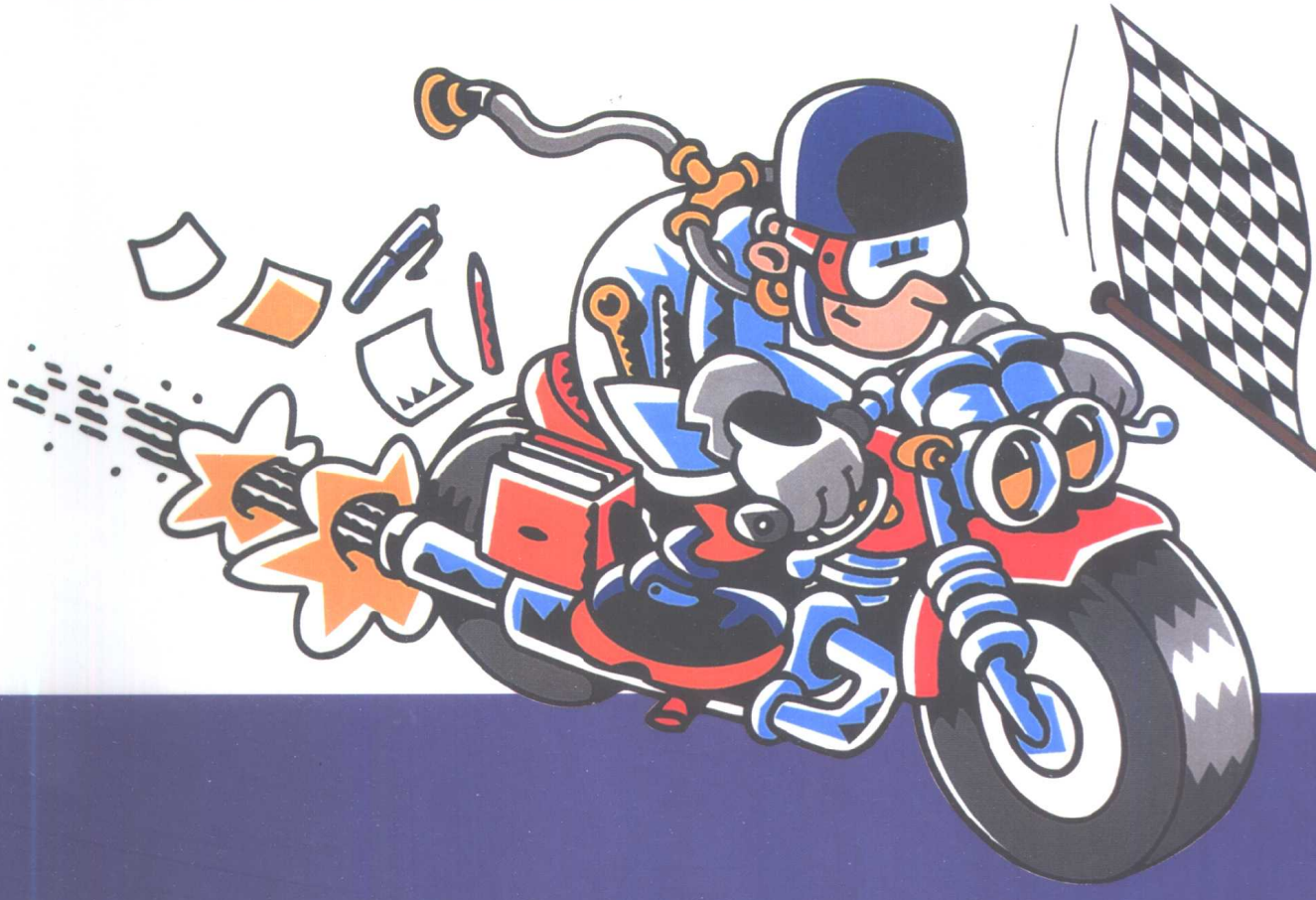
风暴式医学教程 MOSBY'S CRASH COURSE (原版英文医学教程)

肾及泌尿系统

Renal and Urinary Systems

Nisha Mirpuri ⊙ Pratiksha Patel
with Daniel Horton-Szar as Series Editor



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（原版英文医学教程）

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Mosby's Crash Course

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Preface

As the medical curricula have evolved, the scientific basis and clinical aspects of each speciality have become increasingly integrated. *Crash Course Renal and Urinary Systems* reflects today's curricula by integrating the basic science with clinical topics. In this book, we have tried to explain topics in the way we understand them, from the student's perspective.

The information has been set out in a way that is easy to read and learn from. Numerous diagrams and algorithms have been used to simplify some of the more complex principles. We have used hints and tips boxes where we needed to highlight important points and comprehension check boxes help you to check your knowledge as you go along.

The structure of the book follows the renal and urinary systems from basic anatomy and physiology through to history taking, physical examination, and pathology.

We both found the renal and urinary systems to be a very challenging aspect of our course and hope that *Crash Course Renal and Urinary Systems* will provide a complete and simplified review for your learning.

Good luck in your exams!

Nisha Mirpuri
Pratiksha Patel

The primary aim of *Crash Course Renal and Urinary Systems* is to provide the medical student with a framework of knowledge for the study of these systems. The text is designed with the new medical curriculum in mind and interlinks basic science with clinical medicine.

