Carriage of Oxygen:

From Grey’s Anatomy (1918)
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Introduction

I am sure it is unnecessary to explain to you all the importance of the cardiorespiratory system. Respiratory diseases (eg asthma, lung cancer) are a major cause of disability and death in the uk, as are vascular disease (atherosclerosis, strokes).

The teaching methods and course evaluation will be essentially the same as for the movement and posture course, and a similar degree of self directed learning will be necessary. The Marieb text book is now the ‘official’ text book for the undergraduate medical course and it is highly recommended for this course.

Web support:

https://courses.stu.qmul.ac.uk/SMD/kb/GEP2/cardiorespindex.htm

If you have any problems or queries please contact the course organiser Dr. J. Millar (J.Millar@qmul.ac.uk) or Dr. Cathy Baker (Head of GEP course, c.s.baker@qmul.ac.uk)

Course Aims

At the end of this course you should be able to:

Describe the special features of blood that enable it to transport oxygen around the body, to remove carbon dioxide from the body, and how haemostasis is achieved after injury.

1. Measure blood pressure and understand the damage that hypertension can do to the vascular system
2. Interpret the basic features of the ECG
3. Describe the special features of the pulmonary and coronary circulations
4. Describe the significance of cardiac output and how it is measured
5. Explain how the lungs and the kidneys co-operate to maintain a normal body pH
6. Explain the essential mechanics of the lung, and assess lung function at a basic level.
7. Describe the basic mechanisms of the homeostatic regulation of body water
## Lecture List

<table>
<thead>
<tr>
<th>Lecture Title</th>
<th>Lecturer</th>
<th>Venue</th>
<th>Date</th>
<th>Time</th>
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<tbody>
<tr>
<td>1. Introduction to respiratory system</td>
<td>Dr. Patterson</td>
<td>Anatomy</td>
<td>16/10</td>
<td>09.00</td>
</tr>
<tr>
<td>2. Intro to Cardiovascular System</td>
<td>Dr. Millar</td>
<td>Anatomy</td>
<td>16/10</td>
<td>10.00</td>
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<tr>
<td>3. Structure &amp; function of blood</td>
<td>Dr. Syndercombe-Court</td>
<td>Anatomy</td>
<td>16/10</td>
<td>14.00</td>
</tr>
<tr>
<td>4. Blood Vessels</td>
<td>Professor Bird</td>
<td>3.06 OMCB</td>
<td>17/10</td>
<td>14.00</td>
</tr>
<tr>
<td>5. Blood Groups and transfusion</td>
<td>Dr. Ahmed</td>
<td>Anatomy</td>
<td>18/10</td>
<td>09.00</td>
</tr>
<tr>
<td>6. Haemostasis and thrombosis</td>
<td>Dr. Syndercombe-Court</td>
<td>Anatomy</td>
<td>18/10</td>
<td>10.30</td>
</tr>
<tr>
<td>7. Anatomy of the circulation</td>
<td>Dr. Millar</td>
<td>Anatomy</td>
<td>23/10</td>
<td>09.00</td>
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<td>8. Heart as a pump</td>
<td>Dr. Millar</td>
<td>Anatomy</td>
<td>23/10</td>
<td>10.00</td>
</tr>
<tr>
<td>9. Haemodynamics</td>
<td>Dr. Millar</td>
<td>Anatomy</td>
<td>23/10</td>
<td>14.00</td>
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<tr>
<td>10. Conducting system of heart &amp; ECG</td>
<td>Dr. Millar</td>
<td>Anatomy</td>
<td>23/10</td>
<td>15.00</td>
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<tr>
<td>11. Control of BP &amp; Cardiac output</td>
<td>Dr. Millar</td>
<td>Anatomy</td>
<td>25/10</td>
<td>09.00</td>
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<tr>
<td>12. Coronary Circulation</td>
<td>Prof. Bird</td>
<td>Anatomy</td>
<td>25/10</td>
<td>10.00</td>
</tr>
<tr>
<td>13. Kidney structure and function</td>
<td>Dr. Patterson</td>
<td>Pre-clinical</td>
<td>27/10</td>
<td>09.00</td>
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<tr>
<td>14. Body fluid compartments &amp; water balance</td>
<td>Dr. Patterson</td>
<td>Pre-clinical</td>
<td>27/10</td>
<td>10.00</td>
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<tr>
<td>15. Glomerular and tubular function</td>
<td>Dr. Patterson</td>
<td>Pre-clinical</td>
<td>27/10</td>
<td>11.00</td>
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<td>16. Acid base balance</td>
<td>Dr. Patterson</td>
<td>Pre-clinical</td>
<td>27/10</td>
<td>14.00</td>
</tr>
<tr>
<td>17. Breathing muscles and mechanisms</td>
<td>Dr. Patterson</td>
<td>Anatomy</td>
<td>30/10</td>
<td>09.00</td>
</tr>
<tr>
<td>18. Gas exchange and lung function testing</td>
<td>Dr. Patterson</td>
<td>Anatomy</td>
<td>30/10</td>
<td>10.00</td>
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<tr>
<td>19. Carriage of gases in the blood</td>
<td>Dr. Patterson</td>
<td>Anatomy</td>
<td>30/10</td>
<td>14.00</td>
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<tr>
<td>20. Blood gases and control of ventilation</td>
<td>Dr. Patterson</td>
<td>Pre-clinical</td>
<td>03/11</td>
<td>09.00</td>
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<td>21. The lung, mechanics, ventilation and perfusion</td>
<td>Dr. Patterson</td>
<td>Pre-clinical</td>
<td>03/11</td>
<td>10.00</td>
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Learning Objectives for Lectures

