

from his body fluids along with it, or he may retain the salt. In either event the result must be a concentration of his body fluids and an accentuation of his dehydration. We may safely say that Dr Bombard, and those who have emulated him, survived in spite of drinking sea-water, not because of it.

A convincing argument against the drinking of sea-water by castaways is provided by figures for the mortality rate among members of the Merchant Navy who were shipwrecked during the last war (McCance, Ungley, Crosfill & Widdowson, 1956). In those life-craft where sea-water was recorded as having been drunk by one or more of the men the mortality from all causes was 39%. Where no positive statement was made the mortality was 3%. Drinking sea-water was sometimes reported as having caused delirium, madness, suicide or death; in no instance was it reported to have prolonged life.

## REFERENCES

- Adolph, E. F. (and associates) (1947). *Physiology of Man in the Desert*. New York: Interscience Publishers Inc.
- Black, D. A. K., McCance, R. A. & Young, W. F. (1943-4). *J. Physiol.* **102**, 406.
- Elkinton, J. R. (1957). *Proc. Nutr. Soc.* **16**, 113.
- Fowler, R. (1871). *A Complete History of the Case of the Welsh Fasting-girl (Sarah Jacob)*. London: Henry Renshaw.
- Gamble, J. L. (1944). *Proc. Amer. phil. Soc.* **88**, 151.
- Hervey, G. R. & McCance, R. A. (1952). *Proc. roy. Soc. B*, **139**, 527.
- Hunt, E. H. (1912). *J. Hyg., Camb.*, **12**, 479.
- Hunt, J. (1953). *The Ascent of Everest*. Appendix 7. *Physiology and Medicine*, by G. Pugh & M. Ward. London: Hodder & Stoughton.
- McCance, R. A., Ungley, C. C., Crosfill, J. W. L. & Widdowson, E. M. (1956). *Spec. Rep. Ser. med. Res. Coun., Lond.*, no. 291.
- Smith, C. A. (1951). *The Physiology of the Newborn Infant*, 2nd ed. Springfield, Ill.: Charles C. Thomas.
- Robinson, J. R. (1957). *Proc. Nutr. Soc.* **16**, 108.
- Rowntree, L. G. (1922). *Physiol. Rev.* **2**, 116.
- Yoshimura, H., Inoue, G., Yamamoto, M., Yamaji, R., Tanimura, Y., Oohara, S., Takaoka, W., Koishi, H., Funaki, H. & Hayashi, M. (1953). *J. Biochem., Tokyo*, **40**, 361.

### The breakdown of the water equilibrium in disease

By D. A. K. BLACK, *Department of Medicine, Royal Infirmary, Manchester*

If the subject delineated by my allotted title is to be reduced to manageable proportions, it will be necessary to exclude from consideration a number of topics which are either too general to warrant discussion here, or which fall within the territory of other speakers in this symposium. It is difficult to conceive of a disease process which is not attended by some local change in tissue hydration, but such changes are mostly secondary effects, and for our present purpose can be omitted. Moreover, the physiological aspects of body water have been discussed by Robinson (1957) and Widdowson (1957), so it will not be necessary for me to discuss normal water balance. Many of the most notable alterations in water content of the body are really determined by primary changes in its content of electrolytes, certainly of sodium

and its accompanying anions (oedema and clinical dehydration), and possibly also of potassium; this topic also I shall neglect, referring to Elkinton's (1957) contribution, and to the monograph of J. L. Gamble on the *Companionship of Water and Electrolytes in the Organization of Body Fluids* (Gamble, 1951). Since treatment will be discussed by Young (1957), I have managed by these somewhat arbitrary excisions to reduce my subject matter to the causes and effects of those alterations of total body water that occur independently of, or at least in excess of, concurrent alterations in body electrolytes; in other words, I am to deal with primary water depletion and water excess.

*Water depletion.* The first suggestion that primary depletions of water and of salt might be significantly different in their causes, effects, and therapy comes, I think, from the studies of Kerpel-Fronius (1935) on animals. The first clinical paper in English was by Nadal, Pederson & Maddock (1941), and the clinical aspects of the distinction between water and salt depletion have been fully reviewed by Marriott (1947). Meanwhile, important experimental studies of water depletion in man were carried out independently by McCance (Black, McCance & Young, 1943-4) and by Elkinton (Elkinton & Taffel, 1942), with their respective colleagues; these studies were largely prompted by their obvious relevance to the fate of men marooned on life-rafts or lost in the desert. The effect of diet on the water requirement was specifically studied by Gamble (1946-7). It is from these basic studies that our present concepts of water depletion are largely derived, though in the past year or two further information of considerable relevance has come from studies of aldosterone output under conditions of severe water depletion (Bartter, Liddle, Duncan, Barber & Delea, 1956).

