

## FEVER(Pyrexia)

Is an elevation of body temperature above the normal circadian range (daily variation) as a result of a change in the *thermoregulatory* center located in the anterior hypothalamus and pre-optic area (i.e. an increase in the hypothalamic set point of 37 C) due to infection, metabolic derangements or increased cell destruction.

*Body temperature is controlled in the hypothalamus, which is directly sensitive to changes in core Temperature. The normal 'set-point' of core temperature is tightly regulated within  $37 \pm 0.5^{\circ}\text{C}$ , as required to preserve normal function of many enzymes and other metabolic processes.*

# CLASSIFICATION OF FEVERS

## A) Based on Duration of Fever:

- ▶ 1. Acute fevers (<7 days): infectious diseases such as malaria and viral-related upper respiratory tract infection
- ▶ 2. Sub-acute fevers (usually not more than 2 weeks in duration): typhoid fever and intra-abdominal abscess
- ▶ 3. Chronic or persistent fevers (>2 weeks duration): chronic bacterial infections such as tuberculosis, viral infections like HIV, cancers and connective tissue diseases. However, any cause of acute fever can become persistent or chronic if untreated.

## B) Based on Height of Fever:

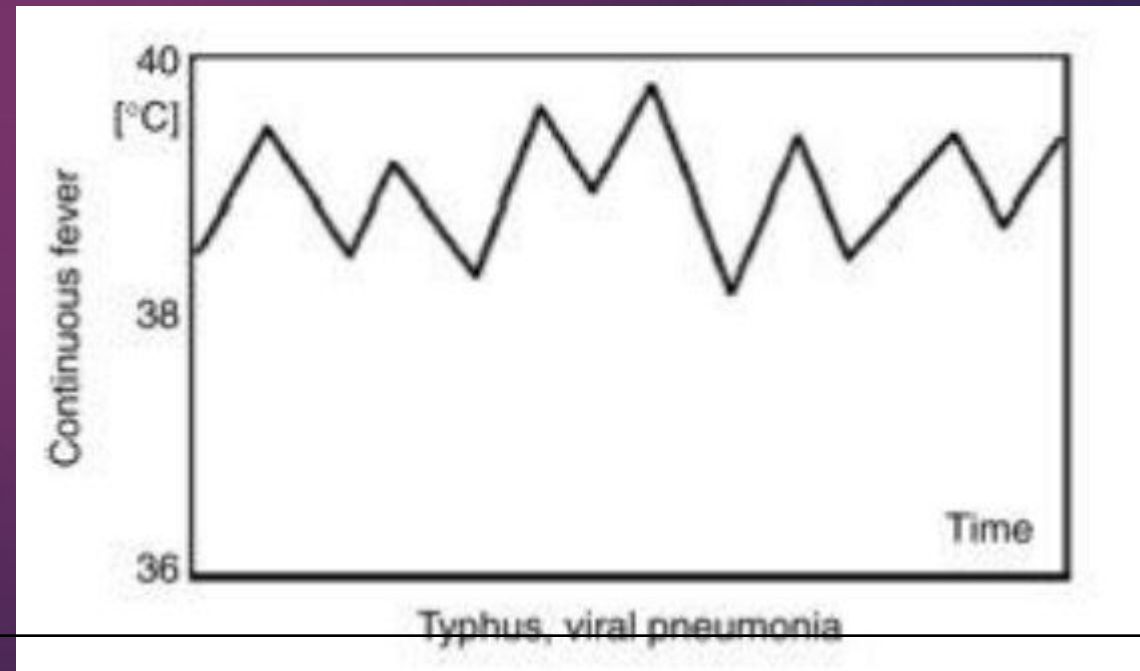
Normal and febrile body temperature ranges (rectal temperatures).

