1 Introduction

Thirst is a subjective sensation aroused by a lack of water. As a powerful and compelling sensation, it is perhaps only exceeded by the hunger for air and by pain. Associated with the sensation of thirst is the desire to drink water, and usually thirsty subjects report a dry feeling in the mouth and find that water tastes pleasant. Some of these different sensations were described vividly by the explorer Sven Hedin (1899) who, after a terrible journey across the western Taklamakan desert during which camels and men of his caravan succumbed for lack of water, finally struggled to safety:

> I stood on the brink of a little pool filled with fresh, cool water – beautiful water.
>
> It would be vain for me to try to describe the feelings which now overpowered me. They may be imagined – they cannot be described. Before drinking I counted my pulse: it was forty-nine. Then I took the tin box out of my pocket, filled it, and drank. How sweet that water tasted! Nobody can conceive it who has not been within an ace of dying of thirst. I lifted the tin to my lips, calmly, slowly, deliberately, and drank, drank, drank, time after time. How delicious! what exquisite pleasure! The noblest wine pressed out of the grape, the divinest nectar ever made, was never half so sweet. My hopes had not deceived me. The star of my fortunes shone brightly as ever it did.
>
> I do not think I at all exaggerate, if I say that during the first ten minutes I drank between five and six pints. The tin box held not quite an ordinary tumblerful, and I emptied it quite a score of times. At that moment it never entered my head that, after such a long fast, it might be dangerous to drink in such quantity. But I experienced not the slightest ill effects from it. On the contrary I felt how that cold, clear delicious water infused new energy into me. Every blood-vessel and tissue of my body sucked up the life-giving fluid like a sponge. My pulse, which had been so feeble, now beat strong again. At the end of a few minutes it was already fifty-six. My blood, which had lately been so sluggish and so slow that it was scarce able to creep through the capillaries, now coursed easily through every blood-vessel. My hands, which had been dry, parched, and hard as wood, swelled out again. My skin, which had been like parchment, turned moist and elastic. And soon afterwards an active perspiration broke out upon my brow. In a word, I felt my whole body was imbibing fresh life and fresh strength. It was a solemn, an awe-inspiring moment.

Recently, we have been able to investigate quantitatively the sensation of thirst, and some of the other sensations associated with thirst (B. J. Rolls, Wood, Rolls *et al.*, 1980). Human subjects were asked to

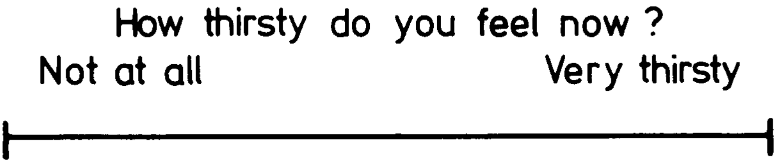

Fig. 1.1. An example of a visual analogue rating scale used by human subjects to provide a measure of thirst. The 10-cm line was marked at the position which corresponded to the degree of thirst felt.

