CARDIOVASCULAR/RESPIRATORY MODULE
Part 1 – Cardiovascular System

HANDBOOK FOR MODULE 2
Part 1 - Cardiovascular System

24th October to 3rd November 2016

UNDERGRADUATE MEDICAL CURRICULUM

UNIVERSITY OF SHEFFIELD
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PLEASE REFER TO THE PHASE HANDBOOK FOR DETAILS OF:

- Assessments
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- Library regulations
- Students with a disability – English language teaching centre, Dyslexia
- Working in a clinical setting
- The Medicine, Dentistry and Health Graduate Statement
INTRODUCTION AND WELCOME

Please read this Handbook carefully – it contains much of the information you need for the course, as well as important information about the examinations!!!

This module is concerned with the structure and function of the cardiovascular and respiratory systems. The module will use a variety of approaches to teach normal structure and function, with case studies illustrating the problems that can arise when abnormalities occur. This handbook focuses on the cardiovascular system and I will refer to this as the ‘CVS module’.

The cardiovascular system is designed to transport and distribute essential materials to all the cells of the body and to remove the waste products that they generate. It is also involved in such homeostatic mechanisms as the regulation of body temperature, humoral communication and protection from infection. Cardiovascular diseases are major causes of morbidity and mortality and affect patients of all age groups.

Please do not hesitate to contact the relevant lecturer or myself, as appropriate, and feel free to give formal or informal feedback about the academic organisation of the module at any time. If for whatever reason you are getting into academic difficulties with the course, let us know sooner rather than later. Many problems when addressed early can be solved before they get too serious! Any purely administrative matters should, in the first instance, be discussed with Karen Kehtarnavaz in the Student Affairs section of the Faculty Office on C Floor, address as below.

All staff involved in teaching the CVS module hope that you will find it interesting and enjoyable, and that you will gain an understanding of the basic properties of the cardiovascular system. We would welcome your opinion on all aspects of the module and your feedback will help us to introduce improvements.

Professor R Storey
CVS Module Coordinator

CVS Module Coordinator
Professor R Storey
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The Medical School
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Phase 1 Administrator

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STRUCTURE OF THE MODULE

The Teaching Staff
The University of Sheffield is a leading research-led institution. Consequently many of the staff who you will meet during this (and subsequent) modules are leaders in their field either nationally or internationally. All are accomplished and experienced teachers.

<table>
<thead>
<tr>
<th>Professor R Storey (CVS Module Co-ordinator)</th>
<th>Dr W Sumaya</th>
</tr>
</thead>
<tbody>
<tr>
<td>Professor of Cardiology and Honorary Consultant Cardiologist</td>
<td>Clinical Research Fellow</td>
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<tr>
<td>Department of Infection, Immunity and Cardiovascular Disease</td>
<td>Department of Infection, Immunity and Cardiovascular Disease</td>
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<tr>
<td>University of Sheffield</td>
<td>University of Sheffield</td>
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<td>The Medical School</td>
<td>The Medical School</td>
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<tr>
<td>Beech Hill Road, Sheffield S10 2RX</td>
<td>Beech Hill Road, Sheffield S10 2RX</td>
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<tr>
<td>Email: <a href="mailto:r.f.storey@sheffield.ac.uk">r.f.storey@sheffield.ac.uk</a></td>
<td>Email: <a href="mailto:w.sumaya@sheffield.ac.uk">w.sumaya@sheffield.ac.uk</a></td>
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<thead>
<tr>
<th>Dr D Hampshire</th>
<th>Dr T J Chico</th>
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<tbody>
<tr>
<td>Postdoctoral Research Associate</td>
<td>Reader and Honorary Consultant in Cardiology</td>
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<tr>
<td>Department of Infection, Immunity and Cardiovascular Disease</td>
<td>Department of Infection, Immunity and Cardiovascular Disease</td>
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<td>Medical School</td>
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<tr>
<td>Beech Hill Road, Sheffield S10 2RX</td>
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<tr>
<td>Email: <a href="mailto:d.hampshire@sheffield.ac.uk">d.hampshire@sheffield.ac.uk</a></td>
<td>Email: <a href="mailto:t.j.chico@sheffield.ac.uk">t.j.chico@sheffield.ac.uk</a></td>
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<table>
<thead>
<tr>
<th>Dr K Suvarna</th>
<th>Professor J Gunn</th>
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<tbody>
<tr>
<td>Consultant Histopathologist</td>
<td>Professor of Interventional Cardiology and Honorary Consultant Cardiologist</td>
</tr>
<tr>
<td>Department of Histopathology</td>
<td>Department of Cardiovascular Science</td>
</tr>
<tr>
<td>Sheffield Teaching Hospitals NHS Foundation Trust</td>
<td>University of Sheffield,</td>
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<tr>
<td>Northern General Hospital</td>
<td>The Medical School</td>
</tr>
<tr>
<td>Herries Road, Sheffield S5 7AU</td>
<td>Beech Hill Road</td>
</tr>
<tr>
<td>Email: <a href="mailto:s.k.suvarna@sheffield.ac.uk">s.k.suvarna@sheffield.ac.uk</a></td>
<td>Sheffield S10 2RX</td>
</tr>
<tr>
<td>Email: <a href="mailto:J.Gunn@sheffield.ac.uk">J.Gunn@sheffield.ac.uk</a></td>
<td>Email: <a href="mailto:Abdallah.Al-Mohammad@sth.nhs.uk">Abdallah.Al-Mohammad@sth.nhs.uk</a></td>
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<tr>
<th>Professor N Wheeldon</th>
<th>Dr A Al-Mohammad</th>
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<tr>
<td>Consultant Cardiologist and Honorary Professor in Inherited Cardiac Conditions</td>
<td>Consultant Cardiologist</td>
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<tr>
<td>Sheffield Teaching Hospitals NHS Foundation Trust</td>
<td>Sheffield Teaching Hospitals NHS Foundation Trust</td>
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<td>Northern General Hospital</td>
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<tr>
<td>Herries Road, Sheffield S5 7AU</td>
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<tr>
<td>Email: <a href="mailto:Nigel.Wheeldon@sth.nhs.uk">Nigel.Wheeldon@sth.nhs.uk</a></td>
<td>Email: <a href="mailto:Abdallah.Al-Mohammad@sth.nhs.uk">Abdallah.Al-Mohammad@sth.nhs.uk</a></td>
</tr>
<tr>
<td>Dr S Laidlaw</td>
<td>Dr E Kritsotakis</td>
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</table>
| Department of Haematology  
Sheffield Teaching Hospitals NHS Foundation Trust  
Northern General Hospital  
Herries Road, Sheffield S5 7AU  
Beech Hill Road, Sheffield S10 2RX  
Email: stuart.laidlaw@sth.nhs.uk | Lecturer in Epidemiology & Statistics  
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<table>
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<tr>
<th>Dr W Parker</th>
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</thead>
</table>
| Clinical Research Fellow  
Department of Infection, Immunity and Cardiovascular Disease  
University of Sheffield  
The Medical School  
Beech Hill Road, Sheffield S10 2RX  
Email: w.parker@sheffield.ac.uk |
AIMS AND OBJECTIVES OF THE CVS MODULE

The aims and objectives indicate the topics to be covered and provide an outline of what you are expected to know by the end of the module. Individual lecture outlines provide information about the material to be covered, the prior knowledge that is required, the clinical relevance of the topic and, where appropriate, references for additional reading.

Aims

This module aims to

- Deliver teaching that is relevant to clinical practice;
- Deliver teaching that allows students to meet the outcome criteria of the curriculum;
- Ensure that students have the necessary information technology and gathering skills needed to complete the course;
- Study the cardiovascular system using an approach that integrates structural and functional aspects.
- Examine the basic structure and function of the cardiovascular system, the mechanisms involved in its regulation;
- Encourage students to use non-contact time to prepare for lectures and practicals and to consolidate core information given in the formal teaching sessions;
- Encourage students to become self-directed learners;
- Give students an opportunity to assess their own progress in formative assessment sessions;
- Provide academic support where necessary;
- Provide students with opportunities to evaluate and comment on the module.