As with the other books in the *Crash Course* series, this book for medical students has been written by medical students with expert input from the Series Editor and myself as the Faculty Advisor. This innovative approach has ensured that the text is user friendly, easy to follow, and accurate.

In using a concise text with extensive illustrations, the emphasis has been to produce a balanced book covering renal physiology and pathophysiology in a way that will give the student a solid overview of the subject. At the same time, the theoretical basis relevant to the problems they will encounter in everyday clinical practice has been provided. Unnecessary complexity has been avoided without loss of relevant practical information.

It is hoped that this book will provide students with a useful supplement to their lecture notes, stimulate them to continue with self-directed learning in this subject, and provide them with a concise yet comprehensive revision aid. To this end a comprehensive set of multiple-choice questions, short-answer questions, and essay topics, together with answers, are provided for the reader to test his or her knowledge.

Any suggestions or criticisms from readers which would help us better attain these objectives in the future would be greatly appreciated.

Kevin Harris
Faculty Advisor

Preface

OK, no-one ever said medicine was going to be easy, but there are very few parts of this enormous subject that are actually difficult to understand. The problem for most of us is the sheer volume of information that must be absorbed before each round of exams. It's not fun when time is getting short and you realise that: a) you really should have done a bit more work by now; and b) there are large gaps in your lecture notes that you meant to copy up but never quite got round to.

This series has been designed and written by medical students and young doctors with recent experience of basic medical science exams. We've brought together all the information you need into compact, manageable volumes that integrate basic science with clinical skills. There is a consistent structure and layout across the series, and every title is checked for accuracy by senior faculty members from medical schools across the UK. I hope this book makes things a little easier!

Danny Horton-Szar
Series Editor

Acknowledgements

Thanks to Danny, Dr Harris, Nigel, and everyone at Mosby for putting in a great amount of time and effort in bringing this book together. It's been hard work, but a very enjoyable and valuable experience. We would also like to thank our families and friends who have supported us and put up with all our moaning over the past year.

Figure Credits

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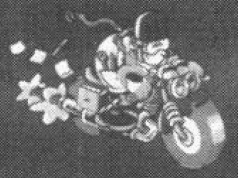

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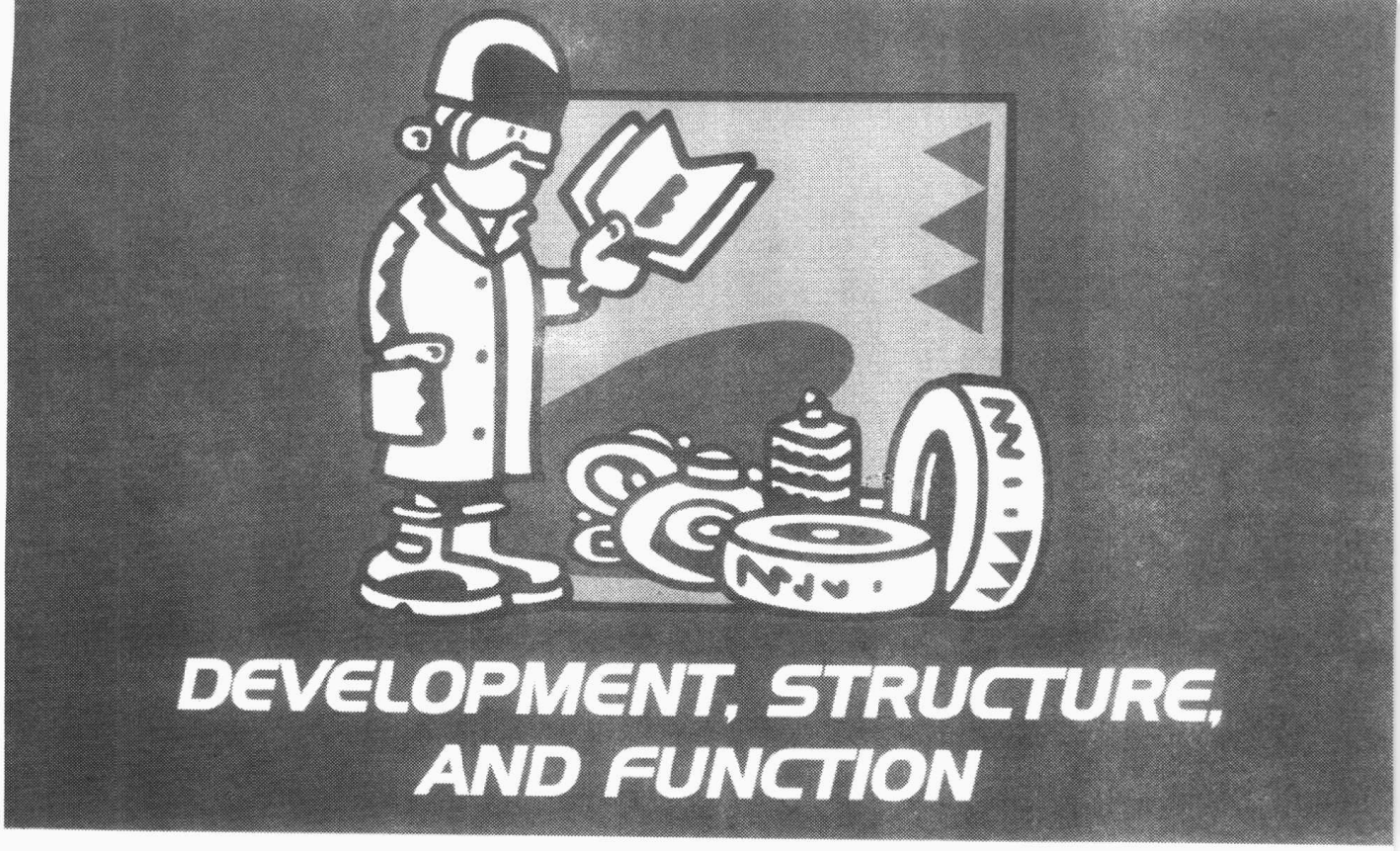

