and chloride ("internal dilution"). Thirst is a prominent postoperative symptom and may possibly be associated with such a cellular dehydration. Alternatively sodium may move into the cells replacing potassium, though direct measurements have not yet shown such a transfer in patients with medically treated heart failure, or may enter bones or the gastrointestinal tract which both contain large stores of sodium.

In patients with a persistently low serum sodium concentration, either before or after operation, several factors may be at work. Sodium depletion may develop as a result of a low sodium diet and treatment with mercurial diuretics or from inadequate restoration of sodium lost in hemorrhage at operation and through drainage of fluid from the chest. Excessive retention of water readily occurs in sick patients placed on a low sodium diet, particularly if they are subjected to the stress of an operation or respiratory infection. Certain of the features seen in the mitral stenosis patients after operation may be reproduced by the administration of antidiuretic hormone. This leads to retention of water, depression of serum sodium concentration and the development of symptoms associated with water intoxication. In patients with heart disease and a low serum sodium concentration there is persistent antidiuretic activity.

Therapeutic Considerations. From the practical therapeutic point of view certain general principles emerge from this study. Patients undergoing mitral valvuloplasty show all the postoperative features commonly seen in general surgical cases. Their significance and therapeutic implications have been described elsewhere. However, the disturbances of fluid and electrolyte metabolism tend to be unduly large in comparison with noncardiac patients and it is in dealing with them that additional care is often required.

In one of the groups, the majority, the serum sodium concentration is normal before operation and the total exchangeable sodium is high. The postoperative fall in serum sodium is not due to body sodium depletion and constitutes part of the physiologic response to trauma. It is transient, is not harmful to the patient and is not an indication for the administration of extra sodium. After operation the patient will readily retain water even in the absence of salt. Excessive fluid intake at this stage depresses still further the serum sodium concentration and may aggravate the patient's condition. Thirst is not a reliable indication of dehydration; it may be present even though there has
been fluid retention of over 3 liters. The most valuable indications in regulating the fluid intake are the patient's weight and urine volume. A series of preoperative weight measurements is of great assistance as a loss normally occurs after operation due to metabolism of fat and lean tissue. If the weight remains steady or increases, excess water is clearly being retained. In general, in a patient of average size the fluid intake in the days immediately after operation should not exceed 2000 ml. a day unless there are special indications such as for example high fever, unduly hot weather, or large drainage from the chest. Similarly the daily excess of fluid intake over urine volume should not be greater than about 1500 ml. unless an exceptionally large extrarenal loss of fluid can be demonstrated.

In another group of patients, a minority, the serum sodium concentration is persistently low. Before operation in the nonedematous patient this is suggestive of salt depletion due to a combination of low sodium diet and administration of mercurial diuretics. The condition may be aggravated or appear later if the sodium loss at operation is not fully replenished. In the postoperative period sodium depletion may be suspected if the serum sodium has not begun to rise after a week from the date of the valvuloplasty and the case is otherwise uncomplicated. In these circumstances administration of hypertonic saline and fluid restriction are indicated to return the body composition to normal. It is very important to emphasize that a persistent low plasma sodium either before or after operation may occur in the absence of sodium depletion (an example is found in case 11, figure 12) and with the "high body water, high body sodium, low body potassium" syndrome of depletion. In such patients water restriction and caloric intake are of much greater importance than giving sodium. High dosage of the latter even over short periods may lead to disastrous pulmonary edema while the plasma sodium still remains low. In this second group with a persistent low plasma sodium, therefore, one must approach sodium therapy with great caution and search diligently for evidence of true sodium depletion before giving over 150 mEq. of sodium. The urine sodium concentration should be determined in all such cases to avoid overlooking the rare "urinary salt loser" in whom energetic sodium replacement is vital.

In none of these patients was the elevation of serum potassium associated with indisputable evidence of potassium toxicity. Were such to occur in the postoperative period, the administration of hypertonic saline intravenously might be of benefit. Such a benefit has been observed in other cardiac surgical patients and in surgery undertaken during the uremic state.

