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

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 awareness 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
- Be able to summarise 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
- Be able to summarise the main effects of paediatric infection on an infant, and identify the main processes involved.
• Be able to identify the effects of paediatric allergic diseases and the main mechanisms involved.

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
28th September – 9th October 2015

Module leaders
Dr. Mark Sullivan (Reprod Develop Sci) mark.sullivan@imperial.ac.uk
Dr. Patricia Cover (Endocrinology) p.cover@imperial.ac.uk

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
12th October – 13th November 2015

Module leaders
Prof. Stephen Franks
Dr. Sadaf Ghaem-Maghami
Prof. Kate Hardy
Dr. Sheba Jarvis
Dr. Channa Jayasena (Endo)

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 pathophysologies 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 5 main subsections, as shown below:

**Central regulation of reproduction**
- Hypothalamic pituitary gonadal axis
- The mechanics and sex and reproductive tissues
- Genetic models of GnRH deficiency
- Kisspeptin as a regulator of mammalian reproduction
- Sex dimorphisms in hypothalamic regulation of human reproduction
- Relationship between metabolic status and reproduction in humans
- Puberty

**Male systems and cancers**
- Spermatogenesis
- Sperm transport
- Mechanisms and treatment of testosterone deficiency
- Male infertility: the azoospermic patient
- Male infertility: genetic disorders
- Male infertility: Influences of lifestyle
- General and clinical aspects of prostate cancer
- Molecular & cellular pathways leading to prostate cancer

**Signalling in reproductive tissues and related cancers**
- The nuclear receptor superfamily
- Control of ovarian steroid hormone production
- Progesterone & oestrogen receptor biology in health & disease
- Control of peptide hormone production
- Epigenetics & cancer
- Angiogenesis & adhesion
- Signalling systems and drug targets

**Female systems and cancers**
- Clinical perspectives: Ovary, breast and reproductive tract
- Cancers and the main pathologies of breast, ovary, uterus & endometrium, cervix, vagina & vulva, prostate
- HPV Vaccines
- Premature ovarian failure
- Follicle growth and development
- Oogenesis & Oocyte maturation
- Aneuploidy
- Fertilisation
- IVF and assisted reproduction.
- Other endocrine disorders of reproductive function & treatments
Post-reproductive health and cancer

- Endocrinology and the physiology of the climacteric
- Anatomical changes in the lower urinary tract and the menopause
- Drug treatment of lower urinary tract disorders
- The Science behind HRT
- Bisphosphonates and statins
- Radiotherapy, laparoscopic surgery & chemotherapy
- Imaging, screening and preinvasive disease

Module 2: Aspects of development: before and after birth
16th November - 18th December 2015

Module leaders
Dr. Wei Cui  
wei.cui@imperial.ac.uk
Prof. Kate Hardy  
k.hardy@imperial.ac.uk
Dr. Mark Sullivan  
mark.sullivan@imperial.ac.uk

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

Physiology and biochemistry of pregnancy
- Decidualisation & implantation
- Fetal membranes & decidua
- Fetal effects of maternal disease
- Immunology of pregnancy
- Multiple pregnancy
- Pre-eclampsia
- Miscarriage
- Labour - mechanisms
- Labour - causes

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

The human infant in pregnancy and early neonatal life
- Overview of development
- Risk factors present in delivery of normal infants at term
- Risk factors present in delivery of preterm infants
- Vulnerability of very preterm infants suffering from growth restriction
- Development of preterm and term infants after delivery.

Module 3: Complications: Paediatric infection & allergy
4th January – 5th February 2016

Module leaders
Dr. Bob Boyle r.boyle@nhs.net
Dr. Paul Langford p.langford@imperial.ac.uk
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.