Integrated Medical Sciences
The Essentials

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John Wiley & Sons, Ltd
Dedicated to the memory of
Dr Y. S. Perera (1919–2002),
physician, teacher, beloved father. A guiding light and source of inspiration that will never diminish with the passage of time.

Shantha Perera
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About this book...

This book aims to present the essential concepts and facts of the basic medical sciences through case scenarios involving a group of characters. It is therefore primarily a revision text.

The book is set out in 10 chapters. Chapters 1–8 cover the organ systems that constitute the human body. Chapters 9 and 10 cover the haematological and immune systems, inheritance and the principles of infection.

Each chapter contains clinical scenarios involving common disease conditions affecting the system under consideration. As you read through these disease scenarios you will be introduced to the underlying basic medical science principles: the anatomical, physiological, biochemical, pharmacological and pathological principles and facts relevant to the system.

For example, the chapter on the digestive system involves several scenarios where common disorders involving the different parts/organs of the digestive system are encountered. As you read these scenarios you will be presented with the anatomy, physiology and biochemistry relevant to that particular part of the digestive system. You will also be introduced to the relevant pathophysiology, pharmacology and microbiology. The scientific facts and concepts would be presented in a fully integrated manner in the context of the clinical scenarios.

The clinical scenarios involve a group of characters that appear throughout the book. You will come across them repeatedly as you read through the chapters and will get to know their medical conditions and personalities. This approach, will aid recall and also be useful when you enter the clinical years where you will encounter patients with multiple clinical problems that require an integrated approach.

For students who do not have a clinical training period as part of their program (e.g. BSc/MSc students) the integrated, case-based approach will aid in better understanding of the underlying scientific principles. In addition to aiding recall, the problem-solving approach will stimulate lateral thinking and allow an appreciation of the interrelationships between the various specialties of biomedical science.

The text is suitable as a revision text for:

A. Preclinical UK Medical Students preparing for integrated preclinical examinations
B. Preclinical US and International Medical Students preparing for the USMLE Step 1
C. Clinical Physiology BSc students
D. Biomedical Sciences BSc/MSc students
E. BPharm Students
F. Advanced Nurse Practitioners and other Health Sciences students.
Key features of this book

A. *Case Scenarios* involving a cast of characters that appear throughout the book.

B. *Questions* that require you to think about the contents of the scenario; e.g. interpretation of physical findings, lab results, etc.

C. Case scenarios are followed by a consideration of the relevant underlying scientific principles (e.g. anatomy, physiology, biochemistry, pharmacology, etc.) presented mainly by annotated figures, tables and descriptive text.

D. *Trigger Boxes* showing key facts – you will need to work out the significance of the terms, which can be used for rapid revision.

E. *Tables* containing more detailed information.

F. *Incomplete tables* – you need to complete these – if required by your programme of study – they can also be very useful for rapid revision.

G. *Learning Tasks* that will get you vital additional information if required.

How to use this book

This book requires *active* learning on your part.

Read through the clinical scenarios and get a feel of what is going on. Try to answer the questions that follow the text. These questions are aimed to get you to think about the key concepts ‘hidden’ within the scenario. Some questions also stimulate further reading.

As you continue reading you will be introduced to the underlying scientific principles and key facts in the form of explanatory passages, annotated figures, and tables. Study these carefully and see how they relate to what’s happening to the patient. You will also come across some incomplete tables. The incomplete tables are designed to cover additional, more peripheral information that may be required by some programs of study. For example BSc/MSC biomedicine students may not need the level of anatomical detail as medical or nursing students.

The learning tasks are also designed to widen knowledge. Carrying them out will give you the depth required in some programs.

Study the Trigger tables which cover the major diseases relevant to a given system. These tables, which require active learning, will be useful for rapid revision, for example just prior to an examination.

