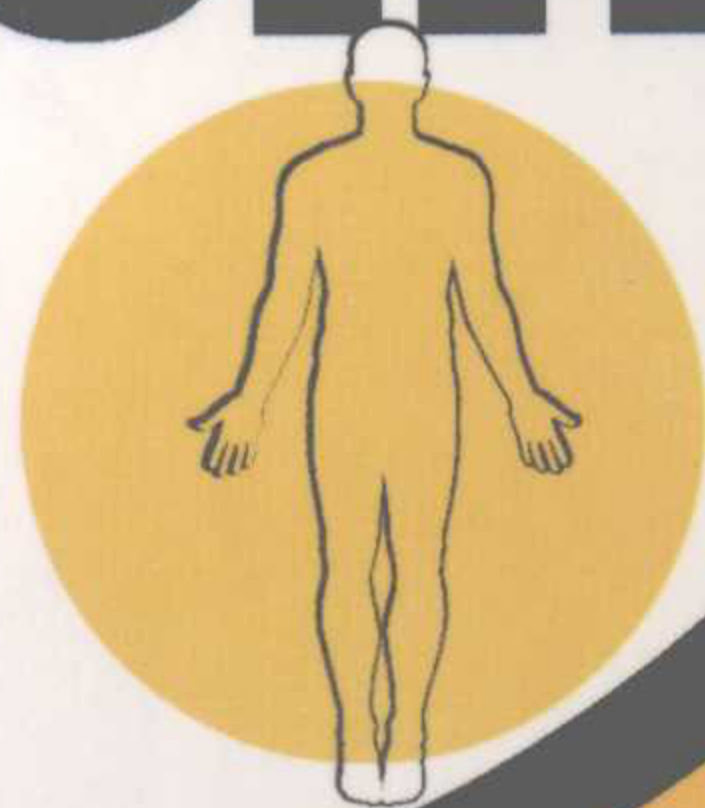


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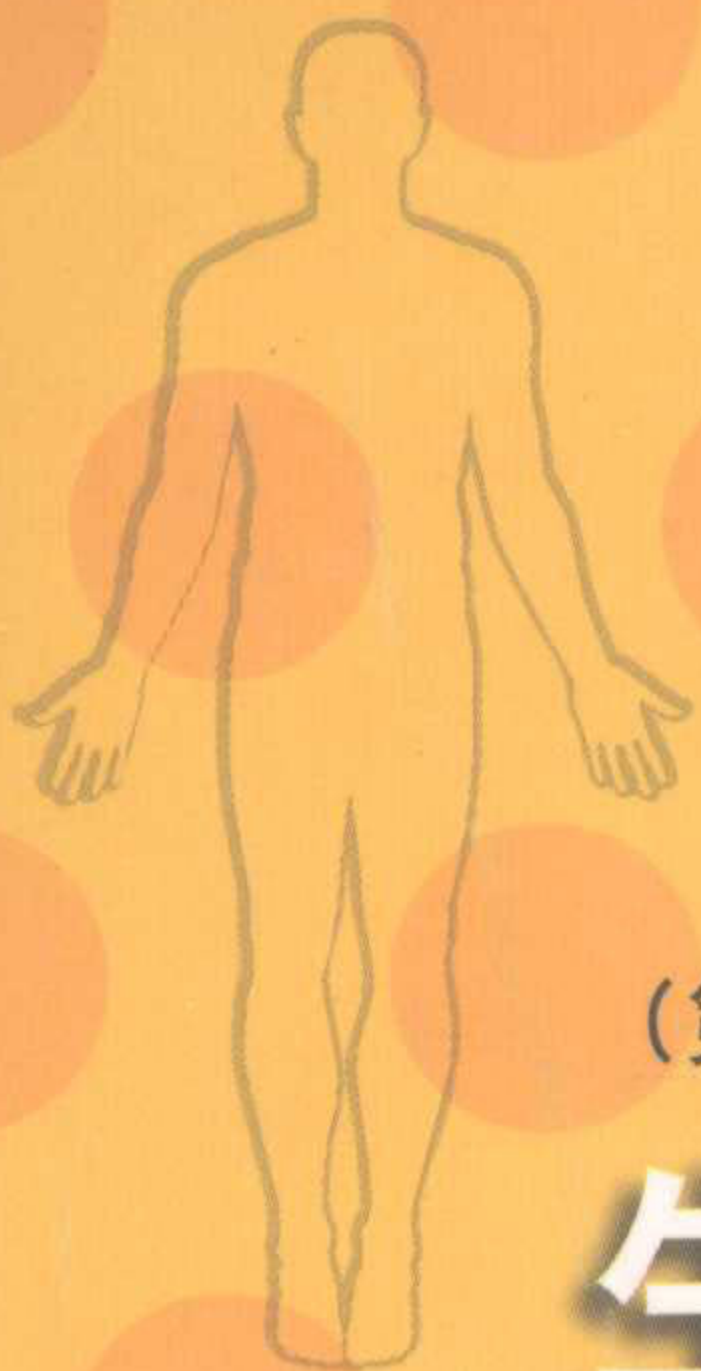
生理学 Physiology

(第3版)

