THE MAINTENANCE OF FLUID BALANCE

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THE FLUID BALANCE of the body is maintained with remarkable accuracy within narrow limits. In health, plus or minus variations seldom exceed 1½ litres or 2½ pints (2 per cent. of body weight). Yet ingestion and excretion per year in average adults is of the order of a thousand litres or a ton of water.

The subject of fluid balance is of great practical importance because deviations, positive (plus) or negative (minus), occur in many common medical and surgical conditions and often cause death. The special interest of the subject to surgeons and anæsthetists is that pre- or post-operative deviations may increase the immediate and subsequent dangers of operations.

The last 15 years have produced great advances in general understanding, especially of the quantitative aspects of the subject, and in adoption of new therapeutic techniques—for example, the continuous intravenous drip. The last seven years have seen increasing general recognition that there are two distinct types of dehydration. In spite of these advances, there is undoubtedly a great deal to be learned.

BASIC PHYSIOLOGICAL CONSIDERATIONS

Slightly over two-thirds of the body weight is composed of water (Peters, 1935; Abbott, 1946)—approximately an Imperial gallon, or 10 pounds per stone. (*Note:*—British Imperial pint = 568 ml. and U.S.A. standard pint = 468 ml.; the respective gallons measure approximately 4½ litres and 3¾ litres; a British stone = 14 pounds.)

A man weighing 70 Kg., or 154 pounds, or 11 stones, contains approximately 50 Kg., or 110 pounds, or 88 pints of water.

The body water is distributed partly within and partly without the cells of all the tissues—the intracellular and extracellular fluids—in the ratio of five-sevenths and two-sevenths. These two fluids differ very greatly in composition. Exchanges between them occur across the innumerable cell membranes.

The extracellular fluid is the " internal environment " which surrounds the cells and is remarkably constant in composition and osmotic pressure.

It is distributed partly in the interstitial tissue spaces and partly in the intravascular blood plasma. In an adult there are approximately 11 litres of interstitial tissue fluid and 3 litres of plasma. It is vital to realise that these are sub-divisions of one and the same fluid—the extracellular fluid. Their composition is the same except for the proteins of the plasma.

The capillary walls are freely permeable to all the components of the extracellular fluid except the very large plasma protein molecules. In all the capillaries of the body this fluid is continuously extruded from the

blood in the proximal parts of the capillary loops under the influence of the hydrostatic pressure generated by the heart. An equivalent amount is continuously reabsorbed in the distal parts of the loops where the osmotic pressure of the plasma proteins exceeds the largely expended hydrostatic pressure. This constant to and fro movement of extracellular fluid, between capillaries and interstitial tissue spaces, amounts to hundreds of litres daily.

The great permeability of capillaries is in contrast with that of cell membranes. It is said that the relative permeabilities are about 3000 : 1 (Landis, 1937).

Extracellular fluid, as regards its dissolved constituents, is mainly composed of salt, i.e., of sodium kations and chlorine anions, with small amounts of potassium, calcium and magnesium, bicarbonate, phosphate, sulphate and organic acids (Gamble, 1947). A nearly constant ratio of 4 : 3 sodium ions to chlorine ions is maintained (Denton, 1949).

For the purpose of this article extracellular fluid may be considered as being very nearly isotonic saline.

Intracellular fluid electrolytes consist mainly of potassium and magnesium kations and phosphate, sulphate and bicarbonate anions.

Perhaps the most important function of the sodium and chlorine ions of extracellular fluid is to maintain isotonicity with the intracellular fluid.

Recently attention has been sharply focussed on the importance of the long known osmotic tie-up between water and salt in extracellular fluid. It has become appreciated that often the primary factor determining water retention or excretion is salt retention or excretion. In deviations from fluid balance salt is often even more important than water.

Although water and salt are tied together, it is simpler at first to consider their separate balances within the body.

Water Balance

Under normal conditions water intake is greater than minimum requirements, and balance is maintained by excretion of the surplus in the urine.

Intake in adults averages daily about 5 pints or 2½ to 3 litres, of which 1,100 ml. are derived from " solid " food and the rest from beverages. Output is the same volume but may be divided into unavoidable losses and surplus water. Unavoidable losses, which go on whether water is ingested or not, are approximately a litre, vaporised from skin and lungs, and half a litre as the minimum volume of urine (" urine obligatoire ") necessary to excrete waste products.

In infants, with their high metabolism, unavoidable water losses are relatively twice as large. This explains the extreme danger of dehydration in babies (Gamble, 1947).

In regard to minimum urine volume for excretion of waste products it is important to realise that this is related to the efficiency of the concentrating power of the kidneys (Lashmet and Newburgh, 1932). In an

adult, daily excretion of only 500 ml. of urine means it must contain 6 to 8 per cent. of dissolved solids and have a specific gravity of 1·030 or more. If the kidneys are inefficient and cannot concentrate urine to a specific gravity of more than 1·012 then the minimum volume required is not less than 1,500 ml. This has most important practical implications. Diminished renal concentrating power of this order is normal in infants, frequent in the aged, and at all ages follows temporary or permanent renal damage from many causes. Severe temporary damage occurs in many conditions of serious illness and " shock," including " shock " due to dehydration.

