

FEVER

Etiology and classification

- Infective fever

- Non-infective fever

Infective fever

- Metabolites from organism can cause fever
- Most common causes of fever (50%~60%)
- Bacteria pyrogens: infective fever (43%)
- Viral pyrogens: (6%)

Non-infective fever

- Absorption of necrotic substances:
injury , ischemic necrosis ,
Allergy Antibiotics
- Endocrine and metabolic disturbances:
hyperthyroidism , dehydration
- Decreased elimination of heat from skin:
heat failure

Non-infective fever

- Dysfunction of central heat regulation

physical: heat stroke

chemical: barbiturate poisoning

mechanical: cerebral hemorrhage

- Dysfunction of vegetative nervous system

Clinical manifestation

- The grade of fever

Low grade fever: 37.3~38°C

Moderate fever: 38~39°C

High fever: 39.1~41°C

Hyperthermia fever: >41°C

Fever pattern as diagnostic clues

Fever Pattern

Cause

Alternate-day fever

Plasmodium vivax, P. Ovale

Fever every third day

P. Malariae

Relapsing fever

daily for 3~6 days

Borrelia sp, rat bite fever

fever-free interval

(Streptobacillus moniliformis;

for about 1 week

Spirillum minus)

supervenes

Continuous “undulating”

Brucellosis, typhoid

Periodic pyrexia

Hodgkin’s disease

(Pel-Ebstein Phenomenon)

with variable cycles

Associated symptoms

- Lymphadenopathy: lymphoma
- Enlargement of liver and spleen: hepatitis
- Rash: drug rash , measles
- Arthralgia: gout rheumatic disease
- Coma: barbiturate poisoning , hemorrhage

Diagnostic points

- Other symptoms besides fever
- Duration and magnitude of fever
- Close contacts with similar illness
- Occupational, travel, recreational exposure
- History of diseases associated with other organ (diabetes chronic renal failure)
- Current medication (antibiotics and antipyretics)
- Allergy

Fever of Unknown Origin (FUO)

- Definition
 - $T > 38.3$ (101 F) on several occasions
 - Duration of fever 3 weeks or longer
 - Cause not diagnosed after 1 week of intensive in hospital investigation

- **Approach to the patient with fever of unknown origin /FUO/**
- FUO refers to a prolonged febrile illness without an established etiology despite intensive evaluation and diagnostic testing.
- The fraction of undiagnosed FUOs has dropped from over 75% in the 1930s to fewer than 10% in most recent studies.
- **Neutropenia associated febrile episodes** without a source are most frequently linked to bacteremia. Fungal infections replace bacterial infections in prominence after acute period-after 7 days.

Etiologies of FUO

- Infection (40%)
- Malignancy (30%)
- Collagen Vascular Disease (20%)
- Undiagnosed (10%)

- The **degree** of fever,
- **nature** of the fever curve,
- **response to antipyretics** have **not** been found to provide enough specificity to guide the diagnosis of FUO.

- Fever may be **attenuated** in older patients, and moderated by use of steroids and nonsteroidal antiinflammatory drugs.

- **Therapeutic trials** rarely establish the diagnosis – **suppress, but not cure**
- /antibiotics, corticosteroids/

History

- Travel
- Immunosuppression
- Drug and toxin history, including antimicrobials
- Localizing symptoms
- Subtle findings
 - subtle changes in behavior granulomatous meningitis;
 - jaw claudication consistent with giant cell arteritis;
 - nocturia consistent with prostatitis.
 - Revisiting the history on several occasions

- **-detailed physical examination**
- **-look for uncommon presentations of common diseases**
- **-look for a mistake or desinterpretation of examination results**

Fever and Rash

Consider the Patient:

- Age of the patient
- Season of the year
- Travel history
- Geographic location
- Immunizations and history of childhood illnesses
- Exposures: insects, animals, and ill contacts
- Medications
- Immune state of the host.

Consider the rash:

- Characteristics of the lesions
- Distribution and progression of the rash
- Timing of the onset in relation to fever
- Progression, if any, of the lesions such as papules to vesicles or petechiae.

Labs

- Complete blood count
- Erythrocyte sedimentation rate
- Routine blood chemistries, including liver enzymes, bilirubin, and lactate dehydrogenase
- Urinalysis, including microscopic
- Chest radiograph
- Routine blood cultures
- Tuberculin skin test with control(s)
- HIV antibody assay
- Antinuclear antibodies
- Rheumatoid factor
- Heterophile antibody test in children and young adults
- CT scan of abdomen.

- **other:**
- gallium 67 or indium-111 labeled leucocyte scanning
- biopsy of bone marrow, liver, lymph node, temporal artery...,pleural biopsy
- **Role of erythrocyte sedimentation rate**
- ESR above 100mm/h:
- -malignancy 58% - lymphoma, myeloma,metastatic colon,breast cancer
- -infections and inflammatory diseases 25%-
endocarditis, RA, giant cell arteritis
- **normal ESR= absence of significant inflammatory process**
- /exception some systemic inflammatory diseases/

Case Series of Fever of Unknown Origin: Prevalent Diagnoses

Diagnosis	Case study					
	Alt 1912-30 n = 93	Petersdorf 1952-59 n = 93	Knockaert 1980-89 n = 41	Pizzo 1966-72 n = 88	Miller 1984-93 n = 72	Sharma 1974-89 n = 143
Rheumatic fever	17	6	0	0	0	0
Abdominal abscess	9	4	5	0	0	2
Endocarditis	0	5	2	3	0	3
Syphilis	4	1	0	0	0	0
Mycobacterial	26	12	15	1	57	27
Lymphoma	9	8	5	2	7	7
Solid tumor	13	10	7	0	1	9
Sarcoid	0	2	2	0	0	2
Lupus	0	5	0	3	0	7
Rheumatoid arthritis	0	0	5	11	0	0
Giant cell arteritis	0	2	19	0	0	0
Drug fever	0	1	7	0	0	0
Factitious fever	0	3	0	0	3	0

Less Common Diagnoses of Fever of Unknown Origin

Infections

Amoebic liver abscess
Brucellosis
Chronic active hepatitis
Cytomegalovirus
Dental abscesses
Diskitis
Epididymitis
Fascioliasis
Gonococcal arthritis
Herpes simplex
 encephalitis
Infectious
 mononucleosis
Kala azar
Kikuchi's disease
Lyme disease
Pyelonephritis
Pyometria
Rheumatic fever
Sinusitis
Typhoid fever
Whipple's disease

Malignancies

Atrial myxoma
Aleukemic leukemia
Kaposi's sarcoma
Lung cancer
Multiple myeloma
Sarcoma

Systemic diseases

Allergic granulomatous
 angiitis
Granulomatous hepatitis
Hypersensitivity vasculitis
Inflammatory bowel disease
Panaortitis
Reiters syndrome
Sarcoidosis

Miscellaneous

Behcet's disease
Chronic fatigue syndrome
Disorders of temperature
 regulation (neurologic and
 dermatologic)
Drug fever
Environmental (metal and
 polymer fume fevers)
Factitious fever
Familial
Mediterranean fever
Periodic fever
Pulmonary emboli
Retroperitoneal hematomas
Thyroiditis