The book has an associated website, containing MCQs and additional topics–please visit www.wiley.com/go/perera
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The Authors
### List of Abbreviations

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<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ab</td>
<td>antibody</td>
</tr>
<tr>
<td>ACE</td>
<td>angiotensin converting enzyme</td>
</tr>
<tr>
<td>ACEI</td>
<td>ACE inhibitors</td>
</tr>
<tr>
<td>ACh</td>
<td>acetylcholine</td>
</tr>
<tr>
<td>ACL</td>
<td>anterior cruciate ligament</td>
</tr>
<tr>
<td>ACTH</td>
<td>adrenocorticotropic hormone</td>
</tr>
<tr>
<td>AD</td>
<td>autosomal dominant</td>
</tr>
<tr>
<td>ADA</td>
<td>adenosine deaminase</td>
</tr>
<tr>
<td>AF</td>
<td>atrial fibrillation</td>
</tr>
<tr>
<td>AFP</td>
<td>alpha- fetoprotein</td>
</tr>
<tr>
<td>Ag</td>
<td>antigen</td>
</tr>
<tr>
<td>AGIs</td>
<td>alpha-glucosidase inhibitors</td>
</tr>
<tr>
<td>AIDS</td>
<td>acquired immunodeficiency syndrome</td>
</tr>
<tr>
<td>ALL</td>
<td>acute lymphoblastic leukaemia</td>
</tr>
<tr>
<td>ALS</td>
<td>amyotrophic lateral sclerosis</td>
</tr>
<tr>
<td>ALT</td>
<td>alanine transaminase</td>
</tr>
<tr>
<td>AML</td>
<td>acute myeloid leukaemia</td>
</tr>
<tr>
<td>ANA</td>
<td>anti-nuclear antibody</td>
</tr>
<tr>
<td>ANP</td>
<td>atrial natriuretic peptide</td>
</tr>
<tr>
<td>ANS</td>
<td>autonomic nervous system</td>
</tr>
<tr>
<td>APC</td>
<td>antigen presenting cell</td>
</tr>
<tr>
<td>aPTT</td>
<td>activated partial thromboplastin time</td>
</tr>
<tr>
<td>AR</td>
<td>autosomal recessive</td>
</tr>
<tr>
<td>ARDS</td>
<td>adult respiratory distress syndrome</td>
</tr>
<tr>
<td>ARF</td>
<td>acute renal failure</td>
</tr>
<tr>
<td>ASD</td>
<td>atrial septal defect</td>
</tr>
<tr>
<td>ASO</td>
<td>anti streptolysin O</td>
</tr>
<tr>
<td>AST</td>
<td>aspartate transaminase</td>
</tr>
<tr>
<td>AXR</td>
<td>abdominal X ray</td>
</tr>
<tr>
<td>AVM</td>
<td>arteriovenous malformation</td>
</tr>
<tr>
<td>AZT</td>
<td>azidothymidine</td>
</tr>
<tr>
<td>BCG</td>
<td>Bacille Calmette-Guérin</td>
</tr>
<tr>
<td>BMT</td>
<td>bone marrow transplant</td>
</tr>
<tr>
<td>BP</td>
<td>blood pressure</td>
</tr>
<tr>
<td>BPH</td>
<td>benign prostatic hypertrophy</td>
</tr>
<tr>
<td>BPV</td>
<td>benign positional vertigo</td>
</tr>
<tr>
<td>CA -125</td>
<td>cancer antigen 125</td>
</tr>
<tr>
<td>CA -15-3</td>
<td>cancer antigen 15-3</td>
</tr>
<tr>
<td>CABG</td>
<td>coronary artery bypass grafting</td>
</tr>
<tr>
<td>CAD</td>
<td>coronary artery disease</td>
</tr>
</tbody>
</table>
C-ANCA circulating anti neutrophil cytoplasmic antibody
CCK cholecystokinin
CEA carcinoembryonic antigen
CF cystic fibrosis
CGD chronic granulomatous disease
CHF congestive heart failure
CIN cervical epithelial neoplasia
CJD Creutzfeld-Jakob disease
CLL chronic lymphatic leukaemia
CM chylomicrons
CML chronic myeloid leukaemia
CMV cytomegalovirus
CN cranial nerve
CNS central nervous system
CO cardiac output
COMT catechol-o-methyl transferase
COPD chronic obstructive pulmonary disease
COX cycloxygenase
CPK-MP creatine phosphokinase MB fraction
CREST (calcinosis, Raynaud’s, oesophageal dismobility, sclerodactyl, telangiectasia)
CRF chronic renal failure
CRH corticotrophin releasing factor
CSF cerebro spinal fluid
CT computer tomography
CVA costovertebral angle or cerebral vascular accident