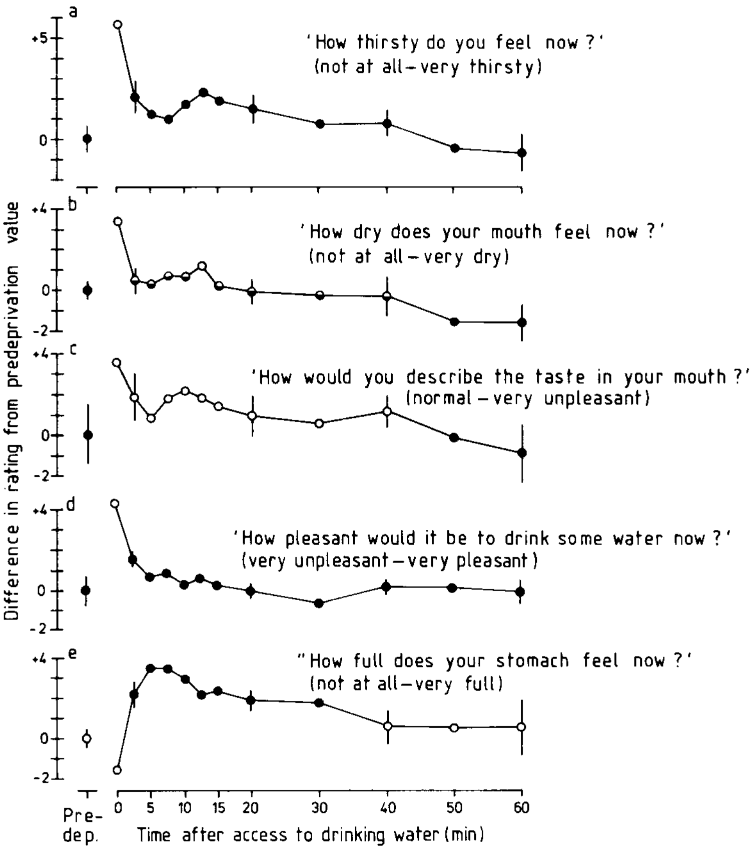

Fig. 1.2. The effect of 24 h water deprivation on human subjective ratings of thirst and other sensations is shown by the difference between the predeprivation rating (pre-dep.) and the rating at time 0, taken 24 h later just before access to water was given. The way in which the ratings changed after drinking started at time 0 is also shown. The significance of the changes relative to the value after 24 h water deprivation, at time 0, is indicated by closed circles ($P<0.01$), half-filled circles ($P<0.05$), or open circles (not significant). (After B. J. Rolls, Wood, Rolls *et al.*, 1980.)

respond to the question 'How thirsty do you feel now?' by marking the position corresponding to their sensation on a 10-cm line labelled at one end 'very thirsty' and at the other end 'not at all thirsty' (see figure 1.1). It is shown in figure 1.2a that, after 24 h deprivation (at time 0, just before access to water), the thirst rating moved more than 5 cm towards the 'very thirsty' end of the scale, compared to the normal, non-thirsty, rating. Water deprivation also usually produces a dry sensation in the mouth. Our subjects, consistent with this, demonstrated a significant shift in the rating of the dryness of the mouth (see figure 1.2b), and also reported a rather unpleasant, almost putrid, taste in the mouth, as shown in figure 1.2c. They also found the taste of water very pleasant after water deprivation, showing a significant shift towards pleasantness (figure 1.2d – see also Chapter 5). Associated with these sensations produced by water deprivation is a desire to drink water, and drinking after water is obtained is avid and remarkably rapid, as illustrated in figure 1.3. Interestingly, the sensation of thirst, and the dryness of the mouth and the pleasantness of the taste of water, diminish very rapidly once drinking is begun, with large and significant changes becoming evident within 2.5 min after starting to drink water (see figure 1.2).

As thirst is a subjective sensation aroused by a lack of water it can strictly only be studied directly in man, according to this definition. However, animals including man, when deprived of water, are in a state of drive in which they will search for and ingest water, and 'thirst' can be used in a different way to that described above as a name for this

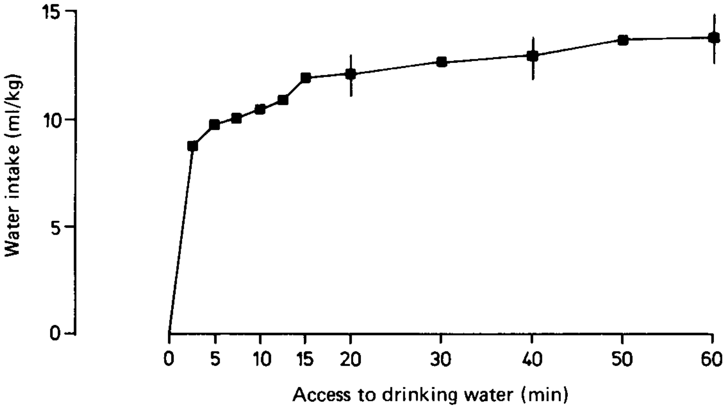

Fig. 1.3. The pattern of water intake over a 1-h period in which the 24-h water-deprived human subjects who provided the ratings shown in Figure 1.2 were allowed free access to drinking water. The drinking was remarkably rapid. (Modified from B. J. Rolls, Wood, Rolls *et al.*, 1980.)

