

APPROACH TO THE FEBRILE PATIENT

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FEVER

Is an elevation of body temperature above the normal circadian range as the result of a change in the thermoregulatory center located in the anterior hypothalamus and pre-optic area.



THERMOREGULATION

Body heat is generated by:

- Basal metabolic activity.
- Muscle movement.

And is lost by:

- Conduction.
- Convection (which is increased by wind or fanning).
- Evaporation which is increased by sweating.

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.



In a hot environment, Sweating is the main mechanism for increasing heat loss.

This usually occurs when the ambient temperature rises above 32.5°C or during exercise.



FEBRILE RESPONSE

The initiation of fever begins when exogenous or endogenous stimuli are presented to specialized host cells, principally monocytes and macrophages.

They will stimulates the synthesis and release of various *pyrogenic cytokines* including:

- interleukin-1, interleukin-6
- TNF- α , and
- IFN- γ .

EXOGENOUS

Stimuli from outside the host like:
microorganism, their products, or toxins which are called **Endotoxin** (lipopolysaccharide).

Lipopolysaccharide (LPS): are found in the outer membrane of all gram negative organisms.

Action :

- Through stimulation of monocytes and macrophages.
- Direct on endothelial cell of the brain to produce fever.

ENDOGENOUS PYROGENS

Polypeptides that are produced by the body (by monocytes and macrophages) in response to stimuli that is usually triggered by infection or inflammation stimuli.

- Pyrogens: substances that cause fever.

What pyrogens are there?

Cytokines: regulatory polypeptides that are produced by:

- Monocytes / macrophages.
- Lymphocytes.
- Endothelial and epithelial cell and hepatocytes.

The most important ones are :

- Interleukin 1α and 1β (the most pyrogenic).
- Tumor necrosis factor α .
- Interferon.
- Interleukin 6 (the least pyrogenic).

↑cytokines → fever develop within 1h of injection.

MECHANISM OF ACTION

Cytokine-receptor interactions in the pre-optic region of the anterior hypothalamus activate phospholipase A.

This enzyme liberates plasma membrane arachidonic acid as substrate for the cyclo-oxygenase pathway.

The resulting mediator, *prostaglandin E₂*, then modifies the responsiveness of thermosensitive neurons in the thermoregulatory center.

- Diurnal variation:

6 am : 37.2 °C

4 pm : 37.7 °C

- Rectal temperature $>0.6^{\circ}\text{C}$ oral temperature

Fever: Morning : AM $>37.2^{\circ}\text{C}$

Evening : PM $>37.7^{\circ}\text{C}$

PRESENTATION OF FEVER

Feeling hot:

A feeling of heat does not necessarily imply fever.

Rigors:

Profound chills accompanied by chattering of the teeth and severe shivering and implies a rapid rise in body temperature. Can be produced by :

- Brucellosis and malaria.
- Sepsis with abscess.
- Lymphoma.

Excessive sweating:

Night sweats are characteristic of tuberculosis, but sweating from any cause is usually worse at night.

PRESENTATION OF FEVER

Headache:

Fever from any cause may provoke headaches.

Severe headache and photophobia, may suggests **meningitis**.

Delirium:

Mental confusion during fever is well described and relatively more common in extreme of age.

Muscle pain:

Myalgia is characteristic of viral infections(influenza), and other infections(malaria and brucellosis etc.)

HYPERTHERMIA

Is an elevation of core temperature without elevation of the hypothalamic set point.

Cause: inadequate heat loss, such as:

- Heat stroke.
- Drug induced such as: tricyclic antidepressant.
- Malignant hyperthermia associated with psychiatric drugs.

FEVER: BENEFICIAL/DANGEROUS?

Elevation of body temperature increases chance for survival.

Temperatures appear to increase the phagocytic and bactericidal activity of neutrophils, and the cytotoxic effects of lymphocytes.

Thus the growth and virulence of several bacterial species are impaired at high temperature.

FEVER PATTERNS

- Intermittent fever.
- Remittent fever.
- Hectic fever.
- Sustained fever.
- Relapsing fever.

Intermittent fever:

Exaggeration of the normal circadian rhythm and temperature. falls daily to normal.

when the variation is large it is called hectic.

Causes:

- Deep seated infection.
- Malignancy.
- Drug fever.