Salt Balance

Salt balance is normally maintained in the same way as water balance ; intake (usually 8-15 g. a day) greatly exceeds minimum needs (about 2 g. daily) and the surplus is excreted in the urine.

Intake is partly from salt combined in foodstuffs and partly by addition in cooking or as a condiment. Output in temperate climates is nearly all in the urine.

An important practical point is that the body has an insistent sensory warning—thirst—when depleted of water, but there is not a similar craving for salt when it is deficient.

The total amount of sodium and chlorine in the body is approximately 1/400 of the body weight or the equivalent of about 6 ounces of salt in an adult of 11 stones—4 ounces being in the extracellular fluid and 2 ounces in the secretions in the alimentary canal. There is little or no sodium or chlorine in the cells of the tissues.

The main functions of sodium and chlorine ions appear to be maintenance of osmotic pressure and acid-base equilibrium.

Regulation of the body's balances of water, sodium and chlorine is chiefly mediated by the kidneys which selectively retain or excrete each of these constituents so that constancy of composition of the extracellular fluid is maintained (relative concentrations appear to have priority over total amounts). Although the kidneys execute the task, they appear to do so largely in response to hormonal control from the pituitary and adrenal glands in regard to water and salt respectively (Verney, 1947, 1948 ; Loeb, 1941).

POSITIVE (PLUS) DEVIATIONS FROM FLUID BALANCE (ŒDEMA)

General body fluid increase will be here considered and not local fluid accumulations.

In severe fluid retention, with generalised œdema, the volume of extra fluid may be of such extreme degree as to cause doubling of the body weight.

Œdema may be said to be " latent " when the tendency for it exists or when the surplus fluid is insufficient to be manifest to ordinary clinical examination. It needs approximately an increase of a gallon (4½ litres) before " pitting " can be demonstrated.

In studying changes in body fluid the most informative and easiest observation is to weigh the patient daily.

Generalised œdema menaces life—especially because of the tendency to pulmonary œdema. It greatly increases operational risk and post-operative mortality. Œdematous tissues heal badly and there is increased liability to wound infection. Œdema is also of interest to surgeons and anæsthetists because many dehydrated patients swing into œdema when dehydration is relieved.

Causes of Fluid Retention

The causes of abnormal increase in total body fluid are as follows :—

(*A*) *Simple Water Retention.*—This is probably rare as water is easily excreted. It can occur from excess administration of pituitary extract containing the anti-diuretic hormone. When water alone is retained the extracellular fluid tends to become hypotonic and water, therefore, enters the cells. This is the possible explanation of the symptoms of " water intoxication " (Weir, Larson and Rowntree, 1922), which follow forced ingestion of large amounts of water or the administration of large doses of anti-diuretic hormone. This unusual type of increase of body fluid will not be further considered as our main concern is with common conditions.

(*B*) *Water Retention Secondary to Salt Retention.*—This is not infrequent. It occurs : (i) Following excess saline administration. (ii) When the kidneys are so damaged that salt excretion is impaired. Normal adult kidneys can excrete sodium and chlorine ions in concentration equivalent to 20 g. per litre of urine sodium chloride (Davies, Haldane and Peskett, 1922). Renal damage, as from nephritis or prolonged lowered blood pressure (for example in dehydration of the secondary type), may reduce renal ability to excrete sodium and chlorine to one-fifth of normal. In normal infants this is the level in any case (McCance and Young, 1941, 1942 ; McCance, 1946) and, therefore, severe renal damage in them may mean maximum excretory capacity as low as 2 g. per litre. (iii) Finally, salt may be retained due to excessive administration of adrenal cortical hormone or of deoxycorticosterone acetate (DOCA).

Whenever salt is retained, water is also retained to the extent of approximately a litre per 6-7 g. of sodium chloride (De Wesselow, 1924). This appears to be because priority is given to maintenance of the electrolyte *concentration* of the extracellular fluid. The body tolerates even gross fluctuations in the volume of this fluid better than changes in its concentration (Stewart and Rourke, 1942). Preservation of isotonicity is the paramount necessity.

(*C*) *Abnormal Shift of Fluid into the Interstitial Tissue Spaces.*—This is frequent and occurs as a result of imbalance in the pressures which determine the continuous to and fro capillary exchange of fluid between

the plasma and interstitial tissue fluid. It may be a matter of increased intra-capillary hydrostatic pressure or diminished plasma protein osmotic pressure. Increased hydrostatic pressure is classically seen in cardiac failure when it affects primarily the distal, or venous, end of the capillary loops, due to general rise of pressure in the systemic veins. Such venous congestion may result in generalised venous distention and rise of venous pressure from the normal level of around 60 mm. (of blood—*not* mercury) to 300 mm. Rise of capillary hydrostatic pressure does not arise in arterial hypertension because such hypertension is due to increased peripheral resistance from generalised arteriolar constriction, and so the arterial high pressure, expended in overcoming the frictional resistance of the narrowed arterioles, has dropped to normal by the time the capillaries are reached. Venous congestion in cardiac failure tends also to cause œdema through decreasing effective glomerular filtration pressure in the kidneys.