Given adequate access to water, clinical water depletion arises most commonly because of insufficient intake in patients who are comatose, lethargic, or simply too weak to bother to drink. The thirst mechanism, normally so compelling, cannot be relied on in ill patients. Gastro-intestinal disease usually leads to equivalent losses of water and electrolyte, and is not therefore a usual cause of pure water depletion; in oesophageal obstruction, however, there may be little electrolyte loss, but the intake of water may be effectively precluded. Deficient intake may be aggravated by abnormal losses of water, most commonly perhaps in febrile patients, whose water needs are increased both by sweating and by hyperpnoea. Inability to concentrate the urine adequately also predisposes to water depletion, as in untreated diabetes insipidus; in renal insufficiency not complicated by vomiting; and in the hyposthenuric states associated with potassium depletion and sometimes with chronic pyelonephritis. The type of food intake is also of some importance in relation to water depletion. The oxidation of carbohydrate supplies an equivalent amount of water, and oxidation of fat rather more; and the carbon dioxide formed is excreted by respiration. On the other hand, protein affords less water of oxidation, and the urea formed in protein katabolism requires water for its excretion. High-protein tube-feeding in comatose patients has been observed to cause significant depletion of water, with an elevated plasma-sodium concentration (Engel & Jaeger, 1954). Clinical water depletion is relatively common in infants, who cannot concentrate their urine

to adult standards, and also in patients with intracranial disease or injury, in whom deficient intake is certainly a major factor, but may not be the whole explanation, as the urine formed may be poorly concentrated. Finally, a depletion of water relative to electrolyte can be induced by giving hypertonic saline solutions; these patients show thirst and a rise in plasma-sodium concentration, but the other signs of an absolute water depletion are of course absent.

The effects of water depletion can be more plainly discerned in the various experimental studies than in clinical water depletion which is often complicated by other abnormalities, or may indeed have arisen because of an impairment of the mechanisms which normally defend us against water depletion. In the normal subject, deprivation of water leads to a loss of weight, the formation of a concentrated urine, and an increase in the osmolarity of body fluid, most conveniently assessed by serial estimates of the plasma-sodium concentration (Black *et al.* 1943-4). The volume of urine formed is a function of the intake of electrolyte and of protein, and it tends to increase as the osmolarity of body fluid rises, whereas it may actually decline with early rehydration, which lowers plasma osmolarity without fully repairing the water deficit (McCance, Young & Black, 1943-4). The contribution made by the extracellular fluid (including the plasma) and the intracellular fluid to the water lost from the body is of considerable interest. Initially, the relative urinary losses of sodium and potassium indicate that these two main compartments of body fluid are each contributing water in proportion to their initial relative volume. This is in notable contrast to sodium depletion, in which the loss of body fluid involves primarily the plasma and extracellular fluid (McCance, 1936), and it has the practical corollary that the circulatory effects of water depletion of a given degree will be less severe than those of a similar degree of water loss induced by sodium depletion. Moreover, with advancing water depletion, a further mechanism enters to maintain extracellular fluid and plasma volume; it was observed by Elkinton & Taffel (1942) in prolonged water deprivation in dogs, and is often described as the 'dehydration reaction'. In it, there is a relatively enhanced output of potassium and a decreased output of sodium, so that by virtue of the 'companionship of water and electrolytes' the volume of extracellular fluid, resting on body sodium, will be less depleted than the volume of intracellular fluid, resting on body potassium. Increase in the sodium: potassium ratio of urine is now largely attributable to action of aldosterone on the renal tubules; and it is of great interest that an increased output of this hormone can be shown in advanced water depletion (Bartter *et al.* 1956). This work suggests that the 'dehydration reaction' of Elkinton & Taffel may constitute an interesting example of volume control of body fluid mediated by the aldosterone mechanism.

The clinical recognition of water depletion, as of most other body-fluid disturbances, depends very largely on the conjunction of an adequate history and awareness of the causes of water depletion. Obviously, not all the features of pure experimental water depletion need be observed in clinical water depletion; for example, an apathetic patient may not complain of thirst, and a patient with renal insufficiency will not be excreting a scanty and concentrated urine. The absence of notable circulatory impairment and hypotension in moderate water depletion is of value in

distinguishing it from moderate sodium depletion. The appearance and turgidity of the subcutaneous tissues are perhaps less helpful, for the combination of wasting and water depletion can mimic the typical 'dehydration' of sodium depletion very closely. In water depletion, the plasma-sodium concentration is increased, whereas in sodium depletion it is usually diminished. The plasma-protein concentration is increased in both water and sodium depletion; the haematocrit percentage is increased in sodium depletion, but not in water depletion; but these estimations are not of great help clinically, because of the usual lack of base-line information.

