

# FEVER OF UNKNOWN ORIGIN

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## Definition:

- (FUO) is best reserved for children temperature  $>38^{\circ}\text{C}$  ( $100.4^{\circ}\text{F}$ ) of at least eight days' duration
- after an intensive **1** week investigation in the hospital.
- Most FUO result from **atypical presentations of common disease.**

# Etiology

- Infectious diseases (**most common**)
- Inflammatory diseases (20%)
- Malignancies (10%)
- Unknown or miscellaneous (15%)

## Infectious diseases:

- **1. *Cat scratch disease***
- **2. *Brucellosis***
- **3- *Salmonellosis***
- **4-*Rickettsia***
- **5- *Intraabdominal, pelvic, intranephric, and perinephric abscesses***

Behçet syndrome  
Drug fever  
Hypersensitivity pneumonitis

Polyarteritis nodosa  
Rheumatic fever  
Juvenile dermatomyositis

**Inflammatory  
diseases**

Juvenile idiopathic arthritis  
Inflammatory bowel disease  
Kawasaki disease

Sarcoidosis  
Serum sickness  
Systemic lupus erythematosus  
Weber-Christian disease

Atrial myxoma  
Cholesterol granuloma

Hodgkin disease  
Inflammatory  
pseudotumor  
Wilms tumor

**MALIGNANCIES**

Lymphoma  
Ewing sarcoma  
Hepatoma

Leukemia  
Neuroblastoma  
Pheochromocytoma

## ***Miscellaneous***

- ***1-drug fever***
- ***2-factitious***
- ***3-hypothalamic dysinnfuction***
- ***4-castlman***
- ***5-idopathic***

# Infectious

## Bacterial:

### 1. Cat scratch disease:

- *-Bartonella henselae*
- *-is one of the most common causes of FUO in children.*
- *-cat to human transmission (through scratch or bite)*
- *-clinical presentation: rash (3-10 days), regional lymphadenopathy (tender , usually in axillary nodes), fever, hepatoseplenomegaly.*
- **Diagnosis:**
- *-Serology (IgM ,IgG)*
- *-lymph node biopsy (usually not required)*
- *Treatment:*
- *Self limited or use azithromycin..*



## **2.Brucellosis:**

-Main way of transmission is ingestion of unpasteurized dairy product from goats or camels.

-classic triad (fever, arthralgia/ arthritis and hepatosplenomegaly).

-Some present as FUO.

### **Diagnosis:**

-Serology

-definitive diagnosis (bone marrow culture, blood culture ).

## Treatment:

<8 years: Rifampicin + bactrim  
(trimethoprim/sulfamethoxazole).  
>8 years: Rifampicin + doxycycline.  
Add IV gentamicin for hospitalised  
patients.  
-Duration 4-6 weeks.

### **3-Salmonellosis:**

- contaminate a number of food products, especially poultry and eggs, and can be transmitted through contact with reptiles or animal feces.
- clinical presentation: high fever, diarrhea , abdominal pain , headache.

#### **Diagnosis:**

- based on clinical signs and symptoms
- confirmed by culture of stool or blood.
- Serologic testing is not recommended

# Mediterranean spotted fever (MSF)

- Mediterranean spotted fever (MSF) is a tick-borne endemic disease caused by *Rickettsia conorii* which is an obligate intracellular bacterium
- mainly in the Mediterranean area and the surrounding countries.

# Clinical manifestation

- It is characterized by fever, maculopapular rash and a tick bite skin lesion (tache noire) The vast majority of patients develops a sparse macular rash which later becomes maculopapular and generalized, usually involving the palms and soles and sparing the face.

- Severe cases progress with splenomegaly, myocarditis, renal impairment, pneumonitis, and shock.

# Laboratory and Imaging Studies

- Thrombocytopenia, anemia, hyponatremia, hypoalbuminemia, and elevated hepatic transaminase levels are common laboratory findings.
- Organisms can be detected in skin biopsy specimens by fluorescent antibodies or polymerase chain reaction, although this test is not widely available
- Serological testing is used to confirm the diagnosis.
- Approximately 50% of patients will not have detectable antibody until the second week of illness, and treatment should not be withheld pending confirmation.

