

WOMEN'S HEALTH AND PAEDIATRICS
 PAEDIATRIC DEPT

**Pyrexia of Unknown Origin (PUO)
 Clinical Guideline**

Amendments			
Date	Page(s)	Comments	Approved by
June 2013	New Guideline		
March 2018		Whole document review	Paediatric Guideline Group

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In Consultation with:

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Target Audience: Doctors, nurses and support staff working in Paediatrics

Impact Assessment Carried Out By:

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Pyrexia of Unknown Origin

Often confused with “Fever Without a Source”.

Pyrexia of Unknown Origin involves a **prolonged duration** of fever.

Fever without a Source may become Pyrexia of Unknown Origin, if it lasts long enough.

The exact incidence of Pyrexia of Unknown Origin is not well defined.

There is no standard definition.

The ability to determine aetiologies has improved over time.

If a diagnosis is eventually determined, then it is no longer of “Unknown Origin.”

More likely to be dealing with an **unusual presentation of a common condition** than a common presentation of an unusual condition. [*Antoon, 2015*]

Definition

Generally requires duration of fever that is deemed to be excessively long for what was expected.

Historically, up to 3 weeks of fever was used. [*Petersdorf, 1961*]

Now, fever lasting **longer than 8 days without a source** is often cited.

Ideally, there are documented fevers (**≥38.0**).

Aetiology

<p>1. Infectious – ~30% The proportion of infectious causes has decreased in recent years, likely due to improved diagnostic testing.</p> <p>Bacterial Pneumonia Urinary tract infection Cellulitis (or line infection) Osteomyelitis, Septic Arthritis ENT Abdominal/pelvic abscess Endocarditis Meningitis</p> <p>TB Pulmonary or extra pulmonary</p> <p>Viral Gastroenteritis Hepatitis EBV CMV Parvovirus Mycoplasma Herpes HIV Recent vaccination</p>	<p>2. Rheumatologic / Autoimmune/Inflammatory – ~20% Juvenile Idiopathic Arthritis <u>Inflammatory Bowel Disease</u> <u>Kawasaki Disease</u> Systemic Lupus Erythematosus <u>Serum Sickness</u> Immunodeficiency Syndromes Inflammatory Bowel Disease Periodic Fevers</p>
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Parasitic Malaria Toxoplasma Toxocara	
3. Oncologic – ~10% Haematological Leukaemias; lymphomas; myeloma Solid organ Any, especially if disseminated malignancy	4. Other Causes – ~5% Familial Dysautonomia Cyclic Neutropenia Thyrotoxicosis Factitious
5. Drug Fever – ~5% Often overlooked [<i>Antoon, 2015</i>] First step in evaluation is stopping all nonessential medications [<i>Antoon, 2015</i>] Many agents, including ibuprofen and acetaminophen, can be a source of drug fever.	6. Undiagnosed (often spontaneously resolved) – ~30%
7. Pseudo-Pyrexia of Unknown Origin Series of benign, self-limited illnesses over a short period of time [<i>Tolan, 2010</i>] This can create the appearance of the child being sick over a protracted course.	

Considerations

Do not under-appreciate the family's concern

- General Appearance: Is the child sick or not sick?

Sick – Higher risk for significant illness with lower threshold for admission.

Not Sick – Lower risk for significant illness (***not no risk***), but likely more appropriately evaluated as an outpatient.

The diagnosis is likely hiding in the History and Physical. [*Tolan, 2010*]

Ask more questions... even the same ones over again (we have all witnessed “historic alternans”).

History of presenting complaint:

Onset: when was temperature first noted; sudden or gradual onset?

Character: constant or intermittent; Frequent peaks in temperature? Has the temperature actually been recorded, if so how high?

Alleviating factors: rest, Paracetamol, Ibuprofen

Timing: night or day, related to exertion?

Associated symptoms/signs (systematic)

- Shivering or rigors
- Sweating (night sweats are particularly important: these are drenching and often require a change of bedclothes)

- Weight loss, Anorexia
- Feeling faint or dizzy; syncope
- Fatigue (has it interfered with daily life?)