J G McGeown



北京大学医学出版社



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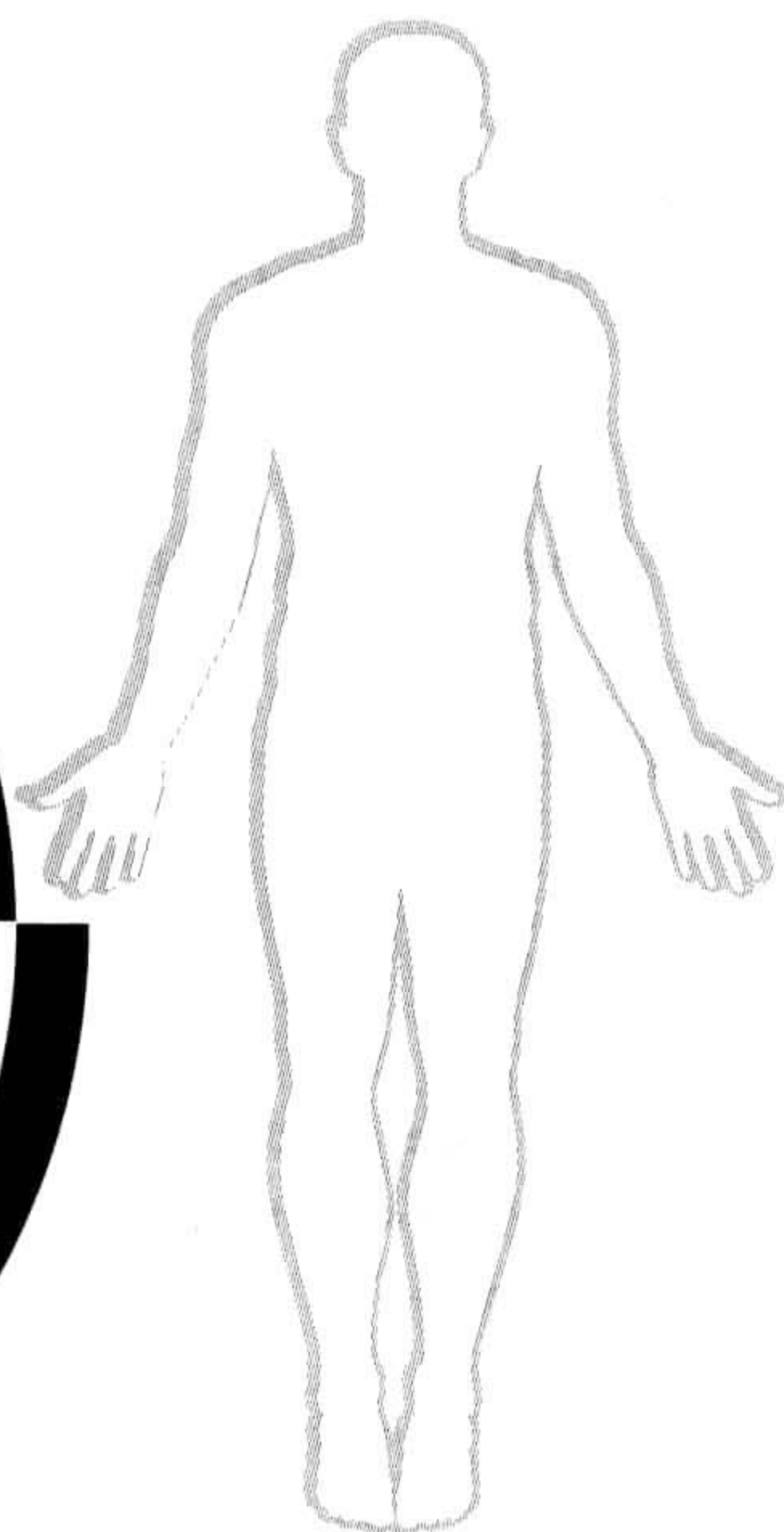
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A clinical core text of human
physiology with self-assessment

(第 3 版)

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Using this book

Philosophy of the book

This section aims to help you:

- understand how self-assessment can make learning easier and more enjoyable
- use the book to increase your understanding as well as your knowledge
- plan your learning.

How much do you know about the control of blood pressure? Are they the right things? Can you answer examination problems on physiological control systems? This book aims to help you with these questions. Principles are illustrated and mechanisms explained while essential information is presented in a concise and ordered fashion. Do not think, though, that this book offers a 'syllabus'. It is impossible to draw boundaries around medical knowledge and learning is a continuous process carried out throughout your career. With this in mind, we want you to develop the ability to discriminate material which must be understood from areas which you need to know about, and topics which you might simply be aware of.

You are probably working towards one or more examinations and one aim is to show you how to overcome this barrier. Learning is not simply for the purpose of passing exams, however, so the book aims both to help you to pass and to develop useful knowledge and understanding.

Layout and content of the book

In order to use this book fully, you need to know why it is laid out as it is. The overview to each chapter sets out the scope of material covered. This has been chosen to reflect those things which anyone starting a medical career needs to know and which an examiner expects them to know. If you have already studied a given system, you might start by testing yourself using the self-assessment section at the end of each chapter. This will help to steer you

towards areas that you need to work on. Alternatively, you may go straight into the main body of the chapter and check at the end that you have grasped the material; if not, then you will need to do further work and perhaps read about the topics elsewhere.

The main part of the text describes the important physiology for the different systems of the body. Within each section, the essential information is presented. These essentials are summarized at the start of each subsection in the form of learning objectives, which provide a guide as to what you should know when you have studied that subject. One useful study technique is to check whether you have achieved these objectives or not. Relevant structural information is given first, both anatomical and histological, followed by a description of the main functions carried out. This will generally involve an outline of what a system does and how its performance is measured. Consideration will then be given to the mechanisms which explain these observed functions. Particular emphasis is placed on the controls which regulate function to meet body needs. Finally, important examples will be given of the consequences of abnormal function in each system to provide a link with your clinical study and training.

You have to be sure that you are reaching the required standards, so the final section of each chapter is there to help you to check your knowledge and understanding. The self-assessment is in the form of multiple choice questions, single best answer questions, matching items questions, short note questions, modified essay questions, data interpretation, clinical scenarios and sample viva questions. Some of these formats may be new to you, but all are used in testing aspiring clinicians. Questions are mainly centred on aspects of physiology which are generally regarded as important in clinical practice and so are emphasized in examinations. Detailed answers are given with reference to relevant sections of the text; the answers also contain information and explanations which you will not find elsewhere, so

you have to do the assessments to get the most out of this book.

Studying the subject

Use of the self-assessment sections will encourage you to store information and to test your ongoing improvement. You must keep testing your current level of knowledge, both strengths and weaknesses.

Overall, the aim is to help you to learn through the use of interlinked steps. Initially you must decide:

- What do you already know about the subject?
- What do you want to learn about the subject?

Knowledge is acquired more easily if it can be put into a framework, so:

- Ask yourself what things need explaining—what do you not understand?
- Try to expand on these things—explain as much as you can and be as specific as possible about what confuses you.
- Use resources such as textbooks, teachers and your peers to address these confusing issues.
- Check that you are no longer confused using relevant self-assessment materials.

