All Wales PIMS-TS & Recovery Trial Pathway Nov '20

Noah's Ark Children's Hospital for Wales Ysbyty Plant Cymru

This guide does not replace comprehensive work up of paediatric fevers
It only aids diagnosis, initial management and timeframes for PIMS-TS and Recovery Trial Entry
Suspected PIMS-TSS requires early involvement of paediatric consult on call and MDT discussion

RCPCH case definition[1]

Possible PIMS-TS?

Use UK National management Consensus[2]

Child has persistent fever, inflammation (↑CRP/↑Neut/↓Lymph), single or multi-organ dysfunction (shock, cardiac, resp, GI, renal, neuro)

FBC, film CRP, ferritin, U/E, bone, LFT, amylase, CK, vit D, blood gas, lactate, clotting, fibrinogen, didimers, troponin, LDH, pro calcitonin & NTproBNP if available, and infection blood tests below

Prompt Infection Work up is crucial: blood culture, urine, LP discretionary, throat swab for COVID PCR and full viral respiratory screen and mc/s, COVID antibody serology, ASOT, EBV viral serology (not monospot), and other tests as clinically indicated. SAVE SERUM to Virology BEFORE IVIG.
CXR, ECG and early ECHO. ***Very low threshold for early Abdominal U/S***

Assess Severity (shock, rising inflammatory markers, abnormal ECG or ECHO – see Appendix for full criteria

General Principles

PIMS TS diagnosis and treatment decisions including RECOVERY TRIAL are reached through early discussion with the MDT: Cardiology, Paeds ID via UHW switch +/- WATCh

Normal Supportive Care, Ceftriaxone (and clindamycin if shocked) pending cultures
Prophylactic Enoxiparin if significantly immobilised; if over 12 yrs, also wear compression stockings

Frequently re-assess, and also monitor mild cases closely (daily bloods)

PIMS -TS diagnosis agreed

	KAWASAKI PICTURE (don't wait 5 days) High Risk: coronary changes and/or age < 1 yr	NON SPECIFIC INFLAMMATORY PICTURE (mild-mod-severe/shock)
0-12 hours	**Early IVIG*** **(also overnight)** **(if high risk : add Methyl Pred + PPI)**	**Recovery Trial** **(IVIG* vs Methyl Pred vs nil)**
0-12 hours	Aspirin: Kawasaki guidelines (d/w Cardiologist)	Aspirin: antiplatelet dose until ECHO normal 6/52

Closely monitor response (incl ECHOs), daily MDT discussion

Consider transfer to Children's Hospital (see criteria page 2)

24-48 hours	**If not improving: Methylpred + PPI**	**If not improving: Recovery Trial** **(Tocilizumab vs nil)**
96 hours	**Infliximab**	**Bespoke treatment as per MDT**

* **IVIG: if available prescribe Iqymmune or Intratect**

On behalf of PIMS-TS MDT, Siske Struik, Consultant Paediatrician UHW 6 November 2020, next review TBC

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Key Points

Fever is common in, whilst PIMS -TS is very rare. The single most important challenge thus is to work through the potential causes of persistent fever in a timely manner.

RCPCH case definition of PIMS-TS [1]
A child (>44 weeks gestation) presenting with persistent fever, inflammation (neutrophilia, elevated CRP and lymphopenia) and evidence of single or multi-organ dysfunction (shock, cardiac, respiratory, renal, gastrointestinal or neurological disorder) with additional features. This may include children fulfilling full or partial criteria for Kawasaki disease. Exclusion of microbiological cause.

Making Diagnosis and Treatment Decisions
Every child with suspected PIMS-TS should be discussed with Paeds ID and Cardiology within 24 hours.
- Treatment for Kawasaki's phenotype follows normal standard of care, but is accelerated, especially in high risk groups. Do not hold up starting IVIG in clear cut Kawasaki's presenting out of hours (discuss with MDT next day).
- Best treatments for non specific phenotypes is unclear and being studied through Recovery Trial [3].

Severity Criteria (see also Appendix next page: panel 2 of national consensus document) [2]
Clinical deterioration, shock, worsening inflammatory markers (note ferritin), cardiac involvement

Recovery trial – instructions (www.recoverytrial.net)
All Paediatric Units are strongly encouraged to recruit eligible patients rather than 'just treat'
Decision to enrol requires Paediatric ID/MDT discussion (Or PICU)
Consenting and randomisation for first step (IVIG vs Methyl Pred vs nil) by clinician at local hospital

Location of Care (see also Appendix next page: panel 2 of national consensus document) [2]
Determined by severity and cardiac status (or need for Tocilizumab)

How to contact UHW Paediatric COVID MDT (includes PIMS TS)
Core: Paediatric IMM/ID, Cardiology, PCCU, Respiratory (for chest) and other specialties as needed
Consultant to Consultant (ideally) via UHW Switch (Paeds ID no formal hours of hours cover – discuss with Gen Paeds on call consultant who can sign post to JE/SS or St Mary's Hospital if needed)

How to transfer to UHW (PICU, HDU or ward level)
Contact WATCh retrieval service 0300 0300 789. WATCh will include on a planning call with UHW:
- PICU consultant and Paediatric Cardiologist on call
- If ward to ward transfer, must also include the UHW General Paediatric Consultant on call
- Paediatric ID consultant on call can be included (optional, via switch)

Please note that depending on their capacity, WATCh may need to request the local team to transfer if felt clinically appropriate.