CXR chest X ray
da dopamine
DDVAP desmopressin acetate
DHEA dehydroepiandrosterone
DIC disseminated intravascular coagulation
DIP distal interphalangeal joint
DIT diiodotyrosine
DKA diabetic ketoacidosis
DM diabetes mellitus
DMARD disease modifying anti-rheumatic drug
DNA deoxyribonucleic acid
DTR deep tendon reflexes
DUB dysfunctional uterine bleeding
DVT deep vein thrombosis
EDV end diastolic volume
EF ejection fraction
EF-2 elongation factor 2
ELISA enzyme linked immunosorbent assay
EPP end plate potential
EPSP excitatory postsynaptic potential
ERPOC evacuation of retained product of conception
ESR erythrocyte sedimentation rate
ESV end systolic volume
FEV1 forced expiratory volume 1
FF filtration fraction
FFP fresh frozen plasma
FSH follicle-stimulating hormone
FT3 triiodothyronine
FTA-ABS fluorescent treponemal antibody - ABS absorption
FVC forced vital capacity
G6PD glucose 6 phosphatase deficiency
GABA gamma amino butyric acid
GBM glioblastoma multiforme/glomerular basement membrane
GFR glomerular filtration rate
GGT gamma glutaryl transferase
GH growth hormone
GHIH growth hormone inhibiting hormone
GHRH growth hormone releasing hormone
GIFT gamete intrafallopian transfer
GM-CSF granulocyte monocyte colony stimulating factor
GN glomerulonephritis
GnRH gonadotrophin releasing hormone
GORD gastroesophageal reflux disease
GTN glycerine trinitrate
5HT 5-hydroxytryptamine
5-HIAA 5-Hydroxyindolacetic Acid
HAART highly active antiretroviral therapy
Hb haemoglobin
HbcAb hepatitis B core antibody
HBeAb hepatitis B e antibody
HBeAg hepatitis B e antigen
HBsAg hepatitis B surface antigen
hCG human chorionic gonadotrophin
HD Huntington's disease
HDL high density lipoprotein
hGH human growth hormone
Hib haemophilus type B vaccine
HIV human immunodeficiency virus
HLA human leucocyte antigen
HONK hyperosmolar hyperglycaemic non-ketotic coma
HPA hypothalamus-pituitary-adrenal axis
HPL human placental lactogen
HPV human papilloma virus
HRT hormone replacement treatment
HSV herpes simplex virus
HTLV human T cell leukaemia virus
HTN hypertension
HUS haemolytic uraemic syndrome
IBD inflammatory bowel disease
IDDM insulin dependent diabetes mellitus
IFN interferon
Ig immunoglobulin
IGF- insulin-like growth factor 1
IGT impaired glucose tolerance
INH isoniazid
INR international normalised ratio
IPSP inhibitory post synaptic potential
IRV inspiratory reserve volume
ITP idiopathic thrombocytopenic purpura
IUGR intrauterine growth retardation
IUI Intra-uterine insemination
IVC inferior vena cava
IVF In vitro fertilization
JRA juvenile rheumatoid arthritis
JVD jugular venous distension
JVP Jugular venous pressure
LAD left anterior decending
LBBB left bundle branch block
LDH lactate dehydrogenase
LDL low density lipoprotein
LFT liver function test
LH lutenizing hormone
LLQ left lower quadrant
LMN lower motor neuron
LSD lysergic acid diethylamide
LV left ventricle
LVH left ventricular hypertrophy
MAOI monoamine oxidase inhibitors
MCH mean corpuscular haemoglobin
MHC major histocompatibility antigen
MCHC mean cell haemoglobin concentration
MD macular degeneration
MEN multiple endocrine neoplasia
MI myocardial infarction
MIBG metaiodobenzylguanadine scan
MIT monoidotryptosine
MMR measles mumps rubella
MPTP methylphenyltetrahydropyridine
MRCP magnetic resonance cholangiopancreatography
LIST OF ABBREVIATIONS