DEVELOPMENT, STRUCTURE, AND FUNCTION

1. Basic Principles

OVERVIEW OF THE KIDNEY AND URINARY TRACT

Functions of the kidney

The kidneys are the major organs responsible for maintaining at a constant level the composition and volume of the body fluids—homeostasis.

They have several functions, which can be summarized as:

- Regulation of water content, mineral composition, and acidity of the body by excreting substances in an amount adequate to achieve total body balance and maintain normal concentration in the extracellular fluid.
- Elimination of metabolic waste products from the blood and their excretion in urine (e.g. urea from protein metabolism, uric acid from nucleic acids, creatinine from muscle creatine).
- Removal of foreign chemicals from the blood and their excretion in urine (e.g. drugs, pesticides, food additives).
- Secretion of hormones (endocrine function)—erythropoietin (controls erythrocyte production), renin (generates angiotensin I from angiotensinogen and controls blood pressure and sodium balance), 1α hydroxylase enzyme (metabolism of vitamin D), and prostaglandins (vasodilator effect).

Embryology of the kidney and the urinary tract

Three consecutive systems form the adult urinary tract:

- Pronephros, which develops in the cervical region of the embryo and is rudimentary.
- Mesonephros, which has characteristic excretory units with their own collecting ducts called mesonephric ducts or wolffian ducts. It develops in the thoracic and lumbar regions as the pronephros regresses. It may function for a short time.
- Metanephros (permanent kidney), which develops at about week 5 in the pelvic region. It forms excretory units (nephrons) from the metanephric mesoderm, and the collecting system is formed from the ureteric bud, which is an outgrowth of the mesonephric duct. The metanephric tissue forms a cap over the ureteric bud, which grows and divides to form the renal pelvis, calyces, and collecting ducts.

The connection between the collecting system and the nephrons is essential to the normal development of the urinary tract. Any failure in this process may cause unilateral or bilateral renal agenesis. Cystic disease can also result from failure of development of the ureteric bud or the kidney tissue. Early division of the ureteric bud results in bifid kidneys, occasionally with ectopic ureters. Abnormal migration of the kidneys into the abdomen from their original position in the pelvis results in pelvic or horseshoe kidneys (see Chapter 9).

Understanding that the kidneys develop in the pelvic region and migrate into the abdominal cavity will help you understand anomalies such as pelvic kidneys.

Structure of the kidneys and urinary tract

The kidneys are located retroperitoneally on the posterior abdominal wall and lie either side of the vertebral column. The right kidney is 12 mm lower than the left (because of displacement by the liver). A kidney measures approximately 11 cm long, 6 cm wide, and 4 cm thick.

Each kidney is composed of about 1 000 000 nephrons bound together by small amounts of connective tissue containing blood vessels, nerves, and lymphatics. Each nephron consists of:

- Glomerulus, which forms a protein-free and cell-free filtrate of blood.
- Tubule, which processes the filtrate as it flows through the tubule before exiting the kidneys as urine.

Fig. 1.1 shows the anatomy of the kidneys and urinary tract.