Introduction to the respiratory system  
Dr John Patterson

1. Outline the causes and social impact (in terms of mortality and morbidity) of airways disease and respiratory infection
2. Comment on the major social, environmental and occupational factors associated with pulmonary disease
3. List the functions of the respiratory system
4. Name the main structural features of the lungs
5. Distinguish between respiratory and non-respiratory components of the lungs and show how histological features are related to function
6. Describe the branching pattern of the respiratory tree, commenting on the significance of the cross-sectional area at different levels.

Structure and functions of blood.  
Dr Denise Syndercombe-Court

1. List the cellular components of blood cells, and outline their roles in the carriage of oxygen and carbon dioxide, immunity/allergy and haemostasis.
2. List the major chemical components of plasma, and comment on the role of these in clotting, immunity, colloid pressure and buffering.
3. Outline the production of blood cells from pluripotent haemopoietic stem cells, and the regulation of erythropoiesis and myelopoiesis.
4. Outline the response to anaemia.
5. Define the parameters of a full blood count and give an outline classification of anaemia.

Large Blood Vessels  
Professor Margaret Bird

1. The chambers of the heart
2. The brachiocephalic veins and the superior vena cava.
3. The ascending aorta, arch of the aorta and the descending aorta and their principal branches.
4. The thoracic aorta
5. The azygos and hemiazygos system of veins.

Blood groups & transfusion  
Dr Ahmed

After this lecture students should have an understanding of:
1. The history of transfusion medicine
2. The nature of blood group molecules and their frequencies in different ethnic groups
3. Antibodies and antigens, and their relevance to blood transfusion
4. Blood collection and processing
5. Compatibility testing and the antiglobulin test: ensuring patient safety
6. Complications of blood transfusion
7. The investigation of a patient with a suspected transfusion reaction

Haemostasis and thrombosis  
Dr Denise Syndercombe-Court

1. Describe the nature and function of platelets, explain what is meant by thrombocytopenia.
2. Describe the normal coagulation pathway and how it is activated by: tissue damage, contact of blood with tissue collagen or glass.
3. Describe the roles of vitamin K, platelets, calcium, serine proteases and modifier proteins in the clotting process.
4. Explain the mechanism of action of heparin, warfarin, aspirin and streptokinase.
5. Indicate under what circumstances it is appropriate to administer the above drugs (see 4).
Anatomy of the circulation Dr Julian Millar

1. Describe the anatomy and physiology of arteries, veins and capillaries
2. Explain the mechanism of capillary filtration and reabsorption
3. Explain the differences between the systemic and pulmonary circulations

Haemodynamics Dr Julian Millar

1. Define the terms systolic and diastolic blood pressure, pulse pressure and mean blood pressure, and state values for these in the normal healthy young adult
2. Explain the relationships between cardiac output, peripheral resistance and blood pressure.
3. Comment on the importance of Poiseuille’s law relating vessel radius and resistance to flow, and the relevance of this to changes in pressure in the circulation
4. Explain the concept of arterial compliance, and describe the relationship between pulse pressure, stroke volume and compliance.