Objectives

At the end of this module, students will have acquired knowledge and understanding of:

Heart

- The basic structure of the heart and surrounding tissues at both the macroscopic and microscopic levels.
- The embryonic development of the heart.
- The ionic bases of cardiac and pacemaker action potentials and the conduction of electrical activity through the heart.
- The electrocardiogram (ECG), recognise its main elements and some basic pathologies such as heart block.
- The pressure changes that occur in the ventricles during the cardiac cycle and relate them to the actions of the valves, the flow of blood and the ECG.
- Cardiac output, and be able to show how it is related to heart rate and stroke volume and outline methods used in its measurement.
- The cellular energy sources in the heart.

Circulation

- The components of the blood and understand their physiological functions
- The general arrangement of the circulation and distinguish between systemic and pulmonary circulations.
- The structure of arteries, capillaries and veins and show how the structure of a vessel relates to its functions.
- The biophysics of the circulation.
- Give an account of the microcirculation and the formation of tissue fluid.
• Explain abnormalities in the circulation illustrated in ILA case presentations in terms of the underlying basic science.

**Control of the cardiovascular system**

• How blood pressure is generated.
• Intrinsic and extrinsic mechanisms that regulate cardiac output.
• Intrinsics and extrinsic mechanisms that regulate peripheral resistance.
• Blood pressure control by regulation of cardiac output and peripheral resistance.
• The effects of posture and exercise on cardiovascular function.
• The fetal circulation and the changes that occur at birth.
STUDENT EVALUATION OF THE MODULE
Student evaluation of the course is one of the most important tools we have to assess whether the aims and objectives have been met. The course continues to evolve in response to comments from students.

At the end of the module you will be asked to complete evaluation questionnaires and to make any free-text comments you may have about the module. When evaluating the module, please avoid making offensive personal remarks about individuals. Such comments will result in your feedback being discarded. I hope that you will make every effort to be constructive in your criticisms and give feedback on the positive aspects of the module as well as any negative comments. A small number of you may also be asked to attend an evaluation session with a member of the faculty staff. Please take student evaluation of the module seriously – we do! In addition to the formal module evaluations, you can pass comments to your student Year Representative, who can present such feedback to the Phase 1 Committee and to the Staff-Student Committee.
<table>
<thead>
<tr>
<th>No</th>
<th>Question</th>
<th>Strongly Disagree</th>
<th>Disagree</th>
<th>Agree</th>
<th>Strongly Agree</th>
<th>Not answered</th>
<th>Mean</th>
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<td>1.</td>
<td>The aims of the module were stated clearly in the Phase handbook</td>
<td>0</td>
<td>3 (4%)</td>
<td>57 (69%)</td>
<td>23 (28%)</td>
<td>0</td>
<td>3.2</td>
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<tr>
<td>2.</td>
<td>The aims of the module were met</td>
<td>0</td>
<td>1 (1%)</td>
<td>66 (80%)</td>
<td>16 (19%)</td>
<td>0</td>
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<tr>
<td>3.</td>
<td>Objectives of the module were stated clearly</td>
<td>0</td>
<td>2 (2%)</td>
<td>58 (70%)</td>
<td>23 (28%)</td>
<td>0</td>
<td>3.3</td>
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<td>4.</td>
<td>The module has allowed me to achieve the objectives</td>
<td>0</td>
<td>2 (2%)</td>
<td>65 (78%)</td>
<td>16 (19%)</td>
<td>0</td>
<td>3.2</td>
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<tr>
<td>5.</td>
<td>The module Handbook (available via My Teaching) was useful</td>
<td>0</td>
<td>14 (17%)</td>
<td>56 (67%)</td>
<td>13 (16%)</td>
<td>0</td>
<td>3.0</td>
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<tr>
<td>6.</td>
<td>There was no unnecessary overlap of subject areas</td>
<td>0</td>
<td>9 (11%)</td>
<td>55 (66%)</td>
<td>19 (23%)</td>
<td>0</td>
<td>3.1</td>
</tr>
<tr>
<td>7.</td>
<td>Staff were approachable/helpful</td>
<td>0</td>
<td>1 (1%)</td>
<td>55 (66%)</td>
<td>27 (33%)</td>
<td>0</td>
<td>3.3</td>
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<tr>
<td>8.</td>
<td>The workload for the module was about right</td>
<td>0</td>
<td>5 (6%)</td>
<td>55 (66%)</td>
<td>23 (28%)</td>
<td>0</td>
<td>3.2</td>
</tr>
<tr>
<td>9.</td>
<td>The Integrated Learning Activities encouraged my learning</td>
<td>4 (5%)</td>
<td>10 (12%)</td>
<td>41 (49%)</td>
<td>28 (34%)</td>
<td>0</td>
<td>3.1</td>
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<tr>
<td>10.</td>
<td>The on-line histology practicals were helpful</td>
<td>5 (6%)</td>
<td>15 (18%)</td>
<td>48 (58%)</td>
<td>12 (14%)</td>
<td>3 (4%)</td>
<td>2.8</td>
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<td>11.</td>
<td>I enjoyed the module</td>
<td>0</td>
<td>2 (2%)</td>
<td>44 (53%)</td>
<td>36 (43%)</td>
<td>1 (1%)</td>
<td>3.4</td>
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<td>12.</td>
<td>The module was well-organised</td>
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<td>7 (8%)</td>
<td>56 (67%)</td>
<td>19 (23%)</td>
<td>1 (1%)</td>
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LECTURE OUTLINES

The remainder of this handbook contains the lecture outlines to accompany the CVS module. Please note that you will receive separate handbooks for the anatomy and histology practical classes.

You are urged to read through the lecture outlines and the practical class handbooks in advance of each lecture/practical so that you can undertake some preparatory work for each session. There is plenty of ‘empty’ time in the timetable to accommodate such reading and preparation work. Additionally, it is anticipated that you will spend time in the evenings studying!

Remember – the core curriculum (i.e. that which can be examined) includes all material covered in the lectures, practicals and ILAs as well as the information in the lecture outlines, the lecture presentations posted on Minerva, and the recommended reading (where given) for each lecture. These information sources define the limits of the minimum that you need to know by the end of the module. Recommended reading is the BARE MINIMUM you are expected to complete and because it is examinable, you are urged to read it! You are welcome to read beyond that and further reading is suggested (or can be suggested by the lecturers) to help you read beyond the core if you wish.

This is a spiral curriculum. At the end of this module you are expected to understand the material within the module only to the depth and breadth covered in the module. You will revisit some subjects again in more depth later in the course, at which point you will be expected to have a deeper knowledge.

The formative assessments in this module have been written with examination revision in mind. To answer the questions it is assumed you have attended the lectures and practicals AND completed the recommended reading.
CRITICAL NUMBERS 1: Risk (Part A: quantifying risks)
(This lecture will be given during the Introductory module)

Dr E Kritsotakis

Lecturer in Epidemiology & Statistics
School of Health and Related Research
The University of Sheffield
Email: e.kritsotakis@sheffield.ac.uk

Aims:
This session aims to present measures of risk and the different ways risks can be estimated in medical research.

Session objectives:
At the end of the lecture, students should be able to:

- Explain the concepts of probability and odds as measures of risk.
- Interpret conditional probabilities in terms of natural frequencies of disease occurrence.
- Explain how risk can be estimated using a sample incidence proportion.
- Briefly describe the problems of variable follow-up and losses to follow-up when estimating risks and explain the use of incidence density rates to address these problems.
- Distinguish between: cumulative incidence, prevalence, attack rate, and case fatality rate.

Core Clinical Problems:
This lecture relates to all core clinical problems.

Assumed knowledge:
None

Relevance to medical practice:
Poor understanding of statistical measures of the risk of diseases, adverse effects of drugs or other medical interventions may cause misinterpretation of the risks of harms. This may have an impact on treatment decisions and might also affect medication adherence. The 1995 contraceptive pill scare and the 2002 menopausal hormone therapy scare in UK, for example, highlight the importance of helping doctors and patients understand risk information. Particularly confusing are single event probabilities and odds, conditional probabilities (such as the sensitivity and the positive predictive value of diagnostic tests), and relative risks. Moreover, lack of standardised terminology and frequent use of the different terms for the same purpose (e.g. “risk” and “rate”) in clinical trials and epidemiological studies seem to raise more confusion. The first two lectures in the “Critical Numbers” series aim to address these difficulties by providing a primer on the measures of risk and the different ways risks can be estimated, compared and communicated in medical research.

