



**UNIVERSITY OF CAMBRIDGE  
SCHOOL OF CLINICAL MEDICINE  
ADDENBROOKE'S HOSPITAL**

**CLINICAL PATHOLOGY  
COURSE HANDBOOK  
FOR STUDENTS**

**2016**

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## THE COURSE

Welcome to the Clinical Pathology Course. This course will allow you to build on your knowledge of the scientific principles of disease (covered in the Part Ib Tripos Cambridge Pathology (Biology of Disease) Course or the equivalent from other Medical Schools), and learn about specific diseases as they affect the major body systems.

Pathology in this course is taught in a variety of ways (covered in detail below). These include:

- \* formal **lectures** including **podcasts** or other electronic reproductions of lectures
- \* **tutorial** classes (small group teaching)
- \* **computer based learning** (CBL) programs and other computer-based systems – see the Virtual Learning Environment [VLE] (MedPortal, previously called ERWEB on the Clinical School's computer system)
- \* **autopsy** room teaching (by individual arrangement made in advance)
- \* interactive large group teaching (often used for revision sessions)
- \* personal study.

The three major components, lectures/podcasts, tutorials and CBL/personal study, form part of an integrated teaching 'package' and each plays an equally important role in the teaching programme. Different aspects of the subject are covered during these various activities. Therefore, it should be appreciated that lectures/podcasts do not completely cover the core material of the course, such that some topics are covered only or mostly in tutorials or CBL, but not in lectures! It is important that you attend each session if maximum benefit is to be derived from the course. It should also be appreciated that the material covered in these sessions is not comprehensive and must be supplemented with personal reading of textbooks and other recommended sources.

### AIMS

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**The Course aims to (1) present the pathological basis of diseases that are commonly seen in clinical practice, and to demonstrate how clinical manifestations may be explained by the underlying pathological processes; and (2) cover investigation of disease processes, including interpretation of test results, for diagnosis and patient management.**

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On successful completion of the Course the student will be able to:

- \* Describe the **aetiology and pathogenesis** of clinically important disease processes.
- \* Describe and interpret the basic **macroscopic appearances** characterising diseased organs & tissues and understand the **pathological processes** that lead to these changes and how they relate to clinical signs & symptoms.
- \* Explain the **mechanisms** by which clinical manifestations of diseases arise.
- \* State the principal **complications and sequelae** of disease processes.
- \* Appreciate how the application of **pathological principles** to the study of diseased tissue and fluids in the pathology laboratory by appropriate **investigation and interpretation** of data relates to diagnosis and patient management.
- \* **Select appropriate pathological investigations** for diagnosis, treatment, assessment of prognosis and monitoring of common diseases (using tissue, blood and other fluids & samples).
- \* **Understand and be able to interpret the results** of pathological investigations in different patients, in health and disease, both in diagnosis and in following treatment.
- \* Communicate an understanding of the role of **autopsy** in clinical audit, education and research.
- \* Understand the **limitations** of diagnostic investigations.

- \* Appreciate the **transmission of microorganisms** between the environment and living hosts, and how this transmission may be reduced or prevented and how host defence mechanisms may be altered.
- \* Understand the principles of how **common bacteria, viruses, fungi, protozoa and parasites** cause disease, and how these infections most commonly present.
- \* Know the **common infectious causes** of dysfunction of each of the body's organ systems.
- \* Understand the principles of how best to use **microbiological tests** to make a diagnosis of infectious disease in patients in and out of hospital.
- \* Be able to use common **antimicrobial agents** and other antimicrobial strategies effectively and efficiently.
- \* Understand the principles of how best to use **chemical pathology tests** to make a diagnosis of various diseases in patients in and out of hospital.
- \* Understand the principles of how best to use **immunological tests** to make a diagnosis of immunological diseases in patients in and out of hospital.
- \* Understand the **pathophysiology** and appreciate the **clinical presentation of haematological** disorders.
- \* Appreciate the **haematological aspects of systemic disease**.
- \* Develop a working knowledge of the use of **haematological investigations** and their clinical **interpretation**.
- \* Be able to appropriately **manage patients** with haematological disorders, in particular **anaemia** and the use of **anticoagulant therapy**.
- \* Understand the **transfusion process** and ensure the safe and effective use of **blood and blood products**.
- \* Integrate **all aspects of laboratory investigation** for individual patients.
- \* Lay the basis for **life-long learning** of integrated clinico-pathological features of disease.
- \* Develop an **evidence-based approach** to the study of clinical pathology.

More **general aims** of the course are:

- \* to give you guidance in personal study
- \* to give you, through your tutors, advice about your personal progress, and offer you assistance and encouragement if your progress is not satisfactory
- \* to give you practice in communicating verbally
- \* to provide you with channels for comment and criticism of all aspects of the course

The Course does **NOT** aim:

- \* to give complete coverage of all of systematic pathology (detailed learning objectives and/or tabulated core curricula are set out below, and these spell out what you need to know and the appropriate level of detail of that knowledge)
- \* to get you to memorise factual information which you do not understand, or which you could easily look up in a book if you ever needed to know it
- \* to make you into a pathologist
- \* to make you into a nervous wreck

## HELP

Your tutors (and the course organisers) will offer a sympathetic hearing to any student who is having academic or other difficulties.



## LECTURES

AIM: Lectures cover many, but not all, of the **major pathological topics** in the **core curriculum**.

Lectures will be delivered by members of the Departments of Histopathology, Medical Microbiology, Chemical Pathology, Haematology, Clinical Immunology and Medical Genetics, who usually have a special interest and expertise in the subjects covered. Some shared lectures will be **given jointly** by 2 or more members of these departments. Lectures are not intended to give comprehensive coverage of each system, but will be used to direct students towards the core knowledge. Some lectures will be available in the form of podcasts or other electronic versions. You will need to supplement lectures by reading the relevant sections of recommended textbooks of Pathology. Handouts are generally given when standard textbooks are considered inadequate and should not be regarded as substitutes for textbooks. Many of the lecture handouts and slides are available on the VLE.

## PODCASTS

AIM: Pathology podcasts, mostly in the form of slides with voiceover explanation, are being used to cover some of the **major pathological topics** in the **core curriculum**. They provide online resources for you to access, during various stages of your course, that act as a support providing aspects of the pathological basis of disease relevant to the placements and themes of the clinical medical course.

The Pathology podcasts have been developed by various Pathology lecturers covering a wide range of topics, including Histopathology, Microbiology, Biochemistry, Immunology and Haematology. Podcasts are available for components of both the Stage 1 and Stage 2 course. They are particularly important for those components of Stage 2 that were previously covered in lectures but are now covered by podcasts, allowing students to access relevant pathological information at a time that is appropriate for their stage of progress through Stage 2 (variable for different groups of students). The podcasts will act as online resources for students on Stage 2 block placements. The podcasts are to be viewed during the placements and will provide core pathological information regarding some of the conditions you will encounter during these attachments. After viewing the podcasts there will be an opportunity to ask questions. Tutorials will be given during the Stage 2 Review & Integration weeks to support the pathological topics in the podcasts and these tutorials will include a "Question & Answer" session at the end to cover relevant questions and discussions arising from podcast viewing. Pathology podcasts will be available throughout Stage 1 and Stage 2 and they can be used as resources for learning or revision by any student at any point.

## TUTORIALS

AIM: Structured tutorials cover selected major topics from the core curriculum in a way designed to stimulate a **problem-solving** approach sometimes using **data interpretation** questions and this approach is intended to foster integration of pathological and clinical features of diseases.

You will be allocated to tutorial groups for various parts of the course. Tutorials will take place at various times set out in the timetable and are held in either Seminar Rooms or Lecture Theatres in the Clinical School Building (or occasionally in other locations according to availability). These structured tutorials are designed to provide you with an opportunity for integration of pathological and clinical knowledge.

Tutorials include:

- **clinico-pathological cases**
- **case problem-solving exercises (CPSE)**
- **data interpretation questions (DIQ)**
- **structured discussions** of key pathological topics with your tutor and fellow students

Both **clinico-pathological cases** and **case problem-solving exercises (CPSEs)** will be used to illustrate important pathological processes and their clinical manifestations, including investigation and interpretation of data. You must be prepared to actively participate in discussing and providing answers for these cases and exercises in the tutorials. Each tutorial group is presented with the same cases and problems which form the basis of the group discussions during the tutorial. A list of titles for these sessions is given below. Whenever possible they will take place after the

relevant lectures. You will gain maximum benefit from these sessions by conscientious preparation beforehand, by reading the relevant lecture notes, handouts, and textbook chapters. **Active participation** is essential for the success of these sessions!

## COMPUTER BASED LEARNING (CBL)

AIM: Computer-based learning provides an opportunity for **interactive learning, problem solving and self-assessment**.

A number of sessions (timetabled below) are devoted to the use of **CBL** resources, which include Computer Aided Learning (CAL) programs and Internet sites (URLs provided). These teaching packages are available for use in the Clinical School Computer Teaching Laboratory at other times during the working day, through the **Virtual Learning Environment (VLE) / Medportal** - a Web-based computer environment that is accessed using a browser, such as Internet Explorer. This environment is structured to guide students to appropriate resources available on computer. CBL resources have a number of purposes:

- Some CBLs provide interactive tutorials on important topics not covered in lectures (e.g. on certain aspects of cervical neoplasia)
- Some CAL programs provide a straightforward introduction to a subject area (e.g. 'Edinburgh PathCALs')
- Other CBL elements are designed to supplement the other parts of the Course, and give you an opportunity for interactive problem-solving
- Some CBLs include self-assessment questions (e.g. practice MCQs, some Internet sites & CAL programs)

### SELF ASSESSMENT QUESTIONS:

Lecturers, tutors and CBL provide MCQs for examinations, covering various aspects of the course. A sample of these questions is available on the VLE/MedPortal for self assessment by students and is similar in style and content to those used in the prize examination and the Final MB examination.

## AUTOPSY ROOM TEACHING SESSIONS

AIMS: Autopsy room sessions provide you with an excellent opportunity to **correlate gross pathological** structural changes at the organ and tissue level, with clinical observations and the natural history of disease.

These take place in the Mortuary / Post Mortem Room / Autopsy Suite on Level 1. You can arrange to attend these teaching sessions on any morning on any day of the week (Monday to Friday) when you have available time that morning and there is a suitable autopsy case being dissected that morning (phone the mortuary / autopsy suite on 3106 or 4549 to arrange this). Please note that only 1 or 2 students at a time can be accommodated each morning. During these sessions, the findings of **diseased organs and tissues** from one or more autopsy cases will be demonstrated and the relevant clinico-pathological correlations considered and discussed. You are strongly encouraged to attend these sessions when possible.

## INTERACTIVE LARGE GROUP TEACHING

**Interactive large-group teaching** sessions are used in Microbiology, Chemical Pathology and other disciplines, in which the session leader selects individual students to **interpret data** to make diagnostic and therapeutic decisions, usually in a case-based teaching format. These may include use of 'branching' decision-based **approaches**.

## CHANGES TO TIMETABLES OR TEACHING ARRANGEMENTS

Students should check for any last minute changes on VLE/MedPortal which lists the timetables or their emails.



## RECOMMENDED READING

A full list of books to accompany the different divisions included in Pathology can be found in the Clinical School Library or in the Course Reading List under General Curriculum Information on the VLE/MedPortal. These lists are updated twice a year to make sure that current editions are included in the list.

## STAFF - STUDENT CONSULTATIONS

Channels of communication will be established between students' representatives and the Histopathology Department. Students will be asked to complete Feedback Questionnaires electronically, in which all major components of the Course will be assessed. This feedback is essential to improve all aspects of the course.

## EXAMINATIONS

### [I] PRIZE EXAMINATION:

A voluntary competitive examination for the Henry Roy Dean Prize will be held prior to the Final MB exam consisting of a multiple choice questionnaire (MCQ), similar in question format to the MCQ paper of the Part I Pathology Final MB Examination (see below) lasting one hour (please see VLE/MedPortal for details).

### [II] FINAL MB EXAMINATIONS:

#### PART I PATHOLOGY FINAL MB

The Pathology Final MB examination will be held in May/June (resit in the following October) at the end of Stage 2. This will give adequate time not only to allow appropriate further study, but also to appreciate the fundamental role of Pathology in the practice of clinical medicine and integrate pathological knowledge with the clinical specialities.

Clinical Pathology includes several disciplines (Biochemistry, Haematology, Microbiology, Immunology, Genetics and Histopathology) which may at first seem unrelated. These disciplines are covered in different lectures and in separate textbooks, and whilst this compartmentalisation provides a logical way to study, sound medical practice requires their integration within appropriate clinical contexts and the Pathology Final MB examination will specifically test for integration.

This examination has two main components:

(a) Multiple choice questions; (b) Practical/Data interpretation questions.

There is also a viva voce exam for selected candidates (for the possibility of achieving a distinction award).

This examination will test core areas covered in the course including biochemical, haematological, immunological, microbiological, genetic and histopathological topics. The relative ratios of questions covering these areas will broadly reflect the time spent studying them in lectures and tutorials during the course.

Candidates must pass BOTH the MCQ component and the Practical component separately. If a candidate fails one component and thus fails the examination overall, then that candidate will have to resit the whole examination (and resit both components).

#### **(a) MULTIPLE CHOICE QUESTIONNAIRE**

AIM: To test understanding and knowledge of a very broad range of topics.

There are 150 best-from-five multiple choice questions (1:5 MCQs – 150 questions). This paper contributes 50% of the total marks and lasts for 3 hours (and is positively marked – no negative marking).

#### **(b) PRACTICAL EXAM/ DATA INTERPRETATION QUESTIONS**

AIM: To test integration of understanding and knowledge of the basic clinical symptoms and signs, with pathological processes and organ changes, and with microbiological, haematological, immunological and biochemical data, by examining data interpretation and problem-solving skills in integrated clinico-pathological contexts.

The types of problem solving and data interpretation questions which will be used, are similar to those used during the course tutorials and in revision tutorials. These relate to integrated clinico-pathological cases, which include case histories, data from laboratory investigations (biochemical, haematological, microbiological, immunological or histopathological) and macroscopical images of diseased organs or tissues. These are drawn from material used in the lectures and tutorials. The Final Practical Examination includes **10 Data Interpretation Questions**. This component contributes 50% of the total marks and lasts for 3 hours.

Although called the "Practical" examination, this is a written exam in which you will not be asked to perform any laboratory procedures, or even to look down a microscope. This exam tests ability to apply your knowledge of pathology in different clinical situations. Junior doctors are no longer called upon to examine urine or look at CSF under the microscope at the bedside or side room, but they must be able to interpret quickly and act upon the results of laboratory tests.

Each of the ten data interpretation questions is in a folder containing a brief, relevant case history, together with the results of a few appropriate laboratory tests (e.g. U & E's, full blood count, LFT's, blood gases, microbiological or serological data etc) and usually one or two good quality colour photographs of a named macroscopic surgical or post-mortem specimen. For each case there will be four or five questions which can be answered briefly, but which require **interpretation of the data. All normal / reference range values are given.** It is unnecessary to memorise these, but essential to be well acquainted with the common tests in order to appreciate the degree of abnormality when a result is abnormally high or low. No credit is given for writing that the sodium is low, potassium high, etc. – the examiners can also read! Candidates are asked to suggest reasons for the abnormalities in the light of the clinical history and photographs.

