Fever of Unknown Origin (FUO)

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FUO

Fever of unknown origin (FUO) was defined in 1961 by Petersdorf and Beeson as: (1) a temperature greater than 38.3°C (101°F) on several occasions, (2) more than 3 weeks' duration of illness, and (3) failure to reach a diagnosis despite 1 week of inpatient investigation.

Contemporary FUO

- Illness greater than three weeks duration
- (Documented) temp greater than 38.3°C (101°F), with lab signs of inflammation on several occasions
- No diagnosis after initial investigation, including negative blood cultures (no recent antibiotics)
- Exclusion of nosocomial causes, and immunocompromised conditions such as HIV

As a rule…..

- FUO’s that persist over extended periods of time w/ little evidence of serious systemic disease generally resolve, often w/o a diagnosis
- The FUO of greater concern is one that is prolonged, w/signs of serious illness, and after a though workup, the etiology remains elusive

Causes of Fever,
but <u>not</u> true “FUO”

- Hospital-associated infections (HAI’s) (respiratory, UTI, wound, catheter, sinusitis, C.difficile)
- Neutropenic fever (ANC < 500)
- HIV, other immunocompromised conditions

With over 200 causes described, typically they are categorized as:

- Infectious
- Malignancy
- Inflammatory

14 disorders ~ 2/3 of the diagnoses

1. Infections:

    Endocarditis

    Tuberculosis

    Abdominal abscesses

    EBV/CMV infections

Vanderschueren S. et al. From prolonged febrile illness to Fever of Unknown Origin:
The challenge continues. Arch Intern Med 2003;163:1033.

Most Common Causes

2. Malignancies:
    - Lymphoma
    - Leukemia
3. Non-infectious inflammatory disorders
    - Adult-onset Still disease
    - Systemic lupus erythematosus
    - Polymyalgia rheumatica – giant cell arteritis
    - Sarcoidosis
    - Crohn’s disease

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4. Miscellaneous disorders

- Habitual hyperthermia
- Drug fever
- Subacute thyroiditis
- Factitious fever

Pel-Ebstein fever

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Viral Hemorrhagic Fevers

5 Families of RNA Viruses:

- Arenaviridae - Lassa Fever
- Bunyaviridae - Hantavirus, Crimean-Congo Hemorrhagic Fever Virus, and Rift Valley Fever Virus
- Filoviridae - Ebola and Marburg virus
- Flaviviridae - Dengue, Yellow fever
- Rhabdoviridae

Lassa Fever

- from contact w/ infected urine/feces of multimammate rat in Africa, with subsequent human-human transmission
- mortality ~ 1%
- Rx: supportive + ribavirin

Hanta Virus

- hemorrhagic fever w/ renal syndrome (HFRS)
  - from contact w/ rodent excreta
  - found in Europe, Asia, Africa
- Hantavirus Pulmonary syndrome (HPS) (“Four Corners Dx”)
  - from inhalation of aerosolized rodent excreta
  - In U.S.(mostly western states), Sin Nombre strain of virus carried by deer mice
  - flu-like symptoms followed by sudden onset SOB/pulmonary edema
  - high fatality rate

Ebola/Marburg

- efficient human-human spread
- high mortality
- treatment: supportive

Yellow Fever

- found in Africa, South America
- from bite of infected Aedes aegypti mosquito
- 200,000 infected each year w/ 30,000 deaths (~1/2 of those who become severely ill w/ jaundice, etc)
- prevention: vaccine

Dengue

- from bite of infected Aedes aegypti mosquito
- ~390 million cases/yr - 96 million symptomatic
- rash, fever, retrorbital pain, bone pain (“Breakbone fever”)
- ~20,000 deaths/yr!
- 4 distinct serotypes - second infection w/ a second serotype appears to significantly increase risk of severe dx
- Prevention: vaccine (plus the usual mosquito avoidance measures)

Dengue

- Warning signs of severe dengue: persistant vomiting, severe abdominal pain

- may need aggressive volume resuscitation w/in 24 - 48 hrs following defervescence, reducing mortality from ~ 10% to 0.1%!

- no ASA products

Thanks and **GOOD LUCK!**