Lecture outline:
Risk literacy: The lecture begins with a short video to introduce the concept of risk and how risk is perceived and communicating in practice.

Quantifying and interpreting risk: Main measures of risk are defined, including probability and odds. Simple calculations are illustrated and the utility of natural frequencies to interpret and communicate conditional probabilities (e.g. sensitivity and specificity of diagnostic tests) is presented.

Estimating risk: The idea of estimating risk using a sample incidence proportion is introduced. Important drawbacks such as competing risks and losses to follow-up and variable follow-up are noted. The utility of the incidence density rate is demonstrated. The link with other
commonly used terms such as cumulative incidence, prevalence, attack rate, and case fatality rate is also noted. The notion of the hazard rate is presented briefly and it is noted that such instantaneous rates are difficult to estimate but the hazard function comes close.

Communicating risks: Perceptions created by the different ways in which risks are described and factors influencing the perception of risk are noted throughout the lecture.

**Recommended reading:**

- Martyn C. Risky business: doctors’ understanding of statistics. BMJ 2014;349:g5619. Available from: http://www.bmj.com/content/349/bmj.g5619 Responses and debates to issues raised in this article are at http://www.bmj.com/content/349/bmj.g5619/rapid-responses


- Hopk

**Videos:**

- Risk literacy by Gerd Gigerenzer. Available at: https://www.youtube.com/watch?v=g4op2WNc1e4

**Further reading:**

CONSTITUENTS OF THE BLOOD: RED AND WHITE BLOOD CELLS

Dr D Hampshire

Postdoctoral Research Associate

Department of Infection, Immunity and Cardiovascular Disease
University of Sheffield
Medical School
Beech Hill Road, Sheffield S10 2RX
Email: d.hampshire@sheffield.ac.uk

Aims
This session aims to:
• Introduce the cellular components of the blood and their functions

Objectives
At the end of this lecture students will be able:
• To describe the structure and function of erythrocytes
• To describe the structure and function of white cells

Core Clinical Problems
This lecture is relevant to problems:
1 Anaemia
2 Bleeding

Assumed Knowledge
Introductory haematology lecture on The Blood in Week One of the IMMS module.

Relevance to Medical Practice
Anaemia, leukaemia, infection, bleeding and thrombosis are commonly encountered disorders with a variety of causes. An understanding of these pathologies first requires understanding of the constituents of the blood.

Lecture Outline
Formation of the blood Haematopoiesis sites related to age, stem cells, growth factors and erythrocytes, life spans and apoptosis
Red cells Number and structure Haemoglobin and oxygen carriage
White cells Neutrophil structure and function Lymphocytes: B cells T cells
Platelets Origins and numbers Structure and function

Recommended Reading

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<th>Chapter</th>
<th>Page Number</th>
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<tr>
<td>Formation of Blood – Haematopoiesis, sites related to age, stem cells, growth factors and erythrocytes, life spans and apoptosis – <strong>Chapter 1</strong></td>
<td></td>
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<tr>
<td>Red Cells – number and structure, haemoglobin, oxygen carriage – <strong>Chapter 2</strong></td>
<td>Pages 12-27</td>
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<td>None.</td>
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CONSTITUENTS OF THE BLOOD: PLATELETS AND PLASMA

Dr D Hampshire

Postdoctoral Research Associate

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University of Sheffield
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Email: d.hampshire@sheffield.ac.uk

Aims
This session aims to:
• Introduce the plasma component of the blood and the function of plasma proteins.

Objectives
At the end of this lecture students will be able:
• To describe the structure and function of platelets
• To describe the constituents and function of the plasma proteins.

Core Clinical Problems
This lecture is relevant to problems:
1 Bleeding

Assumed Knowledge
Introductory haematology lecture on The Blood in Week One of the IMMS module.

Relevance to Medical Practice
Bleeding and thrombosis are commonly encountered disorders with a variety of causes. An understanding of these pathologies first requires understanding of the coagulation system.

Lecture Outline

Plasma Proteins
Albumin and oncotic pressure
Immunoglobins
Carrier proteins
Coagulation proteins and the coagulation cascade
Inhibitors of coagulation

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<tr>
<th>Recommended Reading</th>
<th>Chapter</th>
<th>Page Number</th>
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<tbody>
<tr>
<td>Platelets – origins and numbers, structure and function, decreased and increases numbers – Chapter 22</td>
<td></td>
<td>Pages 264 - 277</td>
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</tbody>
</table>

Further Reading
None.
Aims
This session aims to:
• Examine the development of the heart in utero.

Objectives
By the end of this session the student will:
• Understand and be able to describe the steps involved in the embryological development of the heart

Core Clinical Problems
This lecture is relevant to problems:
45 Cardiac arrest/sudden death
47 Chest pain
54 Palpitations/abnormal heart rhythm

Assumed Knowledge
None

Relevance to Medical Practice
Understanding the embryology of the heart enables the student to understand abnormalities of this development leading to congenital cardiac abnormalities.

Lecture Outline
The heart is one of the few organs which must FUNCTION as well as mature and grow from a very early stage of fetal development. It must continue to function during fetal life, while changing rapidly during the early stage of gestation.

The heart develops from a group of cells in the cardiogenic plate. These cells coalesce and form two parallel 'cardiac tubes'. These tubes then fuse to form one central tube – the heart tube. This heart tube folds and rotates on itself in a particular manner as it elongates. The heart chambers and great vessels are formed by a process of septation, walls which form and grow in particular positions leading to the formation of a structurally normal heart.

This is a very complex process. It is hardly surprising that it sometimes goes wrong.

Recommended Reading

Further Reading


www.med.unc.edu/embryo_images/unit-cardev/cardev_hyms/cardevtoc.htm

www.meddean.luc.edu/lumen/MedEd/GrossAnatomy/thorax0/Heart_Development/HeartIndex.html
STRUCTURE AND EMBRYOLOGY OF THE CIRCULATION

Dr Tim Chico

Lab D38
Centre for Developmental and Biomedical Genetics
Firth Court
Western Bank
t.j.chico@sheffield.ac.uk

Aims
This lecture aims to:
• Outline the general structure of the circulation.
• Outline the histological features of arteries, veins, and capillaries.
• Discuss arterial and venous identity.
• Outline the formation of the mammalian vasculature from early embryonic, to fetal, into post-natal stages.

Objectives
At the end of the lecture, students will;
• Understand the differences between arteries, veins and capillaries, and be familiar with the terms vasculogenesis and angiogenesis.
• Have a working knowledge of how the early embryonic vasculature is patterned.
• Understand how the embryonic aortic arch pattern becomes the post-natal pattern.
• Be aware of some of the medical conditions associated with failure of the vascular structure, or abnormal embryonic patterning.

Core Clinical Problems
This lecture is relevant to problems:
46 Chest pain
47 Leg pain/swelling
49 Cyanosis

Assumed Knowledge
You should understand what a cell is.
You should understand what blood is.
You should understand what a somite is.

Relevance to Medical Practice
The circulation is the first working organ in the developing embryo, and understanding its structure is fundamental to understanding common adult diseases such as aneurysms, or coronary artery disease. In addition, understanding the patterning of the embryonic vasculature is required to understand the causes of vascular malformations which may result in embryonic death, or present to the paediatrician or cardiologist after birth.

