FEVER WITHOUT FOCUS
DEFINITION

• Fever without a focus refers to a rectal temperature of 38 C or higher as the sole presenting feature.

• The terms “fever without localizing signs” and “fever of unknown origin” (FUO) are subcategories of fever without a focus.
FEVER WITHOUT LOCALIZING SIGNS

• Common diagnostic dilemma.

• The etiology depends on the age.

• Traditionally, 3 age groups are considered:
  ➢ Neonates.
  ➢ Infants 1 month to 3 months of age.
  ➢ Children >3 months to 3 years of age.
FEVER WITHOUT LOCALIZING SIGNS

Neonates

• Challenge - as they display limited signs of infection.
• Immature immune responses in the first few months.
• Practice guidelines recommend that if a neonate has had a fever recorded at home by a reliable parent, the patient should be treated as a febrile neonate.
• If body temperature is normal after the covers are removed, then the infant is considered afebrile.
FEVER WITHOUT LOCALIZING SIGNS

Neonates

- Owing to the unreliability of physical findings all febrile neonates should be hospitalized.
- Blood, urine, and cerebrospinal fluid (CSF) should be cultured.
- Stool culture and chest radiograph may also be part.
- Combination antibiotics such as ampicillin and cefotaxime are recommended.
- Acyclovir - owing to the presence of CSF pleocytosis or known maternal history of genital HSV.
FEVER WITHOUT LOCALIZING SIGNS

1 month to 3 years

- The large majority - likely have a viral syndrome.
- RSV and influenza A virus infections - winter.
- Enterovirus infections - summer and fall.
- Pyelonephritis - in uncircumcised boys and infants with urinary tract anomalies.
- Potential bacterial diseases in this age group include otitis media, pneumonia, omphalitis, and SSTI.
FEVER WITHOUT LOCALIZING SIGNS

1 month to 3 years (ill-appearing)

- Hospitalization and cultures of blood, urine, and CSF.
- Ampicillin (to cover *L. monocytogenes* and enterococcus) plus either ceftriaxone or cefotaxime is an effective initial antimicrobial regimen.
- If meningitis is suspected because of CSF abnormalities, vancomycin should be included to treat possible penicillin-resistant *S. pneumoniae*. 
FEVER WITHOUT LOCALIZING SIGNS

1 month to 3 years (well appearing)

• Who have been previously healthy and who have no evidence of skin, soft tissue, bone, joint, or ear infection;

• WBC count of 5,000-15,000 cells/dL, an absolute band count of <1,500 cells/dL, and normal urinalysis and negative culture results are unlikely to have a serious bacterial infection.

• If close observation without antibiotics is planned, a lumbar puncture may be deferred.
FEVER WITHOUT LOCALIZING SIGNS

3 months to 3 years of age

• Approximately 30% - no localizing signs of infection.
• Vast majority - Viral infections.
• *S. pneumoniae*, *N. meningitides*, and *Salmonella* account for most cases of occult bacteremia.
• Bacteremia and/or pneumonia or pyelonephritis, among 3 months to 3 years of age increases as the temperature ( >40C) and WBC count (>25,000) increase.
FEVER WITHOUT LOCALIZING SIGNS

• Well appearing:
  – Reassurance that diagnosis is likely self-limiting viral infection, but advise return with persistence of fever, temperatures >39°C, and new signs and symptoms.

• Ill appearing
  – Vaccinated: only laboratory tests needed in this age group when temperature is >39 C.
  – Unvaccinated: obtaining cultures and administering empirical antibiotic therapy (ceftriaxone, a single dose of 50 mg/kg, not to exceed 1 g).
FEVER WITHOUT LOCALIZING SIGNS

• Empirical antibiotic therapy for well-appearing children <36 mo of age who have not received Hib and S. pneumoniae conjugate vaccines and who have a rectal temperature of >39 C and a WBC count of >15,000/dL is strongly recommended.

• If blood cultures are obtained and S. pneumoniae is isolated from the blood, the child should return to the physician as soon as possible after the culture results are known.
FUO- DEFINITION

• The classification of FUO is best reserved for children with fever documented by a health care provider and for which the cause could not be identified after 3 wk of evaluation as an outpatient or after 1 wk of evaluation in the hospital.
SUBTYPES

1. Classic FUO
2. Health care associated FUO
3. Immune deficient FUO
4. HIV related FUO
CLASSIC FUO

• **Def:** >38°C, >3 wk, >2 visits or 1 wk in hospital.

• **Causes:** Cancer, infections, inflammatory conditions, undiagnosed, habitual hyperthermia.

• **H/O:** Travel, contacts, animal and insect exposure, medications, immunizations, family history, cardiac valve disorder.

• **Examine:** Fundi, oropharynx, temporal artery, abdomen, lymph nodes, spleen, joints, skin, nails, genitalia, rectum or prostate, lower limb deep veins.
CLASSIC FUO

- **Inv**: Imaging, biopsies, sedimentation rate, skin tests.

- **Management**: Observation, outpatient temperature chart, investigations, avoidance of empirical drug treatments.

- **Time course of disease**: Months.

- **Tempo of investigations**: weeks.
HEALTH CARE ASSOCIATED FUO

- **Def:** $\geq 38 \text{ C}, >1 \text{ wk}$, not present or incubating on admission.

- **Causes:** Health care – associated infections, postoperative complications, drug fever.

- **H/O:** Operations and procedures, devices, anatomic considerations, drug treatment.

- **Examine:** Wounds, drains, devices, sinuses, urine.
HEALTH CARE ASSOCIATED FUO

• **Inv**: Imaging, bacterial cultures.

