

BSc in Medical Sciences with HAEMATOLOGY

Introduction

The BSc in Medical Sciences with Haematology is directed at students who have an interest in the scientific basis of medical practice. While directed particularly at students with an interest in the blood and its disorders, it also provides generic skills and provides transferable knowledge that can be readily applied to other disciplines.

The course starts with a 2-week introductory course that provides generic skills and some core knowledge. This is followed by three 5-week taught modules and either a research project or a specialist taught course (two 5-week modules).

Course Directors

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Course Administrator

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Aims

- To gain an understanding of the scientific method and of the scientific basis of haematology

Objectives

After taking this course students will:

- Be able to analyse data and critically review scientific articles
- Be able to explain the principles of research techniques commonly used in haematology
- Be able to discuss and explain the scientific basis of many aspects of haematology, including thalassaemia, haemoglobinopathies and other disorders of red cells, malaria and its relationship to red cell polymorphisms, bone marrow failure syndromes, the science of blood transfusion, thrombosis and normal and abnormal haemostasis, leukaemia, lymphoma and multiple myeloma
- Be able to explain how recent research has contributed to knowledge of haematological disorders and how scientific advances are now influencing the diagnostic approach, the design of drugs and the management of the patient
- Be able to relate the underlying science and the results of recent research to the clinicopathological features of haematological disorders and their management
- Be able to write clear, accurate, scientific English
- Be able to make a scientific presentation

Content

- Introductory two weeks
- Module on haemostasis and thrombosis
- Module on leukaemia, lymphoma and multiple myeloma
- Module on red cells and their disorders
- Research project or specialist taught module

Format of teaching

Teaching takes the form of lectures, seminars, journal clubs, videos, computer-assisted learning, practical classes, demonstrations, student presentations and laboratory visits.

There is also the unique possibility of meeting patients with the specific haematological disorders that you are studying, thus enriching your experience.

Introductory two weeks

Module leaders

Professor Barbara Bain

Professor David Lane

Aims

- To provide the student with some of the core knowledge necessary for an understanding of the scientific basis of medicine – gene structure and function, protein structure and function
- To revise some core skills for acquiring knowledge – critically reading and summarising scientific articles, including interpreting clinical trials
- To provide core knowledge of the scientific basis of some fields of haematology – normal and abnormal haemopoiesis, globin genes and some of their disorders, the normal platelet, normal haemostasis, the scientific practice of blood transfusion, immunological aspects of haematology

Objectives

By the end of the introductory course the student should be able to

- Critically evaluate a scientific article, distinguish a good article from a poor article, explain the relevance of statistical tests used including those applied to clinical trials, and summarize the key points of the article
- Perform basic statistical tests and report on the statistical significance and scientific relevance of the results
- Be able to explain/discuss
 - Normal haemopoiesis
 - The genetic control of haemoglobin synthesis and the clinicopathological features of sickle cell disease
 - The scientific basis of blood transfusion
 - The domain structures of the coagulation proteins, their importance in localising and accelerating the coagulation cascade
 - How haemostasis is achieved
 - How clots and thrombi are lysed
 - How the coagulation system is regulated by anticoagulant proteins
 - How platelets are produced, how they function and how their actions can be inhibited
 - How and why leukaemia occurs, using chronic myeloid leukaemia and acute myeloid leukaemia as examples

Module 1: Thrombosis and Haemostasis

Module Leaders

Professor Mike Laffan

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Aims

- To permit the student to acquire knowledge and understanding of normal and abnormal haemostasis and of haemorrhagic and thrombotic disorders
- To permit the student to acquire generic skills and knowledge, as detailed in the course objectives

Objectives

At the end of this module the student should be able to:

- Explain the domain structures of the coagulation proteins, their importance in localising and accelerating the coagulation cascade
- Explain how haemostasis is achieved
- Explain how clots and thrombi are lysed
- Explain the effects of defects in the coagulation pathways
- Explain the molecular origins of the defects and their implications for treatment, genetic counselling and further understanding of haemostasis.
- Explain how molecular knowledge has led to development of recombinant therapeutic proteins and progress in gene therapy
- Explain the pathogenesis of venous and arterial thrombosis.
- Following attendance at haemophilia clinics and thrombophilia clinics, explain the principles and the clinical utility of thrombophilia testing and implications for genetic counselling.
- Explain the scientific basis of oral and parenteral anticoagulation and fibrinolysis
- Evaluate novel therapeutic options, including their theoretical advantages and their likely impact on the future management of patients with thrombotic disease.