Lecture Outline
Basic plan of the circulation
The basic plan of the (mammalian) circulation is that oxygenated blood is pumped from the left ventricle into the arterial system, which carries blood into its smaller branches (arterioles) until finally it reaches the smallest, thinnest vessels (capillaries) where the blood can perform its purpose, namely provision of oxygen to tissues, and removal of waste products of metabolism, such as carbon dioxide. Blood (now deoxygenated) then passes into the venous system, returning to the right ventricle, where it is pumped to the lungs via the pulmonary arteries. Again, blood passes through arterioles into a capillary network, where it is reoxygenated and looses carbon dioxide by its proximity to the air spaces in the lungs (alveoli). Finally, blood passes back into the left ventricle via the pulmonary veins; this is the double circulation seen in animals with lungs.
Structure of blood vessels

Blood vessels (other than capillaries) conform to a general structural pattern. They are made up of three layers, each layer made up of specialized cell types. A layer of endothelial cells lines the vessel (the tunica intima). These are non-thrombogenic (blood does not clot in contact with these cells). Outside the tunica media is a variably thick layer of vascular smooth muscle cells (the tunica media). These contract and relax according to signals from the endothelium or from nerves, increasing or decreasing blood flow. The most external layer (the tunica adventitia) is a loose layer of fibroblasts with capillaries supplying blood to the cells of the blood vessel itself (the vasa vasorum).

Capillaries are mainly endothelium sitting on a basement membrane, with a patchy smooth muscle layer. There are three types of capillary, dependent upon the pattern of the endothelium. Continuous capillaries, as the name suggests, have an uninterrupted layer of endothelium, whilst fenestrated capillaries (found in the kidney, endocrine glands, and small intestine) have gaps in between the endothelium to allow passage of larger molecules into and out of the circulation. Sinusoidal capillaries (found in the liver and spleen) have even larger gaps to allow passage of cells in between the endothelium.

Arterio-venous identity

Although veins and arteries conform to a similar structure, they differ in several ways. The smooth muscle layer (tunica media) in arteries is thicker in arteries than in veins. In addition, veins possess valves allowing blood to pass only in one direction (failure of these valves leads to varicose veins).

It has been previously thought that these differences were simply due to the different blood flow requirements expected of arteries and veins. Indeed, when a vein is surgically placed into an arterial position (i.e. during coronary artery bypass grafting), the vein becomes “arterialized”, with a much thicker medial layer. However, studies on embryonic vascular development suggest that the identity of arteries and veins is fixed even before the first embryonic heartbeat (see below).

Embryology of the vasculature

Early after fertilization, three layers can be distinguished in the mass of dividing cells that makes up the developing embryo. These are termed the ectoderm, endoderm, and mesoderm. Amidst the mesoderm (the lateral mesoderm to be more precise) are the cells which will become the first blood vessels, called the angioblasts. In addition, outside the embryo itself is an area of mesoderm (extraembryonic mesoderm) from which develop “blood islands”. These are haemoblasts (blasts means a precursor, haemoblasts are precursors of blood) surrounded by endothelial cells.

Vasculogenesis

Between embryonic day 17-21 the endothelial cells of the blood islands spread out to form blood vessels around the yolk sac, chorionic villus and stalk. At day 18, the angioblasts in the lateral mesoderm migrate along the centre of the developing embryo (rostro-caudally, i.e. from head to tail) to form an early vascular loop for the embryonic heart to beat into. This migration is called vasculogenesis.

Somehow, these angioblasts know whether they will be either a vein or an artery, even before any blood is circulating. There are a number of molecules on the surface of the endothelium which are only expressed by arterial or venous endothelium. An example of an arterial specific molecule is Ephrin B2. An example of a venous specific molecule is EphB4, the receptor for Ephrin B2.

Angiogenesis

After the primitive vascular loop is laid in place by vasculogenesis, endothelial cells proliferate and migrate off this loop to form new blood vessels (in a process called angiogenesis), for
example the vessels running between the somites. This process is guided by a number of molecules that either attract the migrating endothelium, or repel it from taking a wrong direction (for example the semaphorins). Angiogenesis is thought to be the mechanism whereby cancers co-opt a blood supply, without which they would not be able to develop beyond a certain size.

Embryology of the aortic arches
Early after onset of the embryonic heart beat, human embryos have a vascular pattern very similar to fish. A heart, with a single atrium and ventricle, pumps blood into a bulbus arteriosus, which pumps blood into the aortic arches which run between the somites of the upper embryo. This pattern has to somehow remodel into the human pattern, and this remodeling occurs between 6-8 weeks.

To summarise what happens to the aortic arches:
- There is no fifth aortic arch in humans.
- The first aortic arch becomes part of the maxillary artery.
- The second aortic arch becomes the artery to stapedius.
- The portion of the dorsal aorta between the third and fourth aortic arches disappears, and the third aortic arches become the common carotid arteries, and proximal internal carotid arteries (the distal internal carotids come from extension of dorsal aortae).
- The right dorsal aorta looses its connection with the midline aorta and 6th arch, remaining connected to the right 4th arch. It acquires the branch 7th cervical intersegmental artery, and the resulting vessel grows into the right upper limb to become the right subclavian artery.
- The left fourth arch becomes the arch of the aorta.
- The left dorsal aorta becomes the descending aorta.
- The right sixth arch becomes part of the pulmonary trunk.
- The left sixth arch becomes the ductus arteriosus.
(This will definitely make sense if you look at the website below, or possibly if you attend the lecture.)

If this process goes wrong, it can lead to clinical consequences such as a right sided or double aorta, or an aortic coarctation.

Recommended Reading

Further Reading
http://www.indiana.edu/~anat550/cvanim/
This highly recommended website’s animations make the process of aortic arch remodeling very clear, and are also useful for other aspects of cardiovascular embryology. There is a helpful self-test section to prepare you for the exam!
ELECTRICAL ACTIVATION OF THE HEART (CELL)

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Aims
The sessions aims to:
• provide students with knowledge of electrical events occurring in the specialised tissues of the heart during the cardiac cycle.

Objectives
At the end of this session students will be able to describe:
• The initiation and conduction of electrical activity across the heart.
• The ionic basis of the pacemaker and cardiac muscle cell action potentials.

Core Clinical Problems
This lecture is relevant to problems:
  45  Cardiac arrest/sudden death
  54  Palpitations/abnormal heart rhythm

Relevance to Medical Practice
Cardiovascular disease is extremely common and is the commonest cause of death in the UK. An understanding of the physiological control of blood pressure is essential to understand the causes of low and high blood pressure, and the treatment for these problems.

Assumed Knowledge:
Basic cardiac anatomy and cell structure

Lecture Outline:
• General basis of the cell membrane potential
• Initiation of electrical activity at the sino atrial node.
• Spread of electrical activity at different velocities through the cardiac tissues.
• AV nodal delay and refractory period.
• Ionic basis of the pacemaker cardiac action potential.
• Control of the pacemaker action potential - neural input, overdrive suppression and latent/ectopic pacemakers.
• Ionic basis of the cardiac muscle action potential.

Recommended Reading:

Further Reading
None
CRITICAL NUMBERS 2: Risk (Part B: comparing risks)

Dr E Kritsotakis

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Aims:
This session aims to present different ways in which risks can be compared and communicated in medical research.

Session Objectives:
At the end of the lecture, students should be able to:
Define what the risk ratio, the odds ratio and the risk difference of an outcome are,
Interpret the value of a risk ratio, an odds ratio and a risk difference in terms of exposure and outcome association.
Define number needed to treat and explain its use as a measure of the effectiveness of a clinical procedure.

Core Clinical Problems:
This lecture relates to all core clinical problems.

Assumed knowledge:
Critical Numbers lecture 1.

Relevance to Medical Practice:
Poor understanding of statistical measures of the risk of diseases, adverse effects of drugs or other medical interventions may cause misinterpretation of the risks of harms. This may have an impact on treatment decisions and might also affect medication adherence. The 1995 contraceptive pill scare and the 2002 menopausal hormone therapy scare in UK, for example, highlight the importance of helping doctors and patients understand risk information. Particularly confusing are single event probabilities and odds, conditional probabilities (such as the sensitivity and the positive predictive value of diagnostic tests), and relative risks. Moreover, lack of standardised terminology and frequent use of the different terms for the same purpose (e.g. “risk” and “rate”) in clinical trials and epidemiological studies seem to raise more confusion. The first two lectures in the “Critical Numbers” series aim to address these difficulties by providing a primer on the measures of risk and the different ways risks can be estimated, compared and communicated in medical research.