MRI magnetic resonance imaging
MS multiple sclerosis
MSAFP maternal serum AFP
MSH melanocyte stimulating hormone
MVP mitral valve prolapse
NAFLD non-alcoholic fatty acid liver disease
NE noradrenaline
NGU non-gonococcal urethritis
NMJ neuromuscular junction
NSAID non steroidal anti inflammatory drugs
NSTEMI non ST elevation myocardial infarctions
OGD oesophagogastroduodenoscopy
OPV oral polio vaccine
PAF platelet activating factor
PAH para aminohippuric acid
PAN polyarteritis nodosa
P-ANCA perinuclear anti neutrophil cytoplasmic antibody
PAP smear Papanicolaou smear
PCL posterior cruciate ligament
PCOS polycystic ovarian syndrome
PDA patent duc tus arteriosus
PE pulmonary embolism
PEFR peak expiratory flow rate
PID pelvic inflammatory disease
PK pyruvate kinase
PMN polymorphonuclear leucocyte
PNH paroxysmal nocturnal haemoglobinuria
PNS parasympathetic nervous system/peripheral nervous system
PPD purified protein derivative
PPI proton pump inhibitor
PPP pentose-phosphate pathway
PROM premature rupture of membranes
PSA prostate specific antigen
PSVT paroxysmal supraventricular tachycardia
PT prothrombin time
PTCA percutaneous transluminal coronary angioplasty
PTH parathyroid hormone
PVB premature ventricular beat
PVC premature ventricular tachycardia
RA rheumatoid arthritis
RBBB right bundle branch block
RBC red blood cell
RBF renal blood flow
RDS respiratory distress syndrome
RF rheumatic fever
<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>RhoGAM</td>
<td>Rh Immune Globulin</td>
</tr>
<tr>
<td>RPR</td>
<td>rapid plasma reagin</td>
</tr>
<tr>
<td>RR</td>
<td>respiratory rate</td>
</tr>
<tr>
<td>RSV</td>
<td>respiratory syncytial virus/ rous sarcoma virus</td>
</tr>
<tr>
<td>RT</td>
<td>reverse transcriptase</td>
</tr>
<tr>
<td>RTA</td>
<td>renal tubular acidosis</td>
</tr>
<tr>
<td>RUQ</td>
<td>right upper quadrant</td>
</tr>
<tr>
<td>RV</td>
<td>residual volume</td>
</tr>
<tr>
<td>RVH</td>
<td>right ventricular hypertrophy</td>
</tr>
<tr>
<td>SCC</td>
<td>squamous cell carcinoma antigen</td>
</tr>
<tr>
<td>SCID</td>
<td>severe combined immunodeficiency</td>
</tr>
<tr>
<td>SHBG</td>
<td>sex hormone binding globulin</td>
</tr>
<tr>
<td>SIADH</td>
<td>syndrome of inappropriate anti diuretic hormone</td>
</tr>
<tr>
<td>SLE</td>
<td>systemic lupus erythymatosus</td>
</tr>
<tr>
<td>SMA</td>
<td>superior mesenteric artery</td>
</tr>
<tr>
<td>SNS</td>
<td>sympathetic nervous system</td>
</tr>
<tr>
<td>SRS-A</td>
<td>slow reacting substance A</td>
</tr>
<tr>
<td>SSRI</td>
<td>selective serotonin reuptake inhibitor</td>
</tr>
<tr>
<td>SV</td>
<td>stroke volume</td>
</tr>
<tr>
<td>SVC</td>
<td>superior vena cava</td>
</tr>
<tr>
<td>SVT</td>