If you can, discuss problems with colleagues/friends. The areas which you understand least well will become apparent when you try to explain them to someone else. You will also benefit from hearing a different perspective on a problem.

Approach to examinations

Your first task is to map out on a sheet of paper an assessment of your strong, reasonable and weak areas. This gives you a rough outline of your revision schedule, which you must then fit in with the time available. Clearly, if your exams are looming large you will have to be ruthless in the time allocated to your strong areas. The discipline of learning is closely linked to preparation for examinations. Many of us opt for a process of superficial learning which is directed towards retention of facts and recall under exam conditions. Ideally, you should acquire a deeper understanding but, recognizing constraints on your time, a pragmatic approach to learning which combines the necessity of passing exams with longer term needs is important.

Next, you need to know how you will be examined. For written examinations you need to know the

length of the exam, the types of question (for example, MCQ, modified essay, etc.), the number of questions to be answered and what choice you will have. The hardest step is to determine the likely scope of the exam; medicine does not draw boundaries around knowledge either in breadth or depth and different teachers may have slightly different emphases. Most medical and dental courses now emphasize a core curriculum and this text seeks to identify aspects of physiology which are clinically relevant. The best approach is to combine lecture notes, textbooks (appropriate to the level of study) and past examination papers. The last of these also helps indicate the depth of knowledge expected in a given area. Trying to 'spot' specific questions, however, is a dangerous practice.

The next stage is to map out the time available for preparation. You must be realistic in this, allowing time for breaks and working steadily, not cramming. If you do attempt to cram, you have to realize that if the examination requires understanding you may be in trouble. An approach based on active learning through the use of key steps, learning objectives and self-assessment has much to commend it. For a subject such as cardiovascular physiology, you might set out the topics to be covered and then attempt to summarize your knowledge about each in note form. In this way, prior knowledge will be brought to the front of your mind and gaps in your knowledge/understanding become apparent. It is much more efficient to go to textbooks having been through this exercise as you are then 'looking' for information and explanations.

As the examination draws near, you should start to attempt practice questions and complete papers. It is not sufficient to have the necessary knowledge and understanding; you need to demonstrate these to the examiners. Many people pay insufficient attention to the type of question they are going to encounter. Moving the focus away from books and lecture notes to actual questions helps in identifying where knowledge is still lacking and what work is still to be done. Additionally, attempting complete exams allows concentration to be built up.

Examination methods

Multiple choice questions or multiple True/False questions

Most multiple choice questions test recall of information. The aim is to gain the maximum marks from what you can remember. The common form consists

of a stem with several different phrases which complete the statement. Each statement is to be considered in isolation from the rest and you have to decide whether it is 'True' or 'False'. There is no need for 'Trues' and 'Falses' to balance out for statements based on the same stem; they may all be 'True' or all 'False'. The stem must be read with great care and if it is long, with several lines of text or data, then you should try and summarize it by extracting the essential elements. Make sure you look out for the 'little' words in the stem such as 'only', 'rarely', 'usually', 'never' and 'always'. Negatives such as 'not', 'unusual' and 'unsuccessful' often cause marks to be lost. 'May occur' has entirely different connotations to 'characteristic'. The latter generally indicates a feature which is normally observed, and the absence of which would represent an exception to a general rule, e.g., regular elections are a characteristic of a democratic society. Regular (if dubious) elections may occur in a dictatorship, but they are not characteristic.

Remember to check the marking method before starting. Most employ a negative system in which marks are lost for incorrect answers. The temptation is to adopt a cautious approach answering a relatively small number of questions. This can lead to problems, however, as we all make simple mistakes or even disagree vehemently with the answer favoured by the examiner! Caution may lead you to answer too few questions to pass after the marks have been deducted for incorrect answers.

Distracters are the technical term for parts of questions which sound as though they are correct but are definitely incorrect in the context of the complete statement. A good example would be to take the stem 'Parasympathetic nervous activity' and have as a completion statement 'leads to a rise in heart rate during exercise'. This is false since, although heart rate does rise in exercise, this is not caused by parasympathetic activity, which slows the heart. Another type of distracter is to give what appears to be the numerically correct value for a variable but to change the units, e.g., systemic arterial oxygen tension is normally about 95 mmHg; 95 kPa would be incorrect but could catch out the unwary. This is the commonest area where students lose marks even though they know the answer.

Single best answer questions

This is another form of multiple choice question which is sometimes favoured over the True/False format discussed above because the increased number of options means that negative marking is

not required. Only one of the possible answers is to be chosen as being the 'most correct'. Care should be exercised, as several of the possible answers may be partially correct and none of them may appear to be absolutely correct. It is the answer which you judge to be the best of the options available which should be chosen. (This reflects some aspects of clinical decision making, in which the best solution has to be chosen among several options, all of which have both benefits and possible drawbacks.) Since there is no negative marking all questions should be attempted.

Essays

Although essays are increasingly rare in examinations, you may be asked to write an essay to test your ability to integrate information. Relevant facts will receive marks, as will a logical development of the argument or theme. Conversely, good marks will not be obtained for an essay which is a set of unconnected statements. Length matters little if there is no cohesion. Relevant graphs and diagrams should also be included but must be properly labelled.

Most people are aware of the need to 'plan' their answer yet few do this. Make sure that what you put in your plan is pertinent to the question asked as irrelevant material is, at best, a waste of valuable time and, at worst, causes the examiner to doubt your understanding. It is especially important in an examination based on essays that time is managed and all questions are given equal weight, unless guided otherwise in the instructions. A brilliant answer in one essay will not compensate for not attempting another because of lack of time. Nobody can get more than 100% (usually 70–80%, tops) on a single answer! It may even be useful to begin with the questions about which you feel you have least to say so that any time left over can be safely devoted to your areas of strength at the end.

Matching item questions

This form of question is another variant of the multiple choice question which is sometimes favoured over the True/False format discussed above because the increased number of options means that negative marking is not required. The main problem that can arise with these questions (other than simply not knowing the answer) is that more than one of the options may seem appropriate to a single statement. All you can do under these circumstances is decide which answer you think is best. Check the instructions carefully to see whether each answer can be used several times (as in my examples) or once only.