Lecture Outline:
Risk communication: The lecture begins with a short video to demonstrate issues related to the perceptions created by the different ways in which risks can be compared and the relevance of the topic in clinical medicine.

Comparing risks: The use of ratios and differences to compare risks is presented and discussed, including the risk ratio, the odds ratio and the risk difference. The relative merits of using ratios and differences to compare risks are discussed. The use of ratios as measures of effect to address the aetiology of a disease/health outcome in clinical studies is outlined, as is the use of differences as measures of potential impact to quantify the public health importance of factors that are determinants of a disease/health outcome. Finally the number needed to treat is introduced and discussed as an effort-to-yield measure which if useful to indicate the potential benefit of a clinical procedure to the patients. Perceptions created by the different ways in which risks can be compared are discussed throughout the lecture.
Recommended Reading:
• Martyn C. Risky business: doctors’ understanding of statistics. BMJ 2014;349:g5619. Available from: http://www.bmj.com/content/349/bmj.g5619 Responses and debates to issues raised in this article are at http://www.bmj.com/content/349/bmj.g5619/rapid-responses


Videos:
• Risk literacy by Gerd Gigerenzer. Available at: https://www.youtube.com/watch?v=g4op2WNc1e4

Further Reading:
CRITICAL NUMBERS 3: Risk tutorial

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Aims:
This small group session aims to elaborate and expand on the calculations and the concepts raised during the lectures on the measures of risk and the different ways risks can be estimated, compared and communicated in medical research.

Session Objectives:
At the end of the tutorial, students should be able to:
Calculate single event probabilities, odds and conditional probabilities and interpret these into verbal descriptions of disease occurrence.
Calculate the risk ratio, odds ratio and risk difference from 2x2 tables and interpret the resulting values into verbal descriptions of exposure – outcome association.
Calculate number needed to treat in simple examples and interpret its value into verbal description of the potential benefit of a clinical procedure to the patients
Distinguish between absolute and relative risks (difference and ratio measures) and identify their merits in influencing the perception of risk.
Distinguish between the different measures of (the risk of) disease occurrence, including prevalence and incidence proportions, incidence and hazard rates.

Core Clinical Problems:
This lecture relates to all core clinical problems.

Assumed knowledge:
Previous Critical Numbers sessions.

Relevance to Medical Practice:
Poor understanding of statistical measures of the risk of diseases, adverse effects of drugs or other medical interventions may cause misinterpretation of the risks of harms. This may have an impact on treatment decisions and might also affect medication adherence. The 1995 contraceptive pill scare and the 2002 menopausal hormone therapy scare in UK, for example, highlight the importance of helping doctors and patients understand risk information. Particularly confusing are single event probabilities and odds, conditional probabilities (such as the sensitivity and the positive predictive value of diagnostic tests), and relative risks. Moreover, lack of standardised terminology and frequent use of the different terms for the same purpose (e.g. “risk” and “rate”) in clinical trials and epidemiological studies seem to raise more confusion. This small group session in the “Critical Numbers” series aims to address these difficulties through tutorial exercises and group work on the measures of risk and the different ways risks can be estimated, compared and communicated in medical research.

Tutorial Outline:
This small group tutorial includes exercises designed to facilitate understanding and interpretation of the concepts raised during the corresponding lectures on risk and the calculations involved. Students will spend some of the time working individually, some of the time working in pairs and some of the time as a whole group.
Recommended Reading:
• Martyn C. Risky business: doctors’ understanding of statistics. BMJ 2014;349:g5619. Available from: http://www.bmj.com/content/349/bmj.g5619 Responses and debates to issues raised in this article are at http://www.bmj.com/content/349/bmj.g5619/rapid-responses


Videos:
• Risk literacy by Gerd Gigerenzer. Available at: https://www.youtube.com/watch?v=g4op2WNc1e4

Further Reading:
CRITICAL NUMBERS 4: Study Design & Sampling

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Aims:
This session aims to present major quantitative study designs, sampling plans and their objectives, strengths and limitations. It also serves as an introductory session for a subsequent series of small-group seminars on the critical appraisal of the medical literature.

Session Objectives:
At the end of the lecture, students should be able to:
• Explain the difference between descriptive vs analytic, observational vs experimental, and prospective vs retrospective studies.
• Outline the setup of main observational designs, including case-series, cross-sectional, case-control, cohort and ecological studies, and list their major strengths and weaknesses.
• Explain briefly the problem of confounding.
• Outline the setup of a randomised controlled trial and explain briefly the role of randomisation.
• Identify the link between the choice of measure of effect and the type of study design.
• (Self-study) Distinguish between random and non-random sampling methods.
• (Self-study) Outline major random sampling plans, including: simple, systematic, stratified and clustered.

Core Clinical Problems:
This lecture relates to all core clinical problems.

Assumed knowledge:
Previous Critical Numbers sessions.

Relevance to Medical Practice:
An understanding of the different ways to design research studies is necessary for both practicing clinicians and researchers, to evaluate existing research evidence and to conduct their own research. This is advocated in the GMC document ‘Tomorrow’s doctors’ (2009), which states that “medical graduates must be able to formulate simple relevant research questions in biomedical science, psychosocial science or population science, and design appropriate studies or experiments to address the questions”. Identifying a study’s design is essential to evaluate the study’s level of evidence, limitations and biases and appropriateness of statistical analysis. This lecture, the third in the “Critical Numbers” series, provides an overview of the major features of study designs used in clinical research and discusses their objectives and the most important strengths and weaknesses of these designs. Additional self-study material is provided to explain the setup of commonly employed sampling plans and the major practical merits and shortcomings of these sampling methods.

Lecture Outline:
Aims and classifications of study designs: The lecture begins with illustrating the main objectives of quantitative studies in medical research and clarifies commonly used categorisations related to study objective and existence of a comparison group (descriptive vs analytic), planned allocation of intervention (experimental vs observational), and direction of inquiry and timing of data collection (prospective vs retrospective).
Observational studies: The planning of observational studies is then considered and major designs are outlined: case-reports and case-series, cohort, case-control, cross-sectional and ecological studies. Their uses and importance are illustrated through historical and contemporary examples from the medical research literature. Potential and implications of selection bias and measurement bias are briefly mentioned. The problem of confounding is illustrated through simple examples and presented as a major problem in the interpretation and strength of evidence provided by observational studies. Finally, the choice of effect measure is linked to the design of the study.

Experimental studies: The randomised clinical trial is introduced as the design providing the greatest justification for concluding causality by avoiding confounding through randomisation and by avoiding biases through blinding and its prospective nature.

Sampling: For any study design, it is necessary to define the subjects chosen for the study and sampling plans were discussed as a key component of study design throughout the lecture (e.g. disease-based sampling in case-control, exposure-based sampling in cohort studies, etc). Additional self-study material is provided in order to explain the distinction between random and non-random sampling methods and outline the setup of major random sampling plans (simple, systematic, stratified and cluster). Major practical merits and shortcomings of each sampling plan are also explained briefly.

Recommended Reading:


Videos:
Intro to Epidemiology Study Types. Available at: https://youtu.be/sdFYHSxq_qo
Introduction to Randomized Controlled Clinical trials by Mike Campbell. Available at: https://youtu.be/8_rR-OL0c08?list=PL1mJ7IZ3qFxYjGZ1cf__ZVC08myM

Further Reading:

MOLECULAR MECHANICS OF CARDIAC CONTRACTION

Dr Abdallah Al-Mohammad

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Northern General Hospital
Herries Road, Sheffield S5 7AU

Aims
This session aims to:
• Describe how cardiac myocytes generate contractile force.

Objectives
At the end of this lecture students will be able to:
• Describe how the architecture of cardiac myocytes relates to force generation;
• Describe the sliding filament mechanism of force generation;
• Outline the mechanisms by which force generation is regulated at the cellular and organ level.

Core Clinical Problems
This lecture is relevant to problems:
46 Chest pain
51 Low blood pressure
54 Palpitations/abnormal heart rhythm
55 Raised blood pressure

Assumed Knowledge
Previous lectures in this module.
The cellular structure of cardiac muscle (histology lectures and practicals in IMMS).