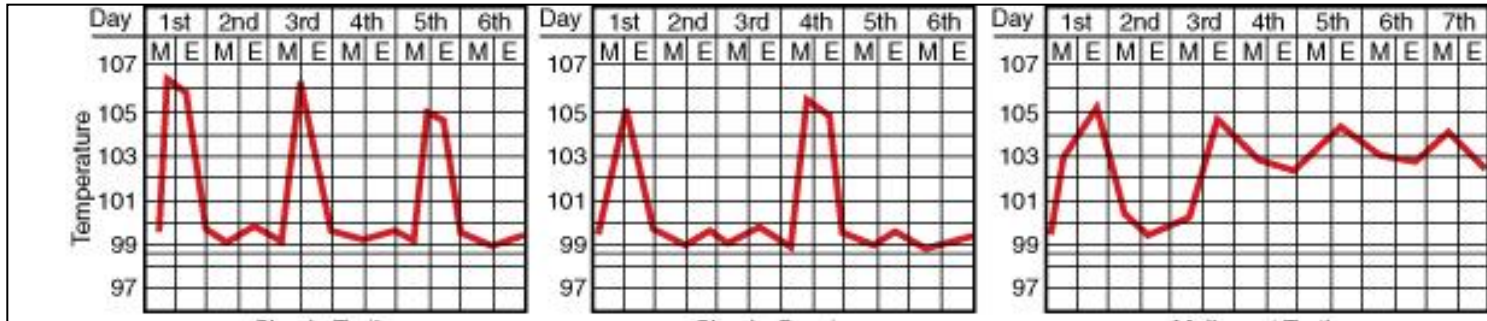
Quotidian fever: hectic fever that occur daily.

Remittent fever:

Temperature falls daily but not to normal.

Causes:

- Tuberculosis.
- Viral infection.
- Many bacterial infections.



Relapsing fever:

Febrile episodes are separated by intervals of normal temperature. Such as:

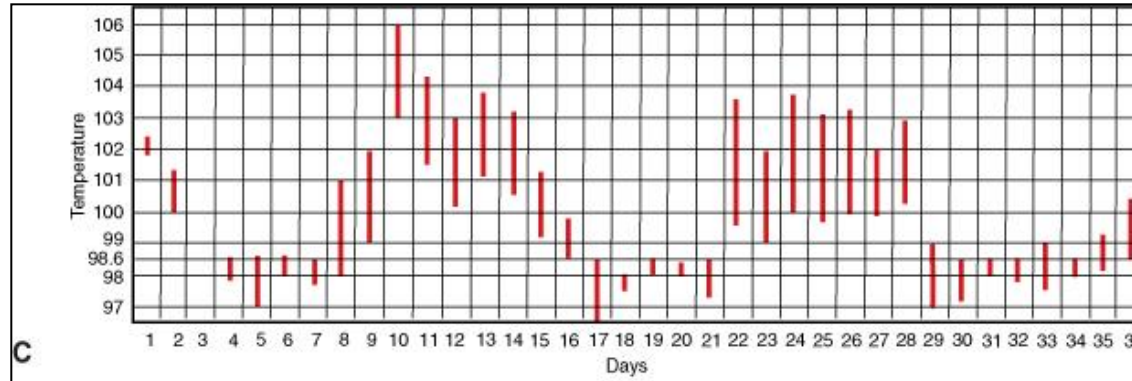
- **Malaria:** fever every 3 days (tertian) caused by (plasm. Falciparum). Or every 4 days (quartan) caused by (plasm. Vivax).
- **Borrelia:** Days of fever followed by days of no fever.

FEVER PATTERN

Fever pattern cannot be considered diagnostic for a particular infection or disease and the typical pattern is not usually seen because of use of :

- Antipyretics.
- Steroids.
- Antibiotics.

FEVER PATTERN

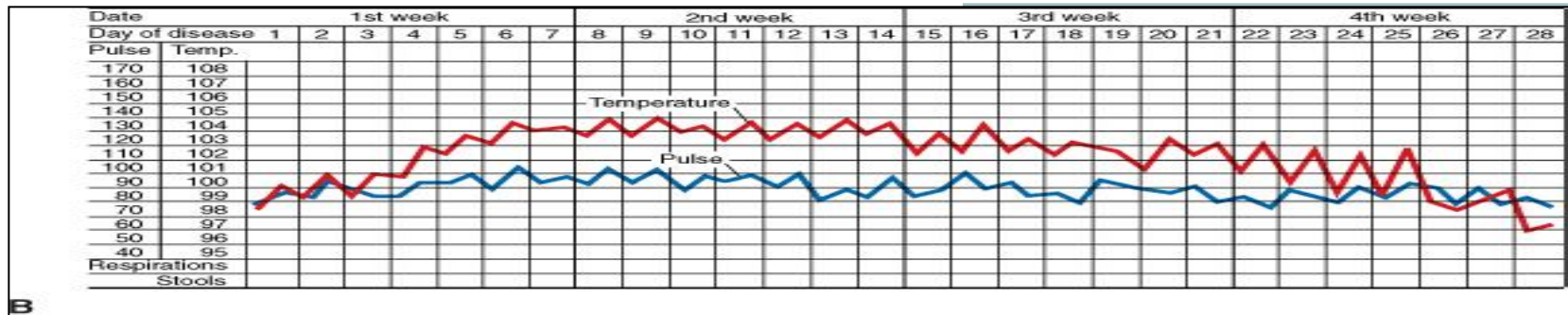


Pel-Ebstein fever:

Fever for 3 to 10 days followed by no fever for 3 to 10 days.

