Recurrent infections – when to investigate

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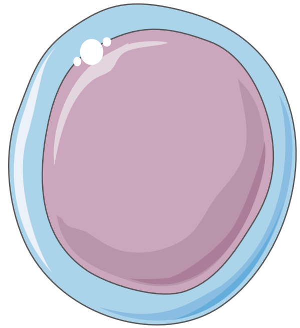
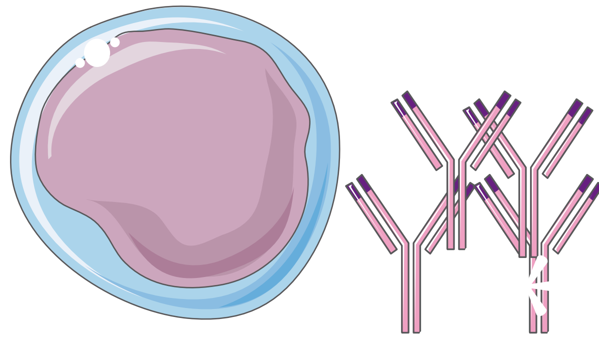
Which children warrant investigation? (SPUR)

- **S**evere infections
- **P**ersistent infections
- **U**nusual infections
- **R**ecurrent infections

Patterns of immunodeficiency



T cells



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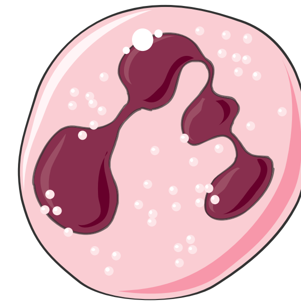
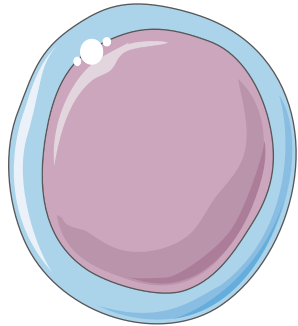


Neutrophils

Patterns of immunodeficiency



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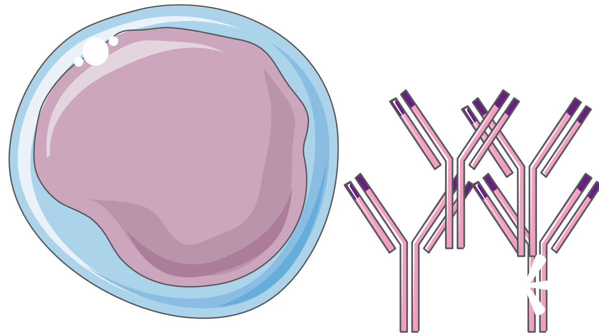
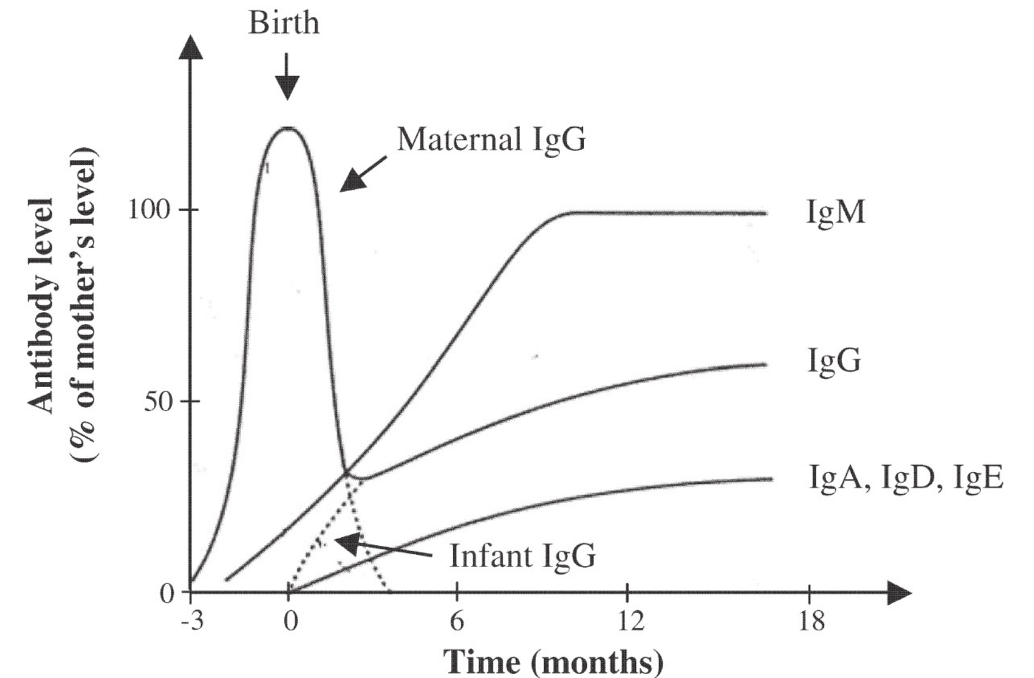
- Tend to be severe (e.g. SCID)
- Present early (first 6mo)
- Severe or persistent respiratory infections
  - Viral, *Pneumocystis jirovecii*
- Diarrhoea
- Persistent candidiasis
- Failure to thrive
- Severe skin rash