Body temperature	°C	°F
Normal	37–38	98.6–100.4
Mild/low grade fever	38.1–39	100.5–102.2
Moderate grade fever	39.1–40	102.2–104.0
High grade fever	40.1–41.1	104.1–106.0
Hyperpyrexia <sup>a</sup>	>41.1	>106.0

## ► C) Based on Pattern of Fever:

1. **Sustained or Continuous Fever:** Fever that oscillates less than 1 °C or 1.5 °F daily; doesn't touch normal

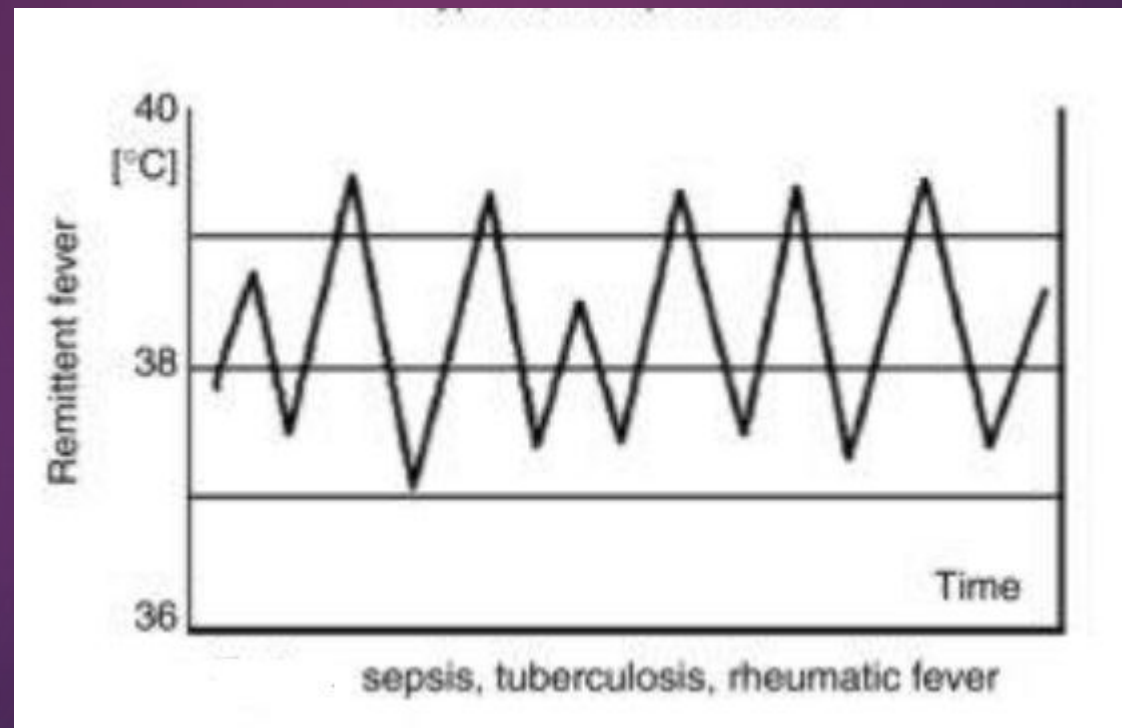
- Typhoid fever
- Drug fever
- Typhus
- Neoplasms



## 2. Remittent Fever:

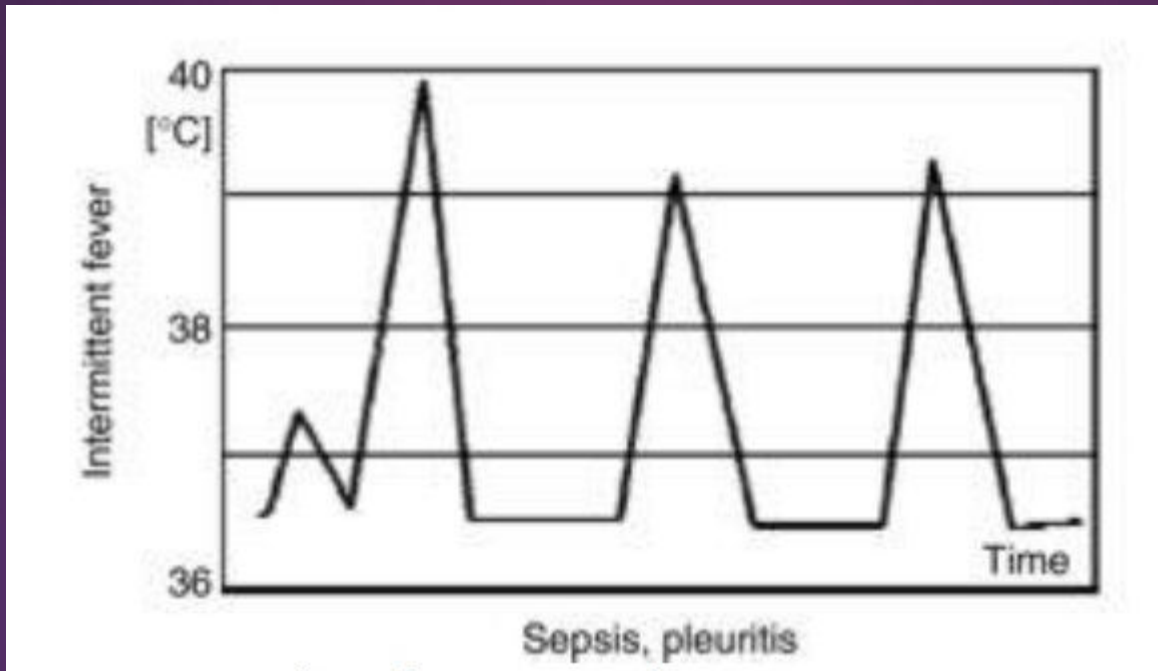
- Fever that oscillates more than  $1^{\circ}\text{C}$  or  $\sim 1.5^{\circ}\text{F}$  ; doesn't touch normal