The best way to prepare is to take an interest in the patients clerked on various firms and to read and interpret their laboratory reports. Students who have done this regularly romp through the 'practical' exam and actually enjoy it. Students who have failed to grasp that pathology is not only lists of causes in textbooks, will find it much harder. The post-mortem demonstrations provide opportunities to see macroscopic specimens and all photographs are taken from autopsies or surgical specimens resected at Addenbrooke's Hospital or other hospitals in the region.

### **(c) VIVA VOCE EXAM:**

**AIM:** This aims to make a decision regarding the award of Distinctions to appropriate students who have performed particularly well in the examination.

Students who have achieved a high standard in the MCQ and practical papers will be invited to attend for oral examination, in which they may have the opportunity to gain a Distinction Award. Students will be requested to attend for oral examination at the discretion of the examiners. All students attending for oral examination will usually have **two 10-15 minute viva voce examination sessions** covering all pathology disciplines.

In each viva voce examination session, the candidate will usually meet two or three examiners, one of whom will usually be an external examiner and they will usually be questioned by at least two examiners during each session. The viva is therefore of significance to the outstanding candidate who may be deemed worthy of distinction.

## **HOW TO APPROACH THIS COURSE**

In the undergraduate (Part Ib Tripos or Biology of Disease or equivalent) Pathology course, you learned the basic scientific principles of disease processes; in Clinical Pathology you will study specific diseases as they affect the major systems of the body. Systemic Clinical Pathology is a vast subject, and in this course we aim to give emphasis to disorders that are common and clinically important. We certainly do not intend to give comprehensive coverage of the pathology of each system.

A good tip to start with is to revise the earlier work in General Principles of Pathology as soon as possible and at all times try to apply it to the various systems as you work through them, as described above. Thus, when learning the causes of gastritis, you might start with the causes of inflammation and consider which of these are important in the case of the stomach.

The list of Systems Objectives and/or tabulated core curricula set out below should help you in your study of each system. This information spells out for each system and discipline what you should have achieved on successful completion of the course. You will find that many of the Systems Objectives are specifically covered in various parts

of the teaching course, but be warned that any part of this is considered “core” knowledge and therefore examinable. If some Systems Objectives have not been specifically covered, it is up to you to do the necessary reading. Do not underestimate the amount of background reading that you will need to do. Use the list of Systems Objectives and tabulated core curricula as a guide for your revision for the Final MB Examination in Pathology, as these core topics (described in the categories “in-depth knowledge” and “familiarity” in the tabulated curricula) are appropriate for testing in the Examination.

## LEARNING OBJECTIVES

Certain broad principles apply to the objectives relating to any given disease. You should be able to:

- define the common terms used to describe or name disease processes.
- describe the epidemiology and have a rough idea about how common a disease is. You do not need to learn precise figures of disease incidence.
- describe the main aetiological factors and pathogenetic mechanisms, if known. You should also be able to state if these are not known to medical science, but you should have some idea of the main theories in current use.
- describe the main macroscopic morphological features of diseased organs and tissues, but the microscopic features are expected only in a few appropriate diseases. By the end of the Pathology course in 2nd Clinical Year you should already be able to work out the main gross changes you would expect in many diseases from first principles and should not find yourself committing a lot to memory by rote. In certain tissues, such as liver and kidney, there are other more specific changes in disease, but again you should be able to work these out from certain principles which apply to these tissues.
- understand how pathological mechanisms affect a patient and become translated into clinical signs and symptoms.
- determine appropriate laboratory investigations to make the correct diagnosis and to monitor disease progress.
- describe the clinical course of the disease and common complications.
- list the disorders which are recognised precursors of certain well-defined clinical syndromes or entities e.g., hypertension, nephrotic syndrome, haematemesis, coma.

You may refer to the accompanying chart for lists of topics to be covered in different degrees of detail for each system.

## CURRICULUM IN HISTOPATHOLOGY

Relative Importance	Heart	Blood Vessels	Pulmonary	Gastro-Intestinal Tract
<b>In-depth knowledge</b>	Ischaemic heart disease  Hypertensive heart disease  "Heart Failure"  Valvular heart disease  Endocarditis	Atherosclerosis  Aneurysms  Hypertension  Aortic dissection	Pulmonary embolism  Pneumonia Tuberculosis  Lung Tumours Emphysema  Asthma  Chronic Bronchitis	Epithelial tumours of large bowel  Malignant gastric tumours  Peptic ulcer disease  Inflammatory bowel disease  Ischaemic bowel disease,  Diverticular disease,  Malabsorption  Oesophageal cancers
<b>Familiarity</b>	Myocarditis  Pericarditis  Congenital heart disease	Vasculitis  PAN  WG  Kaposi's sarcoma  Vascular malformations	Lung abscess  Occupational lung disease  Pleural tumours  Pulmonary Hypertension  Hyaline membrane disease  Adult respiratory distress syndrome	Benign gastric tumours  Achalasia  Meckel's diverticulum.  Gastro-intestinal infections  Carcinoid tumours
<b>Passing knowledge</b>	Cardiomyopathy			Intestinal lymphomas,
<b>Heard of</b>	Tumours			

Relative Importance	Liver, biliary tree & pancreas	Kidney & Bladder	Musculo-skeletal	Male urogenital	Female genital
<b>In-depth knowledge</b>	Hepatitis Cirrhosis Gallstones Alcoholic and drug induced liver disease Pancreatitis Hepatic failure Primary and secondary biliary cirrhosis Portal hypertension Liver cancer Pancreas cancer	Systemic disease affecting the kidney:  hypertension diabetes  SLE,  Amyloid  Pyelonephritis  Renal cell carcinoma  Urothelial Cancer  Proteinuria  Haematuria  Chronic and acute renal failure.  Glomerulo-nephritis	Rheumatoid arthritis:  Osteoarthritis  Infectious arthropathy  Metabolic bone disease  Osteoporosis  Osteomalacia	Prostatic carcinoma  Benign prostatic hyperplasia.  Malignant testicular tumours.	CIN and Cervical cancer  Endometrial hyperplasia & cancer  Fibroids  Endometriosis.  Ovarian tumours  VIN  Vulval cancer
<b>Familiarity</b>	Haemochromatosis,  Wilson's disease  $\alpha$ -1-antitrypsin deficiency  Sclerosing cholangitis	Developmental abnormalities of the renal tract.  Interstitial nephritis  Renal papillary necrosis,  Bladder and renal stones,  Renal artery stenosis,  Reflux nephropathy.	Seronegative spondyloarthropathies  Paget's disease,  Osteosarcoma,  Bone tumours,  Gout,  Pseudogout.  Diseases of muscles	Infections  Benign tumours.  Developmental abnormalities of testis.	Vulval dystrophies  Vaginal tumours.
<b>Passing knowledge</b>	Acute fatty liver				Gestational Trophoblast disease
<b>Heard of</b>	Veno-occlusive disease  Islet cell tumours of pancreas	Haemolytic uraemic syndrome			Fallopian Tube Tumours

Relative Importance	Nervous System	Reticulo-endothelial system	Paediatric and maternal pathology	Tumours	Breast Endocrine & Other
<b>In-depth knowledge</b>	Cerebrovascular disease Trauma Multiple sclerosis Raised intracranial pressure. Dementia Meningitis Abscess	Lymphadenopathy – benign & malignant	Cystic fibrosis Diseases of the preterm infant Pre-eclampsia Intrauterine growth retardation	Lung Colon Oesophagus Breast Prostate Kidney Bladder Stomach Ovary/Uterus Cervix Vulva Testis Melanoma Pancreas Liver Thyroid	Benign and malignant breast disease Graves' disease Hashimoto's thyroiditis. Thyroid tumours Diabetes Mellitus AIDS and HIV
<b>Familiarity</b>	CNS Tumours Degenerative brain disease diseases of peripheral nerves CNS infections Encephalitis	Hodgkin's disease Non-Hodgkin's lymphomas Splenomegaly	Sudden infant death syndrome Birth trauma Hirschsprung's disease Paediatric solid tumours.	CNS tumours Vagina Adrenal Common hereditary neoplasias (eg colon, breast)	Hyperparathyroidism Cushing's & Conn's syndromes. Addison's disease SLE PAN Amyloidosis Sarcoidosis
<b>Passing knowledge</b>				Non-melanoma skin tumours Pituitary	Mult. endocrine neoplasia. Organ transplantation. Iatrogenic disorders Blistering skin disease.
<b>Heard of</b>			Neonatal hepatitis	Salivary gland	Radiation injury Storage disorders

## CARDIOVASCULAR SYSTEM

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**Main topics: atherosclerosis, ischaemic heart disease, cardiac failure, hypertension, valvular disease, aneurysms**

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### 1. Vascular Disease:

#### Atherosclerosis

- understand the aetiology, pathogenesis and risk factors
  - describe the distribution, macroscopic and microscopic features
  - understand the effects on tissues
- describe the complications of atherosclerosis including vascular occlusion, thrombosis, embolism and aneurysm formation

#### Hypertension

- be able to define hypertension
- understand the risk factor and pathogenetic mechanisms, and the relationship with atherosclerosis
- describe the effects on arteries and arterioles both macroscopic and microscopic
- describe the effects on end organs especially kidney and brain
- understand the effects on the heart

#### Diabetic vascular disease

- understand the aetiology and pathogenesis of diabetic vascular disease
- understand the macro-angiopathy
- understand the relationship between diabetes and atherosclerosis
- describe the effects of microangiopathy on specific tissues including kidney, nerves, retina

#### Aneurysms

- be able to define aneurysms and give an aetiological classification
- understand the pathogenesis of different forms of aneurysms
- know the complications including thrombosis, embolism, and rupture
- describe the process of aortic dissection

#### Venous disorders

- define the terms deep venous thrombosis and thrombophlebitis
- understand their risk factors, aetiology and pathogenesis
- have a clear understanding of their complications, including the various forms and outcomes of pulmonary embolism
- define varices; understand the aetiology and pathogenesis

#### Vasculitis

- have a general knowledge of the range of types of vasculitis and their effects

### 2. Heart:

#### Ischaemic heart disease

- review the anatomy and blood supply to the heart
- be able to classify clinical forms of IHD
- understand the relationship with coronary atherosclerosis and its complications
- describe the incidence and risk factors
- recognise and describe the macroscopic sequence of changes in acute myocardial infarction
- list the possible complications of myocardial infarction; understand their pathogenesis; describe their possible outcomes
- be able to correlate pathological changes with clinical effects
- understand the concept of chronic myocardial ischaemia

**Hypertensive heart disease**

- understand the pathogenesis
- describe the macroscopic morphology of the myocardium in left ventricular hypertrophy
- understand the relationship with ischaemic heart disease
- understand the consequences of hypertensive heart disease

**Cardiac failure**

- define cardiac failure
- give an aetiological classification
- understand the pathophysiology of cardiac failure
- be able to discuss clinicopathological features of cardiac failure
- understand the differences between right sided and left sided cardiac failure
- understand adaptive changes in chronic cardiac failure
- describe effects on end organs of cardiac failure
- understand the causes of sudden cardiac death

**Valvular disease**

- be aware of the range of valvular heart disease
- understand the aetiology, pathogenesis, morphology and sequelae of rheumatic carditis
- understand the importance of congenital valvular abnormalities and consequences
- understand the local and systemic effects and complications of infective endocarditis

Students are only expected to be familiar with (but not possess detailed knowledge of) myocarditis, pericarditis, diagnosis of vasculitis, vascular malformations, congenital heart disease and drug-induced myocardial disease.

Students are only expected to be aware of the existence of cardiac tumours and cardiomyopathy (3 types), but should appreciate the genetic basis of the disease.

**RESPIRATORY SYSTEM**


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**Main topics: pneumonia, chronic obstructive airways disease, asthma, pulmonary embolism, tuberculosis, lung cancer, mesothelioma**

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**General**

- understand the definition of respiratory failure, and describe the pathophysiology
- understand the pathogenesis and consequences of pulmonary oedema
- have an outline idea of the concepts of respiratory distress syndrome in adults and neonates
- be aware of the causes, mechanisms, & clinical effects of respiratory distress syndrome and its complications

**Respiratory infections & causative micro-organisms**

- define pneumonia
- be able to define bronchitis and bronchiolitis and describe pathological and clinical features
- recognise and describe the macroscopic features of broncho-pneumonia, lobar pneumonia and interstitial pneumonia, and understand their complications
- be aware of the causes, clinical effects and complications of lung abscess

**Tuberculosis**

- define primary and post-primary TB
- understand the role of the immune system in the sequence of events underlying the pathogenesis of TB
- recognise and describe the macroscopic and microscopic appearances in tuberculous infection
- describe the possible clinical effects
- list the possible complications of pulmonary TB, and understand their pathogenesis, including in the immunocompromised host
- appreciate the clinical importance of drug-resistant strains of TB



**Chronic Obstructive Pulmonary Disease (COPD)**

- understand the concept of fixed airway obstruction
- define chronic bronchitis (clinical definition)
- define emphysema
- be aware of the incidence and relationship of both
- describe aetiology, pathogenesis and risk factors of chronic bronchitis and emphysema
- describe morphological features (macroscopic) of chronic bronchitis and emphysema
- be aware of the different forms of emphysema
- understand the pathogenesis of small airway obstruction
- understand the pathogenesis of pulmonary hypertension in COPD
- understand the pathogenesis of cor pulmonale

**Bronchial asthma**

- understand the aetiology and pathogenesis
- be aware of the macroscopic and microscopic appearances

**Pulmonary Embolism**

- understand the relationship to deep venous thrombosis (DVT)
- understand the possible outcomes of pulmonary thrombo-embolism and their frequency

**Lung Cancer**

- be aware of the importance of lung tumours in clinical practice
- understand the aetiological importance of smoking, be aware of other risk factors
- give a simple histological classification, and understand its clinical importance
- describe the macroscopic features of lung tumours
- understand the clinical presentation and course of lung tumours
- describe the local and systemic complications of lung tumours, and understand their pathogenesis
- be aware of the importance of metastatic tumours in the lungs
- understand the importance and limitations of cytological and biopsy investigations in the diagnosis and management of lung tumours
- appreciate the emerging molecular basis of lung tumours
- have knowledge of malignant mesothelioma, its causes, effects and sequelae

Students are only expected to be familiar with (but not possess detailed knowledge of) the following:

**Interstitial Lung Disease**

- define
- give an aetiological classification
- list the principal conditions giving rise to interstitial lung disease
- be aware of the distribution of disease within the lungs, and the implications for diagnosis
- describe the clinical effects and complications

**Occupational Lung Disease**

- be aware of the principal forms
- be aware of the morphology, clinical effects and outcome of the common types

**Bronchiectasis**

- define bronchiectasis
- be aware of the conditions which predispose
- understand the pathogenesis
- be aware of the clinical effects and complications

**Cystic Fibrosis**

- have knowledge of the pulmonary changes in paediatric Cystic Fibrosis

**Pulmonary Hypertension**

- be aware of the causes, and relationship to right heart disease
- define cor pulmonale; list the disorders which cause it; understand the pathophysiology and consequences

**LYMPHORETICULAR SYSTEM**


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**Main topics: benign lymphadenopathy, malignant lymphadenopathy**

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**Benign Lymphadenopathy**

- know the microarchitecture and normal function of lymph nodes and spleen
- be aware of the importance of lymph node enlargement as a clinical problem
- list the common causes of lymphadenopathy

**Malignant lymphadenopathy**

- be aware of the incidence and clinical importance of Hodgkin's disease and non-Hodgkin's lymphomas
- have a general appreciation of what is the malignant cell in Hodgkin's disease
- be aware that histological classification of non-Hodgkin's lymphomas (NHL) is complex
- understand that NHL may be classified into broad categories according to prognosis and histological features including architecture (diffuse or follicular), cell size and B or T cell type.