<td>supraventricular tachycardia</td>
</tr>
<tr>
<td>T max</td>
<td>transport maximum</td>
</tr>
<tr>
<td>TAH-BSO</td>
<td>total abdominal hysterectomy &amp; bilateral salphingo-oophorectomy</td>
</tr>
<tr>
<td>TB</td>
<td>tuberculosis</td>
</tr>
<tr>
<td>TCR</td>
<td>T cell receptor</td>
</tr>
<tr>
<td>TG</td>
<td>triglyceride</td>
</tr>
<tr>
<td>Th cell</td>
<td>T helper cell</td>
</tr>
<tr>
<td>TIA</td>
<td>transient ischaemic attack</td>
</tr>
<tr>
<td>TLC</td>
<td>total lung capacity</td>
</tr>
<tr>
<td>TMP-SMX</td>
<td>trimethoprim sulphamethoxazole</td>
</tr>
<tr>
<td>TNA</td>
<td>tranexamic acid</td>
</tr>
<tr>
<td>TNF</td>
<td>tumor necrosis factor</td>
</tr>
<tr>
<td>TOA</td>
<td>tuboovarian abscess</td>
</tr>
<tr>
<td>TOF</td>
<td>tracheo-oesophageal fistula</td>
</tr>
<tr>
<td>t-PA</td>
<td>tissue type plasminogen activator</td>
</tr>
<tr>
<td>TPR</td>
<td>total peripheral resistance</td>
</tr>
<tr>
<td>TRH</td>
<td>thyrotropin-releasing hormone</td>
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<td>TS</td>
<td>tumor suppressor</td>
</tr>
<tr>
<td>TSH</td>
<td>thyroid stimulating hormone</td>
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<tr>
<td>TSST-1</td>
<td>toxic shock syndrome toxin 1</td>
</tr>
<tr>
<td>TTP</td>
<td>thrombotic thrombocytopenic purpura</td>
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<tr>
<td>TV</td>
<td>tidal volume</td>
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<tr>
<td>TZD</td>
<td>thiazolidinedione</td>
</tr>
<tr>
<td>UDPGR</td>
<td>UDP-glucuronyl transferase</td>
</tr>
<tr>
<td>Abbreviation</td>
<td>Full Form</td>
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<td>--------------</td>
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</tr>
<tr>
<td>UMN</td>
<td>upper motor neurons</td>
</tr>
<tr>
<td>UOS</td>
<td>upper oesophageal sphincter</td>
</tr>
<tr>
<td>UTI</td>
<td>urinary tract infection</td>
</tr>
<tr>
<td>V/Q ratio</td>
<td>ventilation perfusion ratio</td>
</tr>
<tr>
<td>VC</td>
<td>vital capacity</td>
</tr>
<tr>
<td>VDRL</td>
<td>venereal disease research laboratory</td>
</tr>
<tr>
<td>VIP</td>
<td>vasoactive intestinal peptide</td>
</tr>
<tr>
<td>VLDL</td>
<td>very low density lipoprotein</td>
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<td>VMA</td>
<td>vanillylmandelic acid</td>
</tr>
<tr>
<td>VSD</td>
<td>ventricular septal defect</td>
</tr>
<tr>
<td>VT</td>
<td>ventricular tachycardia</td>
</tr>
<tr>
<td>VWD</td>
<td>Von Willebrand Disease</td>
</tr>
<tr>
<td>VWF</td>
<td>Von Willebrand factor</td>
</tr>
<tr>
<td>VZV</td>
<td>varicella zoster virus</td>
</tr>
<tr>
<td>WBC</td>
<td>white blood cell</td>
</tr>
</tbody>
</table>
The Sickalott family tree

