FEVER OF UNKNOWN ORIGIN

Bino Oommen MD
Established in 1961 by Petersdorf and Beeson based on an analysis of 100 cases

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1. A febrile illness of more than 3 weeks’ duration
2. Temperatures must exceed 38.3°C (101°F) on several determinations
3. No diagnosis reached after 1 week of study in the hospital or after 3 or more outpatient visits
Establishing the Diagnosis

- Detailed History
- Physical examination
- Complete blood count, including differential and platelet count
- Blood cultures (three sets drawn from different sites over a period of at least several hours without administering antibiotics)
- Routine blood chemistries, including liver enzymes and bilirubin
- Hepatitis serology (if liver tests abnormal)
- Urinalysis, including microscopic examination, and culture
- Chest X-Ray
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2. Malignancies (7–31%)
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2. Malignancies (7–31%)
3. Noninfectious Inflammatory Diseases (10–30%)
4. Others (drug-fever, pulmonary emboli, facticious etc.)–15–25%
Most Common Infectious
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VIRAL
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- HIV
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- Hepatic Viruses
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VIRAL
- HIV
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  - CMV
  - EBV
Most Common Infectious

BACTERIAL

VIRAL

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- Herpes Viruses
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BACTERIAL
- Extrapulmonary TB

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Most Common Infectious

**BACTERIAL**
- Extrapulmonary TB
- **Abscesses**: PSHx, trauma, diverticulosis, gynecological procedures

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- Osteomyelitis (s. aureus)

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**BACTERIAL**
- Extrapulmonary TB
- **Abscesses**: PSHx, trauma, diverticulosis, gynecological procedures
- Osteomyelitis (s. aureus)
- Endocarditis (Coxiella, Legionella, Bartonella, Hemophilia, Actinobacillus, Cardiobacterium, Eikenella, Kingella)

**VIRAL**
- HIV
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Most Common Infectious

**Fungal**
- Candida Albicans
- Histoplasmosis
- Cryptococcus

**Parasitic**
- Toxoplasmosis
- Malaria
Most Common Neoplasms

- Lymphoma (Hodgkin and Non-Hodgkin)
- Leukemia
- Solid Tumors (most commonly Renal Cell Ca)
- Hepatocellular Ca or metastasis to Liver
Most Common Connective Tissue Diseases

- Systemic Onset Juvenile Rheumatoid Arthritis
- Giant Cell Arteritis (+50y.o)
- Polyarteritis Nodosa
- RA, SLE, sarcoidosis
Most Common Drug Causes

- Antimicrobials (sulfonamides, penicillins, nitrofurantoin, vancomycin, antimalarials)
- H1 and H2 blocking antihistamines
- Antiepileptic drugs (barbiturates and phenytoin)
- Iodides
- NSAIDS (including salicylates)
- Antihypertensive drugs (hydralazine, methyldopa)
- Antiarrhythmic drugs (quinidine, procainamide)
- Antithyroid drugs
- Contaminants such as quinine that accompany injected cocaine or heroin

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Work-Up of FUO
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History
- PMHx, PSHx
- FHx
- Social Hx (including hobbies, travel, pets, occupation, sexual orientation, sick contacts)
- Medication, Vaccinations
- Immune Status
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History
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- FHx
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Physical
- Any subtle symptoms (tick bites, jaw pain, etc)
- Pay attention to lymph nodes, skin, eyes
- Assess any possible focuses: pain, heat, redness
Diagnostic Labs

- Revisit and repeat previous labs
- ESR or CRP
- Serum LDH
- Creatine phosphokinase
- Tuberculin Skin Test
- Serology (HIV antibody assay, CMV, amebiasis, toxoplasmosis, brucellosis, etc)
- ANA, Rheumatoid Factor
- TSH, thyroxin
- Blood Smear
- Cultures (CSF, Peritoneal, pleural, urine, stool)
Imaging Studies

- CXR
- Abdominal Ultrasound
- Echocardiography
- CT
- MRI
- Endoscopy
- Doppler study
Invasive Procedures

- Lumbar Puncture
- Biopsy
  - Lymph node
  - Temporal artery (if ESR increased in age > 60)
  - Liver
  - Bone marrow
  - Pleural
Prognosis

- Case dependent
- 30–50% of patients, no source identified
- Most unidentified fevers in recent studies have good prognosis
Follow-Up

- Further In-Patient Care: Unnecessary. Careful review of studies show that most patients with FUO have a benign long-term course.
- Out-Patient Care: Periodic re-evaluation of systems, or further work-up in outpatient setting.
Remember:

- A Fever of unknown origin is more likely to be a common disease with a rare presentation, than to be a rare disease.
- Elderly are more prone to lack of symptoms
- Always use MINIMAL diagnostics
References

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