*Water excess ('water intoxication')*. Although it is probably much less common than water depletion, water excess was recognized some 20 years earlier, as a result of the clinical and experimental observations of Rowntree (1922). His description of the clinical effects of overloading with water has not been essentially modified; but additional information has been gained, mainly in the past 10 years, on the frequency of water excess in acute renal failure and postoperatively, and on the detailed effects of water overload on body-fluid distribution and excretion.

It is difficult to induce water excess in the normal organism, because of the effective diuretic response of the kidneys to any load of water that does not provoke vomiting. In disease, however, hypotonic fluids may be given by vein or rectum, but by far the most important factor in causing water excess is impairment of the diuretic response. This failure of water diuresis may arise from intrinsic renal disease, most notably in the anuria or extreme oliguria of acute tubular necrosis; from adrenal or anterior-pituitary insufficiency; or, perhaps most commonly, from excessive production of posterior-pituitary antidiuretic hormone in response to pain or injury, as in the few days following trauma or operation. Electrolyte depletion is a significant factor predisposing to water intoxication, many of whose effects are based on osmolar hypotonicity of body fluid. Because of the conjunction of oliguria, sometimes with sodium depletion, and sometimes with forced parenteral fluids, post-operative water intoxication is fairly frequent, and has been well documented in the past few years (Zimmermann & Wangenstein, 1952; Wynn & Rob, 1954). Before the introduction of water restriction as part of the management of anuria (Bull, Joekes & Lowe, 1949) water excess was common and may have been a cause of convulsions; recent work suggests that in these patients even 1 l. water daily may be excessive, and their requirement is more nearly 500 ml./day (Hamburger & Mathé, 1954; Bluemle, Potter & Elkinton, 1956).

The effects of water excess include fatigue, mental confusion, headache, nausea and vomiting; more severe water excess leads to convulsions and ultimately to death in coma. The protein and electrolytes of plasma are diluted, but the haematocrit shows no striking change, indicating that the water load is divided between cells and plasma. Wynn (1955) has calculated that in experimental water intoxication the excess of water is distributed between body cells and extracellular fluid in proportion to the amount of osmotically active solutes in the two compartments. The urine is copious and dilute when water excess is induced by water loading without pitressin, but later the chloride concentration in the urine tends to increase. This chloruresis, and the natriuresis which accompanies it, have been studied by

Leaf, Bartter, Santos & Wrong (1953) and by Wrong (1956). Their subjects were given several litres of water to drink, and excretion was inhibited by the posterior-pituitary antidiuretic hormone. Leaf *et al.* (1953) regarded the increase in output of sodium which they observed as 'a homeostatic response to over-expansion of fluid volume'. Wrong (1956) showed that the natriuresis was not related to any consistent increase in glomerular filtration rate, and that the time taken for natriuresis to develop was similar to the time that would be needed for aldosterone to disappear from plasma after its production had been inhibited. The view that the natriuresis of water excess is related to diminished output of aldosterone (the converse of the 'dehydration reaction') has received support from the aldosterone assays of Muller, Riondel & Mach (1956).

The clinical recognition of water excess again depends very much on awareness of the circumstances likely to give rise to it. The tissues are well hydrated and the circulation good. Thirst is absent. The plasma-sodium concentration is low, but this finding is of less value than is the converse finding of a raised plasma sodium in water depletion. Low plasma-sodium values are also found in sodium depletion, and in various forms of 'symptomless hyponatraemia' (Danowski, Fergus & Mateer, 1955). When the history is confused or unobtainable, and the patient is convulsed or comatose, it may be justifiable to give 50 ml. of 5% saline intravenously—this amount will alleviate the symptoms of water excess, but will not appreciably correct massive sodium depletion, or influence other states associated with a low plasma sodium.

### Summary

The causes, effects, and clinical recognition of primary water depletion and excess are outlined. These states are less common than the corresponding alterations in body water secondary to electrolyte depletion and excess, but their frequency and importance are sufficient to justify their regular inclusion among the syndromes of body-fluid disturbance.