# Treatment

- Therapy for suspected MSF should not be postponed pending results of diagnostic tests.
- Doxycycline is the drug of choice, even for young children, despite the theoretical risk of dental staining in children younger than 8 years of age.



# Complication and prognosis

- In severe infections, capillary leakage results in noncardiogenic pulmonary edema (acute respiratory distress syndrome), hypotension, disseminated intravascular coagulation, circulatory collapse, and multiple organ failure, including encephalitis, myocarditis, hepatitis, and renal failure.
- Untreated illness may persist for 3 weeks and progress to multisystem involvement.
- the mortality rate is 20-80% without treatment, which is reduced to 1-3% with treatment.

# prevention

preventive measures are focused on modification of human behavior and vector control strategies.

A deeper understanding of the reservoir system of these bacteria is needed for the development of targeted preventive measures, since there are currently no vaccines commercially available.

# Inflammation :

- **Kawasaki disease (KD):** mucocutaneous lymph node syndrome  
Kawasaki disease is an acute febrile systemic **vasculitis** that predominantly occurs in children below five years of age. Its etiopathogenesis is still not clear.
- The disease is characterized by a high fever, desquamative rash, conjunctivitis, mucositis (e.g., "strawberry tongue"), cervical lymphadenopathy, as well as erythema and edema of the distal extremities.
- However, coronary artery aneurysms are the most concerning possible manifestation as they can lead to myocardial infarction or arrhythmias.
- Kawasaki disease is a clinical diagnosis, further supported by findings such as elevated ESR or evidence of cardiac involvement on echocardiography.
- Treatment with IV immunoglobulins and high-dose aspirin is essential and should be initiated immediately after diagnosis.

# Kawasaki Disease

*Small and medium vessel vasculitis*

mnemonic: "Warm CREAM"

## NEEDS:

**Warm** - fever >5d

## PLUS 4 of 5:

1. Conjunctivitis - Bilateral, non-purulent
2. Rash - erythematous, maculopapular, or morbilliform
3. Erythema palms and soles - with swelling
4. Adenopathy, cervical - 1 unilateral node
5. Mucous Membrane - dry, red, strawberry tongue

## Treatment:

1. High dose ASA
2. IVIG

## Complications:

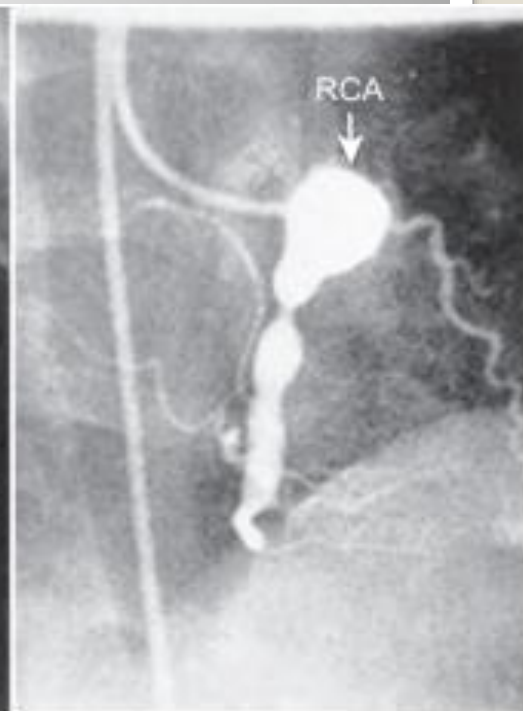
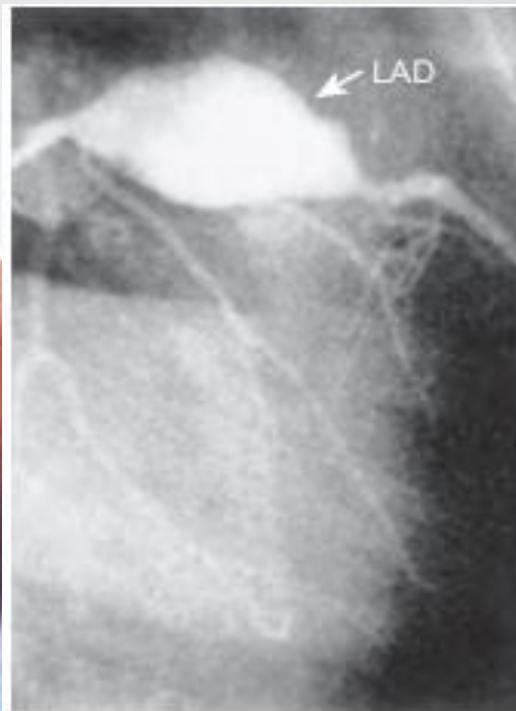
- Coronary artery aneurysm
- Myocarditis
- So do an echo!*