The heart as a pump Dr Julian Millar

1. Explain how the heart is adapted to supply the pulmonary and systemic circulations.
2. Draw a diagram of the pressure profiles in the left atrium, left ventricle and the aorta for a single cardiac cycle. Label the vertical axis in units of pressure. Indicate the points at which the cardiac valves open and close, and the periods of iso-volumetric contraction and relaxation.
3. Explain the origin and significance of heart sounds
4. Describe Starling’s law of the heart and explain how cardiac output is balanced on the two sides.
5. Explain the concepts of preload and afterload.
6. Note the differences between pulmonary and systemic capillaries.
7. Outline the main processes ensuring adequate venous return to the heart

The conducting system of the heart, and the ECG Dr Julian Millar

1. Identify the position in the heart of the sino-atrial and atrioventricular nodes. Describe the course of the atrioventricular bundle and its branches.
3. Briefly explain the term ‘functional syncytium’ and the importance of coordinated contraction of cardiac muscle fibres.
4. Define the term ‘pacemaker potential’ and draw a labelled diagram of the pacemaker potential of a sino-atrial node cell. Briefly explain the reasons for the main potential changes. State the effects on the pacemaker of sympathetic and parasympathetic input.
5. Draw a labelled diagram of a generalised cardiac action potential and briefly describe the ionic currents underlying each phase. Explain the importance of the long refractory period.

Control of blood pressure and cardiac output Dr Julian Millar

1. Describe the physiological sensors and effectors for the control of blood pressure.
2. Explain how blood pressure and blood volume may be independently controlled.
3. Describe the position and innervation of the aortic and carotid sinus baroreceptors, their central connections and the role of the brainstem in the control of blood pressure.
4. Describe the role of the vagus nerve and the sympathetic nervous system in the control of blood pressure.
5. Describe briefly the role of the kidney in the control of blood pressure.

Coronary circulation Professor Margaret Bird
1. Describe the origin and course of the coronary arteries and explain the nature of their anastomoses.
2. Describe the venous drainage of the heart.
3. Describe the specific tasks required of the coronary circulation and how the coronary circulation is structurally and functionally adapted.
4. Describe the sequence of events leading to a myocardial infarction.

### Structure and functions of the kidney

By Dr. Greg Michael

1. Outline the general organisation of the urinary system including the kidney, ureter, bladder and urethra.
2. Identify the parts of the nephron and describe the role of each component in the physiologic processes involved in urine production.
3. Describe the vasculature of the kidney, relating its unique features to the physiology of urine production and nourishment of the nephron.
4. Identify the components of the juxtaglomerular apparatus and describe its role in regulation of blood and urine volumes and renal homeostasis.
5. Outline the structural components of the urinary passageways and bladder and describe how micturition is controlled.

### Glomerular and tubular function

By Dr. John Patterson

1. Describe, and quantify, the forces acting in the glomerular capillary and in the fluid of Bowman's capsule which are responsible for the production of glomerular filtrate.
2. Show, graphically, the effects of molecular size and charge on the composition of glomerular filtrate.
3. Explain the 'clearance concept' and how this is used to measure glomerular filtration rate (GFR). State the properties of suitable marker substances and show how clearance, and hence GFR, are calculated. State normal values for the GFR.
4. Briefly describe the autoregulation of GFR under normal circumstances and the significance of a reduced GFR.
5. Define the terms: filtration; reabsorption; secretion; excretion, as applied to the kidney.
6. Compare the reabsorption of sodium, glucose, amino acids and hydrogen carbonate in the proximal tubule of the nephron.
7. Comment briefly on differences in sodium reabsorption in the proximal tubule, the thick-walled, ascending limb of the loop of Henle and the distal tubule, noting the significance of sodium reabsorption in these regions.
8. By reference to the renal reabsorption of glucose, define the terms: 'renal threshold' and 'transport maximum'. What may be the effects of glucose presence in the final urine?

