Worcestershire Acute Hospitals NHS Trust

Immunodeficiency (PIP)

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The following guidance is taken from the Partners In Paediatrics (PIP)

IMMUNODEFICIENCY

RECOGNITION AND ASSESSMENT

- SPUR to recognition: **S**erious, **P**ersistent, **U**nusual, or **R**ecurrent infections
- The younger the onset, the more life-threatening the immune defect likely to be
  - bacterial infection; early presentation: antibody defect
  - viral/fungal infection; later presentation: cellular defect
- Family history of primary immunodeficiency (PID): focused investigations and refer

Warning signs of PID:

- ≥4 new bacterial ear infections within 1 yr
- ≥2 serious sinus infections within 1 yr
- ≥2 months on antibiotics without resolution of symptoms
- ≥2 episodes of pneumonia within 1 yr
- Failure to thrive with prolonged or recurrent diarrhoea
- Recurrent, deep skin or organ abscess
- Persistent candida in mouth or napkin area
- Need for IV antibiotics to clear infections
- ≥2 severe infections (e.g. meningitis, osteomyelitis, cellulitis or sepsis)
- Family history of PID

Symptoms of immune deficiency

- Delayed umbilical cord separation of ≥3 weeks, omphalitis
- Delayed shedding of primary teeth
- Severe adverse reaction to immunisation e.g. BCGitis
- Unusually severe course of measles or chickenpox
- Family history of any syndrome associated with immunodeficiency, (e.g. DiGeorge anomaly or Wiskott-Aldrich syndrome); or of death during early childhood
- High risk group for HIV and no antenatal HIV test (a negative antenatal HIV test does not exclude HIV in the child)
- Autoimmune liver disease, diabetes, vasculitis, ITP
- Poor wound healing
- Unexplained bronchiectasis or pneumatoceles
- >1 unexpected fracture

Signs of immune deficiency

- Congenital abnormalities: dysmorphic features, congenital heart disease, situs inversus, white forelock, albinism, microcephaly
- Children who appear chronically ill
- Scarring or perforation of tympanic membranes from frequent infection
- Periodontitis
- Enlargement of liver and spleen
- Hypoplastic tonsils and small lymph nodes
- Lymphadenopathy
- Skin: telangiectasia, severe eczema, erythroderma, granuloma, acneiform rash, molluscum, zoster
- Ataxia

Other investigations suggestive of immune deficiency

- Haemolytic anaemia
- Neutropenia
- Eosinophilia
- Hypocalcaemia

Unusual organisms or unusual diseases with common organisms

- Viruses: CMV, EBV, VZV, warts
- Fungi: candida, aspergillus, cryptococcus, pneumocystis, nocardia

- Protozoa: cryptosporidium, toxoplasma
- Bacteria: salmonella, giardia, mycobacterium (including BCG), serratia
- Recurrent infection with common organisms: *H. influenzae, S. pneumoniae, N. meningitidis, S. aureus*

Investigations

- If severe combined immunodeficiency disease possible urgent initial tests below
- failure to thrive, diarrhoea, severe/disseminated infections, opportunistic infections, rash

Table 1: Investigations

Investigations	Sample	Volume	
		Minimum	Ideal
Initial tests (complete all tests for any suspected immune deficiency)			
FBC and differential white cell count	EDTA	1.3 mL	4 mL
Immunoglobulins (G, A, M, D, E)	Clotted	0.5 mL	4 mL
Complement	Clotted	1 mL to reach lab within 2 hr	4 mL to reach lab within 2 hr or separate and freeze immediately
HIV antibody	Clotted	0.5 mL	4 mL
Lymphocyte subsets	EDTA	1 mL	4 mL
Second-line tests (with immunology advice)			
Lymphocyte proliferation	Lithium heparin	Discuss with local immunology centre	
Normal neutrophils			
Neutrophil function test for CGD	EDTA or lithium heparin	0.25 mL	4 mL
		Discuss with local immunology centre	
Recurrent or case with family history of meningococcal disease			
IgG function (antibody response to tetanus, Hib) Retest 4 weeks after vaccination	Clotted	0.5 mL	4 mL

RESULTS

- Isolated neutropenia or lymphopenia: if concerns possible immune deficiency, recheck 1–2 weeks. If persistent:
- auto-antibodies (ANA), allo-antibodies, Coombs' test (neonates), C3, C4, rheumatoid factor, urine/saliva CMV
- pancytopenia: discuss with haematology
- hypogammaglobulinaemia: discuss with local immunology centre

SUBSEQUENT MANAGEMENT

- Avoid live vaccines (e.g. BCG, MMR and varicella)
- Ensure that any blood products given to patients with suspected or proven T-cell immunodeficiency are irradiated and CMV negative
- For specific infections, use same antibiotics as in immunocompetent patients, at higher recommended dosage
- Obtain throat, blood and other culture specimens before starting treatment
- Treat infectious episodes for longer than usually recommended (approximately double)
- In patients with B-cell, T-cell or phagocytic defects, request regular pulmonary function tests and home treatment plan of physiotherapy and inhalation therapy similar to that used in cystic fibrosis
- In children with significant primary or secondary cellular (T-cell) immunodeficiency (e.g. aged <1 yr CD4 <25%, aged 1–5 yr CD4 <15% or aged >5 yr <200 CD4 cells/mm^3), give *Pneumocystis jiroveci* (PCP) prophylaxis with co-trimoxazole