Students are only expected to be familiar with (but not possess detailed knowledge of) the broad principles of the Ann Arbor staging system, the Rye classification of Hodgkin's Disease and the REAL (Revised European and American Lymphoma) classification of NHL, but full description of these classification systems is not required.

Students should be aware that extra nodal NHL occurs in various forms according to site (eg GI MALT lymphomas), and understand their clinico-pathological features. Students should be aware of techniques used in lymphoma diagnosis - immunohistology, DNA analysis, and karyotyping.

**ALIMENTARY SYSTEM**


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**Main topics: chronic gastritis; peptic ulceration; carcinoma of oesophagus and stomach; coeliac disease; ulcerative colitis and Crohn's disease; diverticular disease; colorectal cancer and the adenoma-carcinoma sequence**

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**General**

- be able to list the principal causes of gastro-intestinal haemorrhage
- be aware of the effects of ischaemia on the gastro-intestinal tract
- define the terms "diverticulum", "fistula", and "sinus"

**Oesophagus**

- have knowledge of hiatus hernia
- understand the pathogenesis of reflux oesophagitis and its possible consequences
- define Barrett's oesophagus; describe the morphological changes; be aware of the metaplasia - dysplasia - carcinoma sequence
- understand the clinical importance of oesophageal cancers (2 major types)
- be aware of the nature, causes and clinical consequences of the Mallory Weiss syndrome
- understand the pathogenesis of oesophageal varices; describe the macroscopic morphology and understand their clinical importance

**Stomach**

- be aware of the range of aetiological agents producing acute & chronic inflammation of gastric mucosa
- give an aetiological classification of chronic gastritis
- understand what is known of the relationship between Helicobacter pylori, gastritis and peptic ulceration
- be aware of the incidence, natural history and clinical features of peptic ulceration
- recognise and describe the macroscopic morphology of acute and chronic peptic ulceration in stomach (and duodenum)

- list the complications of peptic ulceration in stomach (and duodenum), and understand the pathogenesis
- understand the clinical importance of gastric adenocarcinoma and its prognosis
- recognise and describe the principal macroscopic types of gastric cancer

#### Small intestine

- understand the concept of malabsorption, and know the range of aetiologies
- recognise and describe the morphological changes of coeliac disease, and understand the role of biopsy in diagnosis
- describe and recognise the morphology of acute ischaemia in the gastrointestinal tract
- be aware that tumours of the small intestine are uncommon
- be aware of the distribution of Crohn's disease in the gastrointestinal tract
- recognise and describe the macroscopic morphology of Crohn's disease of the small (and large) intestine

#### Large intestine

- understand the spectrum of inflammatory bowel disease (IBD)
- have a knowledge of the clinical importance, incidence and natural history of IBD
- be able to compare and contrast the macroscopic features of Crohn's disease and ulcerative colitis
- list the complications of ulcerative colitis and Crohn's disease, and understand their pathogenesis
- have a knowledge of bacterial and viral forms of colitis, including pseudomembranous colitis
- be aware of how ischaemia (acute and chronic) affects the large intestine, and be able to describe the macroscopic morphology
- understand the epidemiology, pathophysiology and complications of diverticular disease
- define polyp; classify the principal polyps of the large intestine
- understand the clinical importance of tumours of the large intestine
- have a knowledge of the adenoma-carcinoma sequence in the large intestine
- understand that some types of intestinal polyp are premalignant, and describe the factors associated with high risk
- have an awareness of the genetic alterations associated with the adenoma-carcinoma sequence
- have an awareness of the inheritance, morphology and clinical implications of familial adenomatous polyposis and hereditary non-polyposis colorectal cancer
- describe the growth and spread of colorectal cancer understand the relationship between morphological features, and clinical presentation and course
- be able to define the Dukes' staging of colorectal cancer, and understand its clinical significance

Students are only expected to be familiar with (but not possess detailed knowledge of) the nature and clinical significance of Meckel's diverticulum, achalasia, benign gastric tumours, gastro-intestinal infections, the common anal and perianal disorders of haemorrhoids, fistulae and anal warts; and be aware of the existence of anal squamous carcinoma.

Students are expected only to have heard of intestinal lymphomas and carcinoid tumours.

## LIVER, BILIARY TREE AND PANCREAS

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**Main topics: hepatitis; cirrhosis; hepatocellular carcinoma; pancreatic carcinoma**

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#### General

- understand the normal microanatomy and function of the liver
- understand the methods of investigation of hepatobiliary disease, and the role of liver biopsy
- be aware of the range of aetiological agents capable of causing acute liver injury

#### Hepatitis (with virology)

- give a classification of viral agents capable of causing acute and chronic hepatitis
- describe the different forms of hepatitis which occur in infections by hepatitis viruses A, B, C and D
- understand the various clinical forms of hepatitis B virus infections, their pathogenesis and clinical outcomes

- be aware of the differing clinical outcomes of different forms of hepatitis
- understand the effects of alcohol on the liver
- describe and recognise the microscopic morphology of alcoholic hepatitis

#### Cirrhosis

- be able to define cirrhosis
- list the aetiological agents, and understand the pathogenesis
- recognise and describe the macroscopic and microscopic morphology
- list the complications of cirrhosis including hepatic failure and portal hypertension; have a clear understanding of their pathogenesis; describe their clinical features
- have a knowledge of the nature of primary biliary cirrhosis, and be able to distinguish it from biliary fibrosis secondary to obstruction

#### Tumours

- be aware of the main forms of malignant liver tumours
- recognise the importance of metastatic tumours in the liver

#### Biliary System

- know the basic anatomy of the biliary tract
- understand the clinical importance of cholelithiasis
- understand the pathogenesis, clinical consequences and complications of cholelithiasis
- be aware of the clinical and pathological effects of biliary obstruction

#### Pancreas

- understand the aetiology, pathogenesis and clinical consequences of acute pancreatitis
- be aware of the nature of chronic pancreatitis and its clinical features
- be aware of the clinico-pathological features of pancreatic carcinoma, and its mode of spread
- describe the clinical and pathological features of cystic fibrosis in relation to the pancreas
- understand the molecular basis and complications of cystic fibrosis

Students are only expected to be familiar with (but not possess detailed knowledge of) benign hepatic tumours, haemochromatosis, Wilson's disease, alpha 1 - antitrypsin deficiency and primary sclerosing cholangitis.

## RENAL SYSTEM

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**Main topics: renal failure; nephritis and nephrosis; tubular and interstitial disease; cancers of kidney & bladder**

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#### Kidney

- define acute renal failure and chronic renal failure
- list the common causes of acute renal failure and chronic renal failure
- understand the pathogenesis of acute and chronic renal failure
- be aware of the effects of diabetes, amyloidosis, SLE, vasculitides, and other systemic diseases on the kidney
- understand the close inter-relationship between systemic hypertension and renal disease
- be aware of the principal congenital and inherited disorders of the kidney with emphasis on polycystic kidney disease.

#### Nephritis and nephrosis

- understand the role of circulating immune complexes, anti-GBM antibodies and *in-situ* immune complexes in the pathogenesis of glomerular injury
- understand the importance and role of the principal mediators of tissue damage in immune disease of the kidney
- define nephrotic syndrome
- list the principal causes of nephrotic syndrome
- describe the clinical features of nephrotic syndrome

**Tubulo-interstitial disorders**

- understand the differences between glomerular disorders and tubulo-interstitial disorders
- be aware of the principal causes of acute tubular necrosis and the possible clinical manifestations and outcomes
- understand the pathogenesis and pathological features of acute and chronic interstitial nephritis, the possible causes, and clinicopathological features
- understand the aetiology, pathogenesis and clinicopathological features of acute pyelonephritis
- understand the aetiology, pathogenesis and clinicopathological features of chronic pyelonephritis
- understand the aetiology and consequences of urinary tract obstruction and hydronephrosis
- understand the pathogenesis of calculus formation in the renal tract, and sequelae

**Renal tumours**

- have a knowledge of the common benign and malignant tumours of the kidney
- be aware of the clinico-pathological features of Wilm's tumour, renal carcinoma and transitional cell carcinoma of renal pelvis

**Bladder**

- understand the effects of bladder calculi
- describe the morphology and clinical features of cystitis
- be aware of the importance of tumours of bladder (ureters and renal pelvis) in clinical practice
- be aware of risk factors for transitional cell carcinoma (TCC)
- describe the natural history of TCC and precursor lesions
- describe and recognise the morphology of TCC's
- understand the importance of histological grading of TCC

Students are only expected to be familiar with (but not possess detailed knowledge of) renal papillary necrosis, renal artery stenosis, and reflux nephropathy.

**FEMALE GENITAL TRACT**


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**Main topics: endometrial hyperplasia and carcinoma; cervical intraepithelial neoplasia and carcinoma; ovarian tumours; ectopic pregnancy**

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**Ovaries**

- be aware of the various forms of non-neoplastic and neoplastic ovarian cysts
- recognise the clinical importance of ovarian tumours
- be able to give a simple histological classification of epithelial, sex cord-stromal and germ cell tumours
- describe the various modes of clinical presentation of ovarian tumours, and correlate with the pathological features
- understand the mode of spread of ovarian cancer and its usual prognosis
- be aware of the clinical features of hormone-secreting ovarian tumours

**Fallopian tubes**

- be aware of the clinical importance of pelvic inflammatory disease and its effects on the Fallopian tubes
- understand the aetiology, pathogenesis, clinical presentation and life-threatening complications of ectopic (tubal) pregnancy

**Uterus**

- recognise the importance of endometrial biopsy in gynaecological investigation and management
- classify endometrial hyperplasia into simple, complex and atypical hyperplasias
- understand the clinical implications of the different types of hyperplasia
- have knowledge of clinical presentation and behaviour of endometrial carcinoma
- be aware of the clinical importance and nature of benign myometrial "fibroids"

**Cervix**

- understand the concept of the cervical transformation zone, and its changes at puberty and menopause
- have a detailed knowledge of the epidemiology, risk factors, aetiology and pathology of carcinoma of the cervix

- understand the concept of cervical intraepithelial neoplasia (CIN), and describe its natural history
- have an understanding of the role of human papillomavirus in CIN & carcinoma of the cervix including the molecular interactions with cell cycle regulators
- describe the microscopic morphology of CIN
- understand the concept of microinvasive carcinoma of the cervix and its clinical significance
- recognise the importance of the cervical screening programme and understand its successes and failings
- appreciate the existence of cervical glandular intraepithelial neoplasia (CGIN)

#### Vulva

- understand the concept of VIN and its progression to vulval cancer

#### General

- review the ovarian & endometrial cycles, and follicular maturation and ovulation
- be aware that diseases of the female genital tract include inflammation, neoplasia, hormonal disturbances and complications of pregnancy
- understand the pathogenesis of endometriosis, its distribution, clinical effects and morphology in affected tissues including ovaries

Students are only expected to be familiar with (but not possess detailed knowledge of) the following:

#### Vagina and vulva

- be aware that vaginal disorders are uncommon, with infection the commonest disease process
- be aware of the existence of vaginal intra-epithelial neoplasia (VAIN) and vaginal squamous carcinoma as an uncommon malignancy
- be aware of the variety of skin disorders affecting the vulva

#### Placenta

- have an outline understanding of the various forms of gestational trophoblastic disease, including hydatidiform mole and choriocarcinoma

## BREAST

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**Main topics: benign breast lumps; carcinoma**

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- know the principal clinical features of breast disease
- be aware of the main diagnostic techniques
- have knowledge of inflammatory lesions affecting the breast
- be aware of the spectrum of degenerative, cystic, fibrotic and proliferative disorders comprising "benign breast disease" (fibrocystic change/disease)
- be aware of the clinical features of fibroadenoma, and recognise its macroscopic morphology
- be aware of the existence of intraduct papilloma and its clinical presentation
- be aware of the size of the clinical problem of breast cancer
- have knowledge of the epidemiology of breast cancer
- have knowledge of the clinical presentation and effects of breast cancer
- describe and recognise the macroscopic morphology of breast cancer
- be aware of the simple classification of breast cancer into special and no special types and their different patterns of behaviour
- be aware of the existence of pre-invasive forms of breast cancer (carcinoma *in-situ*), be able to define, and understand the concepts
- be aware of Paget's disease of the nipple and its implications
- be aware of the National Breast Screening Programme, its techniques, successes and failures

## MALE GENITAL TRACT

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**Main topics: testicular tumours; prostatic carcinoma**

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### Testis

- give a simple classification of testicular tumours
- have an outline knowledge of the clinical features, macroscopic morphology and mode of spread of the common malignant tumours of the testis
- understand torsion and infection (eg Mumps) of the testis

### Prostate

- be aware of the clinical importance of benign prostatic hyperplasia
- understand its clinical effects and complications
- be aware of the clinicopathological similarities and differences between benign prostatic hyperplasia and prostatic carcinoma
- be aware of the clinical importance of prostatic carcinoma
- understand the concepts of latent and occult prostatic carcinoma
- be aware of methods of investigating and monitoring prostatic carcinoma
- have knowledge of the mode of spread, and pattern and type of metastasis

Students are only expected to be familiar with (but not possess detailed knowledge of) the following:

- have a basic knowledge of common infective and inflammatory disorders of testis, epididymis and spermatic cord
- have an understanding of the effects and clinical implications of undescended testis

## ENDOCRINE SYSTEM

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**Main topics: effects of increased and decreased hormone output; thyrotoxicosis; myxoedema; thyroid nodules, thyroid tumours; diabetes mellitus**

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### General

- understand the control mechanisms of hormonal secretion in the endocrine system
- understand the concepts of endocrine hyper- and hypoplasia, end organ effects, and neoplasia
- understand pituitary function as a model of endocrine control systems
- describe the endocrine consequences of functional and non-functional pituitary tumours

### Endocrine pancreas/Diabetes Mellitus

- review the function of pancreatic islets
- understand the pathogenesis of type I and type II diabetes mellitus
- be aware of the pathogenesis of microangiopathic complications of diabetes
- have a knowledge of the multiple systems in which complications of diabetes occur including large and small blood vessels, kidney, retina, nerves, skin, susceptibility to infection, and effects in pregnancy

