PAEDIATRIC IMMUNOLOGY

Primary Immunodeficiencies

	B-cell immunodeficiency	T-cell disorders	Severe combined immunodef. Syndrome (SCID)	Phagocytic disorder	Complement disorder
Epi	most common – 55% of PID	9% of PID	Most severe	12.5% of PID	25% of PID
Age	➢ Present at 3-6/12 of life (as maternal Abs decrease)	1st year of life	1st mths of life	Normally diagnosed at 5yo	SLE,
PP	Cannot produce antibodies causing hypogammaglobulinemia **Selective Immunoglobulin A def.** ➢ Most common ➢ **Low IgA levels** (normal IgM, IgG) ➢ Unable to protect against opportunistic infections of MM (e.g. LRTi, autoimmune) *NB: coeliac disease (falsely normal IgA-TTG and IgA-EMA) → need to test IgG versions **Common variable immunodef..** ➢ Genetic mutation encoding components of B cells ➢ **Low IgA, IgG** (normal IgM) ➢ **No immunity to infections of vaccinations** ➢ High risk of cancers (NHL) and autoimmune (RA) ➢ **Rx: IVIg** **X-linked agammaglobulinemia** ➢ AKA "Bruton's agammaglobulinemaia" ➢ X-linked recessive ➢ Deficiency in all class of Ig	Abnormal or absent T cells ➢ CD4 = cytokine release ➢ Cd8 = Lyse virus infected or cancer cells **DiGeorge syndrome (22q11.2)** ➢ Congenital heart disease ➢ Abnormal facies ➢ Thymus underdeveloped (no functional T cells) ➢ Cleft palette ➢ HypoPTH - hypoCa ➢ 22 chr **Purine nucleoside phosphorylase** def. ➢ Autosomal recessive ➢ Def. of PNPase enzyme to breakdown purines – increases dGTP levels ➢ Lowers T cell levels **Wiscott-Aldrich (WAS gene)** ➢ Thrombocytopenia ➢ Neutropenia ➢ Eczema ➢ Recurrent infections **Ataxia telangiectasia** ➢ Autosomal recessive ➢ ATM serine/threonine kinase protein on Chr 11 ➢ Recurrent infection (low T cell) ➢ Ataxia – uncoordinated movement ➢ Telengiectasia – esp. sclera and skin damage ➢ Cancer risk (esp. haem cancers) ➢ Stunted growth ➢ Accelerated ageing AIDS (acquired immunodef. Syndrome)	Abnormal or absent B **and T cells** **Causes:** ➢ JAK3 mutation ➢ Adenosine deaminase def. ➢ **Omenn syndrome** - X-linked recessive mutation of RAG ½ **(***dysfn T cells attack fetus and neonate***)**	= **no phagocytes** = no removal of catalse +ve organism (e.g. S. aureus, aspergillus, serratia, candida)	➢ **C2 def** – most common ➢ **C1 esterase inhibitor def**. (hereditary angioedema) -no inhibition of bradykinin release during inflammatory response ➢ **Mannose binding lectin def**
Sx			• Persistent severe diarrhoea • FTT • **Opportunistic infection** (E.g. PJP, CMV, chicken pox) • Unwell after vax **Omenn syndrome** ➢ Erythroderma (red scaly, dry rash) ➢ Alopecia ➢ Diarrhoea ➢ FTT ➢ LN ➢ HSM	Chronic granulomatous disease: ➢ recurrent soft-tissue infection by bacteria and fungi → leads to IBD ➢ *pneumonia, abscess, suppurative adenitis, GIT infections, omphalitis (1st sign)*	➢ **Risk of encapsulated organism (**Strep, pneumoniae, HiB, Neisseria) – **normally dealt with by complement** ➢ Unexplained Angioedema esp. lipi swelling for C1 esterase inhibitor def. **(check C4 levels = low)**
Mx	➢ Abx for early infection ➢ IVIg (SC at home)	Haematopoietic stem cell transplant (curative intent)	Urgent specialist paediatric immunologist • IVIg • Sterile environment – minimise risk of new infections • HSCT	Abx for early infection	Abx for early infection Vaccinate against encapsulated

Most useful 3 signs:

- Positive FHx
- Sepsis treated with IVAb
- Failure to thrive

Can lead to identification of:

- 96% of children with neutrophil & phagocytic PID
- 89% with T-lymphocyte PID

*Nb: normal for a healthy child to have 4 – 8 respiratory infections per year.