state of drive. Sometimes, the word thirst has also been applied to the deficits in body water produced by water deprivation, but this use is best avoided, as it is clear and accurate to refer in this case simply to 'water deficit'. The way in which body water is divided into different compartments and the influence which water deprivation has on these compartments, is described in Chapter 2.

The study of thirst and drinking

Thirst, including the control of drinking in animals and man, is the subject of this book. It is a useful and interesting subject to study, not only because it is essential to the survival of most terrestrial vertebrates, and is relevant to clinical conditions of water imbalance in man, as described in Chapter 9, but also because it provides a useful model system with which to analyse how a relatively complex type of behaviour is controlled. The advantages of using drinking as a model system are many. First, it is relatively easy to measure. Even with a behaviour as apparently similar as feeding, measurement is much more complicated in that allowance must be made for the ingestion of a wide range of nutrients, each of which has different effects on the system. Second, with drinking, the initiating stimuli are likely to be related to the effects which lack of water has on the system, and these can be measured and identified relatively straightforwardly. In the case of some other types of behaviour, it may be more difficult to identify and thus to analyse the signals that initiate the behaviour. For example, with feeding it is difficult to know which of the many chemical changes that are part of the metabolism of different nutrients may act as signals to control the behaviour. Third, drinking allows the analysis of body-brain relations in a case of a relatively complex, motivated behaviour. This behaviour can be related to the sensations that accompany it and analysed in terms of the whole range of sensory, control and motor processes which all contribute to the expression and control of drinking.

The causes of drinking

Thirst and drinking normally arise from a lack of water, which acts through resulting changes in the body fluid compartments as described in Chapter 4 to initiate drinking. Thus, drinking in response to a lack of water, or to an alteration in the body fluid compartments, is described as homeostatic in that it reduces the disturbances in the body fluid compartments. Homeostasis is an important concept used by W. B. Cannon (1947) to describe 'the various physiological arrangements which serve to restore the normal state once it has been disturbed'. Drinking in response to a lack of water is an example of a behavioural response which serves to maintain homeostasis. The controls of homeostatic (or 'primary') drinking, which occurs in response to body fluid imbalances, are described in Chapters 4, 5 and 6 in terms of the factors that initiate, maintain, and terminate the drinking. It will be seen that it is possible to specify quite precisely for drinking behaviour which signals lead to the drive for water, which signals reward or reinforce drinking, and which signals stop drinking. It is very interesting that different signals are involved in controlling these different aspects of behaviour. For example, drinking may be initiated in response to a body fluid imbalance, but may be rewarded in the first instance by the taste of water. As a basis for understanding the homeostatic controls of drinking, the fundamental aspects of body fluid distribution and balance are described in Chapter 2.