Œdema, due to generalised rise of venous hydrostatic pressure, tends to be most marked in the dependent parts of the body where the pressure due to gravity reinforces the abnormal intra-capillary hydrostatic pressure.

Diminished plasma proteins (hypoproteinæmia) cause decrease of that difference in osmotic pressure between interstitial tissue fluid and plasma which opposes the intravascular hydrostatic pressure and secures return of extruded fluid. The normal level of the total plasma proteins is $6\frac{1}{2}$ to 8 g. per 100 ml. The normal levels of albumin and globulin are respectively 4-5 g. and $1\frac{1}{2}$-3 g. per 100 ml. From the osmotic point of view the albumin is the more important constituent because its smaller molecules cause there to be about four times as many in a gramme of albumin as compared with a gramme of globulin. Gross œdema, given normal water and salt intake, becomes inevitable when plasma albumin falls below 3 g. per 100 ml. (Bruckman and Peters, 1930; Weech and Ling, 1931; Himsworth, 1946).

Hypoproteinæmia may arise from: (i) Inadequate ingestion of protein due to starvation or inability to eat; (ii) Inadequate absorption as, for example, in gastro-colic fistula or prolonged chronic diarrhœa in such conditions as ulcerative colitis or sprue; (iii) Inadequate synthesis of plasma and tissue proteins when the liver is severely damaged. It is now recognised that in cirrhosis of the liver, the ascites is as much due to this cause as to portal venous congestion (Higgins, *et al.*, 1947); (iv) Gross protein drain from the plasma, as in chronic albuminuria or loss of plasma from extensive burns or crush injuries, causing extravasation into tissues or weeping from surfaces.

The œdema from hypoproteinæmia tends to be generalised and not especially in dependent parts. It affects markedly the laxer tissues.

Hypoproteinæmia represents a very severe decrease of body protein and exhaustion of reserves. Whipple, 1942, has shown, by plasmapheresis experiments, that the normal animal has a reserve of easily mobilised protein equal to several times the total amount of plasma protein and that hypoproteinæmia does not occur until this reserve is all used up.

It is of practical importance to visualise the condition of the blood volume in the common states of general œdema. When salt retention is the primary cause there is increase of plasma volume (Sheftel, 1939; Warren and Stead, 1944; Lyons, *et al.*, 1944). When cardiac failure, with its venous congestion, is the cause, there is also an increase of blood volume (Fishberg, 1940). These are the states in which venesection may be valuable in acute emergency. In hypoproteinæmia, on the other hand, there is decrease in plasma volume which is, indeed, only prevented from being severe by increased tissue pressure due to fluid accumulations, opposing intravascular hydrostatic pressure. The œdema alone prevents oligæmic peripheral circulatory failure and is, therefore, in this respect *beneficial* (Warren, Merrill and Stead, 1943). Hence, treatment by venesection or diuretics is misguided and dangerous. Recognition of the tendency to decrease of blood volume in hypoproteinæmic œdema was retarded by the once prevalent terminology which labelled renal œdema of this type as " hydræmic."

It will be noted that generalised œdema has not above been ascribed to increased general capillary permeability which was at one time freely invoked to explain œdema. This is because it is doubtful whether it is in fact, often or ever a cause of general non-inflammatory œdema in which analyses of dropsical tissue fluid have shown a similar protein content, whatever the cause. Admittedly, extensive extravasation occurs through capillaries locally damaged by burns or crush injuries.

Clinical Features

The clinical features of general œdema are too well known to need description. Its extremely dangerous local effect is pulmonary œdema, of which the first symptoms are shortness of breath and an irritating cough. Later the dyspnœa becomes marked, cyanosis appears, and the cough becomes more troublesome with often copious frothy expectoration, possibly blood tinged, which may pour from mouth and nose as the patient drowns in his own transudate. The physical signs are scattered râles all over the chest and especially at the bases. The X-ray shows woolly areas due to fluid in the alveoli.

Treatment

The emergency treatment of severe œdema, with pulmonary œdema, is the administration of oxygen by an effective method, such as the B.L.B. mask, and venesection.

Apart from these emergency measures, the rational preventive or remedial treatment of generalised œdema is to prevent or attack the cause.

Œdema due to salt retention, from excess saline administration, can be prevented by avoidance of the administration of saline, except in small amounts, in other than hypotonic concentration. This very important point will be further dealt with when the treatment of dehydration is discussed below. Salt retention due to excess administration of extract of adrenal cortex or of DOCA should be prevented by not falling into this error.

Once œdema from salt retention, due to any of the enumerated causes, has developed, the main lines of treatment should be salt restriction and the use of the diuretic mersalyl. Purgation and sweating may also be tried. Mechanical drainage by tapping should be used in all gross cases.

Salt restriction means administration of a diet containing less than 1½ g. of sodium chloride daily. This demands a special diet and not mere avoidance of salt in cooking or as a condiment.

