

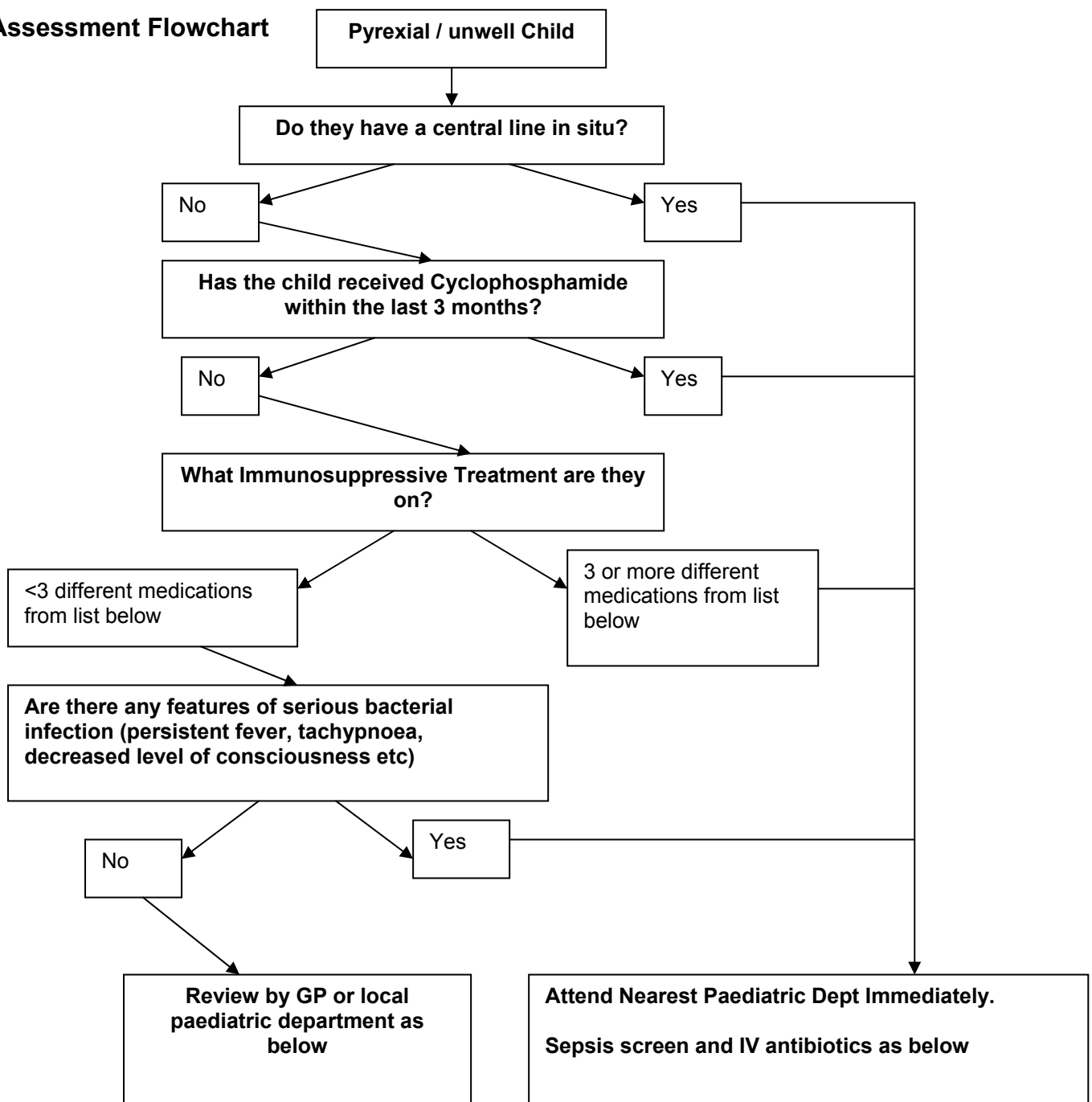
Immunosuppression and Paediatric Rheumatology Patients

Tel: 0191 232 5131
Fax: 0191 201 0155

An increasing number of children with rheumatological diseases are being treated with an increasing variety of immune suppressing drugs (and combinations of those drugs). Children taking these drugs are all at risk of severe infections, both bacterial and viral, although fungal infections are very rare.

These children may become sick quite rapidly, and may present with an incomplete clinical picture. This protocol is aimed to guide doctors when faced with, or answering a telephone query about, a child in these circumstances who may have an infection.

Assessment Flowchart



COMMON DRUGS:

Most of these drugs probably have a similar degree of immunosuppression when taken individually, but combinations may increase the degree of immunosuppression. It is important to remember that **immunosuppression can persist for up to 3 months after stopping these medications** and children within this timescale must be treated as such.

1. **Methotrexate:** affects T-cell function and is given either parenterally or orally. Serious infections are rare but have occurred, especially Chickenpox.
2. **Sulphasalazine:** rarely used and has minimal immunosuppressive activity.
3. **Anti-TNF:** Etanercept (Enbrel®), Infliximab (Remicade®), and Adalimumab (Humira®) all work by interfering with TNF- α . They have been associated with severe infections, especially Tuberculosis and septicaemia
4. **Steroids:** children taking any dose of oral steroids for more than a few weeks must be considered to be immunosuppressed. Doses of $>2\text{mg/kg}$ for $>2\text{weeks}$ are markedly immunosuppressive.
5. **Other drugs:** Cyclophosphamide, Cyclosporin, Azathioprine, Leflunomide (Arava®), and Anakinra (Kineret®) are rarely used in children. Patients taking Cyclophosphamide have a separate protocol, but the other drugs should be treated in the same way as for Methotrexate.