### Body fluid compartments and water balance

By Dr. John Patterson

1. Distinguish between the terms 'osmolarity' and 'osmolality' and between the terms 'isosmotic' and 'isotonic'. State a normal value for plasma osmolality.
2. Name the main fluid compartments of the body, commenting on their volumes and predominant cations.
3. Explain how total body water and total body sodium are regulated by mechanisms that are sensitive to plasma volume and plasma osmolality.
4. Quantify the factors that contribute to the water balance of the body.
5. By means of labelled diagrams show the changes in volume and osmolality of tubular fluid along the length of the nephron, in the presence or absence of anti-diuretic hormone (ADH).
6. Explain how the thick-walled, ascending limb of the loop of Henle plays a key role (in conjunction with ADH) in the production of either a dilute or concentrated urine to meet the requirements of water balance.
7. State the source, nature and mechanisms of release of ADH. Describe the stimuli for the release of ADH and explain how ADH controls urine volume and osmolality.
8. Distinguish between the terms 'water diuresis', 'osmotic diuresis', 'diabetes insipidus' and 'diabetes mellitus'.

### Acid-base balance

By Dr. John Patterson
1. Define 'pH' and state the normal range for arterial pH and the range compatible with life. Comment on the differences between normal arterial and mixed venous pH values.
2. List the sources of bodily acid and comment on the ways in which acid is removed from the body, noting the relative importance of lungs and kidneys.
3. List the principal buffer systems in plasma, extra- and intra-cellular fluid and bone.
4. State the Henderson-Hasselbalch equations for the hydrogen carbonate / carbonic acid buffer system and give normal values for each component. Explain why the hydrogen carbonate / carbonic acid buffer system is important.
5. In terms of the ratio of base to acid and of the absolute values of base and acid, explain the processes of buffering, compensation and correction in acid-base disturbance.
6. Define the terms 'acidosis', 'alkalosis', 'acidaemia' and 'alkalaemia'. Outline how a sample of arterial blood may be used to determine the acid-base status of a patient.
7. Outline the role of hydrogen carbonate, phosphate and ammonium ions in the renal excretion of acid, noting the relationship between tubular pCO2, hydrogen carbonate reabsorption and proton excretion.
8. Name the FOUR simple classes of acid-base disturbance, stating the primary disturbance and the form of compensation for each class. Comment on the time scale for renal and compared with respiratory compensation and give ONE clinical cause for each class of disturbance.

Breathing: muscles and mechanisms

1. Outline the relationships between the lungs, pleura, chest wall and diaphragm.
2. Explain why a negative pressure exists in the (potential) pleural space.
3. Define the terms, pneumothorax, spontaneous pneumothorax and tension pneumothorax and comment briefly on the management of these conditions.
4. Explain why alterations to lung recoil (in for example emphysema and pneumonia) may produce alterations to the shape of the chest.
5. Show, by means of simple diagrams, how the ribs move during breathing.
6. List the muscles active in a) quiet breathing and b) vigorous breathing.
7. Define the terms 'compliance' and 'airways resistance' as applied to the lungs and explain why the work of breathing may be affected in pulmonary disease.

Gas Exchange and Lung Function Testing

1. Draw a simple diagram of an alveolus (and its blood supply), annotated to show how the microscopic structure is suited to efficient gas exchange.
2. What is pulmonary surfactant, where is it produced and why is it important?
3. Tabulate the normal partial pressures of oxygen and carbon dioxide in room air, alveolar air, pulmonary arterial (or 'mixed venous') blood, pulmonary venous (or systemic arterial) blood and expired air. Comment on why these differ.
4. Give an equation for Fick's law of diffusion as applied to gas exchange in the lung the lung, identify the components of the equation, and name one pulmonary disorder affecting each component.
5. Show, by means of simple graphs, how gas exchange comes to equilibrium along a pulmonary capillary. Relate this information to physical exercise and progressive loss of lung function.
6. Define, and give typical values for, commonly used terms in lung function testing and explain how clinically important measures of lung function are obtained.