Water restriction used to be practised in all forms of œdema but modern opinion is that it is unnecessary and harmful (Schroeder, 1941 ; Schemm, 1942 ; Leevy *et al.*, 1946). Œdematous patients should be looked upon as being " brine-logged ", and not " water-logged ". They actually need water as a vehicle for urinary excretion of salt, and œdema is not increased even when water intake is pressed. In generalised œdema, water intake should be normal—neither restricted nor forced.

The mercurial diuretic Injectio Mersalyli (B.P.) is now regarded as possibly acting mainly by promoting increased urinary excretion of sodium and chlorine and so lowering extracellular fluid osmotic pressure.

A secondary water diuresis tends to occur whenever salt is excreted. After mersalyl injection salt excretion precedes and is greater than the water diuresis. Mersalyl is indicated not only in salt retention œdema but also in the œdema of cardiac failure in which much experience has shown it to be most effective. In cardiac failure there is salt retention due to inefficient excretion by the congested kidney (Brod and Fejfar, 1950). Mersalyl is most safely administered by intramuscular injection of ½ to 2 ml. twice a week. It produces a diuresis, usually of several pints, within 3 to 4 hours and is, therefore, best given in the morning to avoid disturbance of sleep.

Purgation producing watery stools causes sodium and chlorine excretion, especially sodium. Therefore, in generalised œdema, due to salt retention, or to cardiac failure, the administration of enough magnesium sulphate (*not* sodium sulphate), usually one to three drachms, every morning is good practice unless the patient is too weak to withstand the exertion involved in the use of the bed-pan. Sweat contains a variable amount of salt but, on the average, about 2½ to 3 g. per litre (Kuno, 1934 ; McCance, 1936 ; Dill, 1938 ; Ladell, *et al.*, 1944). Therefore, promotion of sweating, by increased blankets is helpful if it can be tolerated. In gross œdema the tissues may contain as much as a pound (450 g.) of surplus salt and, therefore, all means of promoting salt depletion should be considered.

Mechanical removal of fluid by puncture of the legs is a very valuable and rapid method of getting rid of water and salt in primary salt retention and primary cardiac œdema. In hypoproteinæmic œdema, as already said, the œdema is beneficial and should not be directly treated (but every effort should be made to restore the plasma proteins). The leg punctures should be made with the point of a tenotome into the lower leg and instep after skin disinfection—about 20 punctures on each side.

The patient should be kept sitting up, with the legs hanging down, for several days in a cardiac bed or chair. Drainage of fluid from the punctures may amount to 10 or more litres with loss of as much as 70 g. of sodium chloride. Pleural effusions, if causing dyspnœa, should be removed by paracentesis in all forms of œdema. Abdominal paracentesis may also be employed to relieve gross ascites.

In the treatment of general œdema due to cardiac failure mention has already been made of the use of oxygen, venesection, salt restriction, mersalyl, purgation, sweating and mechanical drainage. Specifically important measures are bed rest, in a sitting position, and the administration of digitalis in correct dosage. Morphine is very valuable in severe, restless cases.

The treatment of œdema due primarily to hypoproteinæmia should *not* be directed to simple fluid removal, since the fluid has the beneficial effect of maintaining plasma volume, but to restoration of the plasma proteins to normal levels when the œdema will automatically disappear. Therefore venesection, severe salt restriction, mersalyl (definitely dangerous), purgation, sweating and mechanical drainage (except the tapping of large pleural or pericardial effusions) are *not* indicated.

Plasma proteins may be restored by drip transfusion, over six hours, of a litre of plasma on alternate days, and by administration of a high protein diet of which the following is an example of the main components :—

Meat, liver, chicken, fish, 8 ozs. (weighed cooked)	= 56 g. protein
4 eggs	= 24 g. ,,
Cheese, 4 ozs.	= 30 g. ,,
Milk, 2 pints..	= 40 g. ,,
	150 g. protein

Spread out in small meals over the day.

NEGATIVE (MINUS) DEVIATIONS FROM FLUID BALANCE (DEHYDRATION)

Dehydration means reduction in total body water and it arises frequently in many common medical and surgical conditions.

Death occurs when fluid loss reaches about 15 per cent. of body weight or roughly just over one-fifth of total body water—loss of about 10 litres or 2¼ gallons in an adult man.

Causes of Dehydration

Dehydration may be brought about in two main ways :—

(*A*) Insufficient intake of water.

(*B*) Loss of bodily secretions from the alimentary tract or loss of sweat.

Insufficient intake of water occurs when water is not available or when it cannot be drunk due to great weakness, unconsciousness or dysphagia from some local cause.

Loss of bodily secretions in this country usually results from vomiting, diarrhœa, fistulæ or gastric aspiration. Profuse sweating occurs in

tropical climates or under certain industrial conditions; occasionally it arises from mistaken over-heating of patients, especially unconscious patients by blankets or hot air cradles.

There is a most important difference in the effects upon the body of these two causes of dehydration, so much so that they produce two types of dehydration which differ from each other in clinical features and, most important, in the treatment needed (Kerpel-Fronius, 1935; Nadal, Pedersen and Maddock, 1941; Nadal, 1942).