Relevance to Medical Practice:
An understanding of cardiac contraction is fundamental to the understanding of the causes and effects of cardiac disease, and hence underpins knowledge of some of the most commonly encountered diseases in medicine.

Lecture Outline:
• Action potential transmission through the T – tubule system.
• Ca^{2+} interactions with the troponin/tropomyosin system.
• The sliding filament hypothesis.
• The length – tension relationship. Isotonic and isometric contraction.
• The force – velocity relationship. Vmax and contractility. Inotropism.
• The frequency – force relationship. The Bowditch staircase.

Recommended Reading

Further Reading

THE CARDIAC CYCLE

Dr Abdallah Al-Mohammad

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Aims
This session aims to:
• Provide students with knowledge of the major mechanical events within the heart and major vessels during the cardiac cycle.

Objectives
At the end of this lecture, students will be able to:
• Describe the pressure changes that occur in the chambers of the heart during the cardiac cycle and to relate them to the actions of the valves, blood flow and the ECG.

Core Clinical Problems
This lecture is relevant to problems:
46 Chest pain
51 Low blood pressure
54 Palpitations/abnormal heart rhythm
55 Raised blood pressure

Assumed Knowledge
• Previous lectures and anatomy practicals in this module
• Basic cardiac anatomy.

Relevance to Medical Practice
Heart disease is extremely common and is the commonest cause of death in the UK. An understanding of the cardiac cycle therefore underpins the understanding, diagnosis and treatment of many diseases commonly encountered in clinical practice.

Lecture Outline
• The cardiac cycle.
• Diastole and systole.
• Atrial and ventricular pressures.
• Valve openings/closures.
• Relationships of the above to the ECG.
• Ejection and re – filling phases.

Recommended reading:

Further Reading

ELECTRICAL ACTIVATION OF THE HEART (ECG)

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Aims
This session aims to:
• Describe how the ionic events that lead to electrical activation of heart muscle are integrated to produce the surface electrocardiogram;
• Describe how the surface electrocardiogram is used clinically.

Objectives
At the end of this lecture students will:
• Understand how the electrical activity within the heart translates to the recordings obtained by a surface electrocardiogram
• Have a preliminary understanding of how these recordings are used in clinical practice.

Core Clinical Problems
This lecture is relevant to problems:
45 Cardiac arrest/sudden death
46 Chest pain
54 Palpitations/abnormal heart rhythm

Assumed Knowledge
Previous lectures and basic cardiac anatomy
Physiology practicals in IMMS

Relevance to Medical Practice
The electrocardiogram is a widely used method for studying the electrical activity of the heart in clinical practice and plays an important role in the investigation of chest pain, palpitations, and other cardiovascular disorders.

Lecture Outline
This lecture describes the surface ECG and how this is used for clinical diagnosis and monitoring.

Recommended reading
PLATELET BIOCHEMISTRY

Professor R Storey

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Aims
This session aims:
• To describe the biochemical mechanisms leading to platelet activation and functional responses of platelets that follow platelet activation

Objectives:
At the end of this lecture students will be able:
• To understand the essentials of platelet biochemistry that will form a foundation for later teaching about platelet pharmacology and arterial thrombosis

Core Clinical Problems
This lecture is relevant to problems:
2  Bleeding
46  Chest pain

Assumed Knowledge
Introductory lecture on The Blood in Week One of IMMS. Constituents of Blood lectures in this module.

Relevance to Medical Practice
Platelets play a central role in arterial thrombosis which is a significant cause of morbidity and mortality in the UK, and indeed occurs in many cases of fatal ischaemic heart disease. An understanding of the causes and treatment of arterial thrombosis is therefore something that is essential for every junior doctor.

Lecture Outline
Pathways of platelet activation and the role of surface receptors
The roles of glycoprotein IIb/IIIa
Contents of platelet granules
Thromboxane A2 formation as an amplification system in platelet activation
Adenosine diphosphate as an amplification system in platelet activation
Platelet procoagulant activity

Overview of platelet biology
Great advances have been made in the understanding of platelet biology over the last 20 years with knowledge about platelet surface receptors and signalling pathways and this has also enhanced understanding about the action of current antiplatelet agents as well as leading to the development of novel agents. It is now recognised that soluble platelet agonists such as thrombin, ADP, 5 hydroxytryptamine (5HT, otherwise known as serotonin) and thromboxane A2 activate specific receptors that are linked to the G protein Gq (and, for some agonists, other G proteins) and this leads directly to platelet activation. Collagen and other adhesive ligands in the vessel wall, which are exposed following endothelial injury, initiate platelet activation via different signalling pathways that are linked to activation of phospholipase A2, which leads to
the formation and secretion of thromboxane $A_2$ as well as directly activating platelets. This is relevant to understanding how aspirin works.

Platelets release dense granule contents upon activation and these contain high concentrations of ADP and ATP as well as 5HT. These soluble agonists then act on platelet surface receptors to amplify platelet activation. There are two ADP receptors on the platelet surface, P2Y$_1$ and P2Y$_{12}$. The P2Y$_{12}$ receptor is linked to Gi and plays a major role in amplification of platelet activation. Since dense granules are secreted in response to any agonist stimulation, the P2Y$_{12}$ receptor plays a central role in amplification of platelet responses regardless of the stimulus.

The glycoprotein IIb/IIIa receptor (integrin $\beta_{IIIb}\alpha_3$) is converted to an active form upon platelet activation, binding fibrinogen and other ligands, and this allows cross-linking of platelets that culminates in platelet aggregation. Subsequently, further signalling occurs through this receptor, known as ‘outside-in’ signalling, that amplifies platelet activation.

Platelet activation results in not only platelet aggregation and dense granule secretion but also the following processes: (1) $\alpha$ granule secretion, which promotes coagulation and inflammation; and (2) changes in the platelet surface membrane that allow assembly of the prothrombinase complex and catalysis of thrombin generation (‘platelet procoagulant activity’). These processes play an important role in arterial thrombosis and the associated inflammation.

**Recommended reading**

**Further Reading**
None
STRUCTURE OF THE HEART

Professor N Wheeldon

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Aims
This session aims to:
• Relate the gross anatomy and histology of the heart to its function.

Objectives
At the end of this lecture students should be able to:
• Describe the relationship between cardiac ultrastructure and function.
• Describe the function of various structures found within the heart.
• Recognise the importance of the coronary circulation.
• Understand the origin and fetal function of structures such as the ovalis.
• Understand how structural differences between cardiac, skeletal and smooth muscle relate to function.

Core Clinical Problems
This lecture is relevant to problems:
45 Cardiac arrest/sudden death
47 Chest pain
54 Palpitations/abnormal heart rhythm

Assumed Knowledge
A basic understanding of the general anatomy and ultrastructure of the heart.

Relevance to Medical Practice
Heart disease is extremely common and is the commonest cause of death in the UK. An understanding of the structure and function of the heart therefore underpins the understanding, diagnosis and treatment of many diseases commonly encountered in clinical practice.

Lecture Outline
Basic gross structure and general histology of the heart. Function of endocardium, myocardium and epicardium and structures such as purkinje fibres, papillary muscles, valves, atrial endocrine cells, etc. Importance of the coronary circulation. Ultrastructure of cardiac, smooth and skeletal muscle and how the differences relate to function.