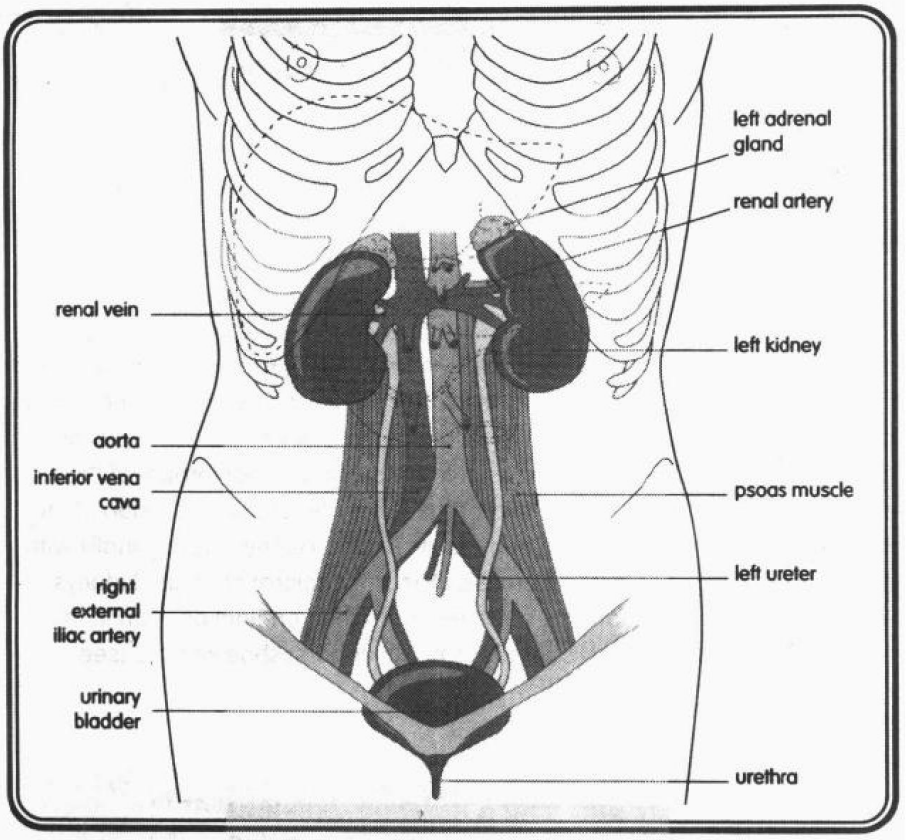

Fig. 1.1 Anatomy of the posterior abdominal wall showing the kidneys and urinary tract.

- **What are the functions of the kidneys?**
- **Give a brief description of the location and structure of the kidneys.**
- **What are the three stages of embryological development?**

FLUID COMPARTMENTS OF THE BODY

Body fluids

Body fluids are divided into:

- Intracellular fluid (ICF), the fluid within cells.
- Extracellular fluid (ECF).

ECF is divided into:

- Plasma—ECF within the vascular system.
- Interstitial fluid (ISF)—ECF outside the vascular system (and separated from plasma by the capillary endothelium).
- Transcellular fluid (TCF)—ECF (e.g. synovial fluid, aqueous and vitreous humour, cerebrospinal fluid) (Fig. 1.2) separated from the plasma by the capillary endothelium and an additional epithelial layer that has specialized functions.

Water is a major component of the human body. Approximately 63% of an adult male and 52% of an adult female is water (i.e. 45 L in a 70 kg male, 36 L in a 70 kg female). One-third of total body water (TBW) is ECF (about 15 L in a 70 kg male) and two-thirds is ICF (about 30 L in a 70 kg male).

Osmolarity and osmolality

Basic concepts

Osmosis is the net passage of a solvent through a semi-permeable membrane between two solutions of different strengths until equilibrium is reached. The osmotic effect can be measured as an osmotic

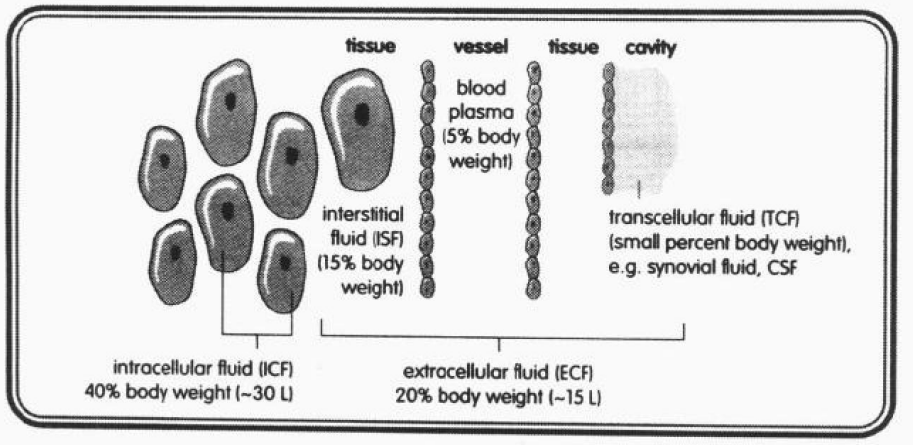

Fig. 1.2 Fluid compartments of the body.

pressure. Hydrostatic pressure is the pressure needed to be applied to the region containing the solute to prevent the net entry of water.

The total solute concentration of a solution is known as its osmolarity—the number of osmotically active particles in solution. The higher the osmolarity, the lower the water concentration. 1 Osm = 1 mole of solute particles.

Osmolarity vs osmolality

Osmolarity is the molar concentration per litre of solution (mOsm/L). Osmolality is the molar concentration of solutes per unit weight of the solvent (water) (mOsm/kg H_2O).

- Normal body fluid osmolality is 280–290 mOsm/kg H_2O.
- Urine osmolality can vary in the range 60–1400 mOsm/kg H_2O.

Plasma osmolality can be calculated from Na, K, urea, and glucose concentrations with the formula:

Plasma osmolality = 2(Na + K) + urea + glucose

Isotonicity and isosmoticity

Changes in the extracellular osmolarity can cause cells to shrink or swell as water will move across the plasma membrane by osmosis out of or into the cells. Therefore a major function of the kidneys is to regulate the excretion of water in the urine so that the osmolarity of the ECF remains nearly constant despite wide variations in intake or extrarenal losses of salt and water. This prevents damage to the cells from excess swelling and shrinkage:

- If cells are placed in a solution of 300 mOsm/kg H_2O (isotonic solution, i.e. 0.9% saline), there is no net movement of water by osmosis and no swelling or shrinkage.
- If cells are placed in a solution of less than 300 mOsm (hypotonic solution), they swell as water osmoses into the cell.
- If cells are placed in a solution of over 300 mOsm (hypertonic solution), they shrink as water moves out of the cell.