Associated symptoms/signs (systems-based)

- Sore throat; difficulty swallowing; ear pain
- Cough and sputum
- Mouth or perianal ulcers
- Hair loss
- Red sore eyes, /oral mucosa
- Diarrhoea and vomiting; abdominal pain
- Urinary frequency; dysuria; haematuria
- Rashes or skin changes; areas of erythema, peeling
- Headache, neck stiffness, photophobia
- New heart murmur; symptoms of heart failure; lethargy;
- Lumps or bumps
- Joint, bone or muscle pains, joint swelling

Past medical history

- Full past medical history but particularly:
- Previous fevers
- Immunosuppression- On steroids, chemotherapy or other immunosuppressive medication
- Tuberculosis- When? Where? Was it drug resistant? What previous treatment given and for how long? (If not sure re: dosing, did their urine go orange? – implies given rifampicin)
- HIV- When diagnosed? When started treatment? Previous treatment? Current treatment? Adherence to medications? Who are they usually looked after by? Do they know their last CD4 count and viral load?
- Recent surgery including dental procedures
- Recent illnesses (including viral) and antibiotic courses

Drug history

- Full drug history including over-the-counter (OTC) and recreational drugs
- Smoking; alcohol
- Immunisations up-to-date?

Family history

- Any family members with contagious diseases (tuberculosis or viral illness)

Social history

- All travel in last year and prophylaxis
- Animal exposures – cats? petting zoos? etc.
- Vector exposures – ticks?
- Swimming (especially in lakes and rivers)
- Pica and Dietary exposures (Toxocara, Toxoplasmosis)
- **TB risks** Contact with people with TB, Recent visit to, or relative visiting from, TB endemic areas

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- **HIV and hepatitis risks** Sexual contact with at-risk individual, no use of barrier protection, Tattoos, Piercings

General examination to include

- Vital signs – Relative Bradycardia?
- Heart murmurs – splinter haemorrhages; Janeway lesions; Osler's nodes; Roth spots; microscopic haematuria (infective endocarditis)
- Hepatosplenomegaly – malignancy, inflammatory, infectious?
- Joints and bones – osteomyelitis, septic arthritis, JIA?
- Skin – Kawasaki Disease, Rheumatic Fever?
- Eyes, mouth, nails – autoimmune?
- Perianal exam – Inflammatory bowel disease?

A completely normal physical exam at time of initial evaluation is suggestive of a benign cause. (*Antoon, 2015*)

Investigations

Resist the urge to order every test available.

Broad laboratory testing is often more harmful than helpful.

<p><u>First Line Investigations:</u></p> <p>FBC + film, U&Es, LFTs, TFTs, CRP, ESR Urate, LDH ASOT, AntiDNase B Thick and thin films, malaria antibodies (based on history) Throat swab – viral, bacterial NPA Urine microscopy & culture x 2 Blood culture Stool – OCP, viral, bacterial culture +/- Lumbar puncture CXR</p>	<p><u>Consider Second Line Investigations if no response to treatment within 72 hours:</u></p> <p>Repeat FBC, film, ESR, CRP Serial blood cultures Autoimmune screen: Autoantibodies, Immunoglobulins and subclasses, C3, C4, Lupus anticoagulant, dsDNA, Antiphospholipid antibody, Ferritin, lipids ANCA Extensive viral serology - Hepatitis, EBV, CMV, Parvovirus, Herpes, Coxsackie, +/- HIV Toxocara, Toxoplasma antibodies Mycoplasma serology Thyroid peroxidase antibodies USS abdomen and pelvis MRI bone, joint ECHO CT scan chest, abdomen pelvis</p>
<p><u>Seek opinion from Immunology and Infectious Diseases, Oncology, Rheumatology if no progress</u></p>	

PUO: Empiric Antibiotics?

Ill Appearing?

Have a lower threshold for obtaining cultures and starting empiric antibiotics.

Well Appearing?

- Observe for fever pattern and progress.
- Do not use of regular antipyretics as fever patterns can be helpful to determine diagnoses

DO NOT give antibiotics at the outset! Empiric antibiotics can delay the diagnosis of many conditions like osteomyelitis and endocarditis. [*Antoon, 2015; Chow, 2011*]

Antibiotic choice is dependent on likely source of fever

If no obvious source, broad-spectrum third generation Cephalosporins are a first line choice.

References

1. <http://pedemmorsels.com/fever-of-unknown-origin/>

2. <http://www.oxfordmedicaleducation.com/history/pyrexia-of-unknown-origin/>

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