Module 2: Leukaemias, lymphomas and multiple myeloma

Module Leaders

Professor Barbara Bain
Dr Sasha Marks

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Aims

- To permit the student to acquire an understanding of the nature of leukaemia, lymphoma and multiple myeloma including their aetiology, pathogenesis, clinicopathological features and the role of oncogenes and tumour suppressor genes in the causation of these disease
- To permit the student to acquire an understanding of the scientific techniques that are leading to new knowledge in this field
- To permit the student to acquire generic skills and knowledge, as detailed in the course objectives

Content

At the end of this module the student should be able to:

- Explain how the cause of leukaemia can be established and describe what is known of the aetiology of acute myeloid leukaemia (AML), acute lymphoblastic leukaemia (ALL), chronic myelogenous leukaemia (CML) and the myelodysplastic syndromes (MDS)
- Describe the main inherited and other constitutional syndromes that predispose towards leukaemias and explain how these syndromes contribute to understanding of leukaemogenesis
- Describe, compare and contrast the clinicopathological features of AML and MDS
- Explain the principles of cytogenetic analysis and be able to interpret a karyotype and a karyogram
- Explain the terms 'oncogene' and 'tumour-suppressor gene' and describe typical oncogenic mechanisms operating in AML, ALL and MDS
- Outline the principle of molecular genetic analysis and be able to give a brief description of the polymerase chain reaction (PCR), reverse transcriptase PCR (RT-PCR) and fluorescence *in situ* hybridisation (FISH)
- Explain how clonality of myeloid cells can be established and the relevance of establishing clonality

- Describe the clinicopathological, cytogenetic and molecular genetic abnormalities of common important subtypes of AML including acute promyelocytic leukaemia
- Describe the clinicopathological, cytogenetic and molecular genetic abnormalities of CML
- Outline the principles of treatment of CML and describe the role of cytogenetic and molecular genetic analysis in monitoring treatment
- Discuss the possibility of cure of AML and CML and how this is influenced by the underlying molecular genetic abnormality
- Describe the clinicopathological, cytogenetic, molecular genetic and immunophenotypic features of acute lymphoblastic leukaemia
- Explain how cytogenetic and molecular genetic analysis has contributed to advancing knowledge in AML, ALL and MDS
- Describe the normal immune system and describe briefly the structure and function of the different classes of immunoglobulin
- Describe the clinicopathological features of chronic lymphocytic leukaemia, non-Hodgkin lymphoma and multiple myeloma
- Explain how the cause of lymphoid neoplasms can be established and discuss what is known of aetiological factors and mechanisms of oncogenesis
- Describe the clinicopathological, cytogenetic, molecular genetic and immunophenotypic features of CLL and typical examples of non-Hodgkin lymphoma (e.g. follicular lymphoma, mantle cell lymphoma, Burkitt lymphoma and adult T-cell leukaemia/lymphoma)
- Explain how the immunophenotype of neoplastic lymphoid cells is established
- Describe the role of immunophenotyping in the differential diagnosis of chronic lymphocytic leukaemia and non-Hodgkin lymphoma
- Describe what is known of oncogenic mechanisms in multiple myeloma, including the role of cytokines
- Describe what is known of the aetiology of Hodgkin lymphoma and describe the clinicopathological features
- Discuss the principles of treatment of lymphoproliferative disorders and multiple myeloma and discuss the prospects of gene therapy in these conditions.

Module 3: Red Cells

Module Leaders

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Professor Irene Roberts

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Aims

- To permit the student to acquire knowledge and understanding of disorders of the red cell
- To permit the student to acquire generic skills and knowledge, as detailed in the course objectives

Objectives

At the end of this module the student should be able to:

- Describe the structure and function of haemoglobin A and explain how haemoglobins A₂ and F differ from haemoglobin A
- Describe the alpha and beta globin gene clusters and explain the control of globin chain synthesis
- Explain what is meant by the terms: beta thalassaemia, beta^o thalassaemia, beta⁺ thalassaemia