Carriage of Gases in the blood

1. List, in order of relative contribution, the ways in which oxygen is transported by the blood.
2. Draw a fully labelled diagram of an oxygen-haemoglobin dissociation curve. Comment on the suitability of the curve for oxygen uptake and delivery and relate this to the cooperativity of the sub-units of haemoglobin.
3. Comment on the properties and roles of fetal haemoglobin and myoglobin.
4. List, in order of relative contribution, the ways in which carbon dioxide is transported by the blood.
5. By means of an annotated diagram, show how red blood cells are involved in the transport of carbon dioxide.
6. Show, by means of graphs, the contributions of dissolved carbon dioxide, bicarbonate ion and carbamino-Hb to carbon dioxide transport in arterial and venous blood.
7. Explain how the allosteric properties of haemoglobin may affect oxygen binding (the Bohr effect) and carbon dioxide transport (the Haldane effect).

Blood gases & control of ventilation

1. Review the definition of gas partial pressure in a mixture of gases and gas partial pressure in a solution.
2. State normal values of the partial pressures of oxygen and carbon dioxide in arterial blood (PaO₂, PaCO₂). How are these measured directly and estimated indirectly?
3. State the location of the central chemoreceptors and describe how these receptors estimate PaCO₂.
4. Describe the location and properties of the peripheral chemoreceptors and show, by means of simple graphs, how alterations in PaO₂ and PaCO₂ alter ventilation.
5. Briefly describe the brainstem structures involved in the production of breathing and list the inputs to the brainstem which influence breathing.
6. State the normal pH of arterial plasma, define the terms acidosis, alkalosis, acidaemia and alkalaemia, and explain the effects on arterial pH of hyper- and hypo-ventilation.
7. Distinguish between the terms hyperventilation and hyperpnoea.

The lung, mechanics, ventilation and perfusion

1. List the components of the total work of breathing.
2. Define the term compliance, as applied to the lungs (or chest wall), comment on the significance of surface tension forces and the role of pulmonary surfactant.
3. Explain the relationship between airflow, airway calibre and airway resistance at different levels in the respiratory tree and name two conditions which may significantly effect the work of breathing.
4. Show, by means of graphs how the main components of the work of breathing contribute to the total work done in normal, tidal ventilation.
5. Outline the responses of bronchiolar and arteriolar smooth muscle which maintain a balance between ventilation of the alveoli and blood flow (perfusion) to the alveoli in normal conditions.
6. Define the term ventilation to perfusion ratio (Va/Q) and give values for the whole lung, the base and the apex of the lung in a normal subject in the upright position, explaining why these differ. Illustrate, by means of diagrams, how the perfusion of the lung may be considered as a ‘three zone model’.
7. Comment briefly on the effects, on blood passing through the lungs, of a high or a low Va/Q.
Learning Objectives for the microanatomy practical sessions

Microanatomy of the blood:
1. To revise the understanding of the anatomical characteristics and functions of different types of leukocytes and identify them in blood smears.
2. To be able to differentiate between erythrocytes found in normal blood smears and those indicative of anaemia.
3. To understand the basic structure and function of bone marrow

Microanatomy of cardiovascular system:
1. To identify arteries and veins and relate the structure of their walls to their physiological function.
2. To revise understanding of the cardiac myocyte and the blood supply to the myocardium.
3. To understand the effects of ischaemia on the myocardium.

Microanatomy of the respiratory system:
1. To identify the components of the respiratory mucous membrane.
2. To compare and contrast the structure of conducting components of the respiratory system and relate their structural differences to differing functions.
3. To identify the respiratory components of the lung and understand their functions.

Microanatomy of the kidney:
1. Describe the basic structural organisation of the kidney, including its vasculature.
2. Describe the structure of the nephron.
3. Relate the structure of the glomerulus to its role in the filtration of blood.
4. List the causes of impaired glomerular filtration and the clinical consequences of this.
5. Describe the structure and microanatomy of the urinary tract, including the bladder.
6. Discuss the pathology of mass lesions of the urinary tract.