When edema is present, even in minimal amounts, restriction of fluid intake to 1200 to 1500 ml. a day often alleviates hyponatremia, and sodium administration with its hazard of increasing already expanded stores of salt and water may be avoided. However, if hyponatremia exists with symptoms such as disorientation, delirium, muscular weakness, apathy or stupor, hypertonic saline and fluid restriction are indicated for the rapid relief of these manifestations.

A quick restoration of the serum sodium level should not be anticipated or attempted. Measurements of total body sodium have shown that after an adequate amount of sodium has been given there may be only a relatively small immediate rise in serum sodium as readjustment of the balance between sodium and water in the body apparently requires several days. In brief:

1. Where surgery has been successful and caloric intake can be resumed the electrolyte pattern will be observed to restore itself gradually to normal if water and salt loading are avoided. The reciprocal nature of the changes in body sodium and potassium and in plasma sodium and potassium will be noted. This restoration is merely a biochemical index of general convalescent rehabilitation.

2. Where surgery has not been successful and caloric intake remains restricted the electrolyte pattern remains distorted, the syndrome of depletion is unrelieved and, in our experience, a wide variety of maneuvers designed for "passive" restoration of water and electrolyte to normal are quite unavailing.

3. Finally there is a third or intermediate group where preoperative depletion has been
maximal, surgical convalescence is slow and caloric resumption hesitant. In these cases, water and salt restriction, daily weight measurement and caloric forcing are indeed lifesaving measures. In addition, as mentioned above, hypertonic saline may be given intravenously under the following circumstances, using 250 cc. of 3.0 per cent sodium chloride: (a) Where plasma potassium is dangerously high and electrocardiographic evidences of toxicity are manifest. (b) Where there is a persistent low sodium without edema, fluid is being restricted, caloric intake has begun, and weight is constant or falling. Here a small dose of hypertonic saline will occasionally initiate a gradual restoration of the plasma electrolyte pattern to normal. This indication is clear if true sodium deficiency can be established by history or NaE, as in case 8, fig. 11. (c) Where an acute depression of plasma sodium after operation progresses to 120 mEq. per liter or below, with associated symptoms. Here again a single dose of hypertonic saline given with caution may be of emergency value even though it appears to exaggerate the high body sodium aspect of the patient’s disorder.

**Summary**

The effect of severe mitral stenosis on body composition has been studied before and after valvuloplasty.

In nonedematous patients immediately before operation there was a slight excess of sodium and water, and a depression of body potassium. Immediately after operation the general features of a response to severe trauma were seen, such as an increased nitrogen and potassium excretion, retention of sodium, a fall in eosinophil count and an increased urinary steroid excretion. The changes in water and electrolyte metabolism were of the same nature but frequently greater in degree than those commonly seen in noncardiac patients after operation. Water retention readily occurred in spite of severe restriction of sodium intake. The serum sodium and chloride concentrations fell and the potassium rose. The fall in serum sodium was not due to loss of sodium from the body; it was greater in those showing considerable weight retention but this was not the sole cause. In a few cases a combination of low salt diet, mercurial diuretics and incompletely restored operative loss led to salt depletion and a persistently low serum sodium concentration.

Body composition slowly returned towards normal over a period of many months after a successful operation. The gain in weight was due to the restoration of lean tissue and fat.

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**Sumario Español**

Pacientes con decompensación cardíaca crónica operados para la corrección quirúrgica de la estenosis mitral han sido repetidamente observados tener una concentración baja de sodio plasmático y una concentración alta de potasio plasmático luego de la operación. Este estudio fue principalmente encaminado a investigar estas anormalidades. Los autores han demostrado que el paciente preoperatorio tiene un desorden característico de composición orgánica, notable por una cantidad grande total de agua, una cantidad alta total de sodio, una cantidad total baja de potasio intercambiable y una concentración de sodio plasmático baja. Los efectos de la cirugía en esta composición anormal del cuerpo y las implicaciones terapéuticas se discuten.

**References**


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