GENERAL APPROACH

Most children taking these medications whose parents ring for advice can be managed by their local GP and should be advised to seek their advice.

However, if there is any concern that the child may have a more serious infection (persistent fever, tachypnoea, signs of decreased peripheral circulation, or altered conscious level, etc.) then the parent must be advised to take their child to the nearest hospital immediately.

Children attending hospital should, of course, receive a full physical examination and should all have the following investigations:

Blood cultures, venous / capillary blood gasses, FBC, U+E, LFT, CRP, Urinalysis

Other investigations (CXR, Lumbar puncture, throat swab, cough swab etc) should be done as clinically indicated. Children with respiratory signs (tachypnoea, hypoxia, etc) must have a CXR and may need Broncho-alveolar lavage to exclude Pneumocystis Carinii infection

If in any doubt the child should be discussed with the on call consultant for paediatrics and admitted overnight for observation. The consultant on-call for Paediatric Infectious Diseases/Immunology is available for further advice if needed.

PROFOUNDLY IMMUNOSUPPRESSED CHILDREN AND CHILDREN WITH INDWELLING VENOUS CATHETERS

Children with an indwelling central line who are on ANY immunosuppressive medication, or within 3 months of doing so must be treated with the utmost speed and seriousness and this same approach should be taken with children taking any combination of 3 or more of the immunosuppressive drugs listed at the beginning of this document.

1. Access central line (or insert peripheral cannula if no central line in situ)
2. FBC, U+E's, LFT's, CRP and venous/ capillary gas sent urgently. Blood cultures, ESR, and viral studies (EBV, HS1+2, CMV, HHV6, respiratory viral screen) should be collected at the same time.
3. Urinalysis (if possible before IV antibiotics are started, but do not delay antibiotics if urine sample not immediately available).
4. Fluid resuscitation if needed.
5. Commence IV antibiotics
 - a. Central line in situ: Teicoplanin 6mg/kg 12hrly for 3 doses then once-daily and Meropenem 20mg/kg tds (max 2g)
 - b. No Central line: Ceftazidime 50mg/kg tds (max. 2g) and Gentamycin 5mg/kg od, or Meropenem 20mg/kg tds (Max 1g) and Gentamycin 5mg/kg od
6. Admit to ward, needs regular review and, if there are any concerns about the patients status deteriorating the case should be discussed urgently with the PICU team at Newcastle General Hospital.

SPECIFIC INFECTIONS

1. VARICELLA:

- a. **Patients who develop chickenpox or shingles must be admitted for IV Acyclovir the same day the spots appear.** Patients who are known to be immune (positive serology, previous documented vaccination, or clear previous history) may have an attenuated disease and may not need the full course to be given IV. The decision to change to oral Acyclovir should be made by the consultant looking after the child.
- b. **Contacts:** Treatment of children with a close contact (Same room for >15mins, or face to face contact) with chickenpox depends on their Varicella immune status, but there is no need to re-check serology before deciding how to proceed.
 - i. Known immunity: no treatment but child must be fully undressed and examined by parent/carer twice a day and if spots develop admitted to hospital as above. For children who are heavily immunosuppressed (ie "Biologics" [Etanercept, Infliximab, Adalimumab, Anakinra], Cyclophosphamide, or high-dose oral

steroids [$>1\text{mg/kg/day}$]) consider giving prophylactic oral Acyclovir (discuss with consultant first)

- ii. Unknown / non-immune: within 72 hrs of exposure these children may be given either of the following:
 1. Zoster immunoglobulin (ZIG) - consider IVIG if child is thrombocytopenic as IM ZIG may cause excessive bruising
 - a. $<5\text{yrs}$ of age: 250mg
 - b. 5-10yrs: 500mg
 - c. $>10\text{yrs}$: 750mg
 2. Oral Acyclovir starting as soon as possible after contact and continuing for 21 days
 - a. $<2\text{yrs}$: 200mg QDS
 - b. 2-6yrs: 400mg QDS
 - c. $>6\text{yrs}$: 800mg QDS
- c. **Role of Vaccine** (Varivax ®). This is recommended for all non-immune patients who may require immunosuppression in the future and must be given at least 2 weeks before starting any immunosuppressive therapy. It is contra-indicated in those already immunosuppressed

2. MEASLES:

Children are infective from 3 days before onset of rash until desquamation (usually ~4 days). Treatment is supportive, but children with measles should be admitted for observation as they are at risk of severe disease. Children within 6 days (most effective if within 3 days) of contact (Same room for $>15\text{mins}$, or face to face contact) with a known case of measles should receive Normal Human Immunoglobulin (available from Public Health Laboratory Service, contact Virologist on-call). Measles is a notifiable disease so the index case must be notified to PHLS.

1. Normal Human Immunoglobulin
 - a. $<1\text{yr}$: 250mg IM
 - b. 1-2yr: 500mg IM
 - c. $>2\text{yr}$: 750mg IM
2. Standard Immunoglobulin may be used only if Normal Human Immunoglobulin is not available
 - a. Dose 0.2mg/kg given IV

3. TUBERCULOSIS:

Treatment for children with TB should always be co-ordinated with the Infectious Diseases team, and specific advice should be sought from the consultant on call. A high index of suspicion must be maintained for children taking "Biologic" Therapies especially Infliximab as these children may be particularly at risk from this infection.

Before starting Biologic therapy or Cyclophosphamide all children should have had a Mantoux test and a CXR and the results of these should be recorded in the medical notes.