### Thyroid

- understand the pathogenesis and clinical consequences of the various forms of goitre
- be aware of the clinical features and underlying pathological conditions in hyperthyroidism
- be aware of the clinical features and underlying pathology in hypothyroidism
- be aware of the underlying immunological mechanisms in some forms of thyroid disease
- be aware of the presentation and investigation (scintiscan & FNA) of thyroid nodules and give a differential diagnosis
- classify the important tumours of thyroid
- be aware of the different clinical behaviour of each type, including mode of spread and prognosis

Students are only expected to be familiar with (but not possess detailed knowledge of) the following:

- classify the various forms of thyroiditis and be aware of their possible clinical features
- be aware of the existence and clinical effects of islet cell tumours
- be aware of the existence of multiple endocrine neoplasia (MEN) syndromes

#### Parathyroids

- review the role of parathyroids in regulation of serum calcium
- be aware of the causes of primary hyperparathyroidism, and its clinical and pathological consequences
- understand the pathogenesis of secondary hyperparathyroidism, and the relationship with chronic renal disease
- be aware of the effects of hyperparathyroidism on bone metabolism and morphology

#### Adrenals

- review the function of the adrenal cortex
- know the various adrenal and extra-adrenal causes of adrenocortical hyper- and hypofunction and their consequences
- understand the pathophysiology of Cushing's syndrome, Conn's syndrome and Addison's disease
- be aware of the benign and malignant, functional and non-functional, primary and metastatic tumours which occur in the adrenals
- understand the function of the adrenal medulla
- be aware of the existence of pheochromocytoma as a rare cause of hypertension

## NERVOUS SYSTEM & MUSCULAR DISEASE

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**Main topics: effects of intracranial expanding lesions; intracerebral haemorrhage; cerebral infarction; dementia; CNS infections; meningitis**

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- review the vascular supply of the brain and skull, anatomy of meninges and circulation of CSF, gross neuro-anatomy of the brain
- have a knowledge of the consequences of hypoxia in the CNS
- be aware of the causes and consequences of cerebral oedema
- list the important causes of increased intracranial pressure
- understand which types of intracranial space occupying lesions cause significant internal shifts, herniations and secondary effects
- classify intracranial haemorrhage according to site, with understanding of the different pathogeneses
- be aware of the consequences of trauma involving CNS
- define "stroke" and be aware of its clinical presentation
- understand the differing pathogenesis of stroke due to haemorrhage, or due to infarction, and the concept of systemic hypotension and infarction of watershed zones
- be aware of the relationship between systemic hypertension and intracerebral haemorrhage, and explain the pathogenesis
- be aware of the effect of HIV infection in the CNS
- be aware of the range of opportunistic infections involving the CNS in AIDS and other immunodeficiency disorders
- understand the pathophysiology of hydrocephalus
- be aware of the concept of demyelination
- have a knowledge of the principal clinical and pathological features of multiple sclerosis
- give a simple classification of CNS tumours
- be aware of the typical clinical features and outcome in CNS tumours
- be aware of the importance of metastatic tumour deposits in the CNS
- be aware of the size of the clinical problem of dementias
- have knowledge of the epidemiology, clinical features and recognised causes of dementia
- be aware of the pathological mechanisms involved in spongiform encephalopathies
- have knowledge of the pathological changes and clinical features of Parkinson's disease
- have knowledge of bacterial meningitis, its causes, effects and sequelae
- have knowledge of cerebral abscess, its causes, effects and sequelae



Students are only expected to be familiar with (but not possess detailed knowledge of) the following

- brain tumour classification
- have a general knowledge of other CNS infections and understand their pathogenesis and clinical effects
- have a general knowledge of degenerative brain diseases
- outline knowledge of peripheral nerve diseases

#### Muscular disease

- be aware of the pathogenesis and clinical features of myasthenia gravis
- know the existence of various forms of muscular dystrophy
- have a general knowledge of the range of other muscle diseases and their effects

## LOCOMOTOR SYSTEM

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**Main topics: osteoporosis; metabolic bone disease; rheumatoid and osteoarthritis**

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#### Bone

- understand the dynamic processes of bone growth, ossification, healing of fractures and remodelling
- be aware of the principal reasons for failure of fracture healing
- understand the differences between osteomalacia and osteoporosis
- have a knowledge of the pathogenesis, clinical features and complications of osteomalacia and osteoporosis
- understand the pathogenesis of bone changes related to parathyroid disorders
- understand the concept and an outline of the pathogenesis of renal osteodystrophy

#### Joints

- know the main causes and complications of infective arthritis
- be aware of the clinical importance of osteoarthritis and rheumatoid arthritis
- describe the pathogenesis and clinical features of osteoarthritis and rheumatoid arthritis
- be aware of the systemic nature and extra-articular manifestations of rheumatoid disease
- be able to contrast the pathology of osteoarthritis and rheumatoid arthritis

Students are only expected to be familiar with (but not possess detailed knowledge of) the following:

#### Bone disease

- be aware of the aetiology, pathogenesis, clinical features and complications of osteomyelitis
- have an outline understanding of the pathology and complications of Paget's disease of bone
- know the general principles of bone tumour classification
- be aware of the clinical importance of osteosarcoma and recognise its macroscopic, radiological and microscopic morphology

## MULTIPLE SYSTEMS

Acquired immune deficiency syndrome (AIDS):

- describe the pathogenesis.
- describe the effects on various tissues and organs and the clinical course.

Students are only expected to be familiar with (but not possess detailed knowledge of) the following:

Systemic lupus erythematosus  
 Polyarteritis nodosa  
 Progressive systemic sclerosis (scleroderma)  
 Amyloidosis  
 Sarcoidosis

## **MOLECULAR BASIS OF DISEASE**

- understand the genetic alterations associated with neoplasia of the cervix and large intestine
- understand the principles involved in transmission of hereditary disorders
- appreciate both the genetic and environmental contributions to multi-factorial diseases

## CURRICULUM IN CHEMICAL PATHOLOGY

Relative Importance	Acid-base balance	Salt & water balance	Potassium	Renal Function
<b>In-depth knowledge</b>	<p>Sampling &amp; precautions for blood gas analysis</p> <p>The <math>[H^+]</math>, <math>pCO_2</math> &amp; <math>[HCO_3^-]</math> buffer system</p> <p>Renal &amp; respiratory regulatory &amp; compensatory mechanisms</p> <p>Metabolic &amp; respiratory acidosis &amp; alkalosis</p> <p>Base excess</p>	<p>Routes of intake &amp; loss of salt &amp; water. Insensible loss</p> <p>Electrolytes &amp; body compartments</p> <p>Causes of hyper- &amp; hyponatraemia</p> <p>Water excess &amp; depletion</p> <p>Renin/angiotensin/aldosterone system</p> <p>ADH system</p>	<p>Body compartment distribution</p> <p>Relationship between <math>[K^+]</math>, <math>[Na^+]</math> &amp; <math>[H^+]</math></p> <p>Renal &amp; non-renal causes of abnormal <math>[K^+]</math></p> <p>Causes of hyper- &amp; hypokalaemia</p> <p>Risks &amp; treatment of hyper- &amp; hypokalaemia</p>	<p>Major pre-renal, renal &amp; post-renal causes of renal failure</p> <p>Biochemistry of acute renal failure,</p> <p>Acute tubular necrosis</p> <p>Biochemistry of chronic renal failure</p> <p>Proteinuria</p> <p>Clearance tests</p> <p>Major tests on urine</p>
<b>Familiarity</b>	<p>Standard &amp; actual <math>[HCO_3^-]</math></p> <p>Principles &amp; dangers of therapy. Use of <math>HCO_3^-</math> therapy</p>	<p>1° &amp; 2° hyperaldosteronaemia</p> <p>SIADH Diabetes insipidus</p> <p>blood &amp; urine osmolality</p>	$[K^+]$ & drugs	<p>Normal renal physiology</p> <p>Nephrotic syndrome</p> <p>Tubular function tests</p> <p>Osmotic diuretics</p> <p>Anaemia of renal failure</p>
<b>Passing knowledge</b>	<p>Anion gap</p> <p>Hyper- &amp; hypochloraemia</p>	Osmolar gap		<p>Principles of dialysis.</p> <p>Role of transplantation</p> <p>Aluminium in renal failure</p>
<b>Heard of</b>		Atrial natriuretic peptides		Fanconi's syndrome

Relative Importance	Calcium, phosphate, magnesium	Liver & intestinal function	Serum proteins & clinical enzymology	Diabetes Mellitus
<b>In-depth knowledge</b>	<p>Intake &amp; loss of <math>\text{Ca}^{2+}</math>. Albumin binding. Free ionised <math>[\text{Ca}^{2+}]</math></p> <p>Physiology &amp; role of PTH &amp; Vit D</p> <p>Causes, consequences &amp; treatment of hyper- &amp; hypocalcaemia</p> <p>Measurements of <math>[\text{Ca}^{2+}]</math>, <math>[\text{PO}_4^{3-}]</math> &amp; alkaline phosphatase</p>	<p>Bilirubin metabolism. Conjugated v unconjugated</p> <p>Causes of hyperbilirubinaemia</p> <p>Hepatocellular damage &amp; transaminases</p> <p>Biliary obstruction &amp; alkaline phosphatase</p> <p><math>\gamma</math>-Glutamyl transferase</p> <p>Albumin</p> <p>Malabsorption syndromes</p>	<p>Causes &amp; consequences of hypoalbuminaemia</p> <p>Acute phase reaction. CRP</p> <p>Hyper &amp; hypogammaglobulinaemia. Myeloma.</p> <p>Para- proteinaemia. Bence-Jones protein</p> <p>Clinical enzymology in myocardial infarction, bone, muscle &amp; pancreatic disease</p>	<p>Hormonal control of glucose metabolism</p> <p>IDDM, NIDDM. Complications &amp; glycaemic control</p> <p>Biochemical diagnosis &amp; monitoring</p> <p>HBA<sub>1c</sub></p> <p>Microalbuminuria</p> <p>Ketoacidosis. Non-ketotic hyperglycaemia</p> <p>Hypoglycaemia</p>
<b>Familiarity</b>	<p>Algorithms of <math>[\text{Ca}^{2+}]</math> correction</p> <p>Metabolic bone disease</p> <p>Hypercalcaemia of malignancy</p>	<p>Congenital hyperbilirubinaemia</p> <p><math>\alpha_1</math>-antitrypsin, ferritin, <math>\text{Cu}^{2+}</math>, caeruloplasmin</p> <p>Digestion &amp; absorption of protein, fat &amp; carbohydrate</p>	<p>Hypogammaglobulinaemia</p> <p>Role of myoglobin &amp; troponins in diagnosis of myocardial infarction</p>	<p>Metabolism of carbohydrates, triglycerides, free fatty acids &amp; ketone bodies</p> <p>2<sup>o</sup> causes of DM. Gestational DM.</p>
<b>Passing knowledge</b>	<p>Hypophosphataemia</p> <p><math>\text{Mg}^{2+}</math> regulation &amp; hypomagnesaemia</p> <p>Calcitonin</p> <p>PTHrP</p>	<p>Faecal fat, Schilling test, <math>^{14}\text{C}</math> glycocholate breath test, hydrogen breath test, pancreolauryl test</p> <p>Ammonia</p> <p>Other markers of liver disease</p>	<p>Enzyme activities v concentrations</p> <p><math>\alpha_1</math>-antitrypsin deficiency</p>	<p>Lactic acidosis</p> <p>Insulinoma</p> <p>Neonatal hypoglycaemia</p> <p>MODY</p>
<b>Heard of</b>		<p>Pancreatic function &amp; intestinal permeability tests.</p>	<p>Cholinesterase deficiency</p>	<p>Insulin, pro-insulin &amp; C peptide measurements</p>

Relative Importance	Pituitary & adrenal	Thyroid	Tumour markers	Toxicology & TDM
<b>In-depth knowledge</b>	<p>Actions of pituitary &amp; adrenal hormones. Negative feedback control</p> <p>Diagnosis of common syndromes of hormonal excess &amp; deficiency</p> <p>Interpretation of laboratory data</p>	<p>Production, regulation &amp; actions of thyroid hormones</p> <p>Common syndromes of thyroid hormone excess &amp; deficiency. Goitre</p> <p>Interpretation &amp; use of thyroid function tests. Effects of anti-thyroid drugs.</p>	<p>Sensitivity, specificity &amp; diagnostic power of tests</p> <p>Theoretical requirements, practical limitations &amp; clinical use of tumour markers</p> <p>T1/2 of clearance of biochemical markers</p>	<p>Overdose of salicylate &amp; paracetamol. Treatment</p> <p>Common poisons</p> <p>Common therapeutic overdoses</p> <p>Principles of &amp; criteria for therapeutic drug monitoring</p>
<b>Familiarity</b>	<p>Dynamic function tests</p> <p>Hormonal changes during puberty, the menstrual cycle &amp; pregnancy</p> <p>Gonadal failure</p> <p>Hypopituitarism</p>	<p>Treatment of hypothyroidism</p> <p>Treatment of thyrotoxicosis</p> <p>Iodine deficiency</p> <p>Sick euthyroid syndrome</p> <p>Thyroid tumours</p>	<p>AFP, hCG, Ca125, Ca199, CEA, PSA</p> <p>Paraproteins</p> <p>hCG in ectopic pregnancy</p> <p>Antenatal screening for neural tube defects &amp; Down's syndrome</p>	<p>Lithium</p> <p>Digoxin</p> <p>Anticonvulsants</p> <p>Theophylline</p> <p>Trough, peak &amp; steady state drug concentrations.</p>
<b>Passing knowledge</b>	<p>Diurnal rhythms, pulsatility &amp; T<sub>1/2</sub> of hormones. Changes in disease states.</p> <p>Acromegaly</p> <p>Congenital adrenal hyperplasia</p> <p>Phaeochromocytoma. Neuroblastoma</p> <p>Polycystic ovary syndrome</p> <p>Androgen excess</p> <p>Prolactinoma</p>	<p>Neonatal screening for hypothyroidism. Thyroid hormone levels in neonates</p> <p>Thyroid antibodies</p> <p>Thyroid function in pregnancy</p> <p>MEN</p>	<p>Ectopic hormone syndromes</p>	<p>Iron, carbon monoxide, methanol, glycol poisoning</p> <p>Aluminium treatment in renal patients</p> <p>Immuno-suppressants</p> <p>Drugs of abuse</p> <p>Heavy metal poisoning</p>
<b>Heard of</b>	<p>Sheehan's syndrome</p>			<p>Forensic &amp; legal considerations</p>