- Describe and explain the clinicopathological features of beta thalassaemia minor, beta thalassaemia intermedia and beta thalassaemia major and relate these terms to the possible underlying genetic defects
- Discuss the significance of beta thalassaemia to individual patients and their families
- Diagnose beta thalassaemia trait and explain how other thalassaemia syndromes are diagnosed (including explaining the principles of molecular diagnostic techniques)
- Explain the terms: alpha⁺ thalassaemia and alpha⁰ thalassaemia and describe how they interact to cause haemoglobin H disease and haemoglobin Bart's hydrops fetalis; describe the clinicopathological features of these alpha thalassaemia syndromes
- Describe and explain the basis of the clinicopathological features of common haemoglobinopathies including haemoglobin S (revision of Foundation Course), haemoglobin C and haemoglobin E
- Explain how mutations in globin genes can cause functional abnormalities in haemoglobin (high or low affinity haemoglobins, methaemoglobinaemia, unstable haemoglobins)
- Explain how thalassaemias interact with haemoglobinopathies
- Discuss how antenatal and neonatal screening for haemoglobinopathies are carried out
- Describe normal and abnormal haemopoiesis
- Discuss inherited and acquired bone marrow failure syndromes
- Evaluate the prospects for gene therapy for inherited haematological disorders
- Explain the structure of the red cell membrane
- Explain the function of red cell enzymes and the effects of their deficiency
- Discuss the inherited causes of haemolytic anaemias
- Discuss the pathology of malaria and the effect of malaria and the red cell genome

Modules 4-5

Projects

Most projects will be laboratory-based projects with relevance to clinical haematology; some of them deal with the scientific basis of the discipline while others are more applied; however all are clinically relevant. There may also be some projects that are performed in other departments. There may be a small number of clinical projects.

Past BSc Project Titles in Haematology

- Do differences in size of fetomaternal haemorrhage account for the difference in cord blood cell dose obtained from Black & Asian versus mixed & Caucasian cord blood donors?
- Mechanisms of Angiopoietin 2 interaction with von Willebrand Factor
- Narrative ethics of sickle cell disease: Screening and the patient's perspective
- Comparison of bone marrow aspirate, flow cytometry and bone marrow trephine biopsy to assess multiple myeloma
- Von Willebrand Factor mutations causing Von Willebrand's disease
- NF Kappa B signalling in aggressive lymphomas
- Aurora Kinase genes and CML blast crisis
- The effect of ethnic neutropaenia on CD34+ stem cell mobilisation and engraftment following autologous stem cell transplant in multiple myeloma

- Narrative ethics of sickle cell disease: The media perspective and its relationship with screening policy
- Imatinib Side effects
- Development of serum-free culture conditions for a 3-D ex vivo model of haemopoiesis
- Exploration of the role of CD1d in the Wnt-dependent regulation of haemopoiesis
- Interaction of ADAMTS13 with VWF A2 domain
- Imatinib Side effects
- Role of calcium in ADAMTS13 function
- Bone density in long term survivors of stem cell transplantation
- Experience in the use of bortezomib in the treatment of relapsed multiple myeloma
- The haematopoietic cell transplantation co-morbidity index (HCT-CI) as a tool for risk assessment pre-BMT in CML.
- Narrative ethics of sickle cell disease: The perspective of health care professionals
- Role of the ADAMTS13 cysteine-rich domain
- Role of the ADAMTS13 disintegrin-like domain
- SNP analysis and transplantation
- Analysis of red cell glycolysis and its disorders by mass spectrometry
- The clinical and pathological differences between secondary iron overload due to increased iron absorption and that due to transfusion and implications on the use of chelation therapy
- Insight into initiation of leukaemia in Down syndrome
- Exploration of the role of CD1d in the Wnt-dependent regulation of haemopoiesis
- Changes in B-cell transcription programme and in pattern of aberrant antigen expression in classical Hodgkin lymphoma during disease evolution and its impact on patient outcome.
- Large scale expression and purification of VWF
- Functional characterization of T-cell subsets in CLL patients
- Routine laboratory abnormalities as a marker for response in chronic myeloid patients
- Chronic lymphocytic leukaemia; assessment of apoptosis and proliferation using multi-parameter flow cytometry.

