The Renal System Explained

An illustrated core text

Sunita R. Deshmukh, BMedSci (Hons)
Fourth Year Medical Student
Faculty of Medicine and Health Sciences, University of Nottingham, UK

Newton W.K. Wong, BMedSci (Hons)
Fourth Year Medical Student
Faculty of Medicine and Health Sciences, University of Nottingham, UK
CONTENTS

Dedications vii
Contributors and acknowledgements viii
Preface ix
Key features x

CHAPTER 1: BODY FLUID BALANCE 1

Body fluid distribution 1
Body fluid compartments 1
Constituents of body fluid 3
ECF ‘reservoir’ 4

General principles of fluid balance 5
Electrolyte solutions 5
Fluid exchange 6

Regulation of body fluid balance 9
ECF volume and NaCl balance 10
Water balance 15
Potassium balance 16

Integrative case study 20
Self-assessment 21

CHAPTER 2: ACID-BASE BALANCE 25

Principles of acids and bases 25
Dissociation (ionisation) 25
Chemical buffers 25
Henderson-Hasselbalch equation 25

Regulation of acid-base balance 26
Chemical buffer systems 27
Respiratory compensation 28
Renal (metabolic) compensation 29

Acid-base disorders 33
Respiratory acidosis 33
Respiratory alkalosis 33
Metabolic acidosis 33
Metabolic alkalosis 36

Integrative case study 38
Self-assessment 41
CHAPTER 3: STRUCTURE OF THE RENAL SYSTEM

Gross anatomy
Kidneys 43
Ureters 51
Adrenal glands 53

Surface anatomy 54

Histology
Kidneys 57
Nephron 57
Renal capsule 62
Renal cortex and medulla 63
Lobes and lobules 63
Interstitium 64
Endocrine components 64
Ureters 65
Adrenal glands 65

Embryology 68
Urinary system 68
Adrenal glands 71

Integrative case study 72
Self-assessment 75

CHAPTER 4: RENAL CORPUSCLE 79

The glomerulus 79
Juxtaglomerular apparatus 79
Mesangium 80

Glomerular filtration 81
Filtration pathway 81
Net filtration pressure 82
Glomerular filtration rate 86
Renal clearance 87
Filtration fraction 89

Renal blood flow 90
Intrinsic mechanisms of autoregulation 92
Extrinsic regulatory mechanisms 94

Integrative case study 99
Self-assessment 101
### CHAPTER 5: RENAL TUBULAR SYSTEM

**Introduction to the renal tubule**
- Tubular transport mechanisms

**Proximal tubule**
- Sodium
- Water
- Bicarbonate
- Chloride
- Potassium

**Loop of Henle**
- Thin descending limb
- Thin ascending limb
- Thick ascending limb

**Other major solutes**
- Urea
- Phosphate
- Calcium
- Magnesium
- Glucose: filtered load calculation

**Distal tubule and collecting duct system**
- Principal cells
- Intercalated cells

**Urine concentration and dilution**
- Counter-current multiplication
- Vasa recta function
- Urea
- Anti-diuretic hormone
- Aldosterone

**Integrative case study**

**Self-assessment**

---

**APPENDIX 1 – DIURETICS OVERVIEW**

**APPENDIX 2 – CLINICAL IMAGING OVERVIEW**

**APPENDIX 3 – NORMAL VALUES**

- Commonly used abbreviations
- References
- Glossary
- Index
The concepts covered in this chapter are all fundamental aspects of the renal system. This system is designed, structurally (anatomically) and functionally (physiologically), to handle fluids within the body in a highly efficient way. Water is the most abundant component of the human body, accounting for roughly two-thirds of the average person’s body weight. The physicochemical processes responsible for maintaining fluid and electrolyte homeostasis in the human body are vital. An awareness of the underlying regulatory mechanisms is also important when considering various pathological changes.

The basic principles are relatively simple to remember and apply, provided you have a clear understanding of them from the outset. The core material in this chapter forms a good starting point for studying the renal system as its relevance can be appreciated throughout.