Short notes

Short notes are usually marked from a 'marking template' or 'model answer' which gives a mark(s) for each important fact (also called criterion marking). Nothing is gained for style or superfluous information. The aim is to set out your knowledge in an ordered, concise manner. The major faults of students are, firstly, devoting too much time to a single question thereby neglecting the rest and, secondly, not limiting their answer to the question asked. For example, in a question about the control of erythrocyte production, all facts about erythropoiesis should not be listed, only those relevant to its regulation.

Modified essay questions and clinical scenarios

These provide for the development of a theme using a series of descriptive paragraphs which set the scene interlinked with specific questions which lead the examinee on as the 'story' unfolds. They are widely used in clinical subjects, where they are often known as 'Patient management problems', but they are sometimes used to test knowledge in basic medical sciences as well. MEQs and clinical scenarios are usually criterion marked so mentioning all the relevant information is vital and a short note format may be used. There is also often a problem-solving element which requires application of basic principles to the specific situation described.

One of the main faults in dealing with this sort of question is for students to attempt to use material from near the end of the problem to help them answer earlier questions. The MEQ is commonly designed to suggest a range of equally likely interpretations based on the initial information. Full marks depend on mentioning all of these. Some explanations may then be excluded, and new possibilities introduced, by providing further information. Your answers to a question should reflect the information given up to that point. Using material which comes later may lead you to exclude some of the most relevant responses. Also, you should attempt all sections of the question (unless the exam instructions indicate negative marking). There is usually some degree of independence of the individual sections of the problem so you should be able to attempt later sections even if you cannot answer the initial questions.

Data interpretation

This involves the application of knowledge to solve a problem. In your revision, you should aim for an

understanding of principles since it is impossible to memorize all the different data combinations. In the exam, a helpful approach is often to translate numbers into a description; for example an arterial blood pH below 7.4 represents an acidosis and the ECG tracing of a heart rate of 120 beats min^{-1} shows a tachycardia. Pattern recognition can then be attempted. This type of question is usually not negatively marked so put down an answer even if you are far from sure that it is right. Conversely, there is no point in listing four possibilities, if the question asks for one response. The examiner will not choose from your answers; the first response is likely to be taken!

Vivas

A few points on technique may be useful. The viva examination can be a nerve-wracking experience. You are normally faced with two examiners who may react with irritation, boredom or indifference to what you say. You may feel that the viva has gone well and yet you failed, or, more commonly, think that the exam has gone badly, simply because of the apparent attitude of the examiners.

Your main aim during the viva should be to control the questioning of the examiners so that they are constantly asking you about things you know about. It is worth running mock vivas with your colleagues to practise this skill. The 'examiner' also learns much in this situation since asking sensible questions requires deep understanding. Major points relating to any of the systems may be asked but if you are aware of having performed badly in an exam essay make sure you cover related material before a 'pass-fail' viva. Always give the simplest possible answer to the question asked; there are very few intentional traps in vivas but many students confuse themselves by looking for them. The examiners are likely to want to explore the limits of your knowledge so do not be upset if they push you hard. It is all right to say you do not know something and this allows the examiners to change tack to see what you do know about.

Normal values

A student is expected to know the values of certain physiological variables as they are essential to any discussion of normal physiology as well as for making decisions in emergency medicine. Values in the text have been limited to those which you are likely to be expected to know. Make sure you are also clear what the units of measurement are in each case.

Conclusions

I have set out a framework for using this book, but you should amend this according to your own needs

and the examinations you are facing. Whatever approach you adopt, your aim should be for an understanding of the principles involved as well as the memorization of facts.

Reference table of normal values Many variables show a considerable range of normal values but mid-values have been quoted in most cases

Variable	Value	Units
Body fluid volumes		
Blood volume	70	ml kg ⁻¹ body wt
Plasma volume	40	ml kg ⁻¹ body wt
Total body fluid volume	60 (males) 50 (females)	% body wt
Intracellular fluid volume	2/3 total body fluid volume	—
Extracellular fluid volume	1/3 total body fluid volume	—
Blood cells/platelets		
Haematocrit (packed cell volume)	45% (0.45)	—
Haemoglobin concentration	14	g dl ⁻¹
Red cell (erythrocyte) count	5	×10 ¹² L ⁻¹
Reticulocyte count	2	%
Erythrocyte sedimentation rate (ESR)	<5 (males) <7 (females)	mm h ⁻¹
White cell (leucocyte) count	6	×10 ⁹ L ⁻¹
Neutrophils	3.5	×10 ⁹ L ⁻¹
Lymphocytes	2	×10 ⁹ L ⁻¹
Eosinophils	0.2	×10 ⁹ L ⁻¹
Monocytes	0.5	×10 ⁹ L ⁻¹
Basophils	<0.1	×10 ⁹ L ⁻¹
Platelet count	250	×10 ⁹ L ⁻¹
Plasma		
Plasma protein concentration	60	g L ⁻¹
Plasma oncotic (colloid osmotic) pressure	25	mmHg
Plasma osmolality	300	mosmol kg ⁻¹
Na ⁺	140	mmol L ⁻¹
K ⁺	4.5	mmol L ⁻¹
Ca ²⁺	2.5	mmol L ⁻¹
Cl ⁻	105	mmol L ⁻¹
HCO ₃ ⁻	25–30	mmol L ⁻¹
Glucose	5	mmol L ⁻¹
Urea	5	mmol L ⁻¹