**NOTE :**  
**Exclude**  
**other**  
**diseases**  
**with similar**  
**findings**







# **APPROACH TO FUO IN PEDIATRICS**

# DIAGNOSIS

- The evaluation of FUO requires a thorough **history** and **physical examination** supplemented by **a few screening laboratory tests**, and **additional laboratory** and **radiographic tests** as indicated by the history or abnormalities found on examination or initial screening.



# History

- **A detailed fever history including:**
  - Onset
  - Frequency
  - Duration of fever
  - Response or nonresponse to therapy
  - Recurrence
  - The impact the fever has on the child's health and activity
  - Weight loss
  - Associated symptoms should be obtained.

# History

- Clues from the general history including:
  - Age (children > 6 years , adolescents)
  - Medication History
  - Genetic Background
  - Social History (exposure to domestic animals , Pica, eating habits)
  - Recent surgical procedure or dental work
  - Hx of chronic infection

# Physical Examination

- The child's general appearance including:
  - Sweating
- The general activity of the patient
- presence or absence of rashes
- Tenderness to tapping over the sinuses or the upper teeth suggests sinusitis.
- Recurrent oral candidiasis may be a clue to various disorders of the immune system.
- Rectal examination
- Muscles and bone examination
- Ophthalmic examination

# Laboratory findings

- A **CBC** with a differential WBC count and a **urinalysis** should be part of the initial laboratory evaluation.
- patients with a **PMN count of  $>10,000/\mu\text{L}$**  or a **nonsegmented PMN count of  $>500/\mu\text{L}$**  have a high likelihood of having a severe bacterial infection.

**ESR and CRP : non specific indicator of tissue inflammation.**

- **Blood cultures:** Multiple or repeated blood cultures may be required to detect bacteremia associated with infective endocarditis, osteomyelitis, or deep-seated abscesses.
- **Urine culture** should be obtained routinely.
- **Tuberculin skin testing (TST)**
- **Serologic tests** may aid in the diagnosis of infectious mononucleosis, CMV infection, toxoplasmosis

- **Radiographic** examination of the chest, sinuses or gastrointestinal tract
- **Total body CT and MRI**
- **Endoscopy or Colonoscopy**
- **Radionuclide scan** may be helpful in detecting abdominal abscesses as well as osteomyelitis
- **Bone marrow biopsy** for cytology and culture

# TREATMENT

**antimicrobial agents should not be used as antipyretics, and empirical trials of medication should generally be avoided.**

- An exception may be the use of anti tuberculous treatment in critically ill children with suspected disseminated tuberculosis.
- **Empirical trials** of other antimicrobial agents may be dangerous and can **obscure the diagnosis** of infective endocarditis, meningitis, parameningeal infection, or osteomyelitis.
- The ultimate treatment of FUO is tailored to the underlying diagnosis.

# Prognosis

- Children with FUO have a better prognosis than do adults. The outcome in a child depends on the primary disease process, which is usually an atypical presentation of a common childhood illness.





THANK YOU