If drinking is not caused by a change in the body fluid compartments or occurs heedless of the state of body fluids, then it is described as non-homeostatic, in that it does not reduce physiological imbalances. This drinking has also been called non-regulatory drinking, or 'secondary' drinking. Examples of non-homeostatic drinking, that is, drinking which is inappropriate given the state of the body fluids, are as follows: (1) The under-drinking which occurs when fluids are made less palatable, for example by the addition of the bitter-tasting substance quinine. (2) Prandial drinking, which is drinking of small draughts taken alternately with small morsels of food in rapid succession in a meal (see Kissileff, 1973). This drinking is at least partly lubricative, and does not just serve to reduce the dehydrating consequences of the meal, in that it occurs primarily when salivation is experimentally reduced, either pharmacologically or by removal of the salivary glands. (3) A dry mouth alone, induced for example by the above methods, or by speaking, excessive smoking, panting or irritation by spicy foods (see Fitzsimons, 1979) or by the removal of the salivary glands (Kissileff, 1973), is sufficient to lead to increased drinking or to an altered pattern of drinking. (4) Schedule-induced polydipsia, in which a rat (reduced to 80% body weight by food restriction), when given 45 mg pellets of food on a spaced-reward schedule with water freely available, drinks excessively between the deliveries of food (Falk, 1961). The effort required to obtain water is another non-homeostatic control of drinking and can affect the drinking pattern as well as the amount ingested (see McFarland, 1971). For example, if the path between the places where food and water is obtained is made longer, then the duration of each bout of drinking and eating becomes longer. Non-homeostatic or secondary drinking is considered further in Chapter 10, together with the question of whether normal, everyday, drinking is in response to body fluid deficits and is thus homeostatic, or whether it anticipates these deficits so that they do not occur, or is in such great excess that it is far greater than that required for homeostasis.

Measures of drinking

A simple way to measure drinking which is widely used in the laboratory is to use an inverted graduated cylinder or tube with a drinking spout at the bottom (figure 1.4). As it allows total intake to be measured, and to be compared perhaps to a fluid-deficit signal, this method is particularly appropriate for determining how accurately drinking is terminated in relation to need. This is thus not so much a measure of how much thirst is being experienced or of the drive to drink, but more a measure of how much water is required to produce satiety, or at least to terminate drinking.

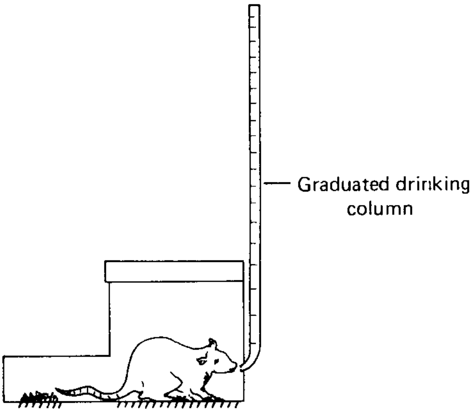

Fig. 1.4. An inverted graduated tube with a drinking spout is a simple way to measure drinking.

If a measure of thirst or the drive for water is required, it is better to measure how hard an animal will work to obtain water, rather than how much water must be consumed before satiety mechanisms terminate drinking. For example, in a progressive ratio test of the animal's motivation, one progressively increases the number of times the animal must press a lever in order to obtain one small delivery of water until the animal stops working. In one study of this type, a progressive ratio of 10 was used, so that rats had to press once for the first water reward, 11 times for the second, 21 times for the third, etc., and it was shown that the hormone angiotensin produced a motivation for water comparable to that produced by moderate water deprivation, in that the rats pressed up to approximately 51 times for one water reward in each of these conditions before they stopped work (B. J. Rolls, Jones & Fallows, 1972). Another example of a schedule in which motivation can be assessed without the complication of satiety produced by ingestion is a variable-interval schedule, in which rewards