Pattern of most fevers



### 3. Intermittent Fever:

Fever that falls to normal each day.





► 4. Hectic or Septic Fever:

When remittent or intermittent fever shows large variation between the peak and nadir

- Kawasaki disease
- Pyogenic infections

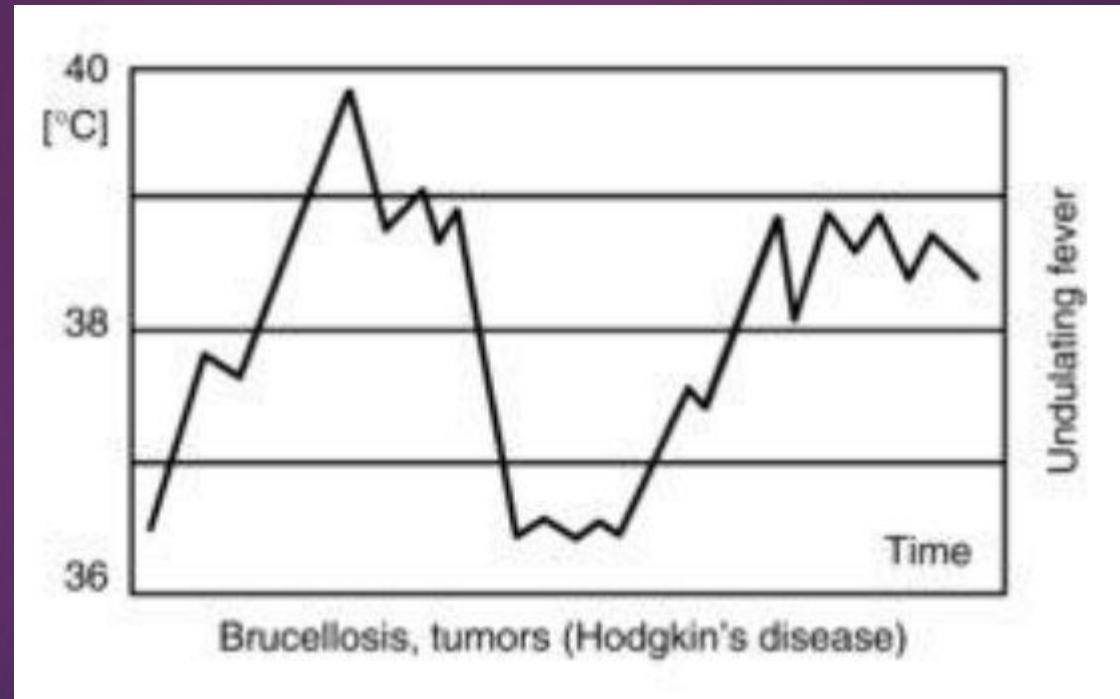
► 5. Periodic or Cyclic Fever: Episodes of fever recurring at regular intervals

- Quotidian (24 hour periodicity): *P. falciparum*
- Double quotidian (12 hour periodicity): Kala-azar, Gonococcal arthritis, Juvenile RA, Some drug fevers (carbamazepine)
- Tertian (48 hour periodicity): *P. vivax*, *P. ovale*
- Quartan (72 hour periodicity): *P. malariae*
  - Pel-Ebstein Fever: bouts of fever lasting 3 to 10 days followed by asymptomatic periods of the same length (Hodgkin's disease)
- Relapsing fever (every 10-14 days): *Borrelia recurrentis*



