

## BSc in Medical Sciences with REPRODUCTIVE AND DEVELOPMENTAL SCIENCES

### Introduction

This course includes all aspects of human reproductive and developmental biology, addressing them from the perspective of the fundamental mechanisms that control these normal physiological processes, and then considering our current knowledge of the most important pathologies.

It is not possible within a period of 15 weeks to consider all possible topics in great depth, so in some parts of the course selected subject areas will be considered, as examples of the understanding that we now have.

This course will include consideration of some selected topics of particular interest, to demonstrate how fundamental science can lead to a better understanding of normal and pathological processes in reproduction and development.

### Course Director

Dr Mark Sullivan      [mark.sullivan@imperial.ac.uk](mailto:mark.sullivan@imperial.ac.uk)

### Aims

- To consider the processes required for successful reproduction, including the detailed mechanisms involved.
- To provide an understanding of how the latest scientific knowledge can inform and improve clinical practice and treatments.
- To appreciate the interactions between events before or during pregnancy, and the impact these can in the short or longer term on mother and infant.
- To assess rigorously how much we understand of the mechanisms underlying the main pathologies of human reproduction and development
- To appreciate the most recent insights from fundamental research, and to consider how these may inform further clinical and translational approaches

### Objectives

After taking this course students will:

- Have an understanding of the main characteristics and events in human reproduction and development
- Have a greater knowledge of the regulatory systems that determine normal and abnormal function of these critical events
- Have been introduced to the most recent science underpinning our understanding of human reproduction, from the earliest stages of life, through pregnancy, to infancy
- Understand more of the mechanisms and impact of the primary complications that are unique in their effect on female health, namely gynaecological cancers and the menopause
- Have been introduced to the normal development of the infant in utero, at the time of delivery and at the beginning of independent life
- Have a greater appreciation for the vulnerability of the preterm human infant, and how the preterm and term infant reacts to their environment
- Appreciate the impact and mechanisms of paediatric infection and allergy

### **Specific skills**

- Be able to integrate knowledge from a range of sources into a deeper understanding of reproduction and development
- Be able to think 'out of the box', integrating information that might be classified as 'obstetrics' or 'gynaecology' or 'paediatrics'
- Have practised presentational skills to a variety of audiences, using different methods

### **Format of teaching**

The taught part of the course will comprise seminars/lectures and small group teaching, including Journal Clubs aimed at critical appraisal of published research papers and debates. For each module a significant portion of time is allowed each week for private study and preparation of in-course assessment. Parts of the Introductory Course and Module 1 will be taught in conjunction with the BSc course in Endocrinology.

### **Taught modules, dates and contact details:**

#### **Introduction**

##### **Module leaders**

Dr Mark Sullivan (Reprod Develop Sci)  
Professor Glenda Gillies (Endocrinology)

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##### **Aims & Content**

The introduction will reprise material on transferable skills with which students may be familiar, emphasising the level of such skills needed for these courses. The ability to critique published material, and use the information gained will be addressed in particular. Fundamental scientific concepts related to the regulation of cell functions and biology will be discussed, so that all students have a secure base of scientific knowledge with which to proceed to the subsequent modules.

#### **Module 1: Hormone dependent systems & cancers: gynaecology and endocrinology**

##### **Module leaders**

Dr Mark Sullivan (RDS)  
Dr Amir Sam (Endo)  
Dr Alan Purohit (Endo)  
Dr Ian Godsland (Endo)

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##### **Aims & Content**

This module starts with an overview of the human endocrine system, including the glands and synthesis and secretion of the various types of hormones. This leads into a detailed study of the endocrinology of human reproduction, including the roles of steroids, inhibins and gonadotrophins in the hypothalamo-pituitary-gonadal axis, and their impact on gametogenesis to produce the female egg and the male sperm. The major changes in female endocrine function (puberty, menstruation and the menopause) are used to illustrate the complex integration between the action of different hormones and other signalling molecules. Defects in signalling mechanisms are probably responsible for all of the major pathophysiological associated with reproduction. The molecular biology of signalling mechanisms of particular relevance to human reproduction and development will therefore be considered in detail with particular reference to the gynaecological cancers and post-reproductive female health.