- Jane
  - Albert
    - Irene
      - Ted
      - John
      - Mary
        - John
          - Debbie
            - Max
              - Zak
            - Susie
        - Zoe
          - Little John
1

The respiratory system

Learning strategy

In this chapter we will consider the essential ‘must know’ facts and concepts of the respiratory system. Our main strategy would involve an exploration of these key principles by following several clinical scenarios.

The first scenario, an asthma attack will introduce us to the anatomy of the respiratory system. A consideration of the pathophysiology of asthma, will lead to a review of the immune system and the mechanism of Type 1 hypersensitivity.

Breathing difficulties will lead us to consider the mechanism of breathing and lung compliance. Lung volumes and capacities will be discussed as we consider the lung function tests of the asthmatic patient. We will also review the key drugs used in asthma treatment.

A second scenario – COPD – leads us to a consideration of acidosis and alkalosis. We will also discuss some key respiratory infections and the important concepts of V/Q mismatch and dead space. Finally we will consider gas exchange, oxygen and carbon dioxide saturation curves and the central and peripheral control of respiration.

Throughout, we will also consider the pathophysiological mechanisms of several key disease states involving the respiratory system, which will, in addition to highlighting the key pathophysiological principles, further reinforce basic principles of anatomy, physiology and pharmacology relevant to the respiratory system.

Try to answer the questions and try to complete the Learning Tasks. The Trigger Boxes should be used as a guide for further reading and revision. At the end of this chapter you should have a sound understanding of the key facts and concepts underlying the respiratory system.
Zoe’s breathing difficulties...

It happened again on Boxing Day. Around 5pm Zoe was sitting on her bed reading when she started to become breathless. Breathing was always her ‘problem’ and Zoe couldn’t understand it.

‘After all it’s supposed to be such a simple thing to do isn’t it?’ she had asked Mary. ‘It’s supposed to be automatic isn’t it? I mean you just breathe in and out. So why is it such an effort sometimes?’

Zoe took a puff out of her blue inhaler. She wondered if her problems had something to do with the fact that she had been a premature baby and that she had to be delivered at 33 weeks, by caesarean section.

‘Maybe my lungs weren’t developed properly’ she thought.

What is in Zoe’s blue inhaler?

Although Zoe was a premature baby, she didn’t have any problems and grew into a healthy child. Had she been born around, say, 26 weeks she would have had serious problems because her respiratory system would have been underdeveloped.

So, let us begin by reviewing the key stages in the development of the respiratory system. First, in terms of origins, the epithelium of the nasopharynx, trachea, bronchi, bronchioles and alveoli are derived from endoderm. The associated cartilage and muscle are mesodermal in origin.

You are expected to know the embryological origins of key anatomical structures. Construct a table listing the main derivatives of endoderm, ectoderm and mesoderm.

So what are the key embryological events in the development of the respiratory system? The respiratory system starts off as an outgrowth of the foregut. In the 4th week the oesophagotracheal septum separates the foregut into the respiratory diverticulum (lung bud) and oesophagus (Figure 1.1). The bud elongates and then branches into two. Each of these two new buds will become the primary bronchus of each lung.

What happens if the diverticulum fails to separate completely from the foregut

What is a TOF (tracheo-oesophageal fistula)?

The left lung bud develops into two secondary bronchi and eventually forms two lobes; the right bud forms three secondary bronchi and three lobes. The tertiary bronchi create the bronchopulmonary segments.

Gas exchange between blood and air in the primitive alveoli is possible in the seventh month of gestation. Lung growth after birth is mainly due to an increase in the number of respiratory bronchioles and alveoli and not due to an increase in size of alveoli. New alveoli are formed for at least 10 years of postnatal life.

What do we mean by the term ‘gas exchange’?

Before birth, the lungs are filled with fluid containing surfactant mainly made up of dipalmitoyl phosphatidylcholine, which is produced by type II epithelial cells. When
respiration begins, lung fluid is reabsorbed but leaves a surfactant coating. If Zoe was born around 26 weeks, her surfactant levels would have been low. She would suffer from respiratory distress syndrome (RDS). Her lungs would be difficult to expand and during deflation her alveoli would collapse. Surfactant decreases the alveolar surface tension and helps the alveoli to expand more easily.

