Guideline

Invasive pneumococcal disease: Assessment and initial investigation to exclude immune deficiency.

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Author/custodian	Director Immunology and Allergy			**Review date**	12/05/2027
Supersedes	NEW				
Applicable to	All clinical staff at CHQ				
Authorisation	Executive Director Clinical Services				

Purpose

Invasive pneumococcal disease (IPD) in fully immunised children; in the absence of other risk factors, can be associated with Inborn errors of immunity (IEI) or primary immunodeficiencies (PID).
While most children with IPD do not have serious immunological abnormalities, up to 12% of patients presenting with IPD, particularly pulmonary or CNS disease are found to have a PID[1].

There are over 400 known PIDs and they have a broad range of presentations ranging from increased susceptibility to infections to significant immune dysregulation[2]. A high index of suspicion is required as diagnostic delay will contribute to excess morbidity and mortality in these patients. This guideline provides a standardised approach to the assessment and initial immunological investigation of children presenting with IPD confirmed invasive pneumococcal disease on PCR or culture.

Scope

This material is published by Children's Health Queensland (CHQ) with the intention of providing a guideline for use at the Queensland Children's Hospital (QCH). This guideline is not intended to be a substitute for professional or clinical advice, or to replace consultation with IMPS (Infection Management Prevention Service or QPIAS (Qld Paediatric Immunology & Allergy Service). Anyone wishing to use this guideline outside of the QCH should refer to their local Medicines Advisory Committee before using.

Related documents

- CHQ-GDL-01221 - Immunisation Guideline for Medically at Risk Children
- CHQ-GDL-01202 - CHQ Paediatric Antibiocard: Empirical Antibiotic Guidelines

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Primary immunodeficiencies are:

- A diverse group of genetically determined defects that can occur in any part of the immune system
- Can lead to increased risk of infections or increased severity of infections
- Early diagnosis of PIDs can prevent complications and reduce morbidity and mortality

Invasive pneumococcal disease is defined as

- Isolation (culture or PCR) of *Streptococcus pneumoniae* from a normally sterile site e.g blood, cerebrospinal fluid, pleural fluid, bone or synovial fluid

Certain children are at increased risk of IPD as shown in the below table

Anatomical cause	Cochlear implants Cerebrospinal leaks and anatomic malformation
Primary Immunodeficiency	X-linked Agammaglobulinaemia Combined variable immunodeficiency Complement deficiency
Acquired immunodeficiency	HIV infection Malignancy Nephrotic syndrome Immune suppression
Asplenia	Congenital asplenia or functional asplenia e.g Sickle cell disease

As rates of immunisation have increased, presentation with IPD in a fully immunised child may indicate an undiagnosed PID and therefore warrants immunological testing[3].

Primary Immune Deficiency should be considered in all children presenting with IPD, particularly those >2 years of age or those with recurrent IPD[4].

A thorough history should be undertaken with particular attention given to the following **red flags**

- History of poor growth
- History of chronic diarrhoea
- Recurrent middle ear, sinus or pulmonary infections
- Recurrent deep skin or organ abscesses

- Recurrent thrush in the mouth, skin or other organs
- Inadequate response to antibiotics (two or more months of antibiotics with minimal effect)
- Repeat hospital admission for intravenous antibiotics
- Invasive pneumococcal or meningococcal disease
- Recurrent, severe or prolonged infections with common pathogens, e.g. adenovirus
- Family history of immunodeficiency, previous sibling death (unexplained or due to infection)
- Parental consanguinity

For all cases of recurrent bacterial meningitis neuroimaging needs to be considered to examine for underlying anatomic defects causing possible CSF breach

Initial management should occur as per the treating team/relevant guideline

Investigations

Any child who has a positive culture or PCR of pneumococcus from a sterile site should have the serotype requested if not already generated.

At a minimum, children should have:

- FBC and film examination to rule out Howell Jolly bodies
- Immunoglobulin levels (IgA, IgM and IgG)
- Complement function (CH50/AH50 and C3/C4 levels)
- If possible collect extra serum for storage in case subsequent serologies are required (ie. pneumococcal antibodies)
- Abdominal ultrasound – spleen present?