Surveillance and studies we participate in
BPSU, RECOVERY, ISARIC and BATS-study

1. https://www.rcpch.ac.uk/sites/default/files/2020-05/COVID-19-Paediatric-multisystem-%20inflammatory%20syndrome-20200501.pdf
2. UK national consensus: https://www.thelancet.com/journals/lanchi/article/PIIS2352-4642(20)30304-7/fulltext

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Appendix (panel 2 of national consensus document) [2]

Panel 2: Management processes for children with PIMS-TS

Classification of PIMS-TS

Primary classification of PIMS-TS should be based on the presenting phenotype*:

(A) Kawasaki disease-like: complete and incomplete, classified using the American Heart Association criteria[17]

(B) Non-specific: children presenting with shock or fever, or both, and symptoms that might include abdominal pain, gastrointestinal, respiratory, or neurological symptoms that do not meet the criteria for Kawasaki disease

Subsequent classification of severity is recommended*

Location of care and features of severity of PIMS-TS

(1) Location of care should be determined by the severity of disease and discussion in a multidisciplinary team will aid risk stratification

(2) Features of severe disease might be indicated by the presence of any of the following factors, particularly when present in combination:

- Physiological features of severe disease: extended capillary refill time†; persistent hypotension†; persistent tachycardia†; requirement for 40 mL/kg fluid bolus†; oxygen saturation <92% in room air†
- Haematological and biochemical features: clinically significant increase in C-reactive protein† (consensus reached for >300 mg/L but subsequent evidence suggests >150 mg/L); clinically significant increase or increasing troponin†; increasing NT-proBNP†; increased or increasing lactate†; clinically significant increase or increasing ferritin†; clinically significant increase or increasing D-dimer‡; increased or increasing lactate dehydrogenase‡; high or low fibrinogen‡; increased creatinine‡
- Cardiac features: abnormal electrocardiogram†; coronary artery aneurysms on echocardiogram†; left ventricular failure*

(3) Children with features of complete or incomplete Kawasaki disease-like phenotype can be cared for in a local hospital with a PICU if they meet the following criteria: they do not have single or multiple organ dysfunction or cardiac involvement and they can have an echocardiogram by a clinician with competency to assess for cardiac involvement including coronary artery abnormalities*

(4) Escalation to a PICU that has clinicians with cardiology expertise should be considered early for any child with single or multiple organ dysfunction†

(5) Children with any evidence of cardiac involvement (increased troponin, increased NT-proBNP, abnormal coronary arteries on echocardiogram or contrast-enhanced CT) should be cared for in a paediatric high dependency unit or PICU with clinicians who have cardiology expertise†

Multidisciplinary team

(1) Early discussion with the core multidisciplinary team should occur for children who are severely unwell

(2) Every child with suspected PIMS-TS should be discussed by a multidisciplinary team within 24 h of admission or identification of PIMS-TS if already an inpatient†

(3) Core members of the team should include paediatric infectious diseases experts or immunologists† or paediatric rheumatologists†, or both, and paediatric cardiologists† and paediatric intensivists†

(4) Additional members of the multidisciplinary team should include general paediatricians caring for children in a local hospital with a PICU for children with multiple comorbidities*, a paediatric transport team for children who are severely unwell in a local hospital with a PICU at the time of discussion with the multidisciplinary team*, and paediatric haematologists for children with haemoglobinopathies, clotting disorders, coagulopathy, or thrombosis‡

Discharge criteria and follow-up

(1) To be discharged from hospital, children who are otherwise well should have stable cardiac function† and no pyrexia for 24 h‡

(2) Children with PIMS-TS should be followed up in the first 1–2 weeks after discharge* and have further follow-up 6 weeks after discharge†; echocardiography should form part of this follow-up for all children with PIMS-TS

(3) Multidisciplinary follow-up should be done for children with coronary artery abnormalities* or who have required organ support due to PIMS-TS*

(4) During follow-up, multidisciplinary clinicians should include paediatric cardiology† and paediatric infectious disease‡ experts

NT-proBNP=N-terminal pro-B-type natriuretic peptide. PICU=paediatric intensive care unit. PIMS-TS=paediatric inflammatory multisystem syndrome temporally associated with SARS-CoV-2. SARS-CoV-2=severe acute respiratory syndrome coronavirus 2. *Determined in phase three of the Delphi process. †Determined in phase two of the Delphi process. ‡Determined during the consensus meeting