**What are type I and II pneumocytes? Where do you find them?**

*Mother of premature babies are treated with steroids. Why?*

*What treatment can be given to a 28-week premature baby having difficulty inflating its lungs?*

**Trigger box  Respiratory distress syndrome (RDS)**

Deficiency of surfactant causes alveolar collapse and poor gas exchange. Majority of infants born before 28 weeks develop RDS within 4 hours of birth. **Features**: Tachypnoea, cyanosis, diaphragm, subcostal and intercostal retraction, grunting. **CXR**: Reticulogranular appearance with air bronchograms. **Treatment**: Glucocorticoids to mother, exogenous surfactant, oxygen, continuous positive airway pressure (CPAP), artificial ventilation.
Next let us consider the gross anatomy of the respiratory system. Figure 1.2 shows the important anatomical structures you need to know.

Note that the right lung has three lobes; the left has two. Each lung lobe is made up of bronchopulmonary segments. Label the oblique and horizontal fissures. The right main bronchus is straighter and shorter than the left main bronchus. This helps to explain why Zoe’s brother John, at age 4, got a small peanut stuck in the right main bronchus when he inhaled it.

When Zoe’s great-uncle Arthur suffered from a really nasty bout of pulmonary tuberculosis the surgeons had to remove several of his bronchopulmonary segments. This was not too difficult because each bronchopulmonary segment is served by its own arteries and vein and is partitioned from other segments by connective tissue.

Define what is meant by the terms (a) ‘respiratory bronchiole’ and (b) ‘terminal bronchiole’.

Let us look at the other main structures that make up the respiratory system. Important structures to know include the nasopharynx, oropharynx, larynx, glottis and trachea. The blood supply of the lungs consists of the pulmonary arteries that run with the airways, the bronchial arteries that branch off from the aorta, and the pulmonary veins that run in the connective tissue septa.

What kind of blood (oxygenated, deoxygenated) is found in these different vessels?

Bronchi have cartilage whereas bronchioles do not. They both have smooth muscle – what is the relevance of these facts to asthma?

Lung connective tissue contains lots of elastic tissue – what is the significance of this elasticity?
The lungs are covered by visceral pleura. This is separated from the parietal pleura which covers the inside of the chest wall by the interpleural space.

**What is pleurisy**

**Trigger box  Pleural effusions**

**Transudate:** (protein < 30 g/L; LDH < 200 iu/l):
Congestive heart failure (CHF), hypothyroidism, nephrotic syndrome

**Exudate:** (protein > 30 g/L; LDH > 200 iu/l):
Pneumonia, carcinoma, tuberculosis (TB), pulmonary infarct.
Can detect clinically if > 500mL; by CXR > 300mL.

**Findings:** Reduced chest movements, stony dull percussion, decreased breath sounds, reduced vocal resonance. Blunting of costophrenic angle on CXR.

**Treatment:** drain exudates, treat underlying cause of transudate.
Sclerosing agents to reduce recurrent malignant pleural effusions.

Three years ago Dr Smith, Zoe’s GP, had told her that she had asthma. Zoe was also told that this was related to her tendency to suffer from allergies. Also, colds, he stated, can lead to an asthma attack – and she got plenty of those especially in winter.

‘The problem is with your immune system’ Dr Smith said.

‘What’s wrong with my immune system?’ Zoe asked. ‘Isn’t it supposed to defend me, zap these nasty bugs?’

‘Your immune system is reacting inappropriately to certain antigens’ replied Dr Smith and then went on to explain how her immune system was causing her asthma and allergic reactions.

This leads us to introduce the basics of the immune system, which needs to be understood in order to appreciate the pathophysiology of Zoe’s asthma. This important system will be considered in detail in Chapter 10 but Figure 1.3 will help to explain what is meant by appropriate and inappropriate immune responses.

Note the central role of the Th cell and the Tc response that can eliminate viruses. This is an *appropriate* immune response. Type I hypersensitivity on the other hand, is an *inappropriate* immune response brought about by the generation of IgE reaginic antibodies against allergens, which leads to mast cell degranulation and the release of mediators that give rise to inflammation and the asthmatic symptoms. Goodpasture’s syndrome is a type II hypersensitivity reaction affecting the lung. A type III disease affecting the lung is hypersensitivity pneumonitis and an important type IV hypersensitivity disease affecting the lung is tuberculosis.
Trigger box  Hypersensitivity reactions

Type I
IgE.
Primary and secondary mediators from mast cells, basophils.
Asthma, allergic rhinitis, eczema, urticaria, food allergies, systemic anaphylaxis.