### REFERENCES

- Bartter, F. C., Liddle, G. W., Duncan, L. E., Barber, J. K. & Delea, C. (1956). *J. clin. Invest.* **35**, 1306.  
 Black, D. A. K., McCance, R. A. & Young, W. F. (1943-4). *J. Physiol.* **102**, 406.  
 Bluemle, L. W., Potter, H. P. & Elkinton, J. R. (1956). *J. clin. Invest.* **35**, 1094.  
 Bull, G. M., Joecks, A. M. & Lowe, K. G. (1949). *Lancet*, **257**, 229.  
 Danowski, T. S., Fergus, E. B. & Mateer, F. M. (1955). *Ann. intern. Med.* **43**, 643.  
 Elkinton, J. R. (1957). *Proc. Nutr. Soc.* **16**, 113.  
 Elkinton, J. R. & Taffel, M. (1942). *J. clin. Invest.* **21**, 787.  
 Engel, F. L. & Jaeger, C. (1954). *Amer. J. Med.* **17**, 196.  
 Gamble, J. L. (1946-7). *Harvey Lect.* **42**, 247.  
 Gamble, J. L. (1951). *Companionship of Water and Electrolytes in the Organization of Body Fluids*. Palo Alto: Stanford University Press.  
 Hamburger, J. & Mathé, G. (1954). In *Ciba Foundation Symposium on The Kidney*. [A. A. G. Lewis and G. E. W. Wolstenholme, editors.] London: J. & A. Churchill.  
 Kerpel-Fronius, E. (1935). *Z. Kinderheilk.* **57**, 489.  
 Leaf, A, Bartter, F. C., Santos, R. F. & Wrong, O. (1953). *J. clin. Invest.* **32**, 868.  
 McCance, R. A. (1936). *Lancet*, **230**, 823.  
 McCance, R. A., Young, W. F. & Black, D. A. K. (1943-4). *J. Physiol.* **102**, 415.

- Marriott, H. L. (1947). *Brit. med. J.* i, 245.  
Muller, A. F., Riondel, A. M. & Mach, R. S. (1956). *Lancet*, 270, 831.  
Nadal, J. W., Pederson, S. & Maddock, W. G. (1941). *J. clin. Invest.* 20, 691.  
Robinson, J. R. (1957). *Proc. Nutr. Soc.* 16, 108.  
Rowntree, L. G. (1922). *Physiol. Rev.* 2, 116.  
Widdowson, E. M. (1957). *Proc. Nutr. Soc.* 16, 118.  
Wrong, O. (1956). *Clin. Sci.* 15, 401.  
Wynn, V. (1955). *Clin. Sci.* 14, 669.  
Wynn, V. & Rob, C. G. (1954). *Lancet*, 266, 587.  
Young, W. F. (1957). *Proc. Nutr. Soc.* 16, 128.  
Zimmerman, B. & Wangenstein, O. H. (1952). *Surgery*, 31, 654.

## The restoration and maintenance of water equilibrium in disease

By WINIFRED F. YOUNG, *Queen Elizabeth Hospital for Children, London, E.2*

The consequences of changes in water equilibrium have been vividly described by previous contributors to this symposium (Robinson, 1957; Elkinton, 1957; Widdowson, 1957; Black, 1957) who have explained to us how both severe depletion and gross expansion of the volume of the body fluids may endanger life itself. Early diagnosis of the diseases likely to cause dehydration can often be made and medical care is easily available in this country. A knowledge of the proper use of water and electrolytes should, therefore, be used mainly for prevention rather than for the treatment of a breakdown of water equilibrium. Unfortunately we are often not quick enough, and severe stages of dehydration may be reached at an alarming speed in very sick patients. Overhydration and water intoxication are usually due to misguided treatment of an individual patient, but the history of events leading up to his clinical state may have been an inadequate guide to his needs. Plans for the management of both depletion and excess must therefore be to hand if successful treatment is to be given when an emergency arises.

### *Assessment of patient's needs*

The objects of treatment are to restore and maintain the volume, and to repair the composition, of the body fluids. Since water equilibrium is dependent upon the concentration of electrolytes in the extracellular and the intracellular fluids, the requirements of water and salt must be assessed together. The estimate of an individual patient's needs must take into account (1) the preceding deficit, (2) current normal daily losses from the skin and lungs and in the urine, and (3) concomitant abnormal losses, e.g. from the alimentary tract or in the sweat. At first, the duration, magnitude and probable site of increased losses, or the extent of a deficient intake may be deduced from the history and clinical state. Later, frequent observations of the clinical state of the patient, variations in his body-weight, and recorded estimates of the output of the urine and stools are used to appraise his needs. It is not always easy to obtain information about the urine output in very sick patients and in young children, but experienced nurses are usually able to give a fair account without