UK PRIMARY IMMUNODEFICIENCY NETWORK
STANDARDS of CARE
This document represents the consensus of the PIN Standard of Care Group.
These Standards of care are for the diagnosis and management of the condition stated, for use by Immunologists and Immunology Specialist Nurses.
Clinical judgement supersedes the Standards of care wherever necessary.

Title	Severe combined immunodeficiency (SCID): initial diagnosis and management
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A list of current standards of care is available at www.ukpin.org.uk

KEY STANDARDS ARE LISTED AT THE END OF THE DOCUMENT

Introduction
Severe combined immunodeficiency (SCID) is a heterogeneous clinical and immunological phenotype that arises from a number of defined molecular defects but also includes a significant number of cases where the underlying molecular abnormality is not known. It is a rare group of diseases, with an overall incidence estimated at 1:50,000 to 1:500,000 births for all forms of SCID. Males are affected more than females because of X-linked inheritance in one specific type. More extensive description of the types of SCID can be found in Reference 1.

Without appropriate treatment, SCID is fatal in the first year of life. Early recognition is vital as an increased infective burden is a significant negative prognostic factor in the success of definitive therapy.

Most importantly, immediate management is not affected by the type of SCID, and prolonged investigation must not delay referral to a specialised centre.

Diagnostic Criteria
These are available on the ESID website
http://www.esid.org/workingparty.php?party=3&sub=2&id=73#Q11

Main Clinical Features
Infections
- Opportunistic infections eg PCP or CMV pneumonitis
- Recurrent, severe or prolonged typical infections eg RSV, parainfluenza, influenza, adenovirus, pneumonia
- Persistent / extensive oral or napkin candidiasis

Failure to thrive
Diarrhoea (including persisting GI infections eg rotavirus)

Other
- Skin rash: maternal engraftment or Omenn's Syndrome
- BCGosis SCID patients who have been given BCG at birth are at risk of disseminated BCG infection.

Key Diagnostic Tests
Where a diagnosis of SCID is suspected the following diagnostic tests must be undertaken:
1. Lymphocyte count: Always use an age-related lymphocyte range: infants normally have higher counts than adults/older children (>2.8 x 10^9/l in infants <3m of age).
2. T and B cell numbers: T, B and NK cell numbers and %.
CD4/8 numbers and % should also be undertaken
3. Immunoglobulin IgG, A and M: these may be low, but maternal IgG may be detected in young infants

The following tests should be considered
1. CD3+4+ and CD3+8+ numbers and %
2. MHC I/II
3. Where appropriate, or in conjunction with a specialist centre, more detailed investigation to define the T cell phenotype or molecular basis of the disease may be undertaken whilst awaiting transfer of the baby to a specialist centre***. It is crucial that this does not delay referral.***

NOTE: A normal or high lymphocyte count or normal or high immunoglobulin levels do not exclude a diagnosis of SCID. Examples of this include Omenn's syndrome and maternal engraftment.

Diagnostic considerations

1. HIV must be considered and excluded where appropriate.
2. A low lymphocyte count in an infant must always be followed up and SCID considered if it persists. Although low lymphocyte counts may be seen in septic infants, immunology advice must be sought if it persists.

Treatment

It is crucial that the diagnosis is recognised quickly and advice sought from the local immunologist in conjunction with the SCID specialist centres:

- Newcastle 0191 273 8811 and ask for the Paediatric immunology consultant or registrar on call
- Great Ormond Street Hospital 020 7405 9200 and ask for the Paediatric immunology consultant or registrar on call

When in hospital, infants with SCID must be cared for in a cubicle (HEPA filtered/Laminar flow where available) with protective isolation measures to protect them from infections.
If a cubicle is not available and child requires inpatient care, they must be transferred to another hospital with a cubical available whilst awaiting transfer to the SCID centre.
If the child is well and does not need to be in hospital, they can be cared for at home by parents. Guidance on this can be obtained from the supraregional centres.

