Structured approach to patients with FUO

A fever of 38.3°C (101°F) or more lasting for at least three weeks for which no cause can be identified after reasonable evaluation and diagnostic testing.(i.e., three days of investigation in hospital or three or more outpatient visits). Petersdorf and Beeson in 1961

FIRST ASSESSMENT

- **History**: fever pattern (continuous or recurrent) and duration; previous medical history, present and recent drug use, family history, sexual history, country of origin, recent and remote travel, unusual environmental exposures associated with travel or hobbies, animal contacts.
- **Stop antibiotic treatment and corticosteroids**
- **Complete physical examination:** with special attention to eyes, lymph nodes, temporal arteries, Liver and spleen, sites of previous surgery, entire skin surface,and mucous membranes.
- **Minimum obligatory investigations**: ESR and CRP, Complete blood count, Electrolytes, urea/creatinine, Total protein, protein electrophoresis, Alkaline, phosphatase, AST, ALT, LDH, bilirubin, creatine kinase, Urinalysis, Blood cultures (x 3), urine cultures, Antinuclear antibodies, rheumatoid factor, ANCA, hepatitis A, B, and C serology, HIV antibody, Tuberculin skin test or interferon-γ release assay, Chest x-ray, abdominal ultrasonography
- **Stop or replace medications to exclude drug fever**
- **Exclude manipulation with thermometer**

Potentially diagnostic clues (all signs, symptoms, and abnormalities potentially pointing toward a diagnosis) → GUIDED DIAGNOSTIC TEST

OTHER TESTS: Peripheral blood smear should be done at this stage if patient has recently travelled to malaria endemic areas or if complete blood count suggests bone marrow involvement, Cryoglobulin, chest/abdominal CT with contrast, temporal artery biopsy (in patients >55 years old), FDG-PET if ESR/CRP elevated (where available) or nuclear scintigraphy, echocardiography, bone marrow biopsy after peripheral blood smear, toxoplasmosis/brucellosis/coxiellosis/EBV/CMV serology

Potentially diagnostic clues (all signs, symptoms, and abnormalities potentially pointing toward a diagnosis) → GUIDED DIAGNOSTIC TEST

INVASIVE TESTS: lymph node or liver biopsy, lumbar puncture, etc, if indicated

Potentially diagnostic clues (all signs, symptoms, and abnormalities potentially pointing toward a diagnosis) → GUIDED DIAGNOSTIC TEST

WATCHFUL WAITING AND RE-EVALUATION

Potentially diagnostic clues (all signs, symptoms, and abnormalities potentially pointing toward a diagnosis) → GUIDED DIAGNOSTIC TEST

DETERIORATION: consider therapeutic trial (antibiotics, corticosteroids)

Causes of pyrexia of unknown origin

Infectious

Bacterial

- **Occult abscess**
- **Complicated urinary tract infection**
- **Culture negative endocarditis**
- **Osteomyelitis**
- **Tuberculosis**
- **Coxiella burnetti (Q fever)**
- **Borrelia Burgdorferi (Lyme disease)**
- **Rickettsial infections**
- **Enteric fever**
- **Brucellosis**

Viral

- **Epstein–Barr virus**
- **Cytomegalovirus**
- **Human immunodeficiency virus**

Parasitic

- **Malaria**
- **Toxoplasmosis**

Fungal

- **Histoplasmosis**

Inflammatory

- **Giant cell arteritis**
- **Adult Still's disease**
- **Systemic lupus erythymatosus**
- **Polyarteritis nodosa**
- **Granulomatosis with polyangitis**
- **Familial Mediterranean fever**

Neoplastic

- **Non-Hodgkin lymphoma**
- **Leukaemia**
- **Renal cell carcinoma**
- **Hepatocellular carcinoma**
- **Metastatic lesions (hepatic from adenocarcinomas)**

Miscellaneous

- **Drugs**
- **Cirrhosis**
- **Pulmonary embolism**
- **Inflammatory bowel disease**
- **Sarcoidosis**
- **Hyperthyroidism**
- **Factitious fever**