The essence of the difference is that in lack of water intake the body becomes depleted of water only. In secretion losses the depletion is of water *and salt*. In both conditions water needs to be administered but the crux of the matter lies in whether or not salt should be given as well. In the first, salt is definitely contra-indicated. In the second, the patient will not recover unless salt is administered too; the reason is that even if water is administered freely the kidneys will excrete it in order to preserve isotonicity of the extracellular fluid because there is a fall in the total osmotic pressure of this fluid, and water can only be " held " in it in proportion to the osmotic pressure.

The two mechanisms which bring about dehydration may produce three types of disturbance of physiology and of the clinical picture:—

(*a*) Simple water depletion or primary dehydration.
(*b*) Pure salt depletion with secondary dehydration.
(*c*) Mixed water and salt depletion.

(*a*) *Simple Water Depletion* (*Primary Dehydration*)

This occurs when the dehydration is due to simple lack of water intake without abnormal secretion losses. The modes of causation have already been mentioned.

Dehydration ensues because the unavoidable water losses, in the form of vaporisation from lungs and skin and minimum urine, continue at the rate of 1,500 ml. (roughly 3 pints) daily. In consequence, the extracellular fluid becomes hypertonic and the sodium and chlorine concentrations rise (Black, McCance and Young, 1944). The hypertonicity causes water to move from the cells to the extracellular fluid. Hence, the water loss is borne by both intracellular and extracellular fluid so that there is not a very marked fall in the volume of the latter. This affects the clinical features because the blood volume is not much shrunken, and so shock symptoms are not prominent.

The first symptom is thirst which becomes worse and worse. Dryness of the mouth soon follows and it may be so dry that swallowing of solid food becomes impossible. The urine volume falls and the urine becomes very concentrated. Weakness is not marked till three or four days have passed but there is a feeling of malaise and headache, though the raging thirst overshadows all other sensory symptoms. The patient looks ill and loses weight in proportion to the water deficit, but there is not the same laxity of the skin which is seen in secondary dehydration. The

blood urea slowly rises. Hæmoconcentration is not a marked feature. Ultimately the patient subsides into a low delirium before death. If water is administered its absorption is very rapid and the beneficial effect may be seen within a few minutes.

A rough quantitative correlation of clinical manifestations with the degree of water deficit (Marriott, 1947) is as follows :—

(i) *Early dehydration.*—Thirst definite but other effects not yet present : deficit approximately 2 per cent. of body weight or 1½ litres in a 70 Kg. (11 stones) man.

(ii) *Moderately severe dehydration* (three or four days without water) :— Marked thirst and dryness of the mouth, oliguria, weakness, ill appearance, slight personality changes, still capable of fair mental and physical performance : deficit of approximately 6 per cent. of body weight or 4·2 litres in a 70 Kg. man.

(iii) *Very severe dehydration.*—All the above manifestations plus mental and physical collapse : deficit of 7-14 per cent. of body weight or 5-10 litres in a 70 Kg. man.

(*b*) *Pure Salt Depletion with Secondary Dehydration*

This condition occurs when abnormal losses of bodily secretions (alimentary or sweat) have occurred *and water has been freely supplied.* The dehydration is not due to lack of water intake but to inability of the extracellular fluid to " hold " water.

This form of dehydration is common at the present time because there is general consciousness of the dangers of dehydration but a tendency to think of it in terms of water only. Patients who have suffered from vomiting or diarrhœa, or have been submitted to continuous gastric aspiration, are plied with water. In consequence their intake and output charts are satisfactory until a late stage and it is erroneously concluded that dehydration cannot be present. Severe cases tend to lapse into a state of collapse but this is not interpreted as being due to dehydration consequent upon salt lack, but is ascribed to other explanations which will be later mentioned. This state of insidious collapse is particularly common in post-operative patients and many lives are lost from lack of understanding of its true nature (Marriott, 1947). It occurs in " heat exhaustion " in the tropics when persons sweat severely, losing salt as well as water, but replace only the water loss.

All the alimentary secretions, except saliva, are isotonic with extracellular fluid and contain mainly sodium and chlorine (Gamble, 1923, 1947 ; McCance, 1936). Severe or prolonged vomiting, diarrhœa, gastric aspiration or loss from fistulæ can drain away as much as three-fourths of the total body stores of salt.

Loss of salt from the body also occurs in Addison's disease in which there is abnormal excretion of sodium and chlorine in urine.

The main effect of salt depletion is loss of total osmotic pressure of the extracellular fluid which, in consequence, proportionally loses volume

as the kidneys excrete water in the attempt to preserve isotonicity. The extracellular fluid tends to become hypotonic and, therefore, there is no withdrawal of water from the cells—rather the reverse. The whole burden of the water loss falls on the extracellular fluid, which consequently becomes much reduced. The contraction of the plasma volume causes the symptoms of oligæmic shock to be prominent at an early stage.

A secondary effect of secretion losses from the alimentary canal is change in the acid-base balance. Thus in severe vomiting alkalosis develops and in severe diarrhœa acidosis occurs. This is because gastric juice contains more than twice as much chlorine as sodium whereas the lower intestinal secretions contain only half as much chlorine as sodium. The general clinical features after vomiting or diarrhœa are similar and, in the writer's opinion, the acid-base changes are of secondary importance compared with the osmotic pressure effects.