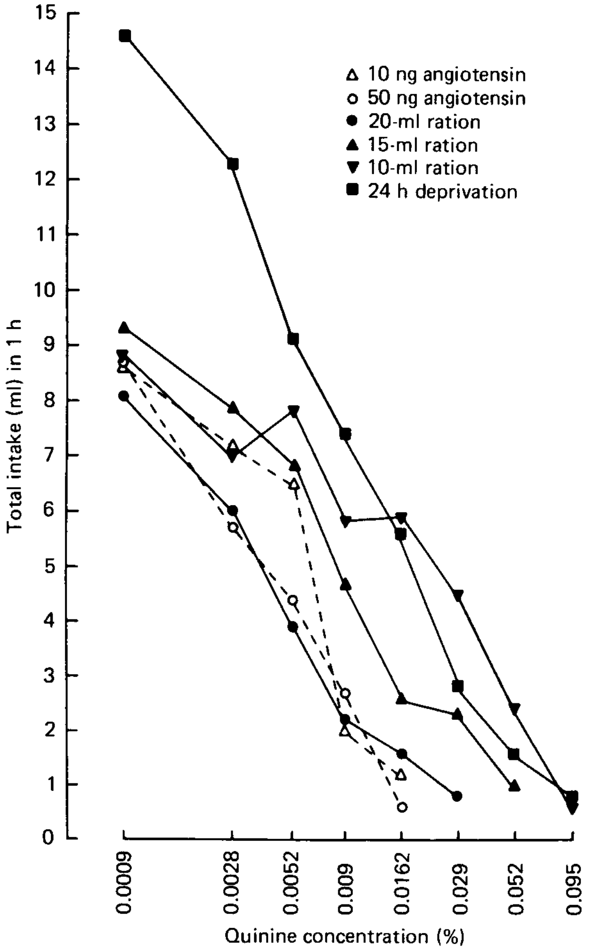

Fig. 1.5. The motivation for water can be estimated by the concentration of bitter-tasting quinine tolerated in the drinking water. In this case rats tolerated the highest concentrations of quinine after 24 h water deprivation, or if they were allowed only a 10-ml ration of water overnight (see text for further details). (From B. J. Rolls, Jones & Fallows, 1972.)

are delivered for the first press made after a variable interval of mean value, e.g. 1 min. On this type of schedule animals work steadily, and at a rate which gives a measure of their motivation, in that the rate is increased by deprivation. Another measure of motivation for water is to assess to what extent animals will tolerate aversive consequences in order to obtain water, using for example electric shock (Warden, 1931), or bitter-tasting quinine added to the water (e.g. B. J. Rolls, Jones & Fallows, 1972).. An example of this is shown in figure 1.5, in which the thirstier rats are because they have been given less water overnight, the more they will tolerate and drink higher concentrations of quinine in a 1-h drinking test. It is also clear that the motivation for water of animals given angiotensin is approximately equivalent to that of rats allowed 15–20 ml of water overnight (compared to the *ad libitum* overnight intake of 25–45 ml). Another way to measure motivation for water is to use a preference test, providing a choice between for example water and food. As implied above, these different measures of motivation for water will not always correlate with the amount of water actually drunk with free access (known as *ad libitum* drinking), as the amount drunk reflects the amount of water required to terminate drinking, rather than just the initial motivation of the animal to obtain water.

The pattern of drinking

Drinking is a behaviour which occurs in many animals at regular, and quite frequent, intervals. Farm animals and dogs kept as pets drink several times a day. Man not only drinks water from time to time in the day, especially when the weather is hot, but also coffee, tea and other beverages, particularly with meals. Rats used in laboratory experiments and allowed free access to water drink at frequent intervals, particularly,

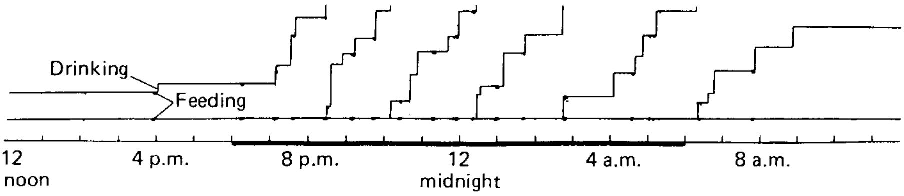

Fig. 1.6. Drinking and feeding patterns in a rat. Each time the rat licked the drinking tube to obtain water, the upper pen moved upward a fraction of a millimetre. (It reset at the top of the paper.) Each time the rat pressed a bar to obtain a 45-mg pellet of food, the upper and lower pens deflected downwards briefly, then returned. Note that most of the drinking was at night, was in long draughts, and was associated with food, occurring just before or just after eating. (From Epstein, 1967.)