**Body fluid distribution**

**Body fluid compartments**

**Intracellular and extracellular fluid**

Fluid is compartmentalised in the body as shown in Figure 1.1. Body fluid volume and distribution can vary with age, gender and proportion of body fat, since adipose tissue has a low water content compared with other tissues (see *Points of interest 1.1*).

The two major divisions of body fluid are separated by the cell membrane:

- **Intracellular fluid (ICF)** – contains a relatively large volume within the body’s cells (about two-thirds of total body water)

- **Extracellular fluid (ECF)** – contains a relatively small volume outside the cells (about one-third of total body water)

**Figure 1.1 – Body fluid compartments**

**Body fluid distribution**

**General principles of fluid balance**

**Regulation of body fluid balance**

**Integrative case study**

**Self-assessment**

**Written by: Sunita Deshmukh**
• **Extracellular fluid (ECF)** – smaller volume of fluid outside cells (about one-third of total body water).

The ECF is further sub-divided into two major compartments, separated by the capillary endothelium, and a minor compartment:

- **Interstitial fluid** – occupies the space between cells and outside capillaries (makes up about two-thirds of ECF volume)
- **Plasma** – the non-cellular part of blood, found inside capillaries i.e. intravascular (plasma accounts for about a third of ECF volume)
- **Transcellular fluid** – contains only a small amount of water, including epithelial secretions such as synovial, pericardial, intraocular and cerebrospinal fluid.

Transcellular fluid is said to occupy a ‘third space’ (3 extracellular fluid compartments in total). Minor compartments of body fluid, like lymph and transcellular (third space) fluids are negligible in terms of their quantitative contribution to ECF.

The major fluid compartments of the body, with average values for volume and percentage of total body weight, are shown in Figure 1.1.

**Clinical relevance 1.1**

In pharmacology, the volume of distribution \( (V_d) \) of a drug is defined as the apparent volume of fluid in which the total dose of the drug is distributed at the same concentration as in the plasma. This value is useful in dosage calculations such as loading doses. Generally the following can be assumed about the nature of drug distribution, based on our knowledge of body fluid compartments (Fig.1.1):

\[
\begin{align*}
V_d &= 3 \text{ L} \quad \text{drug only in plasma} \\
V_d &= 14 \text{ L} \quad \text{drug in plasma and interstitial fluid i.e. ECF} \\
V_d &= 40–45 \text{ L} \quad \text{drug occupying total body water i.e. ICF + ECF} \\
V_d &> 45 \text{ L} \quad \text{drug widely distributed and extensively bound in body tissues}
\end{align*}
\]

**Blood volume**

Blood has intracellular (blood cells) and extracellular (plasma) fluid components, contained intravascularly within the circulation. The fraction of total blood volume that is composed of red blood cells is known as the ‘packed cell volume’ (PCV) or haematocrit. The significance of this value in assessing renal disease is explained in **Clinical relevance 1.2**.

The total blood volume can be calculated from known values of haematocrit and plasma volume, as shown in equation 1.1, using typical values for a normal adult. Plasma volume is measured using serum albumin labelled with radioactive iodine, or less commonly by injecting a dye that binds to plasma proteins in the circulation.

\[
\text{Total blood volume} = \frac{\text{Plasma volume}}{1 - \text{Haematocrit}}
\]

\[
5 \text{ L} = \frac{3 \text{ L}}{1 - 0.4}
\]

**Clinical relevance 1.2**

PCV, or haematocrit, can be calculated from known values of:

- Red blood cell count
- Mean corpuscular volume (MCV) i.e. the average volume of a red blood cell.