The symptomatology of pure salt depletion (McCance, 1936) is as follows. Weakness is early experienced and progresses to extreme lassitude, apathy and final coma. Headache is often present and has the character of a low-pressure headache—it is much worse on sitting up or standing. Giddiness and fainting also tend to occur on standing. The urine volume, if water is being freely supplied, is normal or even increased until a late stage. Thirst is absent and water may be repugnant. Soon anorexia develops and goes on to nausea and vomiting which are present in almost all severe cases. If vomiting was the original cause of the condition then the secondary vomiting is often confused with the primary vomiting. The whole alimentary tract, apart from the sphincters, becomes flaccid and there may be acute dilatation of the stomach and intestinal ileus. There is consequent general abdominal distension. Weight loss is progressive in spite of free water ingestion. Since fluid loss is from the extracellular fluid there is early desiccation of the lax subcutaneous tissues and the patient's skin becomes too large for him so that it wrinkles and pinched up folds do not return in the normal way immediately on release. Even the wrinkled " washerwoman's fingers," originally described in cholera, may be seen. Muscular cramps are marked especially on any attempt to move muscles—they are the same as " heat cramps " or " stoker's cramps." Mental confusion is almost invariable and the patient is in a lethargic, muddled daze.

Most characteristic of all the later manifestations of secondary dehydration, due to salt depletion, are those of peripheral circulatory failure due to contraction of the blood volume. The usual bodily reaction to oligæmia, namely, generalised vaso-constriction, occurs except in the vessels of the heart and brain, designed to divert blood and maintain circulation in the vital centres. It causes generalised skin pallor and coldness of the extremities. At first the vasoconstriction maintains the arterial blood pressure but later this declines until it may ultimately be unrecordable (Caplan, 1942). There is parallel deterioration of the quality of the pulse until it becomes impalpable. In the final stages

cyanosis develops especially in the lips, ears and nails. When the arterial blood pressure falls below 70 mm. Hg., anuria usually occurs.

The blood shows progressive hæmoconcentration, consequent upon the decrease in plasma volume, and the red cell count may rise to 8 million per c.mm., the hæmoglobin percentage to 150, and the packed cell volume (hæmatocrit) to 64 per cent. There is usually a leucocytosis. The hæmoconcentration may cause doubling of the blood viscosity and halving, from this cause alone, of the already scanty peripheral circulation (Marriott, 1947). In extreme cases of vomiting the plasma chloride, expressed as sodium chloride, may fall from the normal level of 560-630 mgm. per 100 ml. to 300 mgm. or even lower. The blood urea rises rapidly and early. The urine shows absence of chloride.

Death is from progressive oligæmic circulatory failure or " shock."

Water, however much is given, does not relieve the condition. Its oral administration, in the later stages, when gastric atony and pylorospasm have developed, may cause death because the stomach may fill up with several pints of water which may then be vomited suddenly. The patient is so enfeebled, and his reflexes so depressed, that the vomit enters the trachea and may cause immediate drowning or later death from bronchopneumonia. The intravenous administration of saline solution produces quick improvement if the condition has not progressed to the irreversible stage.

The state of pure salt depletion with secondary dehydration, arising from secretion losses plus free administration of water, has been so fully described because I believe it to be frequent, especially in post-operative cases, and as yet not generally recognised. Too often the condition is interpreted as being primarily due to pathological manifestations which are, in fact, secondary. The obvious circulatory failure may prompt a diagnosis of " Cardiac failure " or " shock." The high blood urea leads to " uræmia " or " renal failure " being diagnosed. The vomiting and distension are not infrequently regarded, especially in post-operative patients, as indicative of " peritonitis " or " obstruction " or " acute dilatation of the stomach " or " ileus." Many patients have had their abdomens unnecessarily opened or re-opened. An equally serious error, of course, would be to diagnose salt depletion dehydration when, in fact, the patient was suffering from peritonitis or intestinal obstruction.

The picture of salt depletion secondary dehydration is also seen in many medical conditions causing vomiting or diarrhœa and in Addison's disease and diabetic coma.

A few words may be devoted especially to salt depletion arising from prolonged gastric or gastro-intestinal aspiration by Ryle or Miller-Abbott tubes. These therapeutic procedures (Wangensteen, 1942) can be of great value but they can also be lethal if the removed electrolytes are not replaced. Bartlett, Bingham and Pedersen (1938) produced severe chloride depletion in normal volunteers by gastric aspiration. Lyall and Nicol (1939) found that gastric aspiration, prolonged over six days,

caused removal of 93 g. of chloride (expressed as sodium chloride). This is more than half the total amount in the body. When aspiration is being practised, close attention should be directed to maintaining electrolyte balance. Quite a good plan is to filter all aspirated fluid and re-introduce it per rectum. Aspiration of the upper alimentary tract is often adopted to relieve vomiting or distension but may perpetuate these symptoms which are then, mistakenly, interpreted as calling for yet more aspiration.

An approximate quantitative correlation of clinical manifestations with salt deficit (Marriott, 1947) is as follows :—

(i) *Slight to Moderate Salt Depletion.* Absence of chloride in the urine (except in Addison's disease), with lassitude and may be giddiness and faintness on standing : deficit up to 0.5 g. per Kg. of body weight or the equivalent of 4 litres of isotonic saline (8.5 g. per litre) in a 70 Kg. man.