- Production of factor V - role in coagulation and anticoagulation
- Dual cofactor function of protein S
- Epigenetic control of the tumour suppressor gene PTEN in CML
- Role of the ADAMTS13 cysteine-rich domain
- Factor XIII and lytic threshold
- Effect of imatinib on the repair of DNA double-strand-breaks in bcr-abl-negative cells.
- Flow analysis of Von Willebrand Factor collagen binding mutants
- New molecular approaches to potentiate the therapeutic activities of mesenchymal stem cells
- Characterising a Zinc Finger Nuclease targeted to the b-globin gene
- Long-term outcome of donor lymphocyte infusions for the treatment of chronic myeloid leukaemia: tumour eradication or tumour control?
- The Immunoglobulin gene repertoire in B cells
- Role of the TFPI Kunitz domains in anticoagulant function
- Insulin growth factor signalling in normal and leukaemic cells
- Quality of Life after Stem Cell Transplantation
- Secondary malignancies after allogeneic stem cell transplantation
- Plasma determinants of fibrinolysis
- Testing novel proteasome-targeting peptides for effects on myeloma cell viability
- The mechanism of increased thrombotic risk in paroxysmal nocturnal haemoglobinuria
- ADAMTS13 - structure and function
- Mapping the collagen binding site in the VWF A1 domain
- Possible factors associated with long term survival in myeloma
- Investigating soluble CD14 as a marker for graft versus host disease in leukaemia patients
- D positive donor kidneys transplanted into D negative recipients: do recipients form anti-D as a result?
- A new imaging approach to characterize chronic graft-versus-host disease

- Inhibition of deregulated protein kinases in the CML progenitor compartment by novel small molecule drugs
- Molecular basis of Class I G6PD deficiency
- Evaluation of haematopoiesis in response to growth factors in a 3D ex vivo model - 2
- Evaluation of haematopoiesis in response to growth factors in a 3D ex vivo model - 1

What do the students think of the BSc in Haematology?

'Good old Haematology. It really is the only way to go. Just ask any member of Haem Taem! So why choose it? Several reasons really... Firstly, I'd been told by many people that it was the most well taught of BScs. This is very true, and not only are most of the lecturers very enthusiastic and knowledgeable, but they really do know how to deliver a detailed but understandable lecture. In fact, most of the key concepts of the course are reinforced by practicals or tutorials so chances are you'll pick most of the important things up sooner or later. Another reason to do Haematology is that it does *not* involve digging through dozens of research papers after every single lecture, unlike some other BScs. That said, the research papers are definitely needed for the in-course essays that we, like all of the other BScs, are required to do. Also, contrary to the preconceptions that many people have about Haematology, the "dreaded" microscopy is not as bad and all-encompassing as might be expected. In fact, the microscope sessions that we do have are actually very well explained and quite interactive!

But then of course, we cannot forget the X-factor of Haematology and the true reason we all love it - the incredible Professor Barbara Bain. Who wouldn't want her as their course leader? She gives us so many fantastic "trailblazing" lectures, she always goes out of her way to help us and she has even been known to craft a clever joke every now and then ;-)

How is the Year 4 course structured? Three modules – the first is "Red Blood Cells", which mainly focuses on Sickle Cell Disease, Thalassaemia and Malaria. This module is mainly taught via lectures at St Mary's Hospital and is complemented by tutorials and practicals. The second module is "Haemostasis and Thrombosis" – the title is pretty self-explanatory. It is almost exclusively lecture-based and is located at the Hammersmith Hospital, with most of the lectures taking place in the morning (so plenty of free afternoons)! Finally, the third module is "Leukaemias and Lymphomas". This includes learning quite a bit about immunophenotyping and cytogenetic, and how these are used in every-day haematology. This last module is organised similarly to the first one and takes place at St Mary's Hospital with lectures, practicals and tutorials. It must be said that the last module is a little more intense than the other two, but is still very manageable! After the February exams in these three modules, you then do a research project (there are quite a few clinical and laboratory projects to choose from and most people get one of their top choices) or Humanities, History of Medicine, etc.'

'Choosing to do haematology for my BSc was one of the best decisions I have made. The course is very well organised and there is a good balance between lectures, computer-assisted learning (CAL) sessions and individual study time. Apart from lectures and CAL sessions you will be required to participate in microscopy sessions, journal clubs and haematology clinics (this is optional). CAL sessions provide a good opportunity to familiarise yourself with various haematological images, while the microscopy sessions are aimed at consolidating what is being taught in CAL sessions and lectures and will help you improve your microscopy skills! Journal clubs will teach you how to critically appraise research papers in order to be able to appreciate their limitations and the significance of their results. This will prove to be particularly helpful during your project. The part of my BSc which I

enjoyed the most was my research project, which I did in Tokyo. The 3 months that I spent in Japan gave me the chance to travel, meet interesting people and places, find out about different cultures, and experience life in busy Tokyo. I enjoyed every minute of my time there, despite spending very long hours in the pathology laboratory of the Tokyo Medical and Dental University!

In all honesty, 4th year was my best year at medical school. The workload for once was manageable and I very much enjoyed learning haematology, the work in the laboratory, even writing-up my project.

I absolutely recommend it: choose Haematology!