Fig. 1.3 shows the changes in the cells brought about by hypertonic, isotonic, and hypotonic solutions.

Isosmoticity refers to the osmolarity of a solution relative to that of cells regardless of whether the solutes are penetrating or non-penetrating. Isotonicity refers to the osmolarity of a solution relative to its non-penetrating solutes regardless of its concentration of membrane-penetrating solutes (e.g. 300 mOsm/L of non-penetrating solutes).

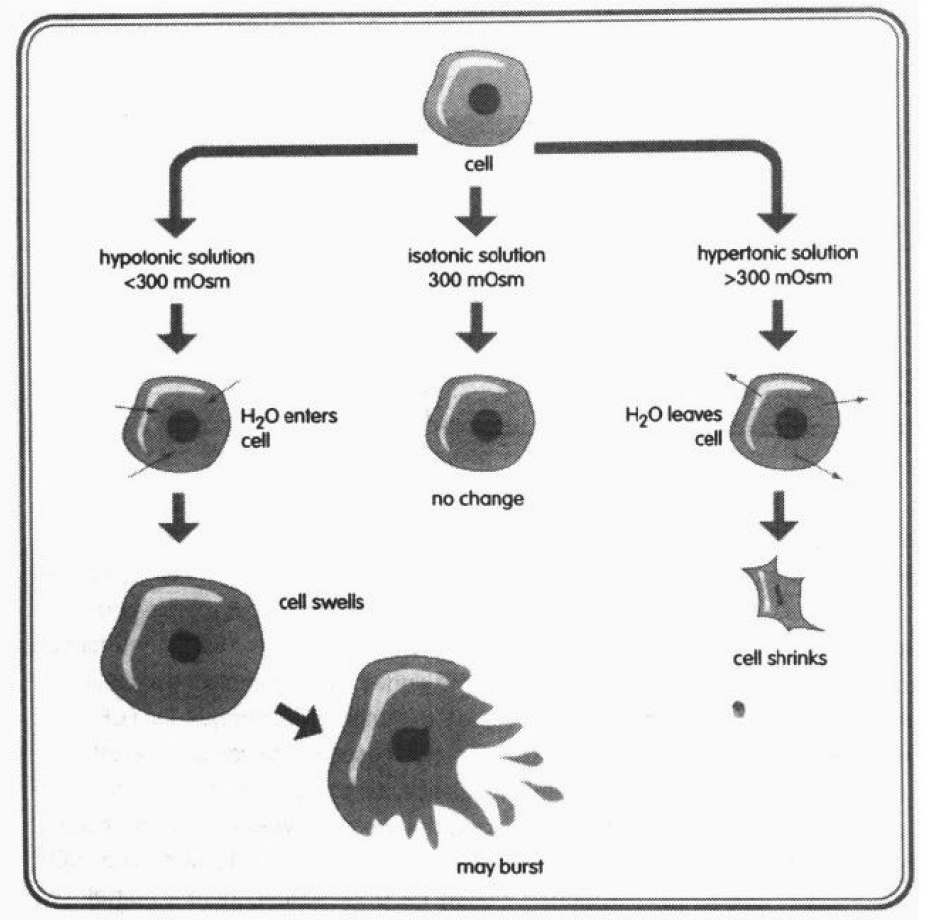

Fig. 1.3 Changes in the cells brought about by hypertonic, isotonic, and hypotonic solutions.

Diffusion of ions across biological membranes

Biological membranes (e.g. cell membranes) are selective in that they allow diffusion of small molecules and ions through them. The concentration gradient and electrical gradient are important in the movement of these molecules.

Diffusion of different molecules occurs at different rates depending upon their shape, size, weight, and charge.

When solutions either side of a membrane contain only freely diffusible ions, the electrical gradient causes ions to move from an area of high ionic concentration to one of low ionic concentration until equilibrium is reached and the ion distribution will be such that the products of the concentration of diffusible ions of the two sides will be equal as follows:

Side A (diffusible cations × diffusible anions) =
Side B (diffusible cations × diffusible anions)

When non-diffusible anionic protein is present on one side of the membrane, cations will cross the membrane to maintain electrical neutrality. This will cause the side containing non-diffusible ions (e.g. protein) to have a slightly greater number of total ions than the side containing only diffusible ions; therefore the osmotic pressure on the side with the non-diffusible ions will be greater. Net water movement will then occur unless the osmotic pressure difference is counterbalanced by hydrostatic pressure.

Sodium (Na^+) is the main extracellular ion.
Potassium (K^+) is the main intracellular ion.

Cell membranes are permeable to:

- Potassium ions (K^+).
- Chloride ions (Cl^-).
- Sodium ions (Na^+).