Variable	Value	Units
Cardiovascular function		
Resting cardiac output	5	L min ⁻¹
Resting heart rate	70	min ⁻¹
Resting stroke volume	70	ml
Systemic arterial pressure	120/80	mmHg
Pulmonary arterial pressure	25/10	mmHg
Central venous pressure	3–8	cmH ₂ O
	2–6	mmHg
Respiratory function		
Compliance (lung + chest wall)	100	ml cmH ₂ O ⁻¹
Intrapleural pressure during quiet breathing	–4 (expiration) –9 (inspiration)	cmH ₂ O
Tidal volume	500	ml
Respiratory rate	12	min ⁻¹
Respiratory minute volume	6	L min ⁻¹
Dead space	150	ml
Alveolar ventilation rate	4.2	L min ⁻¹
FEV ₁ /FVC	>75	%
Blood gases and acid–base balance (also HCO₃⁻ above)		
Systemic arterial pH	7.38–7.42	–
Systemic arterial P _{O₂}	13 98	kPa mmHg
Systemic arterial P _{CO₂}	5.3 40	kPa mmHg
Base excess	–2–+2	mmol L ⁻¹
Renal function		
Renal blood flow	1.2	L min ⁻¹
Glomerular filtration rate	120	ml min ⁻¹
Average urine output (normal hydration)	1	ml min ⁻¹
Renal glucose threshold	11	mmol L ⁻¹
Nutritional status		
Body mass index	20–30	kg m ⁻²
Hormones		
Thyroxine (T ₄)	100	nmol L ⁻¹
Triiodothyronine (T ₃)	2	nmol L ⁻¹
TSH	2.5	mUL ⁻¹
Cortisol	400 (peak) 150 (trough)	nmol L ⁻¹ nmol L ⁻¹
Urinary free cortisol	<300	nmol 24 h ⁻¹

Basic principles and cell physiology

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Overview

The physiology of the body is often described in terms of the homeostatic mechanisms which control the cellular environment. Cell function also relies on an adequate energy supply and the appropriate integration of the activities of the different cells within the body through efficient signalling mechanisms, both electrical and chemical. The cell membrane is very important in many of these functions since it forms a barrier between the intracellular and extracellular environments across which important molecules must be transported. The properties of the membranes of excitable cells also account for the generation of action potentials, and many of the receptors which recognize specific chemical messengers are membrane bound.

1.1 Cells, systems and homeostasis

Learning objectives

- At the end of this section you should be able to:
 - describe the main components of the cell
 - identify the main body fluid compartments and estimate their likely volumes
 - explain the principles of indicator dilution methods and suggest appropriate indicators for specific compartments
 - outline the principles of homeostasis and describe how these apply to temperature regulation.

Physiology is the study of normal biological function. Although the ultimate goal is to understand the intact human, function is often considered in terms of individual physiological systems, each of which consists of different organs and structural elements. The different components of any *system* may be spread widely throughout the body but they serve a *common functional* purpose. Therefore, we talk of the cardiovascular system, consisting of the heart, arteries, capillaries, veins, lymphatics and related control mechanisms, all of which are involved in the circulation of the blood. The fundamental biological unit is the cell, however, and each organ's function reflects the integrated activity of the various specialized cells within it.

Cell structure

Although cells from different organs show considerable differences in shape (morphology) and function, all cells share some general characteristics. Each is bounded by a cell membrane (or *plasma membrane*) which separates the aqueous solution inside the cell (the *cytoplasm* or *intracellular fluid*) from the aqueous solution outside (the *extracellular fluid*). These two fluids have very different ionic compositions (see Section 5.1) and these differences are more easily maintained because ions cannot readily cross the double layer (*bilayer*) of phospholipids in the plasma membrane (Fig. 1). These are oriented with their hydrophilic heads adjacent to the aqueous solutions on either side, while their hydrophobic tails form a fatty core. Membrane proteins move about within the two-dimensional confines of the lipid layer (the fluid mosaic model of the membrane).

Membranes also delimit a number of subcellular units known as *organelles*. These include:

- the *nucleus*, which contains the genetic code for protein synthesis in the form of deoxyribonucleic acid (DNA). Since proteins are key structural and functional molecules in the cell, changes in gene expression regulate how a cell looks and behaves.