1. **Seek and treat any infections promptly**

- Advice must be sought from a specialist SCID unit.
- Antimicrobial therapy may need to be modified in the light of the diagnosis of SCID.
- If SCID is likely and / or lymphopaenia severe treatment should be initiated whilst awaiting diagnostic results (eg CMV/PCP on a bronchoalveolar lavage)
- Any infants who have received BCG vaccination must be commenced on isoniazid and rifampicin (or other suitable drugs).

2. **Avoid further infections**

- Nurse child in a cubicle with protective isolation measures
  - Keep cubicle doors closed
  - Strict hand washing must be adhered to
  - Visitors must be limited to healthy adults
  - Staff with infections (including minor respiratory tract infections or cold sores) should not care for the child
  - If child needs investigations that cannot be undertaken in the cubicle (eg radiology), the department must be aware that the child must be seen immediately, and must not sit in a waiting area with other children. If a wait is unavoidable, a separate room must be provided.
- Give prophylactic co-trimoxazole (Septrin)
- Give prophylactic fluconazole (or other anti-fungal)
- Start replacement immunoglobulin: (even if IgG normal) consider a loading dose of 1g/kg (See SOC on administration of Ig)

3. **Consider definitive treatment**

- This will be undertaken by the specialist SCID unit, and may include stem cell transplantation, replacement enzyme therapy (PEG-ADA) or selected patients may be offered treatment in a gene therapy trial.
- Local units may be asked to assist with initial tissue typing of the immediate family, or extended family members in consanguineous families.

4. **Other**

- No vaccinations should be given
- All blood products must be irradiated and CMV negative

Ongoing management

IT MAY NOT BE POSSIBLE TO TRANSFER THE CHILD TO NEWCASTLE OR GOSH IMMEDIATELY. Attention should be given to a number of general and specific areas, with advice from the specialist Unit:

General – monitor height, weight and head circumference on a regular basis. Attention to skin care (in particular the nappy area in babies with diarrhoea) is crucial.
Nutrition – adequate nutrition is an extremely important aspect of care. NG tube feeding with more basic hydrolysed feeds may be initially necessary. TPN is necessary if enteral feeding is not tolerated
Haematology and Biochemistry – FBC, U+Es and LFTs as clinically indicated.
Immunology – after initial diagnosis, immunology does not need to be monitored regularly unless there is a change in clinical picture.
Radiology – as clinically indicated
Microbiology – Samples should be collected from any potential site of infection, and cultured appropriately for bacteria, viruses and fungi. ***Viral identification by PCR is required as serological testing will be uninformative.*** Hospitalised patients must have weekly monitoring by nasopharyngeal aspirates (IIF/PCR/Culture) or throat swab (PCR) for common respiratory viruses (RSV, influenza, parainfluenza), and blood PCR for CMV, EBV and adenovirus.
Patients cared for at home must have appropriate investigations (NPA/throat swab for viral PCR) at the first sign of any respiratory symptoms.
In the presence of diarrhoea, viral infection (rotavirus, norovirus etc) must be sought.

Referral and governance issues
Patients must be discussed with and referred to one of the 2 supraregional SCID centres as a matter of urgency:

- Newcastle 0191 273 8811 and ask for the Paediatric immunology consultant or registrar on call
- Great Ormond Street Hospital 020 7405 9200 and ask for the Paediatric immunology consultant or registrar on call

If a child cannot be nursed in a cubicle, they must be transferred to another hospital with a cubicle available whilst awaiting transfer to the SCID centre.

Care of the family
It is important to be aware that this diagnosis and its implications will have a profound impact on the family and a great deal of support will be required.
Information given about SCID must be carefully documented in the notes.
Families will require a lot of support.
A booklet for families on SCID can be found at:

http://www.gosh.nhs.uk/factsheets/families/F000207/index.html

As treatment is likely to be lengthy, early referral to social services for financial support should be considered.

Family referral to local genetics services should be undertaken once the diagnosis is confirmed at a molecular basis.