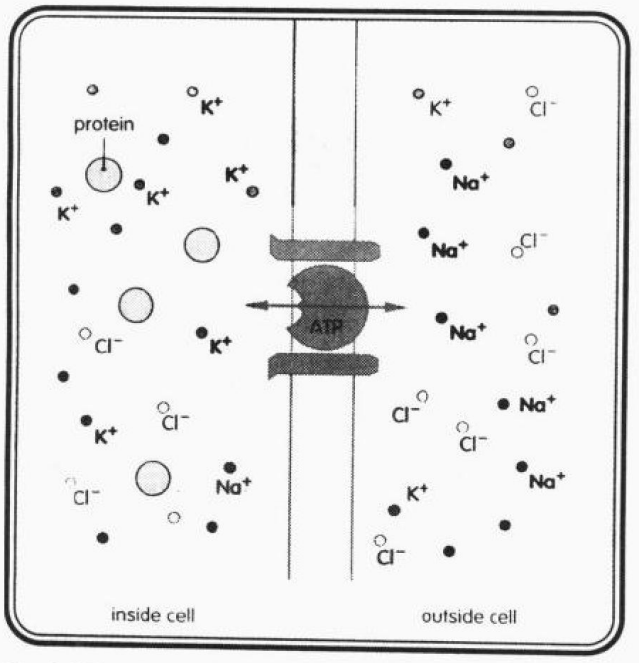

Fig. 1.4 Distribution of ions across cell membranes.

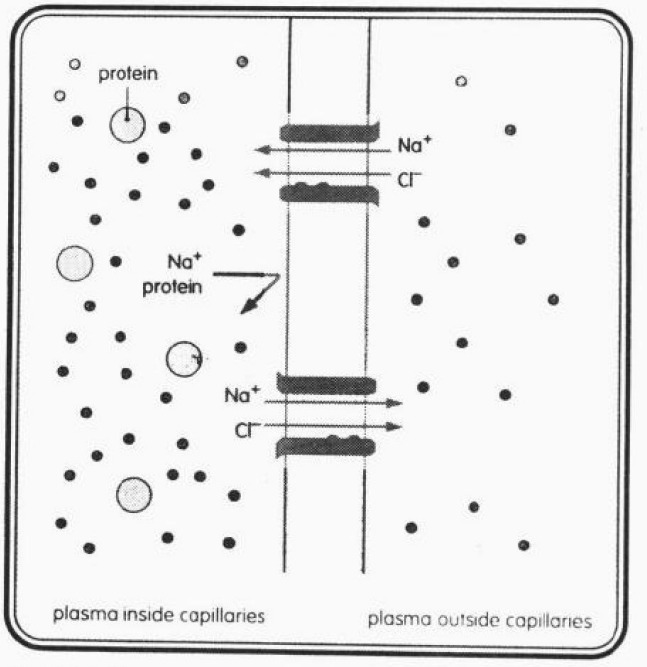

Fig. 1.5 Influence of protein on diffusible ions across cell membrane—demonstrating the Gibbs–Donnan effect.

The permeability of Na^+ is 1/50th of K^+ permeability. The primary active transport mechanism uses adenosine triphosphate (ATP) actively to pump Na^+ out of and K^+ into the cells, but most K^+ in the cell is present as a result of high permeability. Cl^- ions diffuse out of the cell across the cell membrane because there is a net negative charge within the cell. This results in a higher concentration of Cl^- ions outside the cells. At equilibrium, the cell has a net negative charge (–70 mV). Fig. 1.4 shows the distribution of ions on either side of the cell membrane.

Proteins (large molecules):

- Are almost impermeable to the membrane.
- Are mostly anionic and influence the diffusion of other ions, thus causing an imbalance in the distribution of diffusible ions—the Gibbs–Donnan effect (Fig. 1.5).

According to the Gibbs–Donnan effect, there should be more ions inside the cell than outside. These are, however, balanced in biological systems by the sodium pump as Na^+ is effectively non-diffusible.

Fluid movement between body compartments

Body fluid compartments have a relatively constant yet dynamic composition. Equilibrium is maintained by the continual transfer of fluid between the different compartments.

Exchange between ECF and ICF

Water freely diffuses across cell membranes so that equilibrium is reached between the ICF and ECF. Any change in the ionic concentration of the ICF or ECF is followed by the movement of water between these compartments. Na^+ is the most important extracellular osmotically active ion. K^+ is the most important intracellular osmotically active ion.

Exchange between plasma and interstitial fluid

The capillary endothelium separates plasma from interstitial fluid (ISF). Water and ions move between these two compartments, 90% of ions by simple diffusion and 10% by filtration.

Ion filtration between plasma and ISF is carried out through:

- The arterial end of the capillary where there is a hydrostatic pressure of 32 mmHg, which causes fluid to filter out of the plasma into the ISF.
- Proteins that are too large to cross the capillary endothelial cells and therefore remain in the plasma, creating a colloid osmotic (or oncotic) pressure (25 mmHg).
- The venous end of the capillary where there is an osmotic pressure of 25 mmHg, which is greater than the hydrostatic pressure (12 mmHg). This causes fluid to return to the capillary.