• **Management**: Depends on situation.

• **Time course of disease**: Weeks.

• **Tempo of investigations**: Days.
IMMUNE DEFICIENT FUO

• **Def:** ≥38°C, >1 wk, negative cultures after 48 hr.

• **Causes:** Majority due to infections, but cause documented in only 40-60%.

• **H/O:** Stage of chemotherapy, drugs administered, underlying immunosuppressive disorder.

• **Examine:** Skin folds, IV sites, lungs, perianal area.
IMMUNE DEFICIENT FUO

• **Inv**: Chest x ray, Bacterial cultures.

• **Management**: Antimicrobial treatment protocols.

• **Time course of disease**: Days.

• **Tempo of investigations**: Hours.
HIV RELATED FUO

• **Def:** ≥ 38°C, >3 wk for outpatients, >1 wk for inpatients, HIV infection confirmed.

• **Causes:** HIV (primary infection), typical and atypical mycobacteria, CMV, lymphomas, toxoplasmosis, cryptococcosis, immune reconstitution inflammatory syndrome (IRIS).

• **H/O:** Drugs, exposures, risk factors, travel, contacts, stage of HIV infection.

• **Examine:** Mouth, sinuses, skin, lymph nodes, eyes, lungs, perianal area.
HIV RELATED FUO

- **Inv**: Blood and lymphocyte count; serologic tests; CXR; stool examination; biopsies of lung, bone marrow, and liver for cultures and cytologic tests; brain imaging.
- **Management**: Antiviral and antimicrobial protocols, vaccines, revision of treatment regimens, good nutrition.
- **Time course of disease**: Weeks to months.
- **Tempo of investigations**: Days to weeks.
• **Abscesses:** abdominal, brain, dental, hepatic, pelvic, rectal.

• **Bacteria:** cat scratch disease, listeriosis, brucellosis, TB.

• **Localized infections:** cholangitis, mastoiditis, osteomyelitis, sinusitis, infective endocarditis, pyelonephritis.

• **Fungal:** Blastomycosis, Coccidiodomycosis, Ricketssial.

• **Viruses:** CMV, Hepatitis viruses, HIV, EBV.

• **Parasites:** Amebiasis, Giardiasis, Malaria, Toxoplasmosis.
FUO - ETIOLOGY

- **Rheumatologic**: Behcet, JRA, Rheumatic fever, SLE.
- **Hypersensitivity diseases**: Drug fever, Serum sickness.
- **Neoplasms**: Leukemia, Lymphoma, Pheochromocytoma.
- **Granulomatous**: Crohn, Sarcoidosis.
- **Familial**: Ectodermal dysplasia, familial mediterranean fever, familial dysautonomia, Sickle cell crisis.
- **Misc**: Cyclic neutropenia, Kawasaki disease, Pancreatitis, Thrombophlebitis.
FUO - DIAGNOSIS

History

• Origin/ Genetic background
• Exposure to animals
• Ingestion of Meat
• Travel
• Dietary habits
• Pica
• Medication
# FUO- EXAMINATION

<table>
<thead>
<tr>
<th>BODY SITE</th>
<th>PHYSICAL FINDING</th>
<th>DIAGNOSIS</th>
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<tbody>
<tr>
<td>Head</td>
<td>Sinus tenderness</td>
<td>Sinusitis</td>
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<tr>
<td>Oropharynx</td>
<td>Ulceration</td>
<td>Histoplasmosis</td>
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<td></td>
<td>Tender tooth</td>
<td>Periapical Abscess</td>
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<td>Fundi or conjunctivae</td>
<td>Choroid tubercles</td>
<td>Disseminated granulomatosis</td>
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<td>Petechiae, Roth ‘s spots</td>
<td>Endocarditis</td>
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<tr>
<td>Heart</td>
<td>Murmur</td>
<td>Infective endocarditis</td>
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<td>Rectum</td>
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<td>Abscess</td>
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<td></td>
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<tr>
<td>Lower extremities</td>
<td>Deep venous tenderness</td>
<td>Thrombosis or Thrombophlebitis</td>
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FUO- INVESTIGATIONS

• Case to case basis.

• The tempo of diagnostic evaluation should be adjusted to the tempo of the illness.

• The evaluation can proceed in systematic fashion and can be carried out in an outpatient setting.

• If there are no clues in the patient's history or on physical examination then continued surveillance and repeated re-evaluations of the child should be employed to detect any new clinical findings.
FUO- INVESTIGATIONS

- ESR and CRP.
- Cultures.
- Serologic tests – EBV, CMV, Toxoplasmosis, Brucellosis.
- X ray chest, sinuses, mastoids.

- Bone marrow aspiration and culture.
- Radionuclide scans especially for abscesses.
- Total body CT or MRI (both with contrast) permits detection of neoplasms and collections of purulent material without the use of surgical exploration or radioisotopes.
FUO- TREATMENT

- The ultimate treatment of FUO is tailored to the underlying diagnosis.
- Fever and infection in children are not synonymous.
- Antimicrobial agents should not be used as antipyretics, and empirical trials of medication should generally be avoided.
- An exception may be the use of antituberculous treatment in critically ill children with suspected disseminated tuberculosis.
- After a complete evaluation, antipyretics may be indicated to control fever and relieve symptoms.
FUO-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.
• In many cases, no diagnosis can be established and fever abates spontaneously.
• In as many as 25% of cases in whom fever persists, the cause of the fever remains unclear, even after thorough evaluation.
Thank You