Relative Importance	Lipids	Pregnancy, foetus & neonate	Inborn errors of metabolism	Emergencies & intensive care
<b>In-depth knowledge</b>	Epidemiology & risk factors  Hypercholesterolaemia  Hypertriglyceridaemia	Physiological & biochemical changes in pregnancy  Nutritional requirements in pregnancy  Screening tests in pregnancy	Biochemical basis of IEM. Enzyme deficiencies & metabolic blocks  Modes of presentation  Criteria for testing for IEM  Principles of investigation	Common presenting syndromes  Fluid balance  Respiratory & renal monitoring
<b>Familiarity</b>	Metabolism of triglycerides, cholesterol & lipoproteins. role of lipoproteins  Interpretation of laboratory data	hCG in normal, failing & molar pregnancies  Neonatal jaundice  Neonatal monitoring  Pregnancy tests	IEM causes of neonatal disease. Acidosis, organic aciduria, hyperammonaemia & fatty acid oxidation defects. Principles of treatment  Cystic fibrosis  Phenylketonuria  Congenital hypothyroidism  Thalassaemia  IEM causes of adult diseases	Fallability of 'stix' testing. Limitations of blood glucose meters  Amylase & the acute abdomen  CSF tests  Composition of IV fluids  Pulse oximetry  Paediatric problems
<b>Passing knowledge</b>		The pregnant diabetic  Neonatal hypoglycaemia & convulsions  Toxaemia	Haemochromatosis  Wilson's disease  Porphyrias	Effects of age & illness on biochemical tests
<b>Heard of</b>		Obstetric cholestasis  Vit D deficiency	MCAD  Tay-Sachs  $\alpha_1$ -Antitrypsin deficiency  Cystinuria	Effects of hypo & hyperthermia on biochemical tests  Tests for acute porphyrias

Chemical Pathology or Clinical Biochemistry arose because clinicians needed biological fluids to be chemically analysed. It is of limited use in some areas of medicine but is essential in others for diagnosis and/or management. The overall aim of this part of course is to teach the student:

- what constitutes a biochemical test
- what biochemical tests are appropriate in a given clinical situation
- what biochemical tests are not of any use in a given clinical situation
- how to interpret the results of biochemical tests

## SALT AND WATER

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**Main topics: salt and water balance, sodium, water, aldosterone, ADH**

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### Salt and water balance

- understand the major routes of loss and intake of salt and water, including insensible losses
- understand fluid balance measurements
- understand the distribution of electrolytes in the different compartments of the body
- understand the principles of intravenous fluid and electrolyte therapy

### Sodium

- understand the renin/angiotensin/aldosterone system
- note the atrial natriuretic peptides
- understand the major causes of hyponatraemia
- understand the consequences, and principles of treatment and of investigation, of hyponatraemia
- understand the major causes of hypernatraemia
- understand the consequences, principles of treatment and of investigation, of hypernatraemia
- understand the relationships between  $\text{Na}^+$  and  $\text{K}^+/\text{H}^+$  metabolism

### Water

- understand the ADH system
- understand the blood and urine measurements of osmolarity, osmolality and osmotic pressures
- understand the osmolar gap
- understand the major causes of fluid excess and depletion
- understand the consequences, principles of investigation and principles of treatment, of water excess and depletion

### Aldosterone

- understand the major causes, consequences, modes of clinical presentation, investigation, and therapy, of primary and secondary hyperaldosteronaemia and hypoaldosteronaemia

### ADH

- understand the major causes, consequences, modes of clinical presentation including SIADH and DI, investigation, and therapy, of pathologically or inappropriately high or low circulating levels of ADH.

## POTASSIUM

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**Major topics: hyperkalaemia, hypokalaemia, diuretics**

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- understand body compartment distribution
- understand the relationships between circulating  $[\text{K}^+]$  and  $[\text{Na}^+]$  and  $[\text{H}^+]$

- understand the major renal and non-renal causes of abnormalities of circulating  $[K^+]$
- understand the consequences, principles of investigation, and principles of treatment of hyper- and hypokalaemia
- understand the relationships between circulating serum  $[K^+]$  and diuretics

## RENAL FUNCTION

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**Main topics: physiology, pathology, investigations, acute renal failure, chronic renal failure, acute tubular necrosis, nephrotic syndrome**

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### Physiology

- understand the normal function of the glomerulus, proximal and distal convoluted tubules, loop of Henle and collecting duct
- understand the concept of osmotic diuresis

### Pathology

- understand the major pre-renal, renal and post-renal causes of renal failure
- understand polyuria, oliguria and anuria

### Investigations

- understand the clearance tests and the tests of tubular function
- understand the major biochemical tests on urine

### Acute renal failure

- understand why circulating  $[H^+]$ ,  $[K^+]$ , [urea], [creatinine], [urate] and  $[PO_4]$  rise
- understand  $Na^+$  and  $H_2O$  metabolism in acute renal failure
- understand the natural history
- understand the principles of treatment

### Chronic renal failure

- understand the major causes
- understand the natural history
- understand the 'one nephron' hypothesis
- understand the polyuria and the later oliguria
- understand why circulating  $[H^+]$ , [urea], [creatinine], [urate] and  $[PO_4^=]$  rise
- understand why circulating  $[K^+]$  generally rises
- understand why circulating  $[Ca^{2+}]$  falls, and understand the relationship between circulating [urea] and  $[PO_4^-]$
- understand  $Na^+$  metabolism
- understand the anaemia
- understand the principles of conservative treatment and of dialysis and related therapies.
- understand the monitoring of the effectiveness and complications of dialysis
- understand the role of transplantation
- understand aluminium
- Acute tubular necrosis - understand the natural history
- Nephrotic syndrome - understand the major causes, understand the consequences and natural history
- Fanconi's syndrome - understand the major causes and natural history and diagnosis

## CALCIUM, PHOSPHATE AND MAGNESIUM

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**Main topics: physiology, hypercalcaemia, hypocalcaemia, investigations, bone disease, treatment, hypophosphataemia, magnesium**

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### Physiology

- understand the sources of total body calcium intake and loss
- understand the binding of circulating calcium to albumin, free ionized calcium and the algorithms of correction



- understand the regulation of PTH release
- understand vitamin D metabolism, note calcitonin
- understand the hypercalcaemia of malignancy and understand parathyroid hormone-related protein [PTHrP]

#### Hypercalcaemia

- understand the clinical consequences
- understand the major causes

#### Hypocalcaemia

- understand the clinical consequences
- understand the major causes

#### Hypophosphataemia

- understand the major causes, consequences, and treatment  $Mg^{2+}$
- note the parallels with  $Ca^{2+}$  metabolism
- note the dangers of very low  $[Mg^{2+}]$

#### Investigations

- understand the role of serum measurement of  $[Ca^{2+}]$   $[PO_4^{2-}]$   $[PTH]$   $[Urea]$   $[vitamin\ D]$   $[alkaline\ phosphatase]$  and the role of urine measurement of  $[Ca^{2+}]$  and  $[PO_4^{2-}]$

#### Treatment

- understand the relative role of the separate treatments for hypercalcaemia and hypocalcaemia

#### Bone disease

- understand osteomalacia, osteoporosis and Paget's disease

## LIVER FUNCTION TESTS

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**Main topics: Bilirubin, transaminases, alkaline phosphatase, gamma glutamyl transferase, acute hepatocellular damage and obstructive liver disease**

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#### Bilirubin

- Understand the mechanism of bilirubin formation and excretion
- Understand the consequences for the different circulating forms of bilirubin of excessive red cell destruction, biliary obstruction and hepatocellular damage
- Be aware of the congenital disorders of bilirubin metabolism

#### Transaminases

- Know which enzymes are commonly measured to detect hepatocellular damage
- Be aware of the mode of release of cytoplasmic enzymes

#### Alkaline phosphatase and gamma glutamyl transferase

- Know which liver pathologies typically lead to an increase in the serum concentration of these enzymes
- Be aware of the mode of release of these enzymes.

#### Other markers

- Be aware of the changes in the serum concentrations of albumin, choline esterase, clotting factors, immunoglobulins and ammonia which may accompany liver pathology.

## Liver disease

- Know the typical pattern of serum changes in acute hepatocellular damage and obstructive liver disease
- Be aware of the use of the measurement of the serum concentrations of alpha one antitrypsin, ferritin copper and caeruloplasmin in the diagnosis of liver disease
- Be aware of the relative sensitivity and specificity of gamma glutamyl transferase in the detection of alcoholic liver disease.

**CLINICAL ENZYMOLOGY**


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**Main topics: Biochemistry, Myocardial infarction, Bone disease, Muscle disease, Pancreatic disease, Choline esterase deficiency**

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## Biochemistry

- Know the difference between activity and concentration.
- Know that enzyme assays are reported in activities and not concentrations and that the reported serum concentrations are method dependent.
- Know which enzymes and isoenzymes are commonly measured
- Know the tissue distribution of the commonly measured enzymes
- Be aware of the sub-cellular location of the commonly measured enzymes

## Myocardial infarction

- Know the typical pattern of the serum enzyme changes following an MI
- Know the improvement in specificities which the measurement of isoenzymes gives.
- Be aware of the use of myoglobin and Troponins T and I in the diagnosis of MI.

## Bone disease

- Know which enzymes may be elevated in bone disease

## Muscle disease

- Know which enzymes are elevated in muscle disease.

## Pancreatic disease

- Know the typical pattern of the serum enzyme changes in acute pancreatitis.

## Choline esterase deficiency

- Be aware of this condition, its cause and its consequences

**SERUM PROTEINS**


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**Main topics: Albumin, Acute phase reaction, Alpha one antitrypsin, Immunoglobulins**

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## Albumin

- Know the importance of the method used for the measurement of albumin
- Know the causes and consequences of a low serum albumin

## Acute phase reaction

- Know the function of the serum proteins which change in concentration during an acute phase reaction.
- Know the situation in which the measurement of acute phase proteins (particularly C reactive protein) may be useful.

## Alpha one antitrypsin

- Know the causes and the consequences of alpha one antitrypsin deficiency

## Immunoglobulins

- Understand the difference between a polyclonal and monoclonal increase in immunoglobulins.
- Know the protein changes in serum and urine which are typically features of myeloma.
- Be aware of the causes and consequences of hypogammaglobulinaemia.

**TESTS OF INTESTINAL FUNCTION****Main topics: Physiology, Malabsorption, Tests**

## Physiology

- Know how protein, fat and carbohydrate are normally digested.
- Know the sites of normal absorption of vitamins and digested protein, fat and carbohydrate

## Malabsorption

- Know the causes of generalized malabsorption and isolated malabsorption of fat, B12 and disaccharides.

## Tests

- Understand the basis for faecal fat estimation, the Schilling test, the <sup>14</sup>C glycocholate breath test, the hydrogen breath test and the pancreolauryl test.
- Know the serological tests for coeliac disease. Be aware of tests of pancreatic function and of intestinal permeability.

**TUMOUR MARKERS AND THE DIAGNOSTIC POWER OF BIOCHEMICAL TESTS****Main topics: sensitivity and specificity of biochemical tests, half-life of clearance of markers, the nature of tumour markers and their uses and misuses**

*Objectives: Gaining knowledge and understanding of the strengths and weaknesses of some common tumour markers and from this, an appreciation that the same limitations apply to all diagnostic tests. Learning that 'tumour markers' have clinical uses in non-malignant conditions.*

## Understand sensitivity and specificity of a diagnostic test

- understand this in the context of tumour markers and heart enzymes
- understand the importance of prevalence in determining diagnostic power of a test
- (differences and similarities between population screening compared to testing a patient group with a high prior risk of the condition being tested for)
- understand how lack of sensitivity or specificity can produce a misleading 'normal' or 'abnormal' result and how serious clinical consequences can follow from a naive interpretation

## Know how to use the half-life of clearance of a biochemical marker

- be able to calculate and use the half-life of a marker in a clinical context (example of HCG levels in suspected ectopic pregnancy or spontaneous abortion)

## Understand the nature of tumour markers

- products of the normal genome and hence never completely specific for a tumour
- why a 'cancer test' as understood by lay people is unlikely to be found among current tumour markers
- the idea of a tumour marker defined by one or more monoclonal antibodies and that therefore that the results may depend crucially on exactly which antibodies are used

## Understand the practical requirements for a tumour marker

- sensitive - few false negatives
- specific - few false positives
- related to the burden of disease or mass of the tumour - the problem of determining the normal range and the action limits for marker levels - clinically useful in that it helps diagnosis or treatment

Acquire a healthy scepticism about uses and misuses of current tumour markers

Gain an outline knowledge of the following tests in tumour and non-tumour contexts:

- AFP - use in liver disease, cirrhosis, hepatitis, hepatoma, teratoma and testicular tumours; knowing that AFP is normally very high in newborns; use of AFP in antenatal screening for neural tube defects and Down's syndrome
- HCG - use in early pregnancy and ectopic pregnancy; use in antenatal screening for Down's syndrome; use in testicular tumours and tumours of trophoblastic origin; distinction between intact and free beta HCG.
- ectopic hormone syndromes - ectopic meaning either inappropriate in place (site) or inappropriate in time
- syndrome of inappropriate antidiuretic hormone (SIADH) - ectopic ACTH syndrome and its diagnosis
- myeloma proteins - their use and quantitation.
- Ca125 - use in ovarian tumours; non-tumour causes of raised Ca125 (ascites, endometriosis)
- Ca199 - use in pancreatic and gut tumours; non-tumour causes of raised Ca199 (cholangitis) – CEA - general marker of very low specificity and sensitivity
- PSA - use in carcinoma of the prostate and benign prostatic hypertrophy (BPH); non-tumour causes of raised PSA (prostatitis); use of PSA to illustrate the overlap in PSA levels between BPH and carcinoma; bound and free PSA.
- hypercalcaemia of malignancy - PTH versus PTHrP, growth factors causing hypercalcaemia; alkaline phosphatase and other markers of bone turnover

## PITUITARY AND ADRENAL FUNCTION

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**Main topics: adrenal hormones, pituitary hormones, pituitary negative feed-back system, renin-aldosterone system, biorhythms and dynamics of hormones, all the common syndromes of excess and deficiency of adrenal and pituitary hormones**

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*Objectives: Gaining facility in understanding the use of the pituitary negative feedback system and the renin-aldosterone system in diagnosing endocrine disorders; gaining knowledge and understanding of the biochemical diagnosis of the main syndromes of deficiency and excess of pituitary and adrenal hormones and the use of the relevant biochemical tests in monitoring these conditions.*

Know about adrenal hormones

- the adrenal produces mineralocorticoids, glucocorticoids, androgens and catecholamines
- know that the individual hormones and their synthetic analogues have different mixtures of biological activities

Understand the pituitary negative feedback system

- be able to understand and manipulate data related to the negative feedback system to make clinical deductions in a clinical context of endocrine disorders

Know about dynamic function tests (but not protocols):

- synacthen tests (long and short)
- dexamethasone suppression tests (overnight and two-stage) - stimulation tests to investigate the pituitary (ITT, clonidine, glucagon)

Understand the renin-aldosterone system

- be able to understand and manipulate data related to the renin-aldosterone system to make diagnostic deductions in a clinical context of endocrine disorders
- primary hyperaldosteronism (Conn's syndrome)
- secondary hyperaldosteronism - the renin-aldosterone system in ACTH deficiency

Understand biorhythms and dynamics of hormones in outline

- pulsatility of hormones
- diurnal rhythms
- effect of pathological changes, e.g. tumours, on pulsatility and hence bioactivity
- half-lives of hormones and the consequences for interpretation of their levels
- outline knowledge of the biorhythms of: ACTH, cortisol, 17-hydroxyprogesterone, DHEAS, TSH, T3, T4, prolactin, growth hormone, FSH and LH, oestradiol, testosterone, HCG
- the changes in levels during the menstrual cycle.
- the differences which occur in a cycle during which conception occurs.
- the changes in hormone levels which occur as pregnancy progresses

Understand the concepts of 'stress' and hormonal response to stress.