Calculation of PCV is shown in equation 1.2 using approximate average values for a normal adult. Normal ranges are provided in Appendix 3 (haematocrit 0.42–0.45).

\[
\text{Mean corpuscular volume} \times \text{Red blood cell count} = \text{Haematocrit}
\]

\[
90 \times 10^{-15} \text{ L} \times 5 \times 10^{12} \text{L} = 0.45 \text{ (45% of total blood volume)}
\]

**Polycythaemia** is characterised by an abnormally raised concentration of red blood cells (erythrocytes), usually accompanied by increased levels of haemoglobin and PCV. Haemoglobin levels may be affected by other conditions (physiological and pathological e.g. iron-deficiency), therefore clinically PCV is a more reliable indicator of polycythaemia.

Changes in PCV may reflect:

- A change in the actual volume of red blood cells
- A change in the total blood volume.

In **absolute polycythaemia** the red blood cell volume is raised, whereas **relative polycythaemia** occurs due to a fall in plasma volume (the actual volume of red cells remains normal, but the concentration rises).

Absolute polycythaemia may have a primary or secondary underlying cause. Primary polycythaemia (polycythaemia rubra vera, or erythrocytosis) is an example of a
myeloproliferative disorder (uncontrolled clonal proliferation of bone marrow cell lines). Absolute polycythaemia may be secondary to high levels of erythropoietin, the primary stimulus for erythrocyte production. Causes may be:

- Physiological e.g. high-altitude living
- Pathological e.g. diseases of the kidney that inappropriately increase the secretion of erythropoietin, lung disease, cyanotic heart disease.

### Points of Interest 1.1

Water as a percentage of body weight, is influenced by age, gender and percentage of body fat. Body water percentage is highest in neonates and decreases to the normal average adult value of ~60% by one year of age. Body water percentage is typically lower in women than in men because women have a higher percentage of body fat (due to actions of the female sex hormone oestrogen).

### Remember

Water content in adipose tissue is low, relative to water content in other tissue types.

### Remember

Na\(^+\) is the predominant cation of the ECF and K\(^+\) is the major cation of the ICF (Fig. 1.1).

### Ask Yourself 1.1

Q. What is the physiological significance of the difference in Na\(^+\) and K\(^+\) distribution between the extracellular and intracellular fluid?

A. The uneven distribution of Na\(^+\), K\(^+\) and large protein anions (as well as the differential membrane permeability to these ions) are responsible for:

- ECF – Sodium ions (Na\(^+\))
- ICF – Potassium ions (K\(^+\)).

Both of these cations are accompanied by their attendant anions:

- ECF – the major anions accompanying Na\(^+\) are Cl\(^-\) and HCO\(_3^-\)
- ICF – K\(^+\) is accompanied primarily by PO\(_4^{3-}\) (as well as negatively charged cellular proteins which cannot escape the cell).

ECF compartments (plasma and interstitial fluid) are only separated by capillary endothelium which is freely permeable to small ions, so their ionic compositions are similar. The important difference between the two major ECF compartments is the relatively high plasma concentration of plasma proteins, which tend to remain in the capillary due to its low permeability to these proteins.

### Constituents of body fluid

The ionic compositions of the ICF and ECF differ considerably, due to the low electrolyte permeability of the highly selective cell membrane that divides these two fluid compartments. The electrolyte composition of each body fluid compartment is predominated by a particular ion:

- ECF – Sodium ions (Na\(^+\))
- ICF – Potassium ions (K\(^+\)).

Both of these cations are accompanied by their attendant anions:

- ECF – the major anions accompanying Na\(^+\) are Cl\(^-\) and HCO\(_3^-\)
- ICF – K\(^+\) is accompanied primarily by PO\(_4^{3-}\) (as well as negatively charged cellular proteins which cannot escape the cell).