DDx of recurrent infections:

1. **Anatomical defect** (e.g. nasal defect = recurrent sinusitis)
2. **Organic** = cystic fibrosis (LRTi)
3. **Extrinsic** = inhaled foreign objects

SIGNS:

➢ Chronic diarrhoea since infancy
➢ FTT
➢ Unusually **well** despite infection
➢ Unusual pathogens (CMV, candida)

***Secondary (acq. immunodeficiencies):**

1. immunosuppressive drugs
2. malnutrition
3. trauma/surgery/indwelling lines
4. splenectomy
5. chronic disease
6. AIDs

General work up for PID or RECURRENT INFECTIONS

➢ **FBC**
  ➢ ***Low lymphocytes** = T cell disorder*
  ➢ ***Low neutrophils** = phagocytic*
  ➢ ***Low plts** = Wiskott-Aldrich*
➢ **Flow cytometry**
➢ **Serum complement** (C3-C9)
➢ **HIV testing**
➢ **Serum Ig (A/B/G/M/E)** + albumin (is it renal issue, protein malabsorption)

Other

➢ CXR – scarring from previous chest infections
➢ Sweat test (CF)
➢ CT scan chest (bronchiectasis)

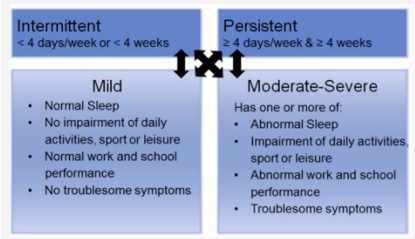
PAEDIATRIC HYPERSENSITIVE REACTIONS

Common types:
- Asthma
- Atopic eczema
- Allergic rhinitis
- Hayfever
- Food allergies
- Animal allergies

General Ix for allergies
- **Skin prick test** (more sensitive) → measure size of wheals (2 controls (histamine and saline)
- **Patch testing (2-3 days)**→ mainly for contact dermatitis
- **RAST testing (poor specificity)** → measure total and allergen specific IgE → for eczema and asthma
- **Supervised Food challenge**

General Mx for allergies
- Remove allergen or taggers
- Change sheets/pillows regularly (house mites)
- Remain indoor if pollen count high

Meds:
- **Prophylactic PO non-sedating antihistamines or prednisone** to dampen immune response and prevent risk of anaphylaxis
- EpiPen (adrenaline auto-injector)
- Immunotherapy