Clinical Cardiac Anatomy - Key Points
1. Apex beat: Left 5th intercostal space, mid-clavicular line
2. Right heart border: SVC – right atrium
3. Left heart border: Aortic knuckle – left pulmonary artery – LA appendage – left ventricle
4. Anteriorly: mainly right ventricle
5. Posteriorly: mainly left atrium and pulmonary veins
6. Mediastinum: Area between right and left pleura, divided as follows:
7. Plane between sternal angle and T4/5 divides superior and inferior mediastinum
8. Pericardium divides anterior, middle and posterior mediastinum
9. Pericardium consists of fibrous (parietal) and visceral layers
10. Push your fist into a soft balloon – explains two layers and pericardial reflections
11. Pericardial space is a potential space
12. Rapid collection of pericardial fluid is restricted and impairs filling – cardiac tamponade
13. Pleural reflection allows drainage of pericardial fluid from the left of the xiphisternum
14. Atrioventricular valves (mitral and tricuspid) are an intrinsic part of their ventricle
15. Disorders of the ventricle often affect function of the relevant Atrioventricular valve
16. Papillary muscles (part of ventricle) attach to atrioventricular valves via chordae tendinae
17. Semilunar valves (aortic and pulmonary) are an intrinsic part of their great artery
18. Disorders of the aorta or pulmonary artery often affect function of their respective valves
19. Arterial blood is blood leaving the heart – not always fully oxygenated (PA)
20. Venous blood is blood returning to the heart – not always deoxygenated (PV)
21. The pulmonary artery carries deoxygenated blood from the heart
22. The pulmonary veins carry oxygenated blood back to the heart
23. LV is thick walled and muscular (systemic ventricle)
24. RV has thin muscular wall
25. Atria are thin walled
26. Four pulmonary veins (usually 4) drain into the left atrium
27. Coronary sinus drains blood from the heart muscle into the right atrium
28. Right atrium has smooth (from sinus venosus) and trabeculated (from original atrium) portions
29. Crista terminalis separates smooth and trabeculated portions of right atrium
30. Fossa ovalis is the remains of the foramen ovale which was patent in foetal life
31. Cardiac muscle cells cross link and join at intercalated discs
32. Coronary arteries arise from the aortic root sinuses and supply the heart itself
33. Coronary arteries are epicardial and therefore accessible to the surgeon (bypass surgery)
34. Two main coronary arteries, left and right
35. Coronaries are functional end arteries, unless collateral supply has developed
36. The left main stem divides into left anterior descending (LAD) and circumflex (Cx) branches
37. The LAD runs in the anterior interventricular groove
38. The LAD gives off septal and diagonal branches to the septum and left ventricular myocardium
39. The Cx runs in the left atroioventricular groove
40. The Cx gives off obtuse marginal branches to the posterolateral LV wall
41. In 10% the Cx provides the posterior descending artery (PDA)
42. The RCA runs in the right atrioventricular groove
43. Usually supplies sinus node, AV node and branches to the anterior RV wall
44. Distal RCA branches into posterolateral and posterior descending arteries (latter in about 70% of people)
45. The posterior descending artery runs in the posterior interventricular groove and supplies inferior septum and LV
46. Dominance refers to the artery (RCA or Cx) which supplies the posterior descending artery
47. Most people (70%) are right dominant – RCA supplies the PDA
48. About 20% are co-dominant – RCA and Cx both help supply the PDA
49. About 10% are left dominant – Cx supplies the PDA

**Recommended Reading**

**Further Reading:**
"Histology - a text and atlas". Edited by M.H. Ross & L.J. Romell. Published by Williams Wilkins International.
Aims
This session aims to describe the basic histology of arteries, veins and the heart.

Objectives
At the end of this lecture students should be able to:

- Describe the microscopic substructure of blood vessels and lymphatic vessels
- Describe the histological features of the cardiac myocyte
- Understand the histology of the cardiac conduction system
- Understand how pathological processes may affect the cardiovascular system

Core Clinical Problems
This lecture is relevant to problems:
45 Cardiac arrest/sudden death
47 Chest pain
54 Palpitations/abnormal heart rhythm

Assumed Knowledge
A basic understanding of the general anatomy and ultrastructure of the heart.

Lecture Outline
The microscopic substructure of blood vessels (arteries/veins/lymphatics). The normal cardiac myocyte. The conduction system. Pathology affecting the cardiovascular system.

Recommended Reading
Human Histology. A. Stevens, J.S. Lowe.
Aims
This session aims to:
• Describe the general feedback loops involved in the maintenance of circulatory homeostasis and normal blood pressure.

Objectives
At the end of this lecture, the students will:
• be able to state the goal of the controlling mechanisms of the circulation;
• have a reasonable knowledge of the role of components of the peripheral circulation as effectors;
• be able to describe the site, mechanisms and effects of arterial and cardiopulmonary baroreceptors, their afferent pathways and central radiation/location and their role in circulatory control;
• be able to describe the site, mechanisms and effects of central chemoreceptors, their afferent pathways and central radiation/location and their role in circulatory control;
• be able to describe the principle of a feedback loop and its role in circulatory control;
• be acquainted with Cushing’s phenomenon and the possible mechanisms involved.

Core Clinical Problems
This lecture is relevant to problems:
  51  Low blood pressure
  55  Raised blood pressure

Assumed Knowledge
Previous lectures in this module.

Relevance to Medical Practice
Cardiovascular disease is extremely common and is the commonest cause of death in the UK. An understanding of the physiological control of blood pressure is essential to understand the causes of low and high blood pressure, and the treatment for these problems.

Lecture Outline
This lecture describes mechanisms which control the circulation, focusing on the mechanisms of the various receptors that regulate the circulation and blood pressure. These mechanisms are an example of feedback loops, and these play a central role in the maintenance of homeostasis.

Recommended Reading:

Further Reading  None
PERIPHERAL CONTROL OF THE CIRCULATION AND BLOOD PRESSURE

Professor Julian Gunn

Professor & Hon. Consultant cardiologist
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Aims
This session aims to:
• Describe the concepts and determinants of blood flow, blood pressure and cardiac output

Objectives
At the end of this lecture, students will understand:
• The concepts and determinants of blood flow, blood pressure and cardiac output

Core Clinical Problems
This lecture is relevant to problems:
19 Fall, collapse
46 Chest pain
51 Low blood pressure
53 Oedema
55 Raised blood pressure
56 Dyspnoea

Assumed Knowledge
Previous lectures in this module.

Relevance to Medical Practice
Cardiovascular disease is common and is the commonest cause of death in the UK. An understanding of the physiological regulation of blood pressure and blood distribution is essential to understand the causes and treatment of high blood pressure, fainting, heart failure, angina and shock.

Lecture outline
• General principles: determinants of blood flow; arterioles; resistance
• Peripheral control: intrinsic and extrinsic
• Blood pressure
• Cardiac output and the Frank-Starling mechanism
• Relevance

Recommended reading:

BLOOD GROUPS AND BLOOD TRANSFUSIONS
(This lecture has been rescheduled to a later date)

Dr S Laidlaw
Department of Haematology
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Herries Road
Sheffield

Aims
This session aims:
• To introduce blood groups and their relevance
• To introduce the safe transfusions of red cells and blood components

Objectives
At the end of this lecture students will be able:
• To describe blood groups, especially the ABO and Rhesus systems
• To describe the rhesus and method of blood transfusions
• To describe alternatives for blood transfusions
• To describe the use of non-red cell components

Core Clinical Problems
This lecture is relevant to problems:
1 Anaemia
2 Bleeding

Assumed Knowledge
Introductory lecture on The Blood in Week One of IMMS. Constituents of Blood lecture in this module.

Relevance to Medical Practice
Blood transfusions are commonly given during surgery, when treating trauma and other medical conditions. An understanding of human blood groups is essential to the safe administration of blood transfusions.

Lecture Outline
Blood groups their number and variety
The ABO system Structure
Naturally occurring antibodies
Consequences for transfusions

The Rhesus system The D/d antigen
Its importance
Consequences of antibody formation

Other blood groups
Group and save
Cross match
Indications for transfusion

Hazards of transfusions immediate
long term
infections
Alternatives to transfusions

Transfusion triggers
Cell Salvage
Pre-donation
Erythropoiesis

Other components
Fresh frozen plasma
Cryoprecipitate
Albumin
Anti-D globin
Intravenous immunoglobulin

Recommended Reading

Further Reading
None
FORMATIVE ASSESSMENT AND REVIEW SESSION

Dr William Parker

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Aim
This session aims:
• To discuss the answers to the formative assessment completed this week

Objectives
By the end of this lecture you should be able to:
• Answer and understand the answers to all the questions in this week’s formative assessment
• Have had an opportunity to ask any questions about the content of the formative assessment of other aspects of the teaching in this week

Core Clinical Problems
As for the lectures delivered in the last 1-2 weeks

Assumed knowledge
The content of this week’s lectures and practical classes

Relevance to medical practice
To graduate as a doctor you will need to pass a number of summative assessments. These assessments are designed to ensure that you have acquired the clinical competencies, medical science knowledge and professional attitudes and behaviours that will enable you to practice medicine. Formative assessments are designed to assist your personal studies by showing you how much you know and also by highlighting areas of work on which you need to spend more time.