Nursing and other health professionals

- Further information and guidelines are available from nursing staff at the 2 supraregional units (Ward 23A Newcastle General Hospital and Robin Ward, Great Ormond Street Hospital).
- Reverse barrier nursing in a cubicle is essential
- Nursing staff must be supported in enforcing visiting precautions (ie no young children, no adults with infections, limited numbers of visitors).

Key references

1. Fischer A, Notrangelo LD Combined immune deficiencies in Immunologic Disorders in Infants and Children, 5th Edition, pp447-479 2004, Elsevier.

Appendix A
Guide for General Paediatricians

When do I suspect SCID?

In any infant with:

- Low lymphocyte count (< 2.8 x 10^9/l)
- Persisting thrush
- Persisting diarrhoea
- Failure to thrive
- Persisting or severe viral infection especially RSV, rotavirus, CMV
- Atypical infection especially PCP

What Should I do?

- Contact your local immunologist and arrange further testing
- Contact one of the 2 supraregional units* to discuss transfer and care
- Try to prevent further infection:
    - Nurse child in a cubicle (HEPA filtered/laminar flow if available) with protective isolation measures
        - Keep cubicle door closed
        - Strict hand washing must be adhered to
        - Vistors must be limited to healthy adults
        - Staff with infections (including minor respiratory tract infections, cold sores) must not care for the child
        - If child needs investigations that cannot be undertaken in the cubicle (eg radiology), the department must be aware that the child must be seen immediately, and must not sit in a waiting area with other children. If a wait is unavoidable, a separate room must be provided.
    - Give prophylactic co-trimoxazole (Septrin)
    - Give prophylactic fluconazole
    - Start replacement immunoglobulin (after discussion with immunologist)

*Supraregional SCID centres:
Newcastle 0191 273 8811 and ask for the Paediatric immunology consultant or registrar on call
Great Ormond Street Hospital 020 7405 9200 and ask for the Paediatric Immunology consultant or registrar on Call

SCID: Key standards of care

1. **Where a diagnosis of SCID is suspected the following diagnostic tests must be undertaken**
    a. Lymphocyte count
    b. T and B cell numbers
    c. T, B and NK cell numbers and %.
    d. Immunoglobulin IgG, A and M

2. **If a diagnosis of SCID is suspected the following actions must be taken**
    a. Contact the local immunologist
    b. Discuss with one of the SCID specialist centres (Newcastle or GOSH)

3. **A child with probable SCID must be cared for as follows:**
    a. When in hospital they must be cared for in a cubicle (HEPA filtered/Laminar flow where available)
    b. Protective isolation measures must be used to protect them from infections. [1]
    c. If a cubicle is not available and child requires inpatient care, they must be transferred to another hospital with a cubical available whilst awaiting transfer to the SCID centre.
    d. If the child is well and does not need to be in hospital, they can be cared for at home by parents.

4. **The following treatments must be instigated in discussion with the local/ supra-regional immunology/SCID team:**

    a. If a possibility of active infection:
        i. Seek and treat promptly considering empirical CMV/PCP or other atypical organism therapy
        ii. If BCG has been given, start isoniazid and rifampicin (or other suitable drugs).

    b. **Avoid further infections**
        i. Nurse child in a cubicle with protective isolation measures[1]
        ii. Give prophylactic co-trimoxazole (Septrin)
        iii. Give prophylactic fluconazole (or other anti-fungal)
        iv. Start replacement immunoglobulin: (even if IgG normal) consider a loading dose of 1g/kg (See SOC on administration of Ig)

5. **Avoid complications**
    a. No vaccinations should be given
    b. All blood products must be irradiated and CMV negative

[1] Single cubicle
Keep cubicle doors closed
Strict hand washing must be adhered to
Visitors must be limited to healthy adults
Staff with infections (including minor respiratory tract infections or cold sores) should not care for the child
If child needs investigations that cannot be undertaken in the cubicle (eg radiology), the department must be aware that the child must be seen immediately, and must not sit in a waiting area with other children. If a wait is unavoidable, a separate room must be provided.