as shown in figure 1.6, at night and in association with feeding. They usually lap at a relatively constant rate of 7 laps/s in short bouts of 30 s to 5 min, and intersperse these bouts with other behaviours such as feeding, grooming or resting. Although one or several bouts of drinking usually follow, or sometimes precede, a bout of feeding and the drinking is thus associated with feeding, it should be noted that this is different from the prandial drinking noted above in which the feeding and drinking are continually intermingled within a bout in desalivate animals (Kissileff, 1973). Prandial drinking appears to occur partly for lubrication, in that it is attenuated if water is infused into the mouth, but not if water is infused into the stomach. However, it is more difficult to know whether drinking that is normally associated with feeding occurs for lubrication or because of actual or anticipated dehydration produced by the food, or for other reasons. This important question, of whether normal drinking is often associated with feeding because dehydration arises or is anticipated as a result of the ingested food, is dealt with in Chapter 10.

After water deprivation, animals drink to satiety with different time-courses. Dogs typically drink very rapidly, gulping down enough in 2–3 min to replace eventually their body needs after 24 h water deprivation. Man and monkeys also drink quite rapidly after 24 h water deprivation, drinking much of what they need in 2.5 min, and most of it in 5 min (see figure 6.2). Rats are slower drinkers, continuing to drink significant quantities in the second half of a 1-h test session following 24 h water deprivation. These different patterns of drinking have important implications for the mechanisms by which drinking is terminated. In relatively slow drinkers, such as the rat, there may be sufficient time for water to be absorbed before drinking is terminated, so that simple replacement of the body fluid deficit may be sufficient to account for the termination of drinking. In species which drink relatively rapidly, there may be insufficient time for water to be absorbed by the gut to allow the deficit signals to be neutralized, so that specialized, pre-absorptive satiety systems are required. It is important to separate and analyse these different possibilities, as shown in Chapter 6.

Another feature in the pattern of drinking is a circadian rhythm. In the rat for example most of the drinking occurs at night (figure 1.6), and this rhythm persists even when food is not available (Morrison, 1968). It is not yet known whether this reflects a circadian rhythm in the drinking mechanism itself or whether the increased drinking at night could be due to a homeostatic need for water, resulting from the water lost in the saliva which is used for grooming as well as for behavioural thermoregulation in the rat (Kissileff, 1973).

2 Fundamentals of fluid intake and output

Life originated in the sea. In this environment the simplest strategy was for animals to evolve with an internal composition similar in concentration to that of the sea water surrounding them. However, as animals colonized dry land they retained a sea-like internal composition and therefore had to meet the problems of conserving and obtaining water. The way in which some terrestrial mammals, including man, have coped with these problems forms the basis of this book. Before attempting to understand the complexities of behavioural regulation it is necessary to explain the fundamental features of fluid composition and balance. The ways of measuring and manipulating the body fluids will also be introduced as these procedures form the backbone of our experimental understanding of the controls of thirst.

Water content of the body

The functions of all the cells of the body depend on water. Oxygen and nutrients are taken up from water and wastes are discharged into it. Water is the largest single component of the body and its volume must be maintained within narrow limits. In the nineteenth century Claude Bernard attempted to define the proportion of water in the body by comparing the weights of the desiccated bodies of Egyptian mummies with the weights of living persons of the same general size and shape. His estimate was that the body is 90% water, which we now know from the more direct method of drying the tissues of corpses is too high. The proportion of body water in man can vary widely in individuals and ranges from about 45% to 70%. Within an individual the proportion of body water tends to decrease with age. This is partly because the proportion of water decreases as the amount of body fat increases. The proportion of water to the lean body mass (the body without fat) is essentially constant at 70%. The proportion of body water and the distribution of water in the various organs tends to be similar in all terrestrial animals.

Total body water can now be measured by injecting a non-toxic substance (e.g. antipyrine, deuterium oxide or tritiated water) which distributes evenly throughout the body water. The volume of fluid in which the substance is distributed is then calculated by dividing the