(ii) *Moderate to Severe Salt Depletion.* Absence of chloride in the urine, lethargy, giddiness, faintings, anorexia, nausea and possibly vomiting, fall of blood pressure but systolic pressure above 90 mm.Hg. : deficit 0·5 to 0·75 g. per Kg. of body weight or the equivalent of 4 to 6 litres of isotonic saline in a 70 Kg. man.

(iii) *Severe to Very Severe Salt Depletion.* Absence of chloride in the urine, stupor, vomiting, blood pressure below 90 mm.Hg. : deficit 0.75 to 1·25 g. per Kg. or equivalent of 6 to 10 litres of isotonic saline in a 70 Kg. man.

(*c*) *Mixed Water and Salt Depletion.* This form of dehydration is common in practice. It arises when there is loss of secretions but water intake is not free. It is particularly prone to occur following vomiting which precludes liberal ingestion of water.

In such cases there is reduction of the total osmotic pressure of the extracellular fluid and, therefore, fall in its volume. At the same time, the continuance of unavoidable water losses (1·5 litres daily) causes water loss to outstrip salt loss if water ingestion is below 1·5 litres daily.

The patients present a mixture of the symptoms of water and salt depletion (primary and secondary dehydration). They are thirsty, have dry mouths and secrete a scanty amount of high specific gravity urine. They are also weak, apathetic and show the signs of oligæmic circulatory failure. Anorexia, nausea and vomiting may be present. Chloride is absent from the urine. The blood urea is raised.

Diagnosis

The diagnosis of dehydration and differentiation of the three types must mainly depend, as in all diagnoses, on an alert awareness of mind due to clear understanding. The simple symptom of thirst and the sign of oliguria at once suggest dehydration which may be due to simple water depletion or mixed water and salt depletion. Vigilance is needed to avoid

missing pure salt depletion dehydration in non-thirsty patients with adequate urine output.

A considerable help to diagnosis, particularly in surgical cases, is institution of routine measurement of urine volume and chloride content. Inadequate urine volume suggests water depletion and absent or low chloride indicates salt depletion. Measurements of both should be made at intervals not longer than eight hours because, in acute cases, fatal dehydration will often develop during longer periods.

Urine volume should be not less than 500 ml. (approximately a pint or 20 ounces) per eight-hour period. This is because cases of potential or actual dehydration are liable to have renal damage, making excretion of waste products impossible in smaller volume.

Urine chloride may be estimated by a very simple quantitative test (Fantus, 1936).*

With a fountain-pen filler pipette drop ten drops of urine into a small test tube. Add one drop of 20 per cent. potassium chromate solution and then add, drop by drop, 2·9 per cent. silver nitrate solution until the whole mixture turns from yellow to brown. Shake the tube after the addition of each drop of silver nitrate. The same pipette should be used throughout to ensure the same size drops but must be rinsed with distilled water between using each solution. The number of drops of 2·9 per cent. silver nitrate solution needed gives the grammes per litre of chloride expressed as sodium chloride in the urine, e.g., 3 drops = 3 g. per litre, 10 drops = 10 g. per litre.

Urine sodium would be an even more valuable estimation because sodium is more important than chlorine and chloride estimations do not necessarily always parallel sodium concentrations. Hitherto no simple quantitative methods of estimation of sodium have been known. However, such methods are now being developed (Wynn, Shirley Simon, Morris, McDonald and Denton, 1950) but are not yet easy bedside manœuvres.

Blood investigations may be helpful in diagnosis. Blood counts, hæmoglobin estimations or hæmatocrit values will all reveal the hæmoconcentration of severe salt depletion (pure or mixed) dehydration. The blood urea is informative. It tends to be raised in either water or salt depletion but rises more steeply in the latter condition and may reach as high as 300 mgm. per 100 ml. Estimations of plasma sodium or chloride will reveal depletion but urine estimations are probably more valuable as well as being easier (Abbott, 1946; Marriott, 1947).

Treatment

The crucial question in regard to the treatment of dehydration is whether the patient requires water alone or water and salt.

* Exceptional situations in which this test may be partially misleading are discussed by Denton (1949) and Marriott (1950). Its value has been confirmed by Evans and Van Slyke (1948) and by Paine and Duff (1949).

The answer is to be derived from consideration of the clinical features and diagnostic precedures described above but the simplest way to settle the question is to ask oneself how dehydration is threatened or has come about. *Is it a matter of simple lack of water intake or have alimentary secretions or sweat been lost?* If there has been loss of secretions or sweat, salt is indicated as well as water. If not, it is contra-indicated.

Preventive Treatment

The key to prevention lies in alert anticipation and in the institution of routine eight-hourly measurement of urine volume and chloride content. Water depletion is certain in any patient not drinking enough and salt depletion is likely whenever loss of alimentary secretions or sweat is taking place.

Water intake should be about five pints or three litres daily to ensure 1,500 ml. of urine. If it cannot be taken by mouth then parenteral methods, discussed in connection with remedial treatment, must be used.