### Table 1.1 – ECF and external environment: processes of transfer between internal and external environment

<table>
<thead>
<tr>
<th>Site of transfer</th>
<th>Input (to ECF)</th>
<th>Output (from ECF)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Digestive tract</td>
<td>Ingestion</td>
<td>Defecation</td>
</tr>
<tr>
<td>Lungs</td>
<td>Inspiration</td>
<td>Expiration</td>
</tr>
<tr>
<td>Body surface</td>
<td>Absorption through skin or mucosal surface, by injection</td>
<td>Perspiration, lacrimation, open wound (haemorrhage)</td>
</tr>
</tbody>
</table>

### Table 1.2 – ECF and other internal sites: processes of transfer

<table>
<thead>
<tr>
<th>Internal processes</th>
<th>Input (to ECF)</th>
<th>Output (from ECF)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metabolism</td>
<td>Production</td>
<td>Consumption (irreversible)</td>
</tr>
<tr>
<td>Storage depots</td>
<td>Retrieval of stored constituents for temporary restoration of their plasma concentration</td>
<td>Storage of excess constituents for temporary maintenance of their normal plasma concentration</td>
</tr>
<tr>
<td>Reversible incorporation into more complex structures</td>
<td>Retrieval of ECF constituent</td>
<td>Removal of constituent from ECF by its conversion</td>
</tr>
</tbody>
</table>
• Resting cell membrane potential (separation of opposite charges across the plasma membrane)
• Generation of action potentials in excitable tissues (nerve and muscle cells) via changes in these variables.

**ECF ‘reservoir’**

The concentrations of different substances in the ECF vary. The ECF acts as a readily available internal reservoir of its constituent substances. Transfer of substances can occur between the ECF and the external environment or between the ECF and other internal sites, via a number of exchange mechanisms summarised in Table 1.1 and Table 1.2.

Storage depots of ECF constituents have a limited capacity, therefore processes of transfer between the ECF (the body’s internal reservoir) and other internal sites can only temporarily compensate for deviations in the normal plasma levels of ECF constituents.

**Remember**

Ultimately the maintenance of a stable balance of ECF constituents relies on the following equation:

**TOTAL BODY INPUT = TOTAL BODY OUTPUT**

This in turn depends on:

• Exchanges between the ECF and the external environment i.e. the balance between ingestion and excretion
• Metabolism i.e. the balance between anabolism (synthesis) and catabolism (breakdown) of ECF constituents.

**Key Points 1.1**

Table 1.3 provides a summary of the normal volume and distribution of body fluids, given a total body water volume of 45 L.

Total body water in a normal healthy adult is 40–45 L on average, accounting for 60% of body weight.

The ICF and ECF are divided by the highly selective plasma membrane.

Major differences between the ICF and ECF include:

• Presence of cellular proteins in the ICF, that cannot leave cells
• Unequal distribution of Na⁺ and K⁺ (and their accompanying anions).

**Table 1.3 – Summary of the major body fluid compartments**

<table>
<thead>
<tr>
<th>Body fluid compartment</th>
<th>Volume (and as a fraction of total body fluid volume)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intracellular fluid (ICF)</td>
<td>30 L (2/3)</td>
</tr>
<tr>
<td>Extracellular fluid (ECF)</td>
<td>15 L (1/3)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>ECF component</th>
<th>Distribution</th>
<th>Volume (and as a fraction of total ECF volume)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Interstitial fluid</td>
<td>Outside the capillary, bathing cells</td>
<td>11.5 L (~3/4)</td>
</tr>
<tr>
<td>Plasma</td>
<td>Inside the capillary i.e. contained within blood vessels</td>
<td>3.5 L (~1/4)</td>
</tr>
</tbody>
</table>

**Remember**

The ICF is characterised by a relatively high concentration of potassium ions (K⁺) i.e. 150 mmol/L.

The ECF is characterised by:

• Relatively high sodium ion (Na⁺) concentration i.e. 135–145 mmol/L
• Low K⁺ concentration i.e. 3.5–5.0 mmol/L.

The ECF compartments are separated by the highly permeable capillary endothelium.

The main difference between ECF compartments is the higher concentration of plasma proteins in the blood plasma (only a small amount of plasma proteins leak into the interstitial fluid).

The regulation of ECF constituents is summarised by the balance concept, which applies to the long-term balance of any substance within the body:

**TOTAL BODY INPUT = TOTAL BODY OUTPUT**

When input > output a POSITIVE balance exists
When output > input a NEGATIVE balance exists