Ideally these bloods should be collected after the resolution of the acute phase of the illness before discharge. In children with less severe disease, investigations can be arranged to coincide with other planned venepuncture.

Additional investigations that QPIAS may suggest include: lymphocyte subsets, memory B cells, CD62L shedding, vaccine challenges, HIV antibody (if no maternal antenatal HIV screen)

Management

Patients with normal initial investigations and no additional red flags/risk factors (as above) can be reassured by the treating team. No further investigations would be required.

Patients with normal initial investigations but notable red flags should be discussed with the QPIAS team (immunology fellow or SMO on call).

All patients with any abnormal investigations should be discussed with the QPIAS team and referred if requested.

Immunisations

All children presenting with IPD should be recommended to receive additional pneumococcal vaccines as per the NIP[5]. Additional pneumococcal vaccination course can be commenced on the ward prior to discharge or patients can present to the Immunisation Centre (2g) upon discharge. Families will need to be given a plan on how to complete the course of recommended pneumococcal vaccine. Funded vaccines can also be accessed through GP

Please refer to the Immunisation Guideline for Medically at Risk Children and The Immunisation Handbook for further details.

Abbreviation

CEWT	Child early warning tool
CHQ	Children's Health Queensland
CNS	Central nervous system
FBC	Full blood count
HIV	Human immunodeficiency virus
IPD	Invasive pneumococcal disease
MDT	Multi-disciplinary team
NIP	National Immunisations Program
PCR	Polymerase chain reaction
PID	Primary immunodeficiency
QPIAS	Queensland Paediatric Immunology and Allergy Service
QSIS	Queensland Specialist Immunisation Service

Consultation

Key stakeholders who reviewed this version:

- Director – Infection Management
- Immunology SMO
- Infection Management SMO

References and suggested reading

1. Butters C, Phuong LK, Cole T, Gwee A. Prevalence of Immunodeficiency in Children With Invasive Pneumococcal Disease in the Pneumococcal Vaccine Era A Systematic Review. *JAMA PEDIATRICS.* 2019;173(11):1084-1094.
2. Yamashita, M., Inoue, K., Okano, T. *et al.* Inborn errors of immunity—recent advances in research on the pathogenesis. *Inflamm Regener* **41**, 9 (2021). https://doi.org/10.1186/s41232-021-00159-6
3. Jayasinghe S, Menzies R, Chiu C, Toms C, Blyth CC, Krause V, et al. Long-term Impact of a "3 + 0" Schedule for 7- and 13-Valent Pneumococcal Conjugate Vaccines on Invasive Pneumococcal Disease in Australia, 2002–2014. Clinical Infectious Diseases. 2017;64(2):175-83.
4. Ingels H, Schejbel L, Lundstedt AC, et al. Immunodeficiency among children with recurrent invasive pneumococcal disease. The Pediatric infectious disease journal 2015;34:644-51

5. Australian Technical Advisory Group on Immunisation. Australian Immunisation Handbook,. In: Australian Government Department of Health, ed. Canberra, Australia 2018.
6. The Australasian Society of Clinical Immunology and Allergy (ASCIA) provides free primary immunodeficiency e-training for health professionals- https://immunodeficiency.ascia.org.au/

Guideline revision and approval history

Version No.	Modified by	Amendments authorised by	Approved by	Comments
1.0 23/03/2023	Director of Infection Management Service	Director of Infection Management Service	Executive Director Clinical Services	
1.1 27/08/2025	Governance Officer (Documents)	Director, Immunology and Allergy	N/A	Change in custodianship

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Accreditation references	NSQHS Standards (1-8): 3 Preventing and Controlling Healthcare Associated Infection

Appendix 1:

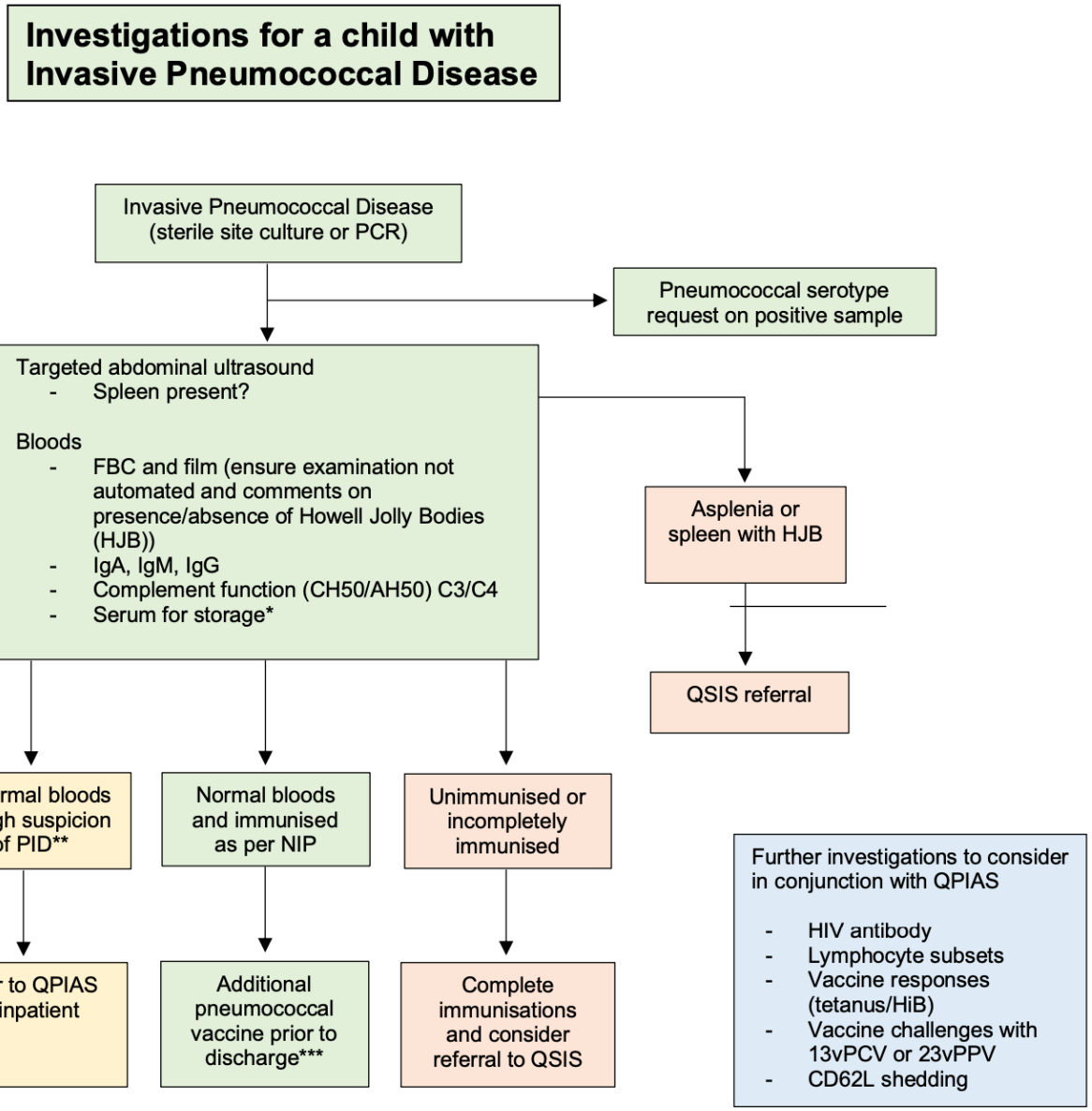

Figure 1. Flowchart of investigations and management of children presenting with IPD
*If possible, collect extra serum for storage in the event Immunology request vaccine responses
**Signs that suggest increased risk of PID include recurrent IPD, consanguinity or unusual site of pneumococcal infection
***Additional vaccinations as per Immunisation Handbook, can be accessed via QSIS at 2g on discharge
Pneumococcal disease | The Australian Immunisation Handbook (health.gov.au)

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Appendix 2:

Preferred blood collection (volume 5mL)				
Tube type	**Tube description**		**Volume required**	**Tests required**
EDTA	Purple pedi-pot		0.5 mL	• FBC • Film to rule out HJB
Serum	Yellow pedi-pot or paed SST		2.5 mL	• IGs (IgA, IgM, IgG) • CH50/AH50 • C3, C4
Serum	Yellow pedi-pot or paed SST		2 mL	• PNABS • Add on