Patients expect their doctor to be well trained and to be able to demonstrate that they have achieved a suitably high standard of knowledge, skills, behaviours and attitudes. Accordingly, the summative assessments are rigorous and the formative assessments help you reflect on your abilities at many points during the programme as you develop and work towards the summative assessments.

Lecture Outline
In this session we will review the formative assessment questions that you will have completed on Minerva this week (see below). We will consider why the correct answers were correct and why the incorrect answers were wrong. We will explore the range of answers given by the class.

Essential work before this session
Completion and submission of your answers (via Minerva) to this week’s formative assessment.

Recommended reading
You are encouraged to read your lecture notes and textbooks to help you answer the formative assessment questions.

Further reading
None
CRITICAL NUMBERS 5: Confidence and significance (part A)

Dr E Kritsotakis

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The University of Sheffield
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Aims:
This session aims to present statistical inference through the use of confidence intervals and p-values illustrate practical aspects of these methods and discuss their relative merits in medical research and clinical practice.

Session Objectives:
At the end of the lecture (part A), students should be able to:

Specify the difference between sample vs population, statistic vs parameter, and descriptive vs inferential statistics.

Explain what is meant by the terms: standard deviation, sampling variation, sampling distribution, standard error and precision of a sample statistic.

Interpret confidence intervals as applied to means, proportions, mean differences, risk differences, risk ratios and odds ratios.

Determine how to control the width of a confidence interval.

Core Clinical Problems:
This lecture relates to all core clinical problems.

Assumed knowledge:
Previous Critical Numbers sessions.

Relevance to Medical Practice:
Clinical trials and epidemiological studies aim to generate new knowledge on the effectiveness of healthcare interventions, identify disease aetiology and assess prognosis. This involves estimating a key parameter of interest, the size of the effect of an intervention or exposure in a certain population. The findings of a single study provide a point estimate of the effect, and this raises a dilemma: are the findings from this sample also likely to be true about other similar groups of patients? Could any apparent treatment benefit or exposure effect arise simply because of chance? Researchers rely on the p-value to report whether an observed effect is trustworthy or robust (statistically significant). Clinical significance, on the other hand, is a decision based on the practical impact or relevance of a particular treatment or exposure effect, and this may or may not involve statistical significance as an initial criterion. Confidence intervals are one useful way for clinicians to decide if a particular effect (whether statistically significant or not) may be of relevance in practice. This session, consisting of the fourth and fifth lectures in the “Critical Numbers” series, aims to address these issues by providing an introduction to statistical inference through the use of confidence intervals and p-values.

Lecture Outline:
Part A:
Basic ideas in inferential statistics: Basic concepts in statistical inference are explained and contrasted, including sample vs population, statistic vs parameter, and descriptive statistics vs inferential statistics, standard deviation vs standard error.

Sampling distributions and standard errors: Using the notion of repeated sampling, variability in statistics from sample to sample is explained. It is noted that sampling error is expected
when a sample from a population is used to provide estimates of the population parameters. The concept of the sampling distribution of the mean is then illustrated. Standard error is introduced as a measure of the variability in the sampling distribution that indicates the precision of a sample estimate.

Confidence intervals: Using the sampling distribution of the mean and the properties of the Normal distribution it is pointed shortly how an expression for a 95% confidence interval for the population mean is derived. The factors that affect the width of a confidence interval are noted and discussed. Examples from the medical literature are used to illustrate the interpretation of confidence intervals for other statistics, including differences in means and proportions, risk ratios and odds ratios. The basics of calculating confidence intervals are briefly mentioned.

**Recommended Reading:**


**Further Reading:**


CRITICAL NUMBERS 6: Study design and sampling tutorial

Dr E Kritsotakis

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Aims:
This small-group session aims to elaborate and expand on concepts raised during the lecture on quantitative study designs and sampling plans and illustrate practical aspects of these methods. It serves as an introductory session for a subsequent series of small-group seminars on the critical appraisal of the medical literature.

Session Objectives:
At the end of the tutorial, students should be able to:

Recognise the study design, sampling plan, exposure and outcome variables, measure of outcome and measure of effect and identify practical shortcomings and feasibility issues in these choices in pragmatic scenarios of medical research studies.
(Self-study) Draw simple, systematic, cluster and stratified random samples from a given population frame using a table of random numbers.

Core Clinical Problems:
This lecture relates to all core clinical problems.

Assumed knowledge:
Previous Critical Numbers sessions.

Relevance to Medical Practice:
An understanding of the different ways to design research studies is necessary for both practicing clinicians and researchers, to evaluate existing research evidence and to conduct their own research. This is advocated in the GMC document ‘Tomorrow’s doctors’ (2009), which states that “medical graduates must be able to formulate simple relevant research questions in biomedical science, psychosocial science or population science, and design appropriate studies or experiments to address the questions”. Correctly identifying a study’s design is not just an exercise in terminology but helps to evaluate the study's level of evidence, limitations and biases and the appropriateness of statistical analysis. This small-group session in the “Critical Numbers” series aims to address these issues through tutorial exercises and small-group work on the different study designs and sampling plans used in clinical research and their objectives, strengths and limitations. Additional self-study material is provided to work on drawing a sample and using a table of random numbers.

Lecture Outline:
This small-group tutorial includes exercises designed to facilitate understanding and interpretation of the concepts raised during the corresponding lecture on study designs and sampling plans and illustrate practical aspects of these methods. Students will spend some of the time working individually, some of the time working in pairs and some of the time as a whole group. Self-study material is included.

Recommended Reading:


Videos

Intro to Epidemiology Study Types. Available at: https://youtu.be/sdFYHSxq_qo

Introduction to Randomized Controlled Clinical trials by Mike Campbell. Available at: https://youtu.be/8_rR-OL0c08?list=PL1mJ7lZ3qFxiYIj-jGZ1cf__ZVC08mymM

Further Reading:


ILA INTRODUCTION – CHEST PAIN

Online

Aims
This session aims to:
• Launch the Chest Pain ILA

Objectives
At the end of this lecture, students will:
• Appreciate how a patient may present with chest pain and understand some of the contemporary issues related to the management of chest pain

Core Clinical Problems
This session is relevant to problem: 46  Chest pain

Assumed knowledge
None

Relevance to medical practice
Patients frequently complain of chest pain and a firm understanding of the relevant physiology is therefore essential to every junior doctor.

Recommended Reading

Further Reading
None
ILA FORMATIVE ASSESSMENT

Aim
This session aims:
• To discuss the answers to the formative assessment completed this week

Objectives
By the end of this lecture you should be able to:
• Answer and understand the answers to all the questions in this week’s formative assessment
• Have had an opportunity to ask any questions about the content of the formative assessment of other aspects of the teaching in this week

Core Clinical Problems
As for the lectures delivered in the CVS module

Assumed knowledge
The content of the CVS module lectures and practical classes

Relevance to medical practice
To graduate as a doctor you will need to pass a number of summative assessments. These assessments are designed to ensure that you have acquired the clinical competencies, medical science knowledge and professional attitudes and behaviours that will enable you to practice medicine. Formative assessments are designed to assist your personal studies by showing you how much you know and also by highlighting areas of work on which you need to spend more time.
Patients expect their doctor to be well trained and to be able to demonstrate that they have achieved a suitably high standard of knowledge, skills, behaviours and attitudes. Accordingly, the summative assessments are rigorous and the formative assessments help you reflect on your abilities at many points during the programme as you develop and work towards the summative assessments.

Lecture Outline
In this session we will review the formative assessment questions that you will have completed on Minerva this week (see below). We will consider why the correct answers were correct and why the incorrect answers were wrong. We will explore the range of answers given by the class.

Essential work before this session
Completion and submission of your answers (via Minerva) to this week’s formative assessment.

Recommended reading
You are encouraged to read your lecture notes and textbooks to help you answer the formative assessment questions.

Further reading
None