The topics are divided into 4 main subsections, as shown below:

### **Reproductive endocrinology**

- Hypothalamic pituitary gonadal axis
- Clinical perspectives: Ovary, breast and reproductive tract
- Puberty
- Menstrual cycle I & II
- Follicle growth and development
- Control of steroid hormone production
- Control of peptide hormone production
- Progesterone & oestrogen receptor biology in health & disease
- Infertility and ART
- Transcription factors
- Other endocrine disorders of reproductive function & treatments
- How does gene organisation determine gene expression?
- The nuclear receptor superfamily: hormonal signalling with a difference
- Endometrial biology & regeneration
- The impact of steroids on endometrial structure

### **Gametogenesis and fertilisation**

- Follicle growth and development
- Oogenesis & Oocyte maturation
- Aneuploidy
- Spermatogenesis
- Sperm transport
- Fertilisation

### **Endocrine cancers**

- Cancers and the main pathologies of breast, ovary, uterus & endometrium, cervix, vagina & vulva, prostate
- Imaging, screening and preinvasive disease
- Tumour Suppressor Genes & molecular profiling
- Epigenetics & cancer
- Gene Therapy
- HPV Vaccines
- Radiotherapy, laparoscopic surgery & chemotherapy

### **Female health – an endocrine perspective**

- Endocrinology and the physiology of the climacteric
- Anatomical changes in the lower urinary tract and the menopause
- Drug treatment of lower urinary tract disorders
- Premature ovarian failure
- Imaging and screening in the post-menopausal patient
- The Science behind HRT
- Bisphosphonates and statins
- Pathophysiology of bone loss

## **Module 2: Aspects of development: before and after birth**

### **Module leaders**

Dr Wei Cui

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Dr Mark Sullivan

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### **Aims & Content**

In this module students will learn about the fusion of male and female gametes to give rise to a genetically unique embryo. The physiology, biochemistry, anatomy and genetics of human preimplantation embryogenesis will be described. The ability to physically and genetically manipulate the preimplantation embryo of both domestic and laboratory species will be examined and the scientific and agricultural benefits explored, with reference to the application of such techniques to human assisted reproduction. Stem cells will be considered in the context of pre-implantation development, as their physiological role starts at this point of pregnancy.

In pregnancy, two genetically distinct individuals co-exist for 9 months. The nature of the feto-maternal interface, which permits this, and defects in its formation which can lead to pregnancy loss or complications in an on-going pregnancy will be considered. To appreciate these complications in context, the nature of the factors controlling the formation of the interface, and the roles of the interface will be assessed. The impact of pregnancy on the mother will be considered, with reference to particular common complications that may in turn affect the infant. This will include pre-eclampsia, alloimmunisation, and preterm labour. This last complication is particularly related to intrauterine infection, and will be considered in detail.

In parallel with the placenta, development of the infant will be considered in general terms, and then describe the development of selected organs and systems in the infant. The effects of maternal health on fetal development will be considered. The process of normal term labour will be discussed, and the adaptations in the infant necessary for successful transition from intrauterine to postnatal environment will be considered. One of the most vulnerable organs in the human infant is the brain. The technology is now available at Hammersmith Hospital to image the brain of very premature infants within a few hours of birth. On-going studies have provided novel insights into the causes and mechanisms of the damage observed in these infants. This module will include consideration of the timing of when the damage occurs, how it develops subsequent to the initial insult, and what the consequences might be.

The topics are divided into 5 main subsections, as shown below:

### **Preimplantation development and IVF**

- Cell biology of preimplantation development
- Human preimplantation development
- Growth factors, the environment and preimplantation development
- Genetic regulation of development
- Genomic imprinting
- Ageing and reproduction
- IVF cycles and their management
- Micromanipulation in ART: Embryo biopsy & PGD: Parthenogenesis

### **The development of the fetus and placenta**

- Basic embryology
- Fetal development mechanisms

- Determinants of in utero growth
- Fetal growth
- Fetal circulation
- Fetal lung development and pathology
- Placental development
- Placental vasculature
- Growth factors in the placenta

### **Stem cell biology**

- Embryonic stem cells
- Mesenchymal stem cells & their applications
- Comparison of embryonic and adult stem cells
- Epigenetics and stem cell biology
- Somatic cell re-programming