Causes:

- Hodgkin lymphoma.
- Tuberculosis.



Temperature-pulse dissociation (Relative bradycardia) is seen in:

- Typhoid fever.
- Brucellosis.
- Leptospirosis.
- Factitious fever.
- Acute rheumatic fever with cardiac conduction abnormality.
- Viral myocarditis.
- Endocarditis with valve ring abscess affecting conduction.

FEVER PATTERNS..DEGREE

Fever with extreme degree:

- Gram-negative bacteremia.
- Legionnaires' disease.
- Bacteremic pyelonephritis.

Noninfectious cause of extreme pyrexia:

- Heat stroke.
- Intracerebral hemorrhage.

APPROACH TO THE FEBRILE PATIENT

What is the easiest and most cost effective way of reaching a diagnosis and thus offering the right treatment for a febrile patient?

**METICULOUS DETAILED
HISTORY.**

APPROACH TO FEVER

Rule out common infection.

Remember:

UNCOMMON MANIFESTATIONS OF COMMON DISEASES ARE COMMONER THAN COMMON MANIFESTATIONS OF UNCOMMON ONES.

Careful history:

Chronology of symptoms:

Detailed complain of the patient with the symptoms arranged chronologically.

Use of drugs:

Drug fever is uncommon and therefore easily missed. The culprits include:

- Penicillin.
- Cephalosporin.
- Sulphonamide.
- anti tuberculous agents.
- anticonvulsants particularly phenytoin.

Surgical or dental procedure:

Patient known to have rheumatic heart disease is at risk to develop infective endocarditis if not given prophylaxis.

Occupational history:

- Exposure to animals: brucellosis & Q fever.
- Exposure to infected person tuberculosis or influenza.

Symptoms of common respiratory infections:

- Sore throat, nasal discharge, sneezing ...?URTI (VIRAL).
- Sinus pain and headache.....? Suggesting sinusitis.
- Elicit symptoms of lower respiratory tract infection cough, sputum, wheeze or breathlessness.

Genitourinary symptoms:

Ask specifically about:

frequency of micturition, dysuria, loin pain, and vaginal or urethral discharge, suggesting:

- Urinary tract infection.
- Pelvic inflammatory disease.
- Sexually transmitted infection (STI).

Abdominal symptoms:

Ask about diarrhea, with or without blood, weight loss and abdominal pain, suggesting:

- Gastroenteritis.
- Intra-abdominal sepsis.
- Inflammatory bowel disease.
- Malignancy.

Joint symptoms:

Joint pain, swelling or limitation of movement . If present ask about:

- Distribution: mono, oligo or poly arthritis.
- Appearance: fleeting or additive.

It suggests:

- Infective arthritis...oligo.
- Collagen vascular disease.....Fleeting.
- Reactive arthritis.

Family history of:

- Tuberculosis.
- Arthritis.
- Other infectious diseases.
- Any one with symptoms of Polyserositis or bone pain.

Ethnic origin of the patient:

Turks, Arabs, Armenians likely to have Familial Mediterranean fever (FMF).

Geographic area of living:

If the patient has been in an endemic area common diagnoses include:

- Malaria.
- Typhoid fever.
- Viral hepatitis.

Dengue fever & other viral diseases:

- Hemorrhagic fevers (eg: Rift valley)
- Ebola
- CORONA(MERS-COV)
- Zika virus
- Nipah virus

Malaria must be excluded whatever the presenting symptoms.

FURTHER POINTS IN HISTORY

- Household pets.
- Ingestion of unpasteurized milk or cheeses.
- Sexual practice.
- Iv drug abuse.
- Alcohol intake.
- Prior transfusion or immunization.
- Drug allergy.

PHYSICAL EXAMINATION

Approach considerations:

Fever may sometimes be absent in some cases, such as:

- Seriously ill newborns.
- Elderly patients.
- Uremic patient.
- Malnourishment.
- Corticosteroid use.
- Continuous treatment with anti-inflammatory or antipyretic agents.

Repeated meticulous examination on a regular basis
(better by different colleagues) until diagnosis is reached.

Temperature should be taken

- Orally or,
- Rectally.
- Axillary temperature is notoriously unreliable .

Cautions while taking oral temperature

