

FEVER OF UNKNOWN ORIGIN

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CRITERIA:

1. A febrile illness of more than **3 weeks' duration**
2. Temperatures must exceed **38,3°C (101F)** 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%)
3. **Noninfectious Inflammatory Diseases** (10– 30%)
4. **Others** (drug– fever, pulmonary emboli, factitious etc.)– 15– 25%

Most Common Infectious

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- Extrapulmonary TB

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- **Abscesses**: PSHx, trauma, diverticulosis, gynecological procedures

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- **Osteomyelitis**(s. aureus)

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Most Common Infectious

BACTERIAL

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

VIRAL

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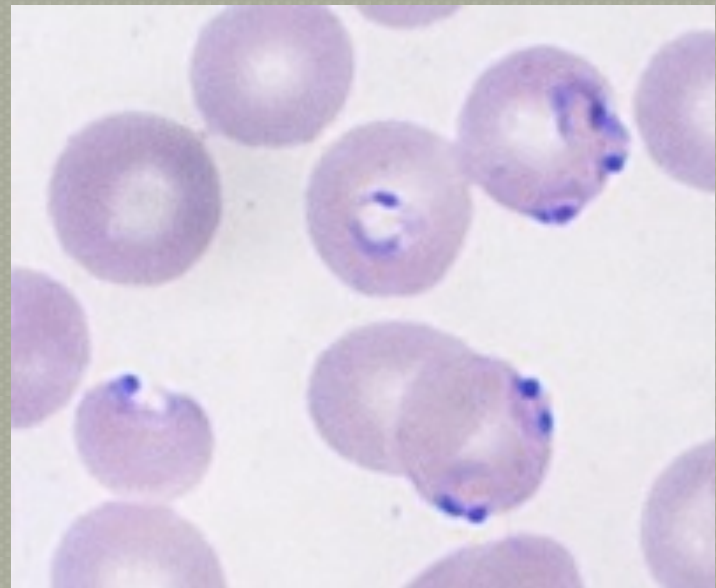
Most Common Infectious

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

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

Work-Up of FUO

History

- PMHx, PSHx
- FHx
- Social Hx (including hobbies, travel, pets, occupation, sexual orientation, sick contacts)
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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

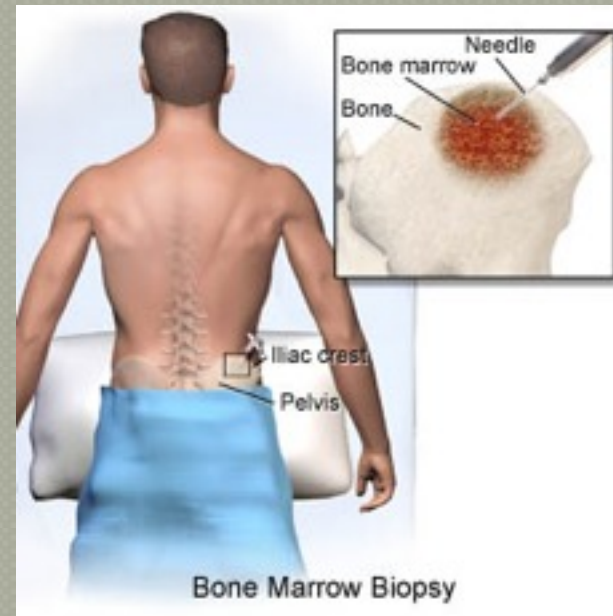
- Revisit and repeat previous labs
- ESR or CRP
- Serum LDH
- Creatine phosphokinase
- Tuberculin Skin Test
- Serology (HIV antibody assay, CMV, amebiasis, toxoplasmosis, brucellosis, etc)
- ANA, Rheumatoid Factor
- TSH, thyroxin
- Blood Smear
- Cultures (CSF, Peritoneal, pleural, urine, stool)

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

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