- the hormones which respond to 'stress' (ACTH, cortisol, growth hormone, prolactin)
- different kinds of 'stress'; the kind which affects these hormones is not exactly definable

Know about the common syndromes of deficiency and excess in detail:

- adrenal insufficiency (Addison's) - primary adrenal failure, pluriglandular syndrome, hypoadrenalism due to pituitary failure and its compensation by the intact renin-aldosterone system.
- excess of adrenal hormones Cushing's syndrome: adrenal tumours, pituitary Cushing's, ectopic ACTH syndrome; Conn's syndrome
- excess of growth hormone - acromegaly, interpretation of growth hormone levels in diagnosis; use of GTT with growth hormone assay as a confirmatory test; use of IGF1 and IGFBP3
- deficiency of growth hormone - methods of screening children and adults for growth hormone deficiency; confirmatory tests including clonidine (children), insulin tolerance test, glucagon test.
- prolactin excess- prolactinoma; other factors which raise prolactin hypothyroidism, phenothiazines pregnancy, lactation prolactin deficiency - Sheehan's syndrome
- FSH and LH 'excess'- revise the changes of hormone levels in the normal menstrual cycle - revise the changes of hormone levels in the menopause - know that primary gonadal failure is marked by raised FSH and LH - understand that the effect of primary gonadal failure in children is only manifested as raised FSH and LH after the time for puberty has arrived - know a little about polycystic ovary syndrome - the effect of excess FSH and LH (hyper stimulation of ovulation) in causing multiple ovulation - be aware that tumours secreting FSH and or LH occur but are very rare indeed
- FSH and LH deficiency - hypogonadotropic hypogonadism - reversible hypothalamic effects causing hypogonadism such as occur in low body weight – hypopituitarism - know that in progressive pituitary disorders, the order in which hormone systems are ablated is usually: first FSH, LH and GH; last TSH and ACTH - understand how LHRH-analogues cause hypogonadism
- oestrogen deficiency states and the effect on bone turnover - tachyphylaxis in HRT - androgen excess, its causes and diagnosis
- catecholamine excess in pheochromocytoma and neuroblastoma

Know about congenital adrenal hyperplasia (in outline only):

- a compound heterozygote condition and hence variable expression - an enzyme defect causing cortisol deficiency which is compensated for by high ACTH in turn causing adrenal hyperplasia and excess of other steroids such as androgens
- 21-hydroxylase defect is by far the commonest type - presentation and diagnosis of the acute 'classical' form
- presentation and diagnosis of the 'non-classical' or late onset form; - diagnosis by measuring 17 hydroxy progesterone
- methods of monitoring of replacement therapy

## THYROID FUNCTION

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**Main topics: thyroid hormones and TSH, pituitary negative feed-back system, synthesis and metabolism of thyroid hormones, effects of antithyroid drugs, thyroid failure, hyperthyroidism, thyroid antibodies, thyroid function in pregnancy, binding of thyroid hormones to serum proteins, iodine deficiency, sick euthyroid syndrome, thyroid hormone replacement therapy, treatment of hyperthyroidism**

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*Objectives: Gaining facility in understanding the use of the pituitary negative feedback system in the context of thyroid function. Know about the different causes of hypothyroidism and hyperthyroidism. Know the scientific and medical issues underlying diagnosis and management of thyroid disease. Know how to interpret thyroid function tests in various clinical contexts.*

Know about thyroid hormones and TSH (thyroid stimulating hormone, thyrotrophin)

- thyroxine (T4), tri-iodothyronine (T3), reverse T3
- know that TSH is pulsatile and has diurnal rhythm.
- know the main thyroid biosynthetic and metabolic pathways and the effect on them of: TSH, iodine, antithyroid drugs (PTU and carbimazole), TSH-receptor stimulating antibody
- know about the differences in thyroid hormone levels in newborns

Understand the pituitary negative feedback system

- be able to understand and manipulate data related to the negative feedback system to make clinical deductions in a clinical context of thyroid disorders

Understand peripheral conversion of T4 to T3 or reverse T3

- factors which affect peripheral conversion (fasting and illness, drugs (PTU and amiodarone); TSH is not a factor affecting peripheral conversion

Know the main causes of and use of diagnostic tests in thyroid failure

- Hashimoto's thyroiditis
- pluriglandular syndrome - treatment of thyrotoxicosis - dyshormonogenesis (in outline only)
- interpretation of TSH levels
- interpretation of T4 and T3 (Free T4 and Free T3) levels
- pituitary failure and the interpretation of T4 and TSH levels in hypopituitarism
- use of TRH test
- neonatal hypothyroidism

Know the main causes of and use of diagnostic tests in hyperthyroidism

- Grave's disease - nodular and multi-nodular goitre - viral thyroiditis
- interpretation of TSH levels
- interpretation of T4 and T3 (Free T4 and Free T3) levels
- use of TRH test - thyrotropinoma
- hypercalcaemia of thyrotoxicosis
- neonatal thyrotoxicosis

Know about TSH-receptor stimulating antibodies (TRAB)

- be aware of the multiple names used: LATS, TBII, TRAB etc - be aware of the difficulty and multiple methods of measuring TRAB (not in detail) - use of TRAB in predicting the occurrence of neonatal thyrotoxicosis

Thyroid function and dysfunction in pregnancy

- pregnancy-associated hyperthyroidism - post-partum thyroiditis
- neonatal thyrotoxicosis

Know about diagnostic thyroid antibodies

- Thyroid Peroxidase antibody (TPO, also known as thyroid microsomal antibody)
- thyroglobulin antibody
- know that positive TPO together with mildly raised TSH predicts future thyroid failure

Know the nature and prognosis of thyroid tumours

- use of thyroglobulin as a tumour marker
- 'hot' and 'cold' nodules

Understand the nature of binding of thyroid hormones to serum proteins;

- serum free T4 and free T3 and the difference between total T4 and free T4
- binding of T4 and T3 to Thyroxine-Binding Globulin (TBG), albumin and prealbumin the factors which affect TBG levels
- understand that the practice of use of tests of thyroid function varies from country to country.
- use of 'T3-uptake' tests
- the effect of drugs which bind to TBG displacing T4 (phenytoin, salicylate, NSAIDs)

Know about iodine deficiency in a world-wide context

- World – Europe – UK - the consequences for population and individual thyroid pathology - know where iodine comes from in the UK diet;
- know that Grave's disease causes iodine deficiency and hence the mechanism of T3 toxicosis - know the effect of supplying iodine to someone with Grave's Disease (Jod-Basedow effect) - effects of amiodarone on thyroid function.

## Understand sick euthyroid syndrome

- the effects of fasting and illness on thyroid hormones - the effect of raised serum lipase and free fatty acids on free T4 levels
- understand why thyroid function tests can be misleading in ill or fasting patients

## Understand screening for thyroid disease

- know the approximate prevalences at different ages - strengths and weaknesses of the strategies of use of thyroid function tests - know how to manage a patient with a borderline raised or borderline low TSH

## Understand thyroid hormone replacement therapy

- consequences of giving thyroxine in patients with hypoadrenalism
- need to start on a low dose and increase the dose slowly - the need to avoid too frequent biochemical testing - the potential consequences of over or under-treating hypothyroidism - how to interpret thyroid function tests in patients taking replacement therapy

## Understand methods and monitoring of treatment of thyrotoxicosis

- antithyroid drugs (carbimazole, propylthiouracil) - radio-iodine - surgery
- the more rapid rate of change in T3 than T4 because of T3's shorter half-life - the refractory nature of a suppressed TSH
- detecting recurrence of hyperthyroidism
- detecting over-treatment resulting in hypothyroidism - the effects of hyperthyroidism on bone

**PREGNANCY, FOETUS, NEONATE**


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**Main topics: modified physiology; diabetes; screening of mother, foetus, and neonate; acute neonatal illness; prolonged jaundice**

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## Physiological resetting in normal pregnancy

- understand the fluid dilutional and renal changes and their consequences
- understand the various risks of haematinic deficiency for mother and foetus
- understand early and later effects of micronutrient deficiencies, and of gross nutritional deficiencies
- note endocrine effects on proteins and protein-bound substances in serum
- know about effects of age and pregnancy on alkaline phosphatase
- know about HCG assays in normal, failing, and molar pregnancies

## Be familiar with conventional criteria for Screening Tests, and:

- understand the reasons and techniques for diabetes mellitus screening
- understand the significance and current procedures for Down's screening
- understand selective screening of at-risk families and sub-populations
- understand the national /east anglian neonatal screening programme, and the main disorders being tested for
- note testing and management of rhesus D+ haemolytic disease

## Medical problems - the mother

- understand the importance of diabetes monitoring in pregnancy
- understand the effects of vitamin D deficiency on mother and on foetus
- understand the use of lab tests in toxemia and related disorders
- know about itching and obstetric cholestasis, and other liver disorders

## Medical problems - the neonate

- understand the use of early investigation of minimal symptomatology
- understand the tests for hypoglycaemia and other causes of convulsions
- understand the monitoring of respiratory and other major illnesses
- note tests for organic acidurias and other acute inherited disorders
- note the main differential diagnoses and important investigations in a baby with prolonged jaundice

## INTENSIVE CARE

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**Main topics: good liaison; monitoring of ventilation, of fluid balance and of renal function; routine lab tests; tests with problems for ICU patients**

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Good liaison between ICU staff and support services, and timely lab results.

Know about respiratory monitoring at the bedside

- understand pulse oximetry and arterial gases/acid-base
- know about training, and monitoring the quality of bedside procedures
- know about lactate, renal, septicemic, glycol-induced, and other acidoses

Know that the fluid balance is charted in detail as it happens

- understand how clinical problems are solved and anticipated in this way
- understand how a detailed sodium balance can help in diagnosis and care
- know effects of age, renal impairment, other organs, and of treatment
- note that blood products equal saline, and dextrose is water, if given iv
- ICU renal monitoring relies on creatinine clearance (despite disadvantages)
- understand the effects on serum urea and creatinine of age, nutrition, organ function, and muscle wasting during prolonged acute illness
- understand the diagnostic use of urine tests in acute oliguria
- note use and limitations of tests for rhabdomyolysis
- note "stix" screening is fallible in ICU patients and needs lab confirmation

Be aware that routine lab monitoring may give problems:

- understand that a low serum albumin means an acute phase reaction, but does not reflect nutrition or synthesis
- know about "corrected" calcium, and that other metals behave similarly
- note effects of tissue damage, drugs, or hypothermia on serum enzymes
- know that serum phosphate falls on iv glucose, especially in alcoholics
- note methods and results vary between labs for albumin and enzymes
- avoid thyroid testing, if possible, until a patient is well and recuperated

## ACUTE TOXICOLOGY

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**Main topics: overdoses – salicylate, paracetamol and common poisons; therapeutic overdose; drugs of addiction, forensic issues, rare poisons**

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Assays in possible overdose patients only if a result may alter treatment given

- understand relevant epidemiologico-social aspects, assay if in doubt
- understand the metabolic effects of different serum salicylate levels
- know about principles, pros, and cons of forced alkaline diuresis
- be aware of the metabolic basis of paracetamol toxicity and antidote
- know the use of a timed assay for the predictive graph in the BNF and the effects of chronic factors increasing paracetamol risk
- understand the use of urgent assays in potential iron, carbon monoxide, methanol, or glycol poisoning
- be aware of the use of different measurements of ethanol excess

Serum assays are routinely crucial for a few causes of iatrogenic toxicity:

- assay lithium if in doubt, always if unwell or if any fluid disturbance
- understand careful digoxin use and assays in susceptible patients, and the use and limitations of its immunological antidote
- note reasons for monitoring aluminium in a few renal patients

Addiction patients may present in many medical ways, or psychiatric, or social

- be aware of effects of honesty & compliance on samples and assays
- be aware of limitations of screening tests including stix tests



- be aware of common drugs of abuse, also solvents, and sports doping
- understand the causes and effects of hyperthermia, rhabdomyolysis

Assays for possible forensic or legal evidence are planned before taking samples:

- know about chain of custody; assay methods differ from routine lab
- be aware of consent difficulties, and that a non-consenting live patient can now be over-riden only on the order of a Judge

A few rarer causes of poisoning must not be overlooked, and are easily tested:

- be aware of lead, mercury, cadmium as occupational and other risks
- note organophosphates need red-cell enzyme assay
- note "herbal" drugs may contain steroids, oestrogens, or metals
- remember arsenic, thallium, etc in the rarest mystery patient

## EMERGENCIES

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**Main topics: plan for emergencies; illness and age affect investigations; acute abdomen; diabetes mellitus; neuro and muscular problems**

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Be prepared what to do and when; know local arrangements for agreed protocols, data transmission, and specimen transport

- understand times and temperatures needed to sample unstable analytes
- understand the need for training & quality testing in bedside procedures
- note differing analytical methods and reference ranges between labs
- know the importance of using full correct patient identity
- distinguish urgent taking of samples from urgent need for analysis

Effects of a patient's age and illness on lab testing:

- understand acute phase effects - low albumin, high glycoproteins eg CRP; calcium may be "correctable", other albumin-bound tests are also low
- understand common presenting syndromes due to abnormal fluids, salts, and diet; also sick euthyroid syndrome; all these commoner in elderly
- understand children need faster investigation and consequent action; also collecting pre-treatment or pre-mortem inborn error samples

Acute problems in patients with diabetes mellitus:

- know limitations of blood glucose meters; confirm extreme results
- understand how to diagnose ketoacidosis, how to monitor treatment, and the pros & cons of bicarbonate administration
- understand acute syndromes of non-ketotic and of lactate acidosis

Acute abdomen syndromes

- understand the use of routine urine and blood tests
- use the local lab's criteria, not textbook data, to interpret serum amylase
- note local protocols for cardiac markers and pre-treatment tests
- note occasional value of tests for pregnancy and for acute porphyrias

Know how to manage acute neuro and muscular problems

- understand the role of cerebrospinal fluid studies
- be aware hypothermia may affect enzymes and other metabolism
- be aware of the various causes and effects of acute hyperthermia
- know about inherited and acquired cholinesterase deficiencies
- understand the wider and faster investigation of undiagnosed sick babies

## THERAPEUTIC DRUG MONITORING (tdm)

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**Main topics: basis of tdm and criteria for use; drugs monitored routinely**

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Basis for monitoring therapy in clinical practice