- Undulant fever :

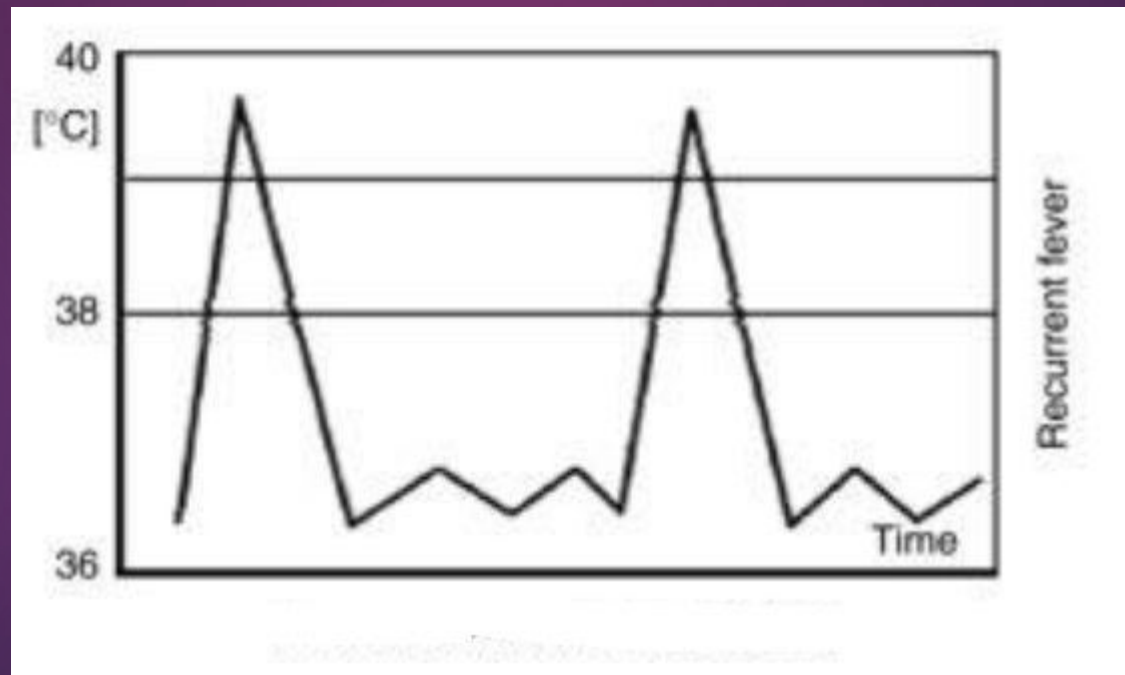
(gradual increase in temperature that remains high for a few days, and then gradually decreases to normal):Brucellosis



► 6. Recurrent Fever:

Illness involving the same organ (e.g. urinary tract) or multiple organ systems in which fever recurs at irregular interval:

Familial Mediterranean Fever



# GENERALISED APPROACH TO FEVER / FUO

The approach to a patient presenting with fever of unknown origin (FUO) should include:

- a comprehensive history,
- physical examination and
- appropriate diagnostic testing

Definitions:	Common Etiologies:
<p><b>A. <u>Classic FUO:</u></b></p> <ul style="list-style-type: none"> <li>(1) Daily or intermittent fever &gt; 101°F</li> <li>(2) Duration of at least 3 consecutive weeks</li> <li>(3) No source identified by clinical evaluation despite: <ul style="list-style-type: none"> <li>a.) 3 days of hospital evaluation OR</li> <li>b.) 7 days of outpatient evaluation OR</li> <li>c.) Three outpatient visits</li> </ul> </li> </ul>	<p>Infection (especially TB, endocarditis, osteomyelitis, intra-abdominal abscess), malignancy (especially lymphoma, renal cell carcinoma, hepatocellular), collagen vascular disease</p>
<p><b>B. <u>Nosocomial FUO:</u></b></p> <ul style="list-style-type: none"> <li>(1) Daily or intermittent fever &gt; 101°F</li> <li>(2) Hospitalized ≥ 24 hours with no fever on admission</li> <li>(3) Fever evaluation of at least 3 days</li> </ul>	<p><i>Clostridium difficile</i> colitis, drug-induced fever, alcohol/drug withdrawal, pulmonary embolism, septic thrombophlebitis, sinusitis, acalculus cholecystitis, pancreatitis</p>
<p><b>C. <u>Immune-deficient FUO:</u></b></p> <ul style="list-style-type: none"> <li>(1) Daily or intermittent fever &gt; 101°F</li> <li>(2) ANC &lt; 500/mm<sup>3</sup></li> <li>(3) Fever evaluation of at least 3 days</li> </ul>	<p>Opportunistic bacterial infections, aspergillosis, candidiasis, herpes virus</p>
<p><b>D. <u>HIV-associated FUO:</u></b></p> <ul style="list-style-type: none"> <li>(1) Daily or intermittent fever &gt; 101°F</li> <li>(2) Inpatient fever &gt; 3 days OR</li> <li>(3) Outpatient fever &gt; 4 weeks</li> </ul>	<p>Cytomegalovirus, <i>Mycobacterium avium-intracellulare</i> complex, <i>Pneumocystis jirovecii</i> pneumonia, drug-induced, Kaposi's sarcoma, lymphoma</p>
www.FirstRanker.com	