Note: Students will be required to go over the Web based learning resources prior to coming to the practicals. Prior reading in textbooks and revision of notes is advised. Please be prepared to contribute to class discussion. Students are advised to take notes during the practicals as answers will not be posted until at least after the in course assessment. Material covered may be included as part of both written and practical exams; the latter focussing primarily on recognition of important features of pathology specimens and photomicrographs.
PROBLEM BASED LEARNING SCENARIOS

PBL1: Excessive bleeding

Scenario:
An 11 year old boy is admitted to hospital for removal of his tonsils. After the operation, he is found to be bleeding badly and to require a blood transfusion. Two months later, he is seen again in outpatients. His mother says that her father bled badly after dental extraction. Blood test results are as follows (normal values are given in brackets):

<table>
<thead>
<tr>
<th>Test</th>
<th>Value</th>
<th>Normal Range</th>
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</thead>
<tbody>
<tr>
<td>Hb</td>
<td>13.9g/dl</td>
<td>(male 13.5-17.5 g/dl)</td>
</tr>
<tr>
<td>MCV</td>
<td>86 fl</td>
<td>(80-100 fl)</td>
</tr>
<tr>
<td>WBC</td>
<td>7 x 10^9/l</td>
<td>(4-11 x 10^9/l)</td>
</tr>
<tr>
<td>Platelets</td>
<td>225 x 10^9/l</td>
<td>(150-400 x 10^9/l)</td>
</tr>
<tr>
<td>Bleeding time</td>
<td>3 min.</td>
<td>(2-7 min.)</td>
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<tr>
<td>Prothrombin ratio</td>
<td>1.0</td>
<td>(1-1.3)</td>
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<tr>
<td>Kaolin cephalin time</td>
<td>65s</td>
<td>(35-40s)</td>
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<tr>
<td>Thrombin time</td>
<td>10s</td>
<td>(10-12s)</td>
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<tr>
<td>Factor VIII</td>
<td>15 i.u./dl</td>
<td>(100 i.u./dl)</td>
</tr>
<tr>
<td>Factor IX</td>
<td>94 i.u./dl</td>
<td>(100 i.u./dl)</td>
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PBL 2 A pain in the chest

Scenario:
Mr Charles Creed is a chef aged 52 who is overweight and has smoked cigarettes for the past 35 years. He has noticed over the past month chest pain on exertion that has radiated into the neck. This has affected his daily activities. At first he thought this pain was due to lifting heavy trays at work. His wife, who knows that his father died, aged 50, of a myocardial infarction and one of his brothers recently died suddenly, urges him to visit the GP.
PBL3 A bad attack of asthma

Scenario:

Richard is a 16 year old, still at school, of 52kg body weight and height 167cm. He has a long history of asthma. He monitors his condition with a peak flow meter and has used a salbutamol metered dose inhaler for four years. He is brought to an Accident and Emergency department in the early hours of the morning having woken in the night with a severe asthmatic attack. These nocturnal attacks are common, but this one is particularly severe. Richard’s parents are anxious about their son’s condition. Richard is also suffering from a bad chest cold.

On examination Richard is dyspnoeic, tachypnoeic and sweating. He is not cyanosed, but he can only speak 2 or 3 words at a time. His nostrils are flared and he is using his accessory muscles of ventilation. The chest is hyperinflated and his rapid, shallow breathing is at the top end of the total lung capacity. There are widespread, polyphonic wheezes in the chest. There is tachycardia (120 b.p.m.) and his blood pressure is 140/90 (normal 120/80) mmHg. The cardiovascular system is otherwise normal as are other body systems.

A test on a sample of venous blood reveals a high but normal Haemoglobin, a high normal white cell count, with increased numbers of eosinophils. Chest X-Ray shows no visible abnormalities, but confirms the hyperinflation of the chest. Peak Expiratory Flow (PEF) is less than 60 l/min, essentially unmeasurable. An ear lobe pulse oximeter gives a value for the haemoglobin saturation of 94%. A sample of arterial blood is taken for immediate analysis and the following values are returned (normal values in brackets):

\[
\begin{align*}
\text{pH} & = 7.1 (7.36-7.44) \\
\text{PaO}_2 & = 10 \text{ kPa (13.9)} \\
\text{PaCO}_2 & = 8 \text{ kPa (5.3)}
\end{align*}
\]

Richard is clearly in respiratory distress, but not as yet in respiratory failure. He is admitted to hospital, and given oxygen therapy. He is treated aggressively with intravenous (iv) hydrocortisone, iv theophylline, nebulised salbutamol and nebulised ipratropium. Within 2-3 hours Richard is talking well, respiratory rate is reduced and he is using his accessory muscles of ventilation less. His PEF can now be measured at 120 l/min. He still has a wheeze, but is better able to ventilate. Arterial blood gases and pH are now normal. He will remain in hospital for the next night and, if all goes well, he will return home the following day.