- **Primary immune deficiencies (PID's)**
  - There are 8 classes of PID's spanning the adaptive and innate immune systems
  - PID's are a large group of disorders that result in recurrent infections and that are NOT caused by other diseases, treatments or environmental exposure to toxins
  - Mostly genetic disorders, most are diagnosed in children under 1 year
  - Results in the patient being unable to make an appropriate immune response to one or more groups of pathogens – can be lethal
  - Most are not associated with lymphocytes

PID classification	Examples of PIDs	
Combined T and B cell deficiencies	• Severe combined immunodeficiency disorder (SCID) • Complete DiGeorge syndrome • CD40 and CD40L deficiencies (HIGM)	LECTURE 1 LECTURE 2
Well-defined syndromes with immunodeficiency	• Wiskott-Aldrich syndrome (WAS) • Ataxia telangiectasia • Hyper IgE syndrome	
Diseases of immune dysregulation	• Lymphoproliferative syndromes • Familial haemophagocytic lymphohistiocytosis • CD24 deficiency	
Congenital defects of phagocyte number or function, or both	• Severe congenital neutropenia, X-linked neutopenia • X-linked chronic granulomatous disease (CGD) • Leukocyte adhesion deficiency (LAD)	
Innate immunity deficiencies	• TLR3/TBK1/UNC93 deficiency (Herpes encephalitis) • IL17A, IL17F, IL17R deficiency, STAT1 GOF (candidiasis)	
Auto-inflammatory disease	• Familial Mediterranean fever • TNF-R-associated period syndrome (TRAPS)	
Complement deficiencies	• Various	
Antibody deficiencies	• CD40 and CD40L deficiencies (HIGM) • Ig deficiencies (X-linked agammaglobulinaemia, XLA; X-linked lymphoproliferative disease, XLP; selective IgA deficiency) • Common Variable Immunodeficiency (CVID)	LECTURE 2 LECTURE 1 LECTURE 2

- Common inherited disorder particularly in people of northern European background
- Variable severity – severe forms have poor prognosis – no present cure – will eventually lead to death
- Improvements in treatment have resulted in increased lifespans over the years
- Death usually due to respiratory failure/cardiac complications
- Multiple systems affected: including respiratory, digestive, reproductive
    - All systems are affected by the production of excessively thick, dehydrated secretions of mucus in epithelial cells
    - Caused by mutation in a key protein which results in the failure of salt (specifically chloride ions) and subsequently water transport by epithelial cells lining ducts

- Clinical features: **respiratory**
- Frequent coughing
- Chronic infections
- Lung damage
- Due to:
    - Obstruction of bronchioles by mucus
    - Colonisation by bacteria, especially antibiotic resistant strains
    - Damage (fibrosis) caused by inflammatory responses

- Clinical features: **digestive**
- Failure to thrive (malnutrition)
- Chronic malabsorption of certain nutrients
- Due to:
    - Blockage of various intestinal and pancreatic ducts by mucus
    - Poor digestion of fats (mainly) and proteins
- Intestinal obstruction in newborns (‘meconium ileus; 15% of neonates with CF)
- Pancreatic insufficiency (85% patients) – depends upon the particular mutations involved
- Chronic pancreatitis (and diabetes, 40% adults), liver disease (>5%) – long term complications

- Clinical features: **reproductive**
- Infertility in males
- Sub-fertility in females
- Due to:
    - Blockage of vas deferens in males leading to fibrosis or usually atrophy: congenital bilateral absence of the vas deferens (CBAVD)
    - Cervical mucus in females acting as a barrier to passage of sperm
    - Females may be anovulatory