- understand in principle the reasons for monitoring therapy, the factors underlying variability in drug levels, and criteria to be satisfied for tdm
- note that tdm is only needed in practice for a very few drugs in the BNF
- understand what steady state, trough, peak & other measurements are, and the reasons why particular drugs differ as to which of these we use
- be aware of other factors affecting interpretation in sick patients, and the importance of monitoring these to assist tdm decisions
- note the use of a random assay during iv therapy of acute symptoms

Main examples of drugs monitored routinely

- antibiotic levels: understand why both peak and trough may be crucial digoxin: note handling in different patients is affected by other factors which requiring monitoring eg renal, electrolytes, drugs, and body-size
- lithium: be aware how Li is routinely managed, and its chronic effects, also why acute symptoms or fluid disturbances are urgent problems
- antiepileptic drugs: know why and how tdm is useful for only 3 of these
- cyclosporin etc: know about the use of tdm, also what factors affect interpretation such as which organs are transplanted or abnormal
- theophylline: note how assays are used in seriously ill patients

## INHERITED DISORDERS - inborn errors of metabolism (IEM)

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**Main topics: metabolic effects of IEM; diagnostic approach; screening for IEM; the sick infant; older children; some adult problems and IEM**

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NB: be aware in particular of those IEM emphasised in the clinical student texts

Appreciate the biochemical basis of a patient's symptoms and management

- understand how abnormal genes affect protein structure and synthesis
- understand the different modes of inheritance of abnormal genes, and the importance of a careful family history
- understand how a deficient enzyme blocks a metabolic pathway, modifies amounts of precursors, products, and minor-pathway metabolites, and how abnormal concentrations of metabolites can lead to clinical effects

It is important to test for IEM in certain situations:

- unexplained abnormalities in routine tests, e.g. in sick infants
- presentation at an unusual age, e.g. cataracts, thrombi, calculi
- exclude rarer causes of e.g. neonatal jaundice, rickets, emphysema, serious liver disease, recurrent infections, acute abdomen
- bizarre features, e.g. odd appearance, funny smell, coloured urine
- abnormal development, or regression
- relatives at risk from e.g. cholesterol, scoliosis, porphyria, etc

Principles of investigation:

- screen metabolites, test enzyme if known, confirm by DNA ideally, using methods which distinguish affected, carrier, and normal persons
- note the growing possibilities of primary DNA testing
- samples may include blood and urine, cells in blood, or fibroblasts
- note methods by which the above is applicable during pregnancy, with limited foetal access but to a wider range of tissues
- important to get pretreatment or perimortem samples in the very ill
- if a risk is diagnosed, mark the notes, discuss card or bracelet for patient

Be aware of the conventional list of criteria for an ideal Screening Test

- know about such terms as sensitivity, specificity, and reference ranges
- be aware of the national and east anglian neonatal screening programme
- understand the metabolic basis, consequences untreated, and preventive care of phenylketonuria and of congenital hypothyroidism patients
- note the biochemical basis of cystic fibrosis, its diagnosis, and care
- be aware of screening programmes for subpopulations at risk of an IEM, eg for thalassaemia, and for Tay-Sachs disease
- note feasibility of CAH, MCAD, and other IEM in neonatal programmes

Include IEM in the differential diagnosis of significant neonatal symptoms such as hypoglycaemia, vomiting, diarrhoea, failure to thrive, haemolysis, or just ill

- be aware why many IEM of amino acids, vitamins, and near pathways may present with acidosis, organic aciduria, or hyperammonaemia & fatty acid oxidation defects eg MCAD (an acyl-CoA dehydrogenase)
- note the diagnosis and care of congenital adrenal hyperplasia (CAH)
- note the investigation of prolonged neonatal jaundice

During childhood

- consider recurrent illness as possible IEM, plan list of tests for next time
- be proactive with odd symptoms for early diagnosis and treatment
- parents may be very aware of IEM and armed with internet data
- offer counselling regarding further pregnancies as soon as possible

In general adult medicine

- important IEM can present, eg haemochromatosis, Wilson's disease, hypercholesterolaemia, antitrypsin deficiency, cystinuria, porphyrias, multiple endocrine neoplasias
- the lab can help and advise you how to investigate
- be ready to suspect an acute porphyria with relevant acute symptoms, investigate appropriately; suspect and test possible skin porphyrias; be aware of skin-plus-acute porphyrias, also acquired porphyria
- inherited homocystinurias differ from acquired hyperhomocystinaemia

## DIABETES MELLITUS

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**Main topics: Insulin, OGTT, HbA1c, ketoacidosis, hypoglycaemia**

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Physiology

- understand normal carbohydrate metabolism
- understand production and action of insulin
- understand actions of glucagon, adrenaline, growth hormone, cortisol
- understand hormonal control of glucose metabolism and its relationship to the metabolism of triglycerides, free fatty acids and ketone bodies

Diabetes

- understand aetiology and clinical features of IDDM, NIDDM
- understand the secondary causes of diabetes
- understand diabetic complications and relationships to glycaemic control
- understand gestational diabetes
- note MODY

Biochemical diagnosis and monitoring

- appreciate significance of hyperglycaemia and glycosuria
- know WHO criteria for diagnosis using OGTT
- understand difference between frank diabetes and impaired glucose tolerance
- understand importance of correct sampling (fluoride-oxalate v. serum)
- appreciate common artefacts (drip arm, old samples)
- understand blood/urine monitoring using 'stix', glucometers

- understand HbA1c and microalbuminuria
- appreciate the place of insulin, proinsulin and C peptide measurements
- understand non-diabetic causes of glycosuria

#### Ketoacidosis

- understand pathophysiology
- understand clinical and biochemical features
- understand biochemical responses to treatment
- understand in particular the role of  $[K^+]$ ,  $[HCO_3^-]$  and water balance in the diagnosis and therapy

#### Hyperosmolar, non-ketotic hyperglycaemia

- understand pathophysiology
- understand clinical and biochemical features
- understand biochemical responses to treatment

#### Lactic acidosis

- be aware of historical association with biguanides
- understand the non-diabetic causes

#### Hypoglycaemia

- know clinical features
- appreciate differences between reactive and fasting hypoglycaemia
- understand relationships to insulin and sulphonylureas
- be aware of PHHI (persistent hyperinsulinaemic hypoglycaemia of infancy), insulinoma and other endocrine causes and their diagnosis
- understand neonatal hypoglycaemia and its causes

## ACID BASE BALANCE

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**Main topics: blood gases, metabolic acidosis, respiratory acidosis, metabolic alkalosis, respiratory alkalosis, compensation, therapy**

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#### Blood gases

- understand how the sample is taken and the major precautions
- understand the parameters reported, including  $[H^+]$  and pH,  $pCO_2$ , total  $CO_2$ , standard  $[HCO_3^-]$ , actual  $[HCO_3^-]$  and base excess.
- understand the  $CO_2/HCO_3^-$  buffer system
- understand the mechanisms of renal regulation of  $[H^+]$
- understand the mechanism of respiratory regulation of  $[H^+]$

#### Metabolic acidosis

- understand the major causes including lactic acidosis, renal tubular acidosis, renal failure, diabetic ketoacidosis, acetazolamide and salicylates
- understand and calculate the anion gap and the significance of hyperchloraemia and hypochloraemia in metabolic acidosis

#### Respiratory acidosis

- understand the major causes

#### Metabolic alkalosis

- understand the major causes

#### Respiratory alkalosis

- understand the major causes including salicylates

**Compensation**

- understand how primary and compensatory changes are distinguished by blood gas, and urea and electrolyte analysis

**Therapy**

- understand the principles and the dangers

**LIPIDS**

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**Main topics: Physiology, epidemiology, hypercholesterolaemia, hypertriglyceridaemia**

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**Physiology**

- understand the metabolism of the major lipoproteins of serum
- understand the role of the major lipoproteins, circulating lipoprotein enzymes and lipoprotein receptors
- understand triglyceride metabolism
- understand cholesterol metabolism
- understand the VLDL LDL link between the two

**Epidemiology**

- understand the relationships between cholesterol, atherosclerosis and other factors including smoking and hyperhomocysteinaemia

**Hypercholesterolaemia**

- understand the major causes, modes of clinical presentation, consequences, investigations and treatment

**Hypertriglyceridaemia**

- understand the major causes, modes of clinical investigation, consequences, investigations and treatment.

## CURRICULUM IN MEDICAL MICROBIOLOGY

This tabulated curriculum provides a guide to the standard required: a student who shows several significant gaps in knowledge in the areas “in depth knowledge” and “familiarity” categories (these include the core topics) would be unlikely to pass. A student who lacks gaps in these areas and demonstrates a good level of understanding of this knowledge, and shows some knowledge of several areas in “passing knowledge” and “heard of” categories, would be in the running for a distinction. The course aims to build a clinical perspective on to the scientific basis of micro-organisms and infection, and on to the practical experience you gained of manipulating micro-organisms, in the pre-clinical course. The tabulated Core Curriculum in Microbiology includes those areas of the syllabus that were mainly covered in the pre-clinical course. We have little time to review these areas during the Block Course, but we remind you of such information when it is vital to understanding of the new material.

Textbooks in microbiology rapidly go out of date, and many on the market are:

- too detailed and advanced, and/or
- too focussed on laboratory aspects of micro-organisms, and/or
- too focussed on clinical aspects of patient management.

Hence, we provide handouts for most lectures and symposia in the Microbiology course. Our handouts in microbiology are aimed to present the necessary information in a way that will be of practical use to you when you are house staff dealing with patients. Such core information is sometimes **boxed** or **highlighted** to make it clearer.

Extra information appears as smaller font text: this may be about less common infections, drugs or syndromes, or may cover the scientific or patho-physiological background to infectious diseases. Many of our handouts also give references to recent reviews or primary publications in the medical literature, and occasionally web-based resources - these are recommended to students who wish to read further, at distinction standard.

The well-rounded student will be able at the end of the course to view their microbiological knowledge from several perspectives: for example, the questions:

- which micro-organisms commonly cause wound infection?
- which infections are commonly caused by *Staphylococcus aureus*?
- which antibiotics are often used to treat *Staphylococcus aureus* infections?
- name some infections commonly treated with flucloxacillin.
- which antibiotics are often used to treat IV catheter infections?

all draw on the same closely-related fund of knowledge.

### LECTURES

In microbiology, we cover most (but not all) the topics in the “in depth knowledge” and “familiarity” sections of the core curriculum during the lectures and tutorials.

### PODCASTS

There are also a number of Microbiology podcasts, which have been developed by the Microbiology lecturers to cover some of the major microbiological topics in the core curriculum.

### TUTORIALS

In microbiology these are usually case-based, and we encourage a high degree of student participation. They are usually based on written details of cases, which are therefore similar in format to the Data Handling questions in the final examination. The aims are for students to involve themselves in the management of real cases, to see the impact of their diagnostic and therapeutic decisions, and to appreciate the interaction of the microbiology laboratory with clinical services in and out of hospital.

Please read the relevant lecture notes and look at the appropriate CBL resources before the sessions - it is a waste of resources if these sessions have to become mini-lectures because of lack of preparation on the part of the participants! Because of time limitations elsewhere in the course, some new primary knowledge is introduced during

these sessions. We do not have enough staff to allocate a single tutor to groups of students throughout their course, and students may have the same broad subjects covered by a bacteriologist or a virologist.

## CURRICULUM IN MEDICAL MICROBIOLOGY

Relative importance	Use of the laboratory in diagnosis	Prevention of infection	Clinical syndromes
<p><b>In depth knowledge</b></p> <p>{You will need an in-depth knowledge, and be able to integrate pathogenesis, epidemiology, treatment, and prevention of infections, with clinical manifestations and rational laboratory investigation.</p> <p>i.e. you will be expected to answer questions on these topics}</p>	<p><b>TAKING SAMPLES:</b> Value of clinical details. Confidentiality, safety. Direct microscopy.</p> <p><b>PRINCIPLES OF BACTERIAL CULTURE &amp; PCR:</b> Blood, CSF. Urine, Faeces. Bacterial and viral swabs: nose, throat, skin, genitals</p> <p>Interpretation of common reports: significance of isolates, choice of further investigations, guidance of empirical and definitive antimicrobial therapy; and infection control significance of results.</p>	<p><b>Immunisation:</b> H. influenzae type b (Hib) Pneumococcus Tetanus MMR Influenza Hepatitis B VZV</p> <p>Antibiotic prophylaxis for Clean + prosthetic surgery, Gut surgery, Endocarditis, and Meningitis.</p> <p>Infection control principles: Isolation, Handwashing. Asepsis. Avoidance of needlestick injuries.</p>	<p>Common causes, rational investigation and empirical treatment of:</p> <p>Septicaemia. Meningitis &amp; encephalitis UTI. Cellulitis, Surgical &amp; traumatic wound infection. Infection of IV catheters &amp; prostheses. Rashes. Pneumonia (including atypical pneumonia) Hepatitis. Diarrhoea. Neonatal infection Rash &amp; fever in pregnancy. Post-delivery &amp; congenital infection.</p>
<p><b>Familiarity</b></p> <p>{You will need to be conversant with these subjects, and understand the principles of pathogenesis (etc.) as above.</p> <p>i.e. you may also get questions on these topics.}</p>	<p>Relative speed, reliability, costs of microbiological tests.</p>	<p><b>Immunisation:</b> Diphtheria Hepatitis A <i>Mycobacterium tuberculosis</i> (BCG)</p> <p>Principles of management of needlestick injuries (HIV).</p> <p>Antibiotic and immunisation prophylaxis after splenectomy.</p>	<p>Osteomyelitis &amp; septic arthritis. Sinusitis &amp; Otitis media. Sore throat. Bronchitis, Bronchiolitis. Aspiration pneumonia. Avian influenza Hospital-acquired pneumonia. Lung abscess &amp; Empyema. Cholangitis, Peritonitis. Fever &amp; diarrhoea in the returning traveller. Fever, rash, pneumonia, meningitis &amp; diarrhoea in the immuno-compromised &amp; HIV.</p>
<p><b>Passing knowledge</b></p> <p>{You will need to understand just the major principles of these topics: for example, give one use for each antibiotic, or when each organism may be relevant in differential diagnosis}</p>	<p>Nucleic acid-based diagnosis.</p> <p>Principles of ELISA.</p> <p>Evidence base for common testing strategies (eg value of throat swab before treating sore throat or MSU before treating cystitis); cost effectiveness principles.</p> <p>Concept of pre-and post-test probability of diagnosis.</p>	<p>Antiseptics &amp; disinfectants. Autoclaves.</p> <p>Other immunizations: Polio, Pertussis. Typhoid &amp; Cholera.</p> <p>Chemoprophylaxis of TB, malaria.</p> <p>Use of immunoglobulins in therapy &amp; prophylaxis.</p> <p>Other prophylaxis: Immunocompromised patients, UTI</p>	<p>Conjunctivitis. Bites. Dental sepsis. Otitis externa. Typhoid Toxin-mediated food poisoning Possible bioterrorism clinical presentations Dengue fever</p>
<p><b>Heard of</b></p>	<p>Methods for typing of bacteria, viruses.</p> <p>Whole genome sequencing</p>	<p>Operating theatre design.</p> <p>Rabies immunization.</p>	<p>Endophthalmitis. Infective &amp; reactive arthritis Diabetic foot infections. Tropical sprue, Whipples. Neutropenic &amp; Neonatal enterocolitis. Epiglottitis Middle East respiratory syndrome coronavirus</p>