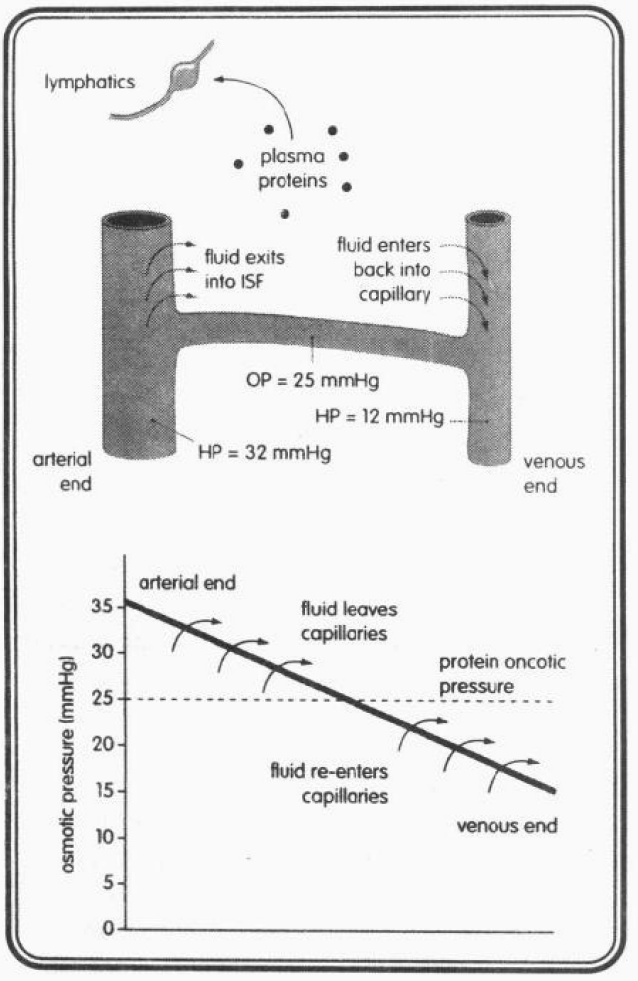

Fig. 1.6 Exchange of fluid between the plasma and ISF across a capillary wall. (HP, hydrostatic pressure; OP, oncotic pressure.)

Composition of fluid compartments

Component	Plasma	ECF	ICF*
Na^+ (mmol/L)	142	145	12
K^+ (mmol/L)	4	4.1	150
Cl^- (mmol/L)	103	113	4
HCO_3^- (mmol/L)	25	27	12
proteins (g/L)	60	0	25
osmolality (mOsm/kg H_2O)	280	280	280
compartment volume (L)	3.0	12.0	30

*ICF compartment is not the same throughout the body, it varies with different types of cells

Fig. 1.7 Composition of the fluid compartments.

The exchange of fluid between the plasma and ISF across a capillary wall is illustrated in Fig. 1.6. Hydrostatic pressure depends upon arteriole blood pressure, arteriole resistance (which determines the extent to which blood pressure is transferred to the capillary), and venous pressure.

Osmotic pressure (25 mmHg) is produced by plasma proteins (17 mmHg—oncotic pressure) and the imbalance of ions—there are more ions (e.g. Na^+) inside the capillary than outside as a result of the presence of negatively charged proteins and the Gibbs–Donnan effect.

Exchange between interstitial fluid and lymphatic vessels

Some plasma proteins can be lost from the vascular system into the ISF. The lymphatic system is composed of a network of lymphatic capillaries in all organs and tissues, which eventually join to drain into the venous system via the thoracic duct in the neck. These lymphatic capillaries are very permeable to protein and thus return the escaped plasma proteins to the circulatory system.

The ionic composition of the fluid compartments is shown in Fig. 1.7.

Fluid and ion movement between the body and external environment

There is a continuous exchange of body fluids with the external environment, but there must be a balance between intake and output.

Water intake and output are illustrated in Fig. 1.8. Water lost from the lungs varies with the climate (e.g. in very dry climates over 400 mL per day is lost). Insensible losses are those due to evaporation of water from the skin (i.e. not sweat). Sweating ('sensible perspiration') is an additional loss. Urinary loss can be varied according to the needs of the body. Intakes also vary considerably and can be adjusted according to need (i.e. thirst mechanism). Despite these variations, the body's ionic concentration is maintained within strict limits by the kidney mechanisms, including control of tubular reabsorption of filtered Na^+ and to a lesser extent K^+.

Water intake and output			
Water intake (mL)		**Water output (mL)**	
drink	1500	lungs	400
food	500	skin	400
metabolism	400	faeces	100
		urine	1500
total	2400	total	2400

Fig. 1.8 Water intake and output.

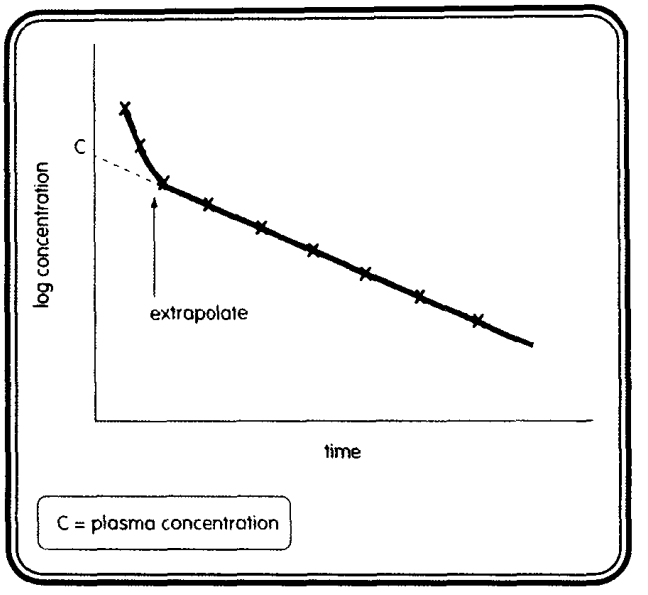

Fig. 1.9 Plasma concentration of an injected substance.