History: A comprehensive history should include questions about:

- A. The fever itself (e.g. route of measurement, peak temperature, patterns, time of day, etc.)
- B. Systemic symptoms (e.g. weight loss, decreased appetite, rash, myalgias, arthralgias, etc.)
- C. Localized symptoms (e.g. cough, urinary symptoms, headache, abdominal pain, bone pain, etc.)
- D. Travel history, sick contacts, animal contacts, family history, and sexual history
- E. Potential causes of drug-induced fever: diuretics, pain relievers, salicylates, anti-arrhythmic agents, anti-seizure drugs, sedatives, antihistamines, barbiturates, cephalosporins, penicillins, sulfonamides.

## Physical Examination:

Physical Exam Finding	Clinical Correlate
Erythema nodosum	Sarcoidosis, Tuberculosis, Histoplasmosis, IBD, Drug reaction
Heart murmur	Endocarditis, rheumatic fever
Hepatomegaly	Hepatitis, Lymphoma, Metastatic cancer, Typhoid fever
Joint swelling or pain	RA, SLE, Gout, Pseudogout, Lyme Disease, Familial Mediterranean fever, Lyme disease
Livedo reticularis	PAN, SLE, cryoglobulinemia
Lymphadenopathy: A. Generalized, tender B. Localized, non-tender	Autoimmune or infectious disease Malignancy
Relative bradycardia	Legionella, Psittacosis, Q Fever, Typhoid Fever, Babesiosis, Brucellosis, Malaria, Dengue Fever, RMSF, Lymphoma, Drug Fever
Palpable purpura	Vasculitis, Meningococcemia, Rickettsial infection
Splenomegaly	EBV, CMV, hematologic malignancy, sarcoidosis, tuberculosis
Temporal artery tenderness	Temporal arteritis
Uveitis	Sarcoidosis, Tuberculosis, Toxoplasmosis, Vasculitis
Vitiligo	Autoimmune disease



## Laboratory Testing:

### First-Line Tests

CBC with manual differential

Chemistry panel

Liver function tests

ESR

Blood culture x 3 sets

Urinalysis and urine culture

Chest x-ray

PPD or TB QuantiFERON

If the above laboratory work-up is negative, obtain a **CT of chest, abdomen and pelvis with contrast.**

## Further diagnostic testing:

A. If an **infectious** disease is suspected...

Second-Line Tests: TTE, sputum culture for AFB, HIV test, Hepatitis A, B, and C serologies, RPR, ASO titer, serology for CMV, EBV

Third-Line Tests: TEE, LP, Sinus CT, Gallium scan

B. If a **non-hematologic malignancy** is suspected...

Second-Line Tests: Mammography, Chest CT with contrast, Endoscopy, Bone Scan, Gallium Scan

Third-Line Tests: MRI of the brain, Lymph node biopsy, Skin lesion biopsy, Liver biopsy, Ex-Lap

C. If a **hematologic malignancy** is suspected...

Second-Line Tests: Peripheral smear, SPEP

Third-Line Tests: Bone marrow biopsy

D. If a rheumatologic disease is suspected...

Second-Line Tests: RF, ANA, cryoglobulin, ferritin

Third-Line Tests: Temporal artery biopsy, Lymph node biopsy

E. Venous Doppler studies should be obtained in relevant patients.