When patients are losing secretions the loss should be directly measured if possible or estimated if measurement is not feasible. The loss should be made good, *as it proceeds*, by the administration of hypotonic saline (see below).

Remedial Treatment

The treatment of established dehydration demands diagnosis as to whether it is pure water depletion, pure salt depletion or mixed water and salt depletion. Then a quantitative estimate of the amount of water and/or salt loss should be made. This is probably best based on the overall clinical picture and the rough correlations already described. The patient will also need in addition the amounts of water and/or salt being lost while repair of the initial deficits is proceeding.

Throughout the period of restoration of water and/or salt balance most careful watch must be kept on the patient as regards his general state and his urine output and urine chloride level. Intake and output and urine chloride must be charted. Dehydrated patients are gravely ill from the dehydration and often before it have been suffering from anæmia or cachexia (with hypoproteinæmia) or cardiac or respiratory disease. Even slight over-dosage of saline may swing them over to œdema and cause pulmonary œdema which may be fatal. At the same time, deficits must be relieved and carefulness not allowed to cause timorous dosage. In the past, large numbers of patients died from dehydration—especially following secretion losses — because of pitifully inadequate treatment.

As regards urine volume, it has already been stated that the aim should be 500 ml. or a pint, per eight hours. The aim for urine chloride should be 2-4 g. per litre in an adult and 2 g. per litre in an infant.

The practical questions which arise in treating a dehydrated patient are : (i) What fluid to administer ? (ii) How much ? (iii) At what rate of administration ? (iv) By what route ?

(i) *What Fluid ?*

In simple water depletion water is indicated and should be given as such or in beverages. Plain water may be administered per rectum but, if intravenous or sub-cutaneous administration is necessary, then isotonic glucose solution (5·0 per cent.) should be employed. The glucose is utilised and the water serves for rehydration.

If salt depletion exists, saline administration is necessary. Saline should generally be administered, by any route, as hypotonic sodium chloride and isotonic saline (0·85 per cent. NaCl) should only be used in extreme salt depletion and then only to the extent of one or two litres. The reason for the interdiction of isotonic saline is that patients receiving it tend to retain sodium and chlorine to a greater extent than water and in consequence may later become œdematous because " brine logged " (Coller, Iob, Vaughan, Kalder and Moyer, 1945). This tendency is particularly marked following operations or anæsthetics (Moyer, 1949 ; Wilkinson *et al.*, 1949). Hypertonic saline, in the author's opinion, should never be used to correct salt depletion. Half normal saline (0·425 per cent.) has very little saltiness of taste and may be given, flavoured, by mouth. It may be administered per rectum. For intravenous or sub-cutaneous use, an isotonic solution of 0·425 per cent. sodium chloride and 2·5 per cent. glucose should be used for adults. In infants the standard dilution should be 0·2 per cent. sodium chloride and 4 per cent. glucose.

(ii) *How much fluid ?*

As stated above, this should be the amount of the deficit plus losses, normal and abnormal, taking place during the period of administration. In minor depletions two or three litres of water or saline solution, depending on the type of dehydration, may be enough but in severe cases the total requirement may be as much as 10 litres or 18 pints. In all mixed depletion cases allowance must be made for the fact that water loss exceeds salt loss. Theoretical calculations may easily be at fault and must be checked continuously as treatment proceeds by the general state of the patient and his urine volume and urine chloride. Relief of depletions may be assumed when clinical manifestations have disappeared and the urine volume reaches 500 ml. per eight hours and its chloride level two to four g. per litre.

(iii) *What rate of administration ?*

As a general routine the rate for water or saline, by any route, should be a litre each six to eight hours. However, in very severe dehydration, especially when there is gross salt depletion, a faster rate may at first be necessary to save the patient's life. In such cases the first litre should be given in one to two hours, the second litre in another two or three hours

and a third litre in a further four to six hours. Whenever there is any doubt, it is wiser to err on the side of slowness.

(iv) *What route ?*

Oral administration is the route of choice whenever practicable except in salt depletion of more than minor degree. In marked salt depletion, oral administration, besides being ineffective, may be dangerous because of the dilatation of the stomach, and associated danger of vomiting and drowning, which have already been mentioned. In patients who have difficulty in drinking, fluid may be introduced into the stomach via a thin stomach tube passed through the nose (Ransome, Gupta and Paterson, 1944). This method is useful in infants (Nauth-Misr, 1946).

Intravenous administration of saline is imperative in patients suffering from severe salt depletion ; such patients are in desperate peril and there is no time to wait upon other methods.

Special routes, useful in certain circumstances, are the rectal, subcutaneous and intra-peritoneal routes. The details of technique may be found in surgical manuals. Rectal administration is best performed by the original method of Murphy (Murphy, 1909 and 1916 ; Kekwick and Marriott, 1937).

CONCLUSION

Deviations from fluid balance, positive or negative, are of great importance in a wide range of medical and surgical conditions and cause much loss of life. Rational preventive or remedial treatment can be almost miraculous. Incorrect treatment may be lethal. Clear understanding is the pre-requisite to proper handling of cases.

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