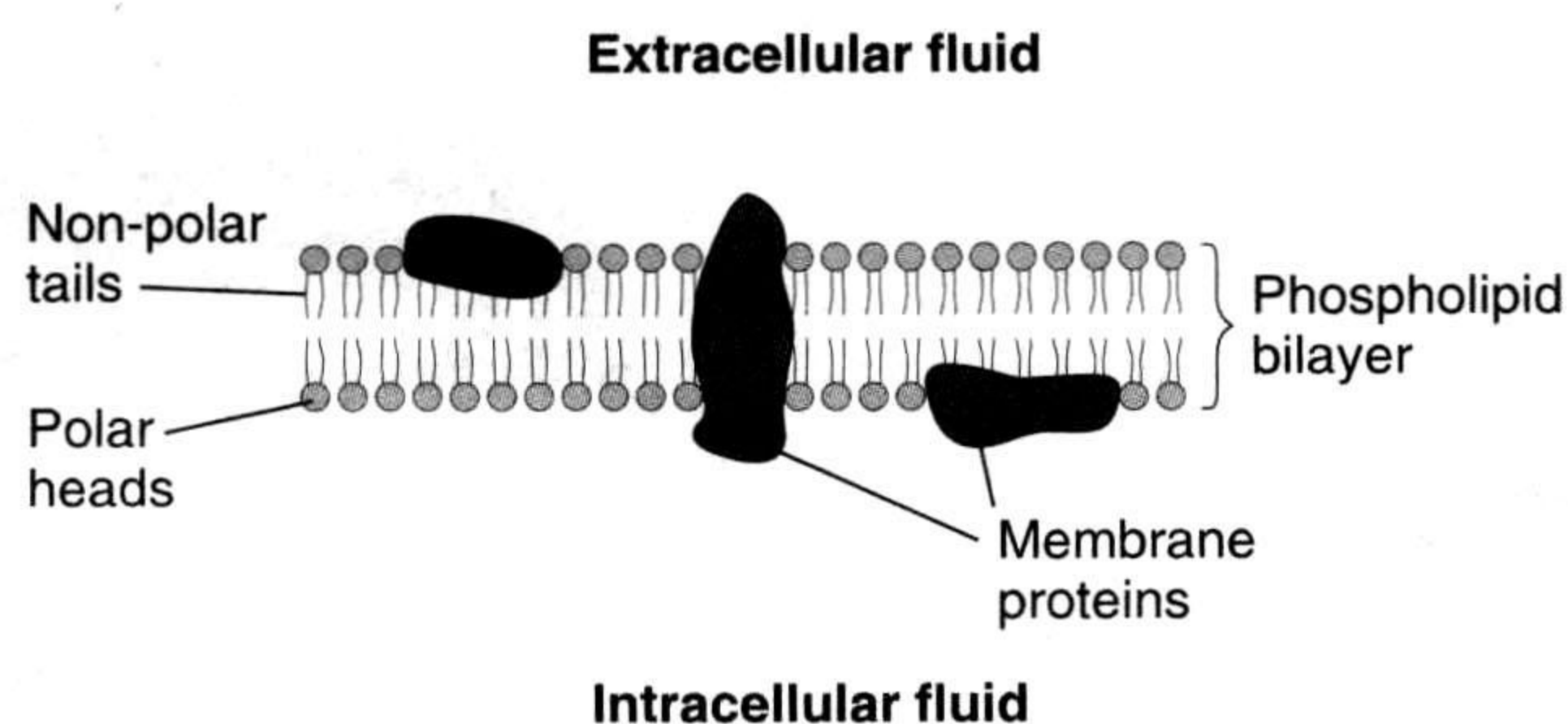
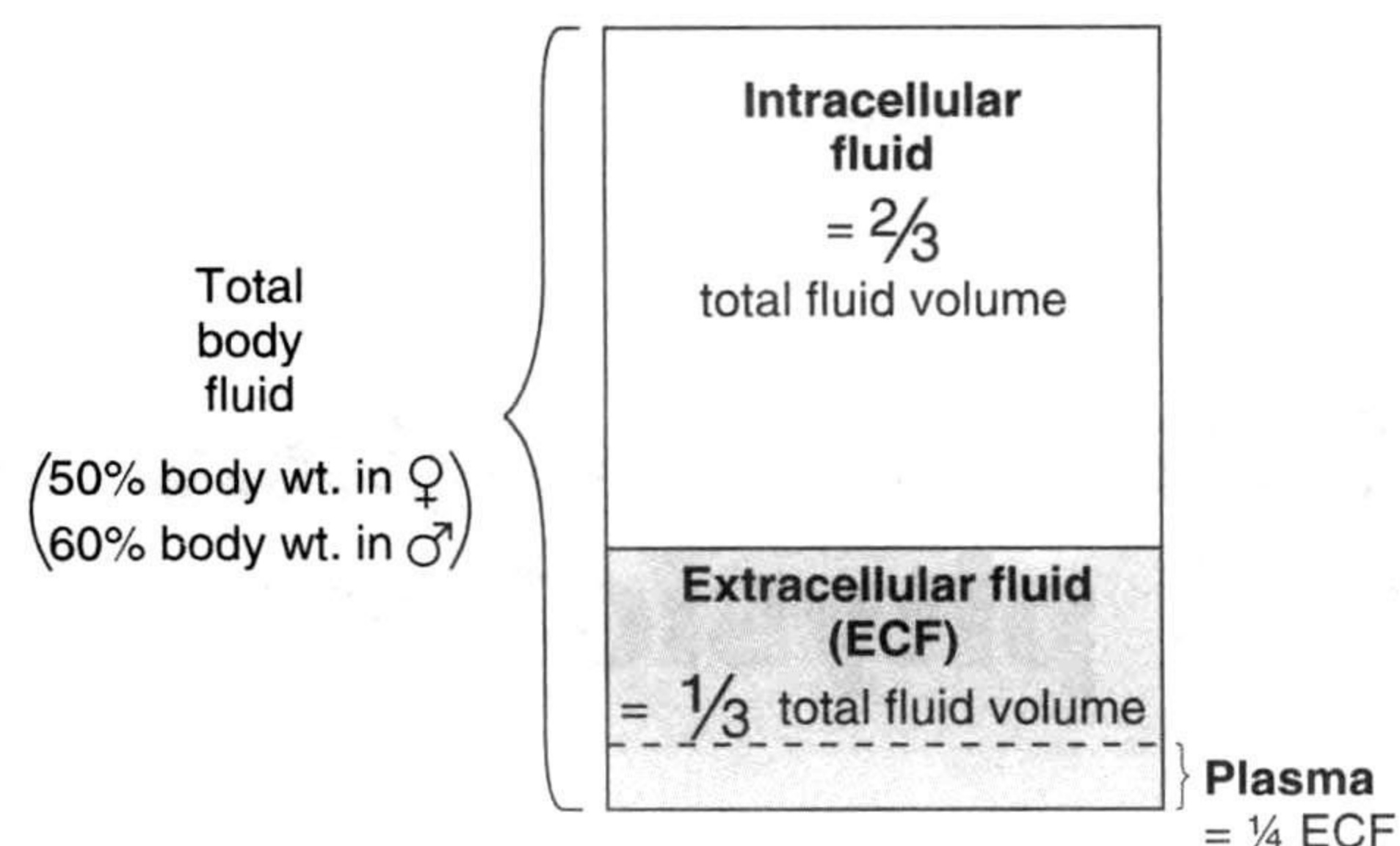


Fig. 1 The plasma membrane. Membrane proteins may be exposed on either side or may cross the whole thickness of the lipid bilayer.

- *mitochondria*, which are surrounded by both an outer membrane and a highly folded inner membrane. Mitochondria are responsible for oxidative breakdown of food molecules, providing the cell with usable energy in the form of ATP.
- the *endoplasmic reticulum* (or *sarcoplasmic reticulum* in muscle cells), which is an interconnecting series of membranous channels and vesicles. In some regions this has a large number of *ribosomes* attached to the surface, thus leading to the distinction between rough and smooth endoplasmic reticulum. Ribosomes play a key role in protein synthesis.
- the *Golgi apparatus*, a system of stacked vesicles found close to the nucleus. This is involved in the formation of secretory vesicles and lysosomes.