### **Physiology and biochemistry of pregnancy**

- Decidualisation & implantation
- Fetal membranes & decidua
- Fetal effects of maternal disease
- Immunology of pregnancy
- Fetal alloimmunisation
- Multiple pregnancy
- Pre-eclampsia
- Labour - mechanisms
- Labour - causes
- Adaptation at delivery
- Programming

### **The human brain in pregnancy and early neonatal life**

- Overview of brain development
- Assessing brain growth in research
- Basic brain development / MR imaging
- Common patterns of injury in preterm infants / risk factors / outcomes
- Common patterns of injury in more mature infants /risk factors/ outcome
- Electrophysiological functions and relevance
- Research methods and assessing brain growth and effects of injury/prematurity
- Neuronal growth and regeneration
- Hormones and the brain
- Genes / gender and brain development / related neurological problems

### **Module 3: Complications: Paediatric infection & allergy**

#### **Module leaders**

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Dr Paul Langford	<a href="mailto:p.langford@imperial.ac.uk">p.langford@imperial.ac.uk</a>
Dr Sandra Newton	<a href="mailto:s.newton@imperial.ac.uk">s.newton@imperial.ac.uk</a>
Professor John Warner	<a href="mailto:j.o.warner@imperial.ac.uk">j.o.warner@imperial.ac.uk</a>

#### **Aims & Content**

In the previous module it was shown that the presence of bacteria, even within the pregnant uterus, does not always lead to a complicated pregnancy. Infection is thus not simply a statement of whether an organism is present; an understanding of how the interaction of host genetic predisposing factors and the virulence determinants of selected paediatric

pathogens influence the outcome of infection will be provided. There will be particular emphasis on the state of the art research methods used to identify host and pathogen factors and the impact of such knowledge on therapeutic intervention/prevention. Allergic responses represent another pattern of responses of the infant to its environment. Our current understanding of paediatric allergy will be considered, including the mechanisms by which allergic responses are activated, the main mediators, the consequences, and how this understanding may inform treatment options.

The topics are divided into 2 main subsections, as shown below:

### **Paediatric infectious disease**

- Overview of host - bacterial interactions
- Virulence determinants & identification of virulence factors
- Genomes & DNA arrays
- Host genetic variability in immune response
- Genetic epidemiology setting up an investigation
- Proteomic approaches
- Vaccines and antibiotics
- Detection of SNPs
- Genetic polymorphisms and the clinic
- Hepatitis C
- Meningitis vaccines then, now & the future
- Epidemiology of infection
- Antibiotic resistance
- Intracellular lifestyle of pathogens
- Bad Rash Days-how we study treatments for serious infections
- Sepsis and tissue injury
- Biology of tuberculosis
- HIV pathogenesis and transmission.
- Mycobacterial infections
- Genetic susceptibility to mycobacterial disease

### **Paediatric allergic responses**

- Allergic responses in infants
- Mechanisms of allergic responses
- Ontogeny of the immune response
- Allergy diagnosis.
- Anaphylaxis
- Genetics of allergy and asthma
- Asthma basic mechanisms
- Basic cellular mechanisms and allergy.
- Food allergy – mechanisms
- Prospects for allergy prevention.
- Rhinitis and asthma – The united airway
- Hygiene hypothesis and Pre/pro-biotics
- Aero-allergen avoidance.
- Atopic eczema
- Epidemiology of Allergy
- Qualitative aspects of allergy
- Food induced enteropathies

## **Modules 4 and 5**

### **Projects**

A wide variety of projects will be offered, based round topics from all three modules. These may be laboratory based, or more clinical in nature.

### **Specialist options.**

Students may take one of the humanities options.