	Atopic Eczema	Allergies	Allergic Rhinitis
PP	➢ **CHRONIC** cutaneous hyperreactivity to environ. stimuli (food and inhalant allergens, irritants, and infection) ➢ Loss-of-function mutations in **filaggrin (*FLG*) gene (**preserves skin barrier)	Immune reaction to food protein ➢ Rising rates in Western world ➢ IgE mediated vs non-IgE Mediated	• **IgE mediated inflammatory** (type 1) • **Sensitisation** (environmental allergen → APC →Th2 →Il-4 → B cells → specific IgE → mast cell and basophils → LLK, histamine
SX	1. Scratching = disrupts skin integrity ➔ erythema, papulation, oozing and crusting, excoriation, and lichenification. 2. Ask about triggers 3. Ask about past skin infections (cellulitis), hospitalisations 4. **Red flags** = poor growth, recurrent infection, **infected eczema** (weeping lesion), pustules, vesicles **Diagnostic criteria:** ➢ Visible **itchy** dry **red** blanching scaly skin ➢ FHx of atopy (1st deg or personal) ➢ Dry skin within past year ➢ Rash distributed across: o **Infants**: Extensor surfaces + face o **Young child**: Flexor surfaces (cubital, popliteal fossa) ➢ Recurrent rash history < 2yo	*Either:* **IgE mediated (within mins)** Type 1 hypersensitivity autoimmune reaction: **1) cow's milk protein *allergy*** a. **before 1yo** b. **GI Sx = distension, abdo pain, V/D** c. urticaria, angio-oedema (facial swelling), cough, wheeze, watery eyes and eczema **2) anaphylaxis** **Urticaria* (hives) affecting epidermis and dermis ➔ anti-histamines, moisturisers ***Angioedema of mucosa** = obstructed upper airway **Non IgE-mediated (hrs – days):** **1) FPIES,** 2) **eosinophilic oesophagitis**, **3) cow's milk protein *intolerance*** a. More common in formula-fed < 1yo b. NOT an allergic process c. Does cause proctolitis	*Types time vs frequency vs severity :* 1) **Occupational** (environmental) 2) **seasonal** (spring = pollen = hayfever) 3) **perennial** (allergen exposure – house dust, house mites, pets)  *Acute Sx (early phase 5-30mins)* ➢ Sneeze + itchy nose, ➢ palate, ear ➢ Rhinorrhoea or blocked nose *Late phase (2-8 hours)* ➢ Swelling + oedema + thick secretions ➢ Nasal congestion → obstruction ➢ Hyperactive + wheezing
Mx	➢ **Parental Education!!!** ➢ ***Sx management (general) – maintain skin hydration*** o Stop scratching (maintain skin integrity) o Reduce stress and bathing time o High oil + low water content moisturiser (QV, Cetaphil) o Bleach baths (↓bacterial load and superinfection) ➢ ***Sx management (flares)*** 1) Increase moisturiser > 4x daily 2) Topical steroids and antihistamines 3) If severe: topical calcineurin inhibitors (eg tacrolimus) 4) Antimicrobials (Abx) if infected eczema or antivirals if herpeticum eczema (HSV)	➢ Education and **food avoidance (e.g. cow's milk, nuts)** ➢ **Allergy action plan** + EpiPen purchase *Medical Mx* 1) **Antihistamines** (e.g. cetirizine) – prevent anaphylaxis 2) **Steroids** (e.g. oral pred, topical or IV hydrocortisone) - prevent anaphylaxis 3) Anaphylaxis ➔ 1:1000 **adrenaline** +call 000 o If HypoTN = IVF NS bolus every 5-10min --- ➢ Most food allergies are 'outgrown' with time, 80% by school age in eggs, milk and wheat. ➢ *lifelong allergies (20% peanut-9% tree nut → REFER TO immunology centre* *Mx for Cow's milk protein **intolerance*** ➢ Avoid consuming dairy products if BF ➢ Replaced formula with hydrolysed formula feeds designs for cow's milk allergy (proteins broken down to avoid triggering immune response) ➢ Most outgrow by age 3 ➢ Can still take milk unlike *Cow's milk protein allergy → step-up milk ladder regime*	Avoid allergen exposure (dust, animal dandur etc.) ➢ Change pillows and clean clothes regularly ➢ Minimise pet contact Medical – started empirically w/o diagnosis: ➢ **Oral anti-histamines for prophylaxis** o **Non-**sedating – *loratadine* o Sedating - *promethazine, chlorphenamine* ➢ **Corticosteroid OR anti-cholinergic nasal spray** (check technique - e.g. do NOT sniff at same time as spraying) If can taste at back of throat (gone too far!!) ➢ **Nasal antihistamines –** *in acute settings* ➢ **Immunotherapy** = Mast cell stabilisers Surgery = resect nasal turbinate hypertrophy