Patterns of immunodeficiency

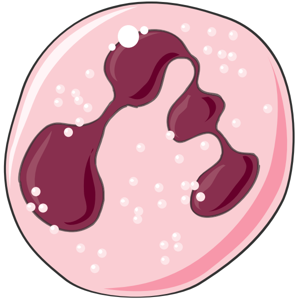


B cells

- Present later (after 6mo)
- Recurrent bacterial infections, e.g. pneumonia, otitis



Patterns of immunodeficiency



Neutrophils

- Delayed separation of umbilical cord (>30 days)
- Recurrent abscesses – e.g. perianal
- Poor wound healing
- Deep-seated abscesses e.g liver
- Fungal infections

Immune dysregulation can also be a sign of primary immunodeficiency

- Immune dysregulation
  - Hepatosplenomegaly, lymphadenopathy
  - Autoimmunity (including cytopenias)
  - Inflammatory bowel disease
  - Coeliac disease
  - Eczema
  - Vasculitis
  - Autoinflammation (fever and rash)
- “Inborn errors of immunity” is emerging term

Thalhammer J et al., J Allergy Clin Immunol 2021

Four important indicators for investigation

- Family history of primary immunodeficiency
  - Ask about sibling death and parental consanguinity
- Need for intravenous antibiotics
- Failure to thrive
- Recurrent deep-seated infections

Subbarayan A et al., Pediatrics 2011; Reda SM, Allergy Asthma Immunol Res 2013

Useful first-line investigations

- FBC – neutrophils, lymphocytes, monocytes
  - *Look for Lymphocytes <2*
  - *Neutrophils <1*
- Immunoglobulins (IgG, IgA, IgM)
- Lymphocyte subsets (T, B, NK)
- Vaccine responses
  - Tetanus, HiB, pneumococcus

Caution with test interpretation

- Mannose binding lectin
- Low IgA levels

Recurrent cough and coryza

- Recurrent coryza and cough is usually viral URTIs
  - Up to 10 per year is normal in pre-school children
  - Especially if siblings, nursery attendance, smokers at home
- Distinguish two forms of “persistent cough”
  - Recurrent wet cough with intermittent cough-free periods (usually viral URTIs)
  - Chronic daily wet cough (>4 weeks, needs investigation)

Recurrent “pneumonia”

- Is this actually recurrent viral wheeze?
- Gastroesophageal reflux / aspiration / unsafe swallow?
- Recurrent confirmed pneumonia could be an underlying respiratory cause, e.g.
  - Cystic fibrosis
  - Primary ciliary dyskinesia
- Immunodeficiency
  - B-cell
  - Complement disorders / combined immunodeficiency
  - Rule out HIV infection

Recurrent acute sore throat

- Recurrent courses of antibiotics
  - Viral versus bacterial
  - FeverPAIN or Centor criteria
- ENT referral
  - Watchful waiting versus tonsillectomy
  - SIGN criteria for tonsillectomy indications
- PFAPA: Periodic Fever, Aphthous ulceration, Pharyngitis and cervical Adenitis

A note on herpes viruses

- Recurrent HSV
  - Often trial a course of suppressive aciclovir for 6 months
- Eczema herpeticum
  - Improve eczema control
- Shingles in childhood
  - Ask about age at varicella infection (< 1 year)
  - Severity of original chicken pox
  - Single versus multi-dermatomal

Recurrent skin abscesses

- Decontaminate
- Whole family

Recurrent urinary tract infections

- Not a sign of immunodeficiency
- Imaging guidelines - NICE
- Structural problem
  - Obstructive uropathy
  - Vesicoureteric reflux (VUR)
- Generally avoid antibiotic prophylaxis
  - Except young children (< 2 years) with *high-grade* VUR

Summary of key points

- Think about the *pattern* of infections
  - SPUR
- Try to explore what antibiotics were prescribed for – oral vs IV
- Remember the family history
- Has the child had unusual or deep-seated infections?
- Look at growth
- Think beyond infections
  - Immune dysregulation
- If investigating for immunodeficiency, start with small focused panel:
  - FBC, immunoglobulins, vaccine responses, lymphocyte subsets