### **Past BSc Project Titles in Reproductive and Developmental Sciences**

- Investigation of immune regulation in early onset eczema
- Sleep disturbance in house mite sensitive asthmas
- Perinatally infected HIV & adolescents/young adults + their attitude to having children
- The national guidelines for chlamydia testing
- The cross-talk between decidualising endometrial cells and placental cells
- Oxidative stress and SUMO-modified proteins
- Apricot kernel exposure and almond allergy
- Obstetric cholestasis: Investigating the role of fibroblast Growth Factor 19
- Larp 1 and malignancy in NIH3T3 cells
- The cross-talk between decidualising endometrial cells and placental cells
- Enhancing medical students' experience in the operating theatre
- Evaluation of the CCM metabolic monitor in mechanically ventilated children
- P-CPAP: the use of Heliox therapy in ventilators - CPAP
- Chemotherapy drugs and the common fragile site
- Trastuzumab (hereceptin) therapy
- Androgen production in theca cells
- Use of Adrenaline autoinjectors in children in the UK
- Hepatitis B and C virus co-infection in our cohort of HIV infected children
- The impact of Reproductive Hormones on Hepatic Lipid Metabolism
- Paediatric respiratory medicine: Medical gas therapy techniques in paediatrics and neonatology

- Corticospinal tract integrity following perinatal hypoxic-ischaemic injury
- Electrophysiological characterization of Taurocholate on resting membrane potential
- Alkaline phosphatase and bone turnover in our cohort of HIV infected children
- BMP agonists and antagonists in mouse follicles
- Stem cells in osteogenesis imperfecta
- Identification of myofibroblasts in human fetal cardiac tissue
- Neonatal Epidemiology - Determinants of length of stay and feeding at discharge of preterm infants.
- Thromboelastography and miscarriage
- An evaluation of the effects of prenatal vitamin D supplementation on childhood immune responses
- Role of TRF2 in hESCs, hECCs and their neural derivatives
- Predicting pre-operatively the risk of sub-optimal debulking in ovarian cancer
- Stem cell biology in transplantation
- Determinants of maternal anxiety in paediatric allergic disease
- Stem cell biology in transplantation
- Children's anxiety in paediatric allergic disease
- The effect of androgen treatment on preadipocyte differentiation and function
- Cardiovascular risk assessment in HIV infected young people aged 10-16 years
- Thromboelastography and miscarriage
- Punctate white matter lesion in the preterm brain
- Regulation of myometrial contractility
- Impact of anaesthetics on ovarian cancer metastasis in vitro

## **What do the students think of the BSc in Reproductive and Developmental Sciences?**

'Reproductive and Developmental Sciences BSc is an amalgamation of the previously separate Obstetrics & Gynaecology and Paediatrics BSc's. The modules consisted of predominantly science-based lectures, given along with clinical context, on topics from both specialties. In the paediatric module, we were given the opportunity to visit the Paediatric Neonatal Intensive Care Unit, which I particularly enjoyed.

There was a large range of project choices available and mine was lab-based. This was my first experience of research and the lab environment and I thoroughly enjoyed my time there. I developed invaluable skills, both practical e.g. performing DNA synthesis & PCR, and academic e.g. literature searches, final write-up. My supervisor and team gave me excellent support and guidance but also encouraged self-directed work. I could organise my days as I wished as long the targets were met in time; I found both the freedom and responsibility refreshing.

All in all, I was very satisfied with the course. The workload was manageable, although stressful around the time of exams. It has also given me a knowledge base which has proved extremely useful during my 5<sup>th</sup> year O&G attachment.'

'Reproductive and Developmental Sciences is a unique course in that it encompasses many fields - obstetrics & gynaecology, paediatrics, immunology, neuroscience, respiratory and cardio. It explores pregnancy, fertility (IVF) and menopause, fetal development and childhood infection and allergy. But don't worry - it's not like Human Life Cycle from first and second year.

This relatively lecture-heavy course has a simple structure; 3 five-week modules, each with 2 pieces of coursework (one essay and one shorter piece, e.g. a presentation or critical appraisal). Creative skills are put to the test when asked to write an original newspaper article on any aspect of pregnancy-not restricted to humans! Based mainly at Hammersmith Hospital for the first one and a half modules, it has the advantage of being located close to Westfields for vital post-lecture retail therapy. The remainder of the course takes place in St. Mary's Hospital, where you also visit a paediatric allergy ward and perform allergy skin tests on each other. Within walking distance of many cafes/eateries, lunch can be a challenge.

Throughout the course days can vary from days off, half-days and 9-to-5's.

So if you're female and interested in a female-dominated course, this one's for you!

And if you're male and interested in a female-dominated course, this one's for you!