



Pyrexia of unknown origin

History and Examination:

- **Family history** of collagen diseases and cancer
- **Immunization status**
- **Occupational history** ? virologist ? Sex worker?
- **Travel history** been to African swamps lately?
- **Nutrition** (including consumption of dairy products)
- **Drug history** (over-the-counter medications, prescription medications, illicit substances)
- **Sexual history**
- **Recreational habits**
- **Animal contacts**
- **Surgical history** could there be a deep abscess?
- **ASK ABOUT ALL ORGAN SYSTEMS**

CHECK EVERY LYMPH NODE!
And feel the spleen...

PUOs are caused by

- **infections (30-40%)**- mainly kids
- **neoplasms (20-30%)**- mainly elderly
- **collagen vascular diseases (10-20%)**
- **miscellaneous diseases (15-20%)**.
- between 5-15% of FUO cases defy diagnosis, despite exhaustive studies.

IN THE OVER-50S:

more than 30% of PUO cases are related to connective-tissue disorders and vasculitic disorders.
Giant cell temporal arteritis } account for 50%
Polymyalgia Rheumatica } of the cases.

Repeat a regular physical examination daily while the patient is hospitalized.

Pay special attention to rashes, new or changing cardiac murmurs, signs of arthritis, abdominal tenderness or rigidity, lymph node enlargement, fundoscopic changes, neurologic deficits and changing patterns of fever peaks.

SO WHAT COULD BE CAUSING THIS? massive list of differentials...

Bacteria

ABSCCESS: Previous abdominal operations, trauma, or histories of diverticulosis, peritonitis, endoscopy, or gynecologic procedures
Most common locations are the subphrenic space, liver, RLQ, retroperitoneal space, and the pelvis in women.

TUBERCULOSIS: especially among migrants and the immunocompromised, so do a **Chest X-ray**

URINARY TRACT INFECTION is easily recognised; so do a **Urinalysis**

ENDOCARDITIS causing new murmurs, so **listen to the heart and take blood cultures**

CHOLANGITIS could be clinically silent, so think about doing the **LFTs** even though they may be normal

OSTEOMYELITIS if there are musculoskeletal symptoms, so do a **Tc99 Bone Scan**

Viruses

COULD IT SIMPLY BE AN ADVANCED HIV INFECTION? Typical and atypical mycobacteria and cytomegalovirus (CMV) are opportunistic infections that frequently cause prominent constitutional symptoms, including fever, with few localizing or specific signs, so do **HIV and CMV serology**

HERPESVIRUSES can reactivate in the immunocompromised and elderly without much external signs; so do **EBV Monospot, Herpes serology and Blood film for Atypical Lymphocytes.**

Speaking of HIV: could it be **CANDIDA** or **CRYPTOCOCCUS**? Could it be **TOXOPLASMOSIS**?

Neoplasms

Lymphomas and Acute leukaemias cause fever, night sweats and **weight loss.**

Renal cell carcinoma: fever being the only presenting symptom in 10% of cases.

Hematuria may be absent in approximately 40% of cases, but there will be anaemia and high **ESR**

Adenocarcinomas of the breast, liver, colon, or pancreas and liver metastases from any site.

Autoimmune

Fever may only be the **FIRST THING THAT GOES WRONG:** watch for arthralgia, rash, nephritis

Systemic Lupus: can get fevery, easily identified with **ANA, DsDNA(Ab), etc...**

Polyarteritis Nodosa: a systemic necrotising vasculitis; **ANCA, high ESR, leucocytosis**

Rheumatoid Arthritis: fever can sometimes present without (rather, before) arthralgia. **RF.**

Granulomae

Sarcoidosis: look for lymph nodes and granulomae with **NON-INVASIVE IMAGING**

Crohns Disease: hard one, need **Endoscopy and Biopsy**

Medications

beta-lactam antibiotics, procainamide, isoniazid, alpha-methyldopa, quinidine, and diphenylhydantoin. Just stop the drugs and the patient will cool down within 2 days

Endocrine

HYPERTHYROIDISM: fever and weight loss often the only signs; run a **TSH and T4**

ADRENAL INSUFFICIENCY: rare but potentially fatal! **Nausea, vomiting, weight loss, skin hyperpigmentation, hypotension, hyponatremia, and hyperkalemia.**

The OTHERS

Giant Cell Arteritis – **ESR will be over 100** ask about jaw claudication and visual loss

Polymyalgia Rheumatica -symmetrical pain and stiffness involving the lumbar spine and large proximal muscles,

INVESTIGATIONS:

FBC: Anemia, leukaemia, leukocytosis, lymphocytosis? Atypical lymphocytes of EBV or CMV?

- **PERIPHERAL BLOOD THICK AND THIN FILMS** for malaria

Urinalysis: Exclude UTIs and cancers of the urinary tract

LFT: mainly to check for viral hepatitis or liver abscess

Culture EVERYTHING!

SEROLOGY– EBV, CMV, HIV, HEP B and C, toxoplasma, chlamydia

ESR: for Giant Cell Arteritis, Polyarteritis Nodosa, etc

ANTIBODIES:

- ANA
- Rheumatoid factor
- ANCA
- Double-stranded DNA

IMAGING:

Chest Xray- who knows what you may find

Abdominal Ultrasound (maybe even in absence of symptoms)

CT scan of abdomen and pelvis (if there are vague abdominal symptoms)

MRI and /or Tc99 Bone Scan if you suspect osteomyelitis

ENDOSCOPY if you suspect Crohns

If all else fails, you may be reduced to doing BIOPSIES.

For MANAGEMENT, you need an underlying cause.

No evidence supports prolonged hospitalization in patients who are clinically stable and whose workup is unrevealing.