Type II
Cytotoxic.
IgG against cell surface antigens – complement-mediated damage.
Blood group incompatibilities in transfusion, autoimmune haemolytic anaemia (AHA),
erthroblastosis fetalis, Goodpasture’s syndrome.

Type III
Antigen/antibody (Ag/Ab) complexes – complement activation, neutrophil infiltration.
Arthus reaction, serum sickness, vasculitis, glomerulonephritis, systemic lupus erethematosus (SLE), rheumatoid arthritis (RA), hypersensitivity pneumonitis.

Type IV
Cell mediated.
Th1 cells release cytokines – macrophage, T-cell activation – tissue damage.
Contact dermatitis, TB.

Figure 1.3  Appropriate (open arrows) and inappropriate (closed arrows) immune responses
**Tuberculosis**

Primary TB – usually lung; usually asymptomatic.
Reactivation leads to post-primary TB (most cases of symptomatic TB), miliary TB.
**Findings:** Ghon complex (caseating lesions in lymph nodes + granuloma).
Kidney most common site of extrapulmonary TB.
**Features:** Malaise, anorexia, weight loss, fever, cough, haemoptysis, mucoid, purulent sputum.
**Investigations:** CXR, ZN stain, Lowenstein–Jensen culture, Mantoux test.
Mantoux positive 5–15 mm in 48–72 h indicates infection and/or bacille Calmette–Guérin (BCG) vaccination.
BCG reduces TB development by 50%.
**Treatment:** Rifampicin, isoniazid (INH), pyrazinamide, ethambutol.
Pyridoxine to reduce INH neurotoxicity.

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**Hypersensitivity pneumonitis**

A type III hypersensitivity reaction secondary to inhaled organic material (e.g. mouldy hay spores).
**Examples:** Farmers’ lung, bird fanciers’ lung.
**Findings:** Thick alveolar walls, granulomas with histiocytes and plasma cells. Fibrosis in chronic.
**Examination:** Bilateral crackles.
**Diagnosis:** CT, lung biopsy.
**Treatment:** Antigen avoidance, steroids, immunosuppressants.

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**What are pneumoconioses?**

Figure 1.4 shows the mechanism of type I hypersensitivity that is responsible for the pathology of Zoe’s acute allergic asthma attack. Note that antigen-binding to IgE stimulates mast cells to release pre-synthesized primary mediators. Synthesis and subsequent release of secondary mediators involve the activation of arachidonic acid and the synthesis and release of prostaglandins and thromboxanes through...
Cyclooxygenase pathway and leukotrienes C4 and D4 (termed slow reacting substance of anaphylaxis (SRS-A)) through the lipoxygenase pathway.

What is anaphylaxis? Can you describe the mechanisms underlying systemic anaphylaxis? How is this condition treated?

At the time of her diagnosis, Zoe had been given a skin prick test to confirm her allergic status. She was inoculated with a series of allergens including grass pollen and dust mite extracts. She got a classic wheal and flare reaction after 20 minutes but was surprised when the reaction reappeared around 5 hours later. Immediate reactions occur within minutes of allergen exposure and are mediated principally by the mast cell granule contents (primary mediators). Some 5–8 hours after the immediate reaction has subsided, a second reaction – the late-phase reaction – occurs due to the release of additional secondary mediators including cytokines. Tables 1.1 and 1.2 show the key

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Note that cross-linking of IgE by allergen leads to receptor cross-linkage. This leads to a transient elevation of cAMP, activation of protein tyrosine kinases, methylation of membrane phospholipids and an influx of calcium which causes fusion of granules with plasma membrane and release of primary mediators into extracellular environment. Secondary mediators are synthesized.