Relative importance	Antimicrobial agents	Organ systems	Micro-organisms
<p><b>In depth knowledge</b></p> <p>{You will need an in-depth knowledge, and be able to integrate pathogenesis, epidemiology, treatment, and prevention of infections, with clinical manifestations and rational laboratory investigation.</p> <p>i.e. you will be expected to answer questions on these topics}</p>	<p>1-2 pharmacokinetic facts, 2-3 major uses and 1-2 major side effects of each:</p> <p>Penicillins (ordinary, broader-spectrum groups plus flucloxacillin). Cephalosporins (oral, parenteral, broad-spectrum groups; 1-2 from each). Gentamicin. Ciprofloxacin. Erythromycin, clarithromycin. Vancomycin. Metronidazole. Aciclovir, ganciclovir, Zanamivir Oseltamivir</p> <p>Current resistance problems (MRSA, pneumococci, MDRTB, VRE)</p>	<p>Infections of: CSF. Lungs. Upper respiratory tract. GIT. Bladder. Kidney. Genitalia. Endocarditis. Skin &amp; soft tissues. Lymphadenopathy.</p> <p>2-3 antibiotics frequently used for infections of each of the above systems.</p>	<p>Basic bacteriology of (eg know Gram stain reaction, rod/coccus/spiral, facultative aerobe/anaerobe, common diseases caused by, virulence factors of, 2-3 antibiotics commonly used to treat):</p> <p><i>Staph aureus, epidermidis, saprophyticus.</i> <i>Strep. pyogenes.</i> <i>Strep. pneumoniae.</i> Lancefield gp. B streps. <i>Mycobacterium tuberculosis.</i> <i>Clostridium perfringens &amp; tetani</i> <i>Neisseria meningitidis + gonorrhoeae.</i> <i>E coli.</i> <i>Campylobacter.</i> <i>Shigella.</i> <i>Non-typhi Salmonella.</i> <i>Corynebacterium diphtheriae.</i> <i>Pseudomonas aeruginosa,</i> <i>Mycoplasma pneumoniae,</i> <i>Pneumocystis jiroveci</i></p> <p>Hepatitis A, B, C. HSV, VZV, CMV, EBV. Influenza viruses. Measles. Parvovirus. HIV. <i>Toxoplasma, Chlamydia,</i></p>
<p><b>Familiarity</b></p> <p>{You will need to be conversant with these subjects, and understand the principles of pathogenesis (etc.) as above.</p> <p>i.e. you may also get questions on these topics.}</p>	<p>Penicillins (other groups). Trimethoprim. Norfloxacin.</p> <p>Fluconazole</p> <p>Principles of susceptibility testing.</p> <p>Importance of monitoring of gentamicin and vancomycin serum concentrations.</p> <p>Principles of anti-HIV therapeutics.</p>		<p>Principles of viral (eg HIV, Herpes viruses) and bacterial replication.</p> <p>Very basic bacteriology of (eg know some of Gram stain reaction, rod/coccus/spiral, facultative aerobe/anaerobe, common diseases caused by, 1 antibiotic commonly used to treat):</p> <p><i>Salmonella typhi</i> <i>Viridans</i> and group D streptococci <i>Clostridium difficile, Bacteroides fragilis.</i> <i>Legionella.</i> <i>Candida.</i> <i>Cryptosporidium, Giardia, Entamoeba histolytica.</i> <i>Plasmodium</i> (Malaria). Parvovirus, Enteroviruses incl. polio. Rabies Novoviruses/SRSV/Norwalk etc.</p>
<p><b>Passing knowledge</b></p> <p>{You will need to understand just the major principles of these topics: for example, give one use for each antibiotic, or when each organism may be relevant in differential diagnosis}</p>	<p>Antibiotic resistance mechanisms. Cephalosporins (long half-life, broad-spectrum oral groups). Tetracyclines Teicoplanin Synercid, Linezolid. Rifampicin. Fusidic acid. Chloramphenicol. Nitrofurantoin. Isoniazid, Ethambutol Amphotericin. Nystatin. Famciclovir, valaciclovir, foscarnet. Valganciclovir</p>	<p>Eye. Brain. Cystic fibrosis.</p>	<p><i>Vibrio.</i> <i>Bacillus anthracis &amp; cereus</i> <i>Haemophilus.</i> <i>Strep 'milleri'</i> <i>Helicobacter.</i> <i>Treponema.</i> <i>Borellia</i> (Lyme disease). <i>Clostridium botulinum.</i> <i>Listeria.</i> <i>Leptospira.</i> Non-tuberculous mycobacteria. <i>Aspergillus.</i> <i>Cryptococcus.</i> <i>Enterobius vermicularis.</i> <i>Coxiella.</i></p>

<b>Heard of</b>	Mupirocin Azithromycin Netilmicin, amikacin Sulphonamides Flucytosine, griseofulvin, terbinafine, voriconazole, caspofungin. Mebendazole, Antimalarials. Cidofovir		<i>Brucella.</i> <i>Moraxella. Yersinia, Aeromonas.</i> <i>Fusobacterium.</i> <i>Rickettsia.</i> <i>Leishmania, Trypanosoma.</i> <i>Toxocara, Taenia, Trichuris, Hookworms.</i> <i>Ascaris, Strongyloides, Schistosoma.</i> Microsporidia, Cyclospora.
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Relative importance	Epidemiology	Mechanisms of pathogenicity
<p><b>In depth knowledge</b></p> <p>{You will need an in-depth knowledge, and be able to integrate pathogenesis, epidemiology, treatment, and prevention of infections, with clinical manifestations and rational laboratory investigation.</p> <p>i.e. you will be expected to answer questions on these topics</p>	<p>Principles of commensalism and pathogenicity. Understand principles of reservoirs, routes and portals of infection.</p> <p>Concept of herd immunity. Principles of vaccination strategies.</p>	<p>Principles of toxigenicity, adhesion, invasion.</p> <p>Principles of host defence.</p> <p>Primary, sometime, opportunist &amp; latent pathogens.</p> <p>Mechanisms of diseases CMV, HSV, VZV, HIV</p>
<p><b>Familiarity</b></p> <p>{You will need to be conversant with these subjects, and understand the principles of pathogenesis (etc.) as above.</p> <p>i.e. you may also get questions on these topics. }</p>	<p>Sources, reservoirs, routes of transmission, &amp; principles of control of common outbreaks in and out of hospital.</p> <p>Normal flora of important body sites (eg 2-3 organisms found in mouth, throat, nose, gut, skin).</p>	<p>Principles of mechanisms of disease caused by:</p> <p>Staphs, Streps, <i>E. coli</i> (EIEC, VTEC, ETEC, uropathogenic)</p> <p>Splenectomy &amp; infection. Neutropenia &amp; infection.</p> <p>Parvovirus, influenza, measles, norovirus</p>
<p><b>Passing knowledge</b></p> <p>{You will need to understand just the major principles of these topics: for example, give one use for each antibiotic, or when each organism may be relevant in differential diagnosis}</p>	<p>Examples of practical uses for typing of bacteria and viruses</p>	<p>Principles of mechanisms of diseases caused by: <i>Salmonella</i>, <i>Shigella</i>, <i>V. cholerae</i>.</p> <p>Glycocalyx as a virulence factor.</p> <p>Endotoxaemia.</p> <p>Rabies</p>
<p><b>Heard of</b></p>		

**CURRICULUM IN HAEMATOLOGY**

<b>Relative Importance</b>		<b>Anaemia</b>	<b>White cells/platelets</b>
<b>In depth</b>	Bone marrow function  Structure and function normal bone marrow and blood cells Clonal and reactive proliferation	Symptoms and signs of anaemia  Causes of anaemia  Laboratory investigation of anaemia  Iron deficiency anaemia  Causes of microcytosis  Megaloblastic anaemia  Causes of macrocytosis	Symptoms and signs of neutropenia  Symptoms and signs of thrombocytopenia or abnormalities of function
<b>Familiarity</b>		Haemolysis  Thalassaemia and sickle cell anaemia  Anaemia of chronic disease	Main causes of neutropenia  Management neutropenia sepsis  Investigation of thrombocytopenia  Main causes of thrombocytopenia – immune, viral + drug induced
<b>Passing knowledge</b>	Control of haematopoiesis		Aplastic anaemia
<b>Heard of</b>			Hereditary cytopenias

<b>Relative Importance</b>	<b>Bleeding disorders</b>	<b>Thrombophilia</b>	<b>Myeloproliferative disorders</b>
<b>In depth</b>	<p>Normal clotting system -</p> <p>Basic coagulation tests – PT, APTT Fibrinogen</p> <p>Clinical presentation of different types of bleeding disorders</p> <p>Haemophilia A + B and von Willibrand's disease – presentation and clinical manifestations</p> <p>Inheritance</p>	<p>Patient risk groups for thrombosis</p> <p>Primary and secondary prevention of venous and arterial thrombosis</p> <p>Anticoagulant therapy – heparin, warfarin. Mode of action, administration, monitoring, complications and their management</p>	<p>Classification: Polycythaemia, essential thrombocythaemia, myelofibrosis, chronic myeloid leukaemia</p> <p>Differentiation of clonal disorders from reactive processes: eg secondary polycythaemia – hypoxia, thrombocytosis - infection inflammation, malignancy by clinical history, examination and laboratory investigations</p>
<b>Familiarity</b>	<p>Laboratory investigations and principles of therapy in haemophilias. Prognosis and complications of therapy</p> <p>Disseminated intravascular coagulation</p>	<p>Inherited thrombophilias Protein C,S Antithrombin Factor V Leiden prothrombin mutations</p> <p>Lupus anticoagulant</p> <p>Laboratory investigations of thrombophilia</p>	<p>Polycythaemia rubra vera and essential thrombocythaemia therapy and prognosis</p> <p>Chronic myeloid leukaemia and myelofibrosis – clinical and laboratory findings Clinical course and therapy</p>
<b>Passing knowledge</b>	Molecular basis of bleeding disorders	Molecular basis of thrombophilias	<p>Relative polycythaemia</p> <p>Cytogenetic and molecular findings in CML</p>
<b>Heard of</b>	TTP/HUS		

<b>Relative Importance</b>	<b>Paraproteinaemia</b>	<b>Leukaemia</b>	<b>Lymphoma</b>
<b>In depth</b>	Myeloma – clinical, radiological and laboratory findings  Prognosis and treatment  Monoclonal gammopathy of uncertain significance	Classification into acute or chronic and lymphoid or myeloid (AML, ALL, CML, CLL)  Clinical and laboratory presentation	Clinical presentation Staging
<b>Familiarity</b>		Epidemiology.  Treatment strategies – observation to single agent or combination chemotherapy.  Supportive care  Prognosis  Myelodysplasia	Management strategies  Clinical course
<b>Passing knowledge</b>	Waldenstrom's macroglobulinaemia	Prognostic features in acute leukaemia in particular cytogenetic abnormalities	
<b>Heard of</b>		Bone marrow/stem cell transplantation	

<b>Relative Importance</b>	<b>Transfusion Medicine</b>
<b>In depth</b>	<p>Red cell transfusion - safe and optimal use of blood</p> <p>Red cell antigens ABO Rhesus D Compatibility testing</p> <p>Transfusion reactions, recognition, prevention and management</p>
<b>Familiarity</b>	<p>Blood components – FFP, Cryoprecipitate and platelets</p> <p>Risks and prevention of transmission of infection including donor issues</p> <p>Strategies to avoid exposure to donor blood</p> <p>Massive transfusion</p> <p>Issues around vCJD and transfusion</p>
<b>Passing knowledge</b>	Albumin
<b>Heard of</b>	<p>Red cell substitutes</p> <p>Virus inactivation of red cells, platelets and FFP</p> <p>Therapeutic apheresis</p>

## CURRICULUM IN CLINICAL IMMUNOLOGY

Relative Importance	Immunopathology of the Autoimmune Diseases	Immune Deficiency Syndromes
<b>In-depth Knowledge</b>	<u>systemic:</u> rheumatoid arthritis SLE scleroderma/CREST Sjogren's syndrome  <u>organ specific:</u> diabetes (IDDM) thyroiditis chronic gastritis adrenalitis myasthenia gravis	immunopathogenesis of HIV infection  inherited and acquired hypogammaglobulinaemia  complement deficiencies  consequences of splenectomy  neutrophil dysfunction syndromes  DiGeorge syndrome  inherited severe combined immunity deficiencies
<b>Familiarity</b>	glomerulonephritis*  vasculitis*	development and neonatal immunity  immunological consequences of immunosuppression
<b>Passing Knowledge</b>	autoimmune liver disease  pemphigus & pemphigoid  autoimmune neuropathies  polymyositis	principles of immuno-therapy & reconstitution

\*histopathological aspects of these diseases can be found in the Histopathology Curriculum



## CURRICULUM IN MEDICAL GENETICS

The parts of the core curriculum which are particularly addressed in the Clinical Pathology Block Course are marked with an asterisk. Other parts are covered in Phase III.

1. Be able to construct a family pedigree.
2. \*Be able to determine from a family pedigree the most likely mode(s) of inheritance.
3. \*Appreciate the implications of a genetic diagnosis for patients, offspring and relatives.
4. Be aware of the anxieties caused by genetic disorders to patients and their relatives.
5. Be familiar with sources of information about genetic diseases and be aware of common genetic disorders (eg Cystic Fibrosis) and common inherited cancer susceptibility syndromes (eg HNPCC, FAP, BRCA).
6. Be aware of the function and organisation of genetic services and how to make referrals.
7. \*Understand the importance of establishing a specific genetic diagnosis.
8. \*Understand the general approaches to determining the genetic status of relatives.
9. \*Appreciate the complexity of genetic disease and the pitfalls of determining genetic risks.
10. \*Be aware of the range of genetic investigations available and their limitations.
11. \*Be able to interpret molecular genetic and cytogenetic laboratory reports.
12. Understand the principles of non-directive counselling.
13. Know about reproductive options and general approaches to prenatal diagnosis.
14. \*Understand the principles of multifactorial inheritance and their relevance to common diseases.
15. Appreciate the ethical and social aspects of medical genetics, particularly with regard to genetic testing (including presymptomatic diagnosis and the testing of children).

## **SPECIMEN FORMATS OF MCQs**

### **1) One-from-five Multiple Choice Questions (1:5 MCQ)**

The scoring system is: +1 for a correct response; 0 for an incorrect response; 0 for no response.

**During the 24 hours before the Pathology exam, the wise medical student:**

- a. decides it's really time to buy a pathology textbook of my own
- b. looks at the computer based learning programs for the first time
- c. brings out his or her seventh colour of highlighter to complete the rainbow of scholarship
- d. complains "I never had enough time to look through all this stuff"
- e. says "I can't know it all, I don't need to know it all", and gets a good night's sleep

Answer: e

Further examples of MCQs are on the VLE / MedPortal.