Measuring body fluid compartments

Dilution principle

The dilution principle is used to measure fluid volume when fluids cannot be directly measured or extracted from the container or compartment holding them. This allows measuring *in situ*. A substance that will mix completely and uniformly in the fluid compartment is used to allow all of the volume present to be measured. Allowances must be made for the excretion and metabolism of substances by the body.

$$V_D = \frac{Q_A - Q_H}{C}$$

Where V_D = volume of distribution; Q_A = quantity administered; Q_H = quantity metabolized after 10 hours; C = concentration.

Two methods are used:

- Single injection method.
- Constant infusion method.

Single injection method

This is used when the substance has a slow rate of excretion from the compartment being measured and is carried out as follows:

1. A known amount of test substance is injected intravenously.
2. Plasma concentration is determined at intervals.
3. A graph (log concentration against time scale) is plotted (Fig. 1.9).
4. Extrapolate the straight portion to time 0—this gives the concentration of substance that will distribute evenly instantly (Fig. 1.9).

Using this method:

$$\text{Compartment volume} = \frac{\text{Amount injected}}{\text{Concentration at zero time}}$$

Constant infusion method

This is used for test substances that are rapidly excreted and is carried out as follows:

1. A loading dose of the test substance is injected intravenously.
2. The test substance is infused at a rate to match renal excretion rate.
3. Plasma concentration is measured at intervals.
4. When the substance comes to equilibrium, the plasma concentration is constant (Fig. 1.10).
5. Stop the infusion.
6. Collect urine until all the test substance has been excreted.

Using this method:

Amount excreted = Amount present in the body at the time the infusion was stopped

And:

$$\text{Compartment volume} = \frac{\text{Amount excreted (mg)}}{\text{Plasma concentration (mg/L)}}$$

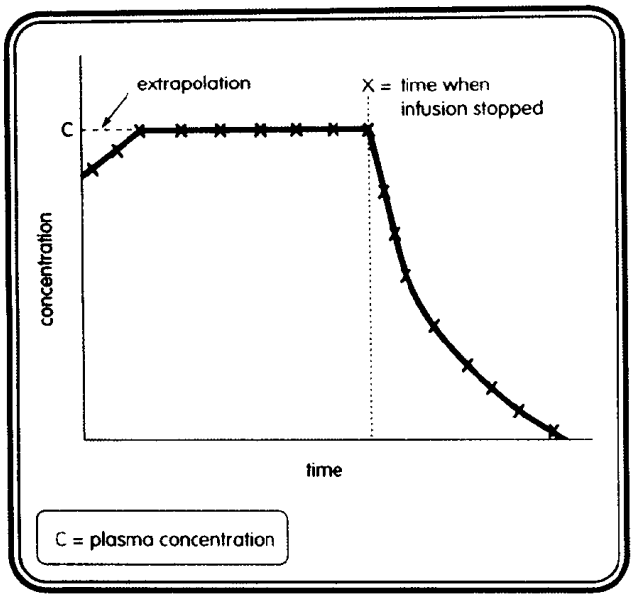

Fig. 1.10 Plasma concentration of an infused substance. (From Principles of Renal Physiology by C Lote, 1993.)

Measurement of plasma volume, red cell volume, and blood volume

Plasma volume, red cell volume, and blood volume are measured as follows:

- Plasma volume—the test substance needs to remain within the vascular system (e.g. plasma protein) and radio-iodinated human serum albumin or Evans Blue dye are used.

  Normal plasma volume = 3 L

- Blood volume—measure the haematocrit (% of red blood cells in total blood volume) by centrifuging a small sample of blood—for example, if the haematocrit is 45%, the plasma volume is 55% of blood volume (measure plasma volume as above and blood volume = plasma volume × 100/55).

  Normal blood volume = 5 L

- Red cell volume can be measured from plasma volume and haematocrit or by direct dilution, which is carried out by taking a small sample of blood, incubating red blood cells in radioactive phosphorus (^{32}P) or chromium (^{51}Cr), resuspending (in saline), reinjecting, and determining the dilution of the label after 15 min.

Measurement of extracellular fluid

As ECF is made up of several compartments, it is difficult to measure accurately. A substance that will diffuse across the endothelial barriers into the ISF, but not into the cells, is required. It is difficult to measure the TCF as it is separated from the capillaries by another membrane in addition to the capillary membrane. Substances used include:

- Inulin (may be excluded from bone and cartilage).
- Mannitol.
- Thiosulphate (most widely used).
- Radiosulphate.
- Thiocyanate.
- Radiochloride or radiosodium (these substances cannot be completely excluded from cells).

  Normal ECF volume = 15 L

Measurement of interstitial fluid

ISF cannot be measured directly. It needs to be calculated as follows:

ECF (15 L) – plasma volume (3 L) = ISF (12 L)

Measurement of total body water

Isotopes of water are used as markers (deuterium oxide or tritiated water) to measure total body water (TBW). A normal value in a 70 kg man is 63% (i.e. 45 L) and in a 70 kg woman, 52% (36 L), being lower in women because of their greater proportion of body fat.

Measurement of transcellular fluid

As this compartment is separated from the rest of the ECF by a membrane, the substances used to measure the ECF do not cross into this compartment. Thus TCF is included in the TBW, but excluded from the ECF, thus:

TBW = ECF + ICF + TCF

There is a large turnover—about 20 L/day for the gastrointestinal tract.