Body fluid compartments

The body contains many different aqueous solutions, which may be classified into a series of fluid compartments depending on their location (Fig. 2). The main subdivision is between intracellular and extracellular fluids. The extracellular compartment represents all fluid not inside cells, including the plasma component of blood, aqueous humour in the eye, synovial fluid in joints and cerebrospinal fluid within the central nervous system. The largest single extracellular subcompartment, however, consists of the *interstitial fluid*, which lies in the connective tissue matrix surrounding most body cells. It is normally this fluid which is in direct contact with the cell membrane and controlling interstitial conditions is vital for normal cell function. Much of this control is achieved by the continuous circulation of blood through the cardiovascular system. The rate of blood flow to any region and the plasma concentrations of different solutes greatly influence the cellular environment since, with the exception of plasma pro-



e.g. 60 kg ♀	Total body fluid = 50% of 60 kg = 30 L
	ECF = 1/3 of 30 L = 10 L
	Plasma = 1/4 of 10 L = 2.5 L

Fig. 2 Fluid compartments within the body showing the relative volumes occupied by intracellular fluid, extracellular fluid and plasma (part of the extracellular space).

teins, water and solutes move freely between plasma and the interstitium.

Volume measurement by indicator (dye) dilution methods

The volume of a given fluid compartment, e.g., the extracellular fluid volume, is usually estimated indirectly using an indicator substance. If a known quantity of indicator becomes evenly distributed through that compartment, measurement of the final concentration of indicator allows the volume of fluid to be calculated using Equation 2 below.

$$\text{Concentration} = \frac{\text{Amount of indicator}}{\text{Fluid volume}} \quad (\text{Eq. 1})$$

$$\therefore \text{Fluid volume} = \frac{\text{Amount of indicator}}{\text{Concentration}} \quad (\text{Eq. 2})$$

This technique is called the *indicator*, or *dye dilution method*, and it relies on finding an indicator which fulfils two main criteria.

- It should become evenly distributed through the whole of the fluid compartment of interest, otherwise the concentration will be artificially high leading to an underestimate of the volume concerned.
- It should not leak out into other fluid compartments or be rapidly metabolized or cleared from the body, since the concentration of indicator would be reduced under such circumstances, leading to an overestimate of the relevant volume.

For these reasons different indicators are appropriate when estimating the volume of different fluid spaces within the body.

Blood and plasma volume

Blood volume can be measured by taking a sample of an individual's blood and radioactively labelling the red cells, e.g., with chromium-51. These cells are reinjected, given time to mix evenly through the blood volume, and another sample of blood is taken. The radioactivity per unit volume is used to calculate the total blood volume (normal value is 4–5 L).

Plasma volume is usually estimated using a dye which binds to plasma protein, such as Evans' blue dye. This is restricted to the plasma space because the protein does not readily escape from the circulation. Plasma proteins radiolabelled with iodine-131 can also be used. These indicators do not enter the red cells so the calculated volume is that of plasma only (2.5–3.0 L), and not the total blood volume.

Extracellular fluid volume

Extracellular fluid volume is not easily measured and different indicators give different results in a given subject. Substances which have been used include radioactive sodium, radioactive bromide, the polysaccharide inulin, and sucrose. Mean values are about 10–15 L. The plasma volume represents about 25% of the extracellular space and, since there is free exchange of fluid across the capillary wall, any increase or decrease in extracellular fluid volume will be reflected by a parallel change in plasma volume. This means that mechanisms which affect the total extracellular fluid volume will also alter the plasma and, therefore, blood volumes, e.g., renal fluid reabsorption (Section 5.4).

Homeostasis

Normal cell function relies on appropriate environmental conditions since the temperature, pH, ionic concentrations, O_2 and CO_2 levels in the extracellular fluid all influence biochemical activity inside the cell. The mechanisms which control the body's internal environment are called *homeostatic mechanisms*. These keep conditions inside the body relatively constant despite considerable changes in the external environment.

The following general elements are present in all homeostatic control systems (Fig. 3).

- *Detectors*, or receptors, sensitive to the variable to be controlled.

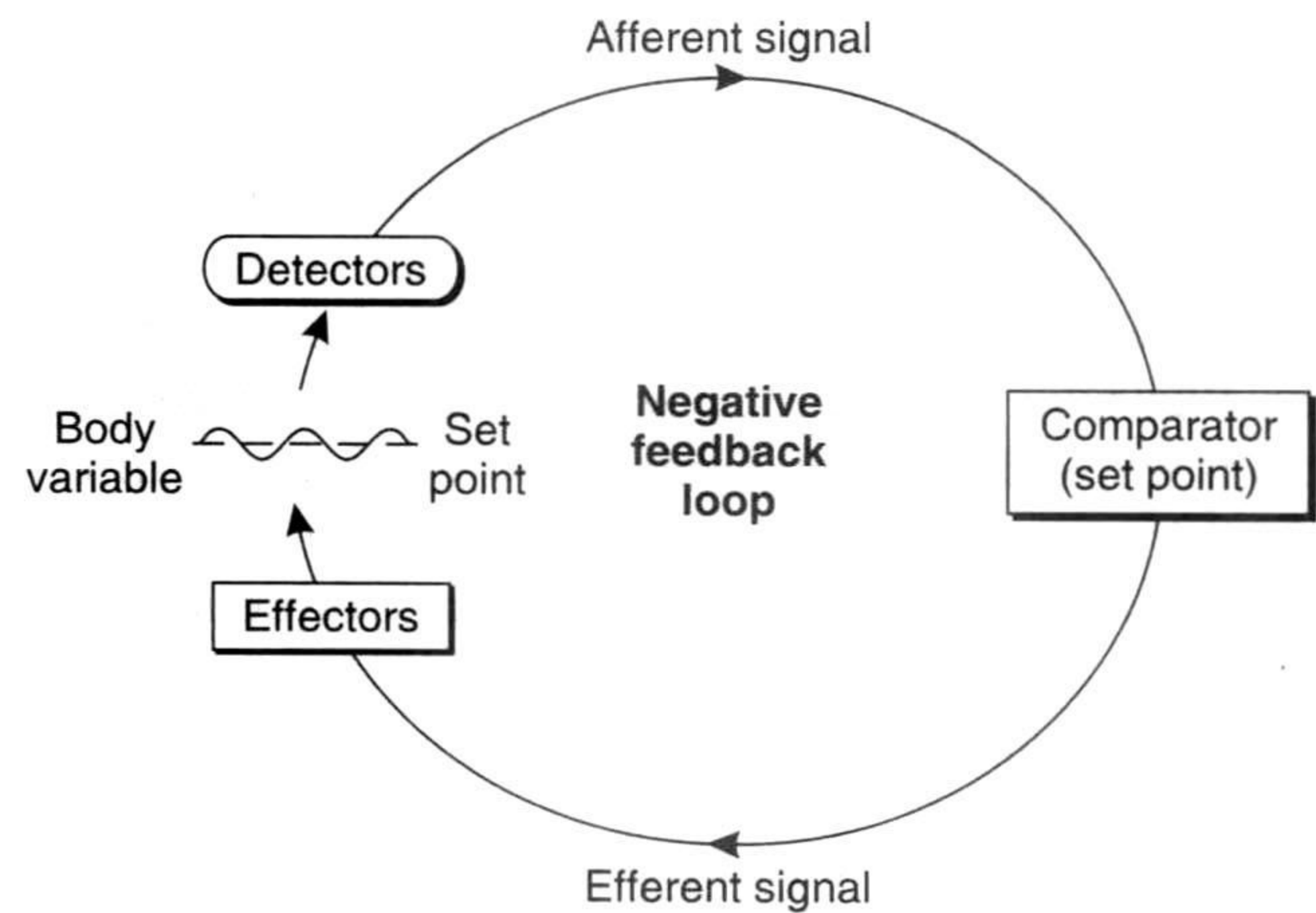


Fig. 3 Elements of a homeostatic control system. The controlled variable may oscillate, or hunt, around a mean value (the set point).

- A *comparator*, or *integrating centre*, which receives the afferent signal from the detectors and compares this measured value of the variable with a preferred value, or *set point*, for the system. If the actual value differs from the set point the integrator generates an efferent (outgoing) signal.
- *Effector* systems which can change the measured variable are activated by the signals from the integrator. Their effect is to bring the variable back towards the set point.

In such a system, any deviation of the variable away from its normal (set) value stimulates responses which reduce that deviation. This is referred to as *negative feedback* control and is an important element of homeostasis. The overall effect is to maintain a constant environment but often a phenomenon known as *hunting* is observed in which the controlled variable oscillates around a fixed mean value rather than remaining exactly at the set point (Fig. 3).

Biological systems may also demonstrate *positive feedback* in which deviations from the steady state are actually amplified, rather than diminished, by a feedback loop. Such mechanisms, however, have no part to play in homeostasis.

Homeostatic regulation of body temperature

Regulation of body temperature provides a good example of homeostasis. The body core is normally held close to 37°C, even though the environmental temperature (which affects the rate of heat loss from the body) and rate of metabolic heat production may vary widely.

Temperature detectors (*thermoreceptors*) monitor both the core temperature (the regulated variable) and the peripheral temperature (a separate but relevant variable). The afferent inputs go to an integrating centre (the *thermoregulatory centre*) in the *hypothalamus* of the brain, which compares core temperature with the set point of 37°C. If these differ, outgoing nerve signals activate a number of effector systems which alter the rates of heat production and heat loss.

In cold conditions:

- reflex increases in muscle tone and shivering liberate metabolic energy as heat
- in infants, there may also be increased heat production in brown fat (Section 9.6)
- heat loss is reduced by sympathetic constriction of peripheral blood vessels, which decreases skin blood flow; erection of skin hair (piloerection) also occurs but has limited significance in humans.

In hot conditions the rate of heat loss can be greatly accelerated by:

- increased sweating stimulated by sympathetic nerves which in this specific case release the neurotransmitter acetylcholine
- dilatation of cutaneous blood vessels caused by reduced activity in vasoconstrictor sympathetic nerves releasing the more typical sympathetic neurotransmitter noradrenaline (norepinephrine). There may also be active dilatation of arterioles (Section 3.7).

Behavioural aspects are important too, e.g., we dress up warmly, exercise and eat hot food when we are cold, while preferring light clothes and cool drinks in hot weather.

Box 1 Clinical note: Pyrexia

Pyrexia or fever is a temporary elevation of the core temperature commonly caused by infection. It is not due to any breakdown of the detector or effector systems responsible for temperature control but results from a change in the set point. Toxins released from bacteria and immune cells cause the hypothalamus to respond to a core temperature of 37°C as if it were abnormally low and so it increases heat production, e.g., through shivering (rigors). This raises body temperature.

1.2 Energy sources in the cell

Learning objectives

- At the end of this section you should be able to:
 - outline the main steps in cellular energy exchange.

Body cells require energy to carry out mechanical work (e.g., in muscle cells), to transport ions or molecules against concentration gradients (e.g., ion pumps) and for the synthesis of complex molecules. These active processes are ultimately fuelled by the energy released through the breakdown of carbohydrate, fat and protein from our diet. The initial series of reactions in the breakdown of glucose is referred to as glycolysis and does not require O₂ (anaerobic metabolism). This leads to the formation of lactic acid and produces small amounts of *adenosine triphosphate* (ATP), the main source of usable energy within the cell. In the presence of O₂ (aerobic conditions), however, intramitochondrial enzymes catalyse the complete catabolism of the products of glycolysis, releasing much greater amounts of ATP and generating CO₂ and water as byproducts (Section 4.7). Whereas glycolysis leads to a net production of two molecules of ATP per glucose molecule, oxidative metabolism can produce an additional 34–36 ATP molecules. Subsequent hydrolysis of the high-energy phosphate bonds in ATP by *ATPase enzymes* makes energy available for the active processes of the cell.

1.3 Transport across cell membranes

Learning objectives

- At the end of this section you should be able to:
 - list the factors affecting solute diffusion across cell membranes
 - identify the conditions necessary for osmosis and understand the differences between osmolality, tonicity and osmotic pressure
 - describe the characteristics of carrier-mediated transport and differentiate between facilitated diffusion, primary active transport and secondary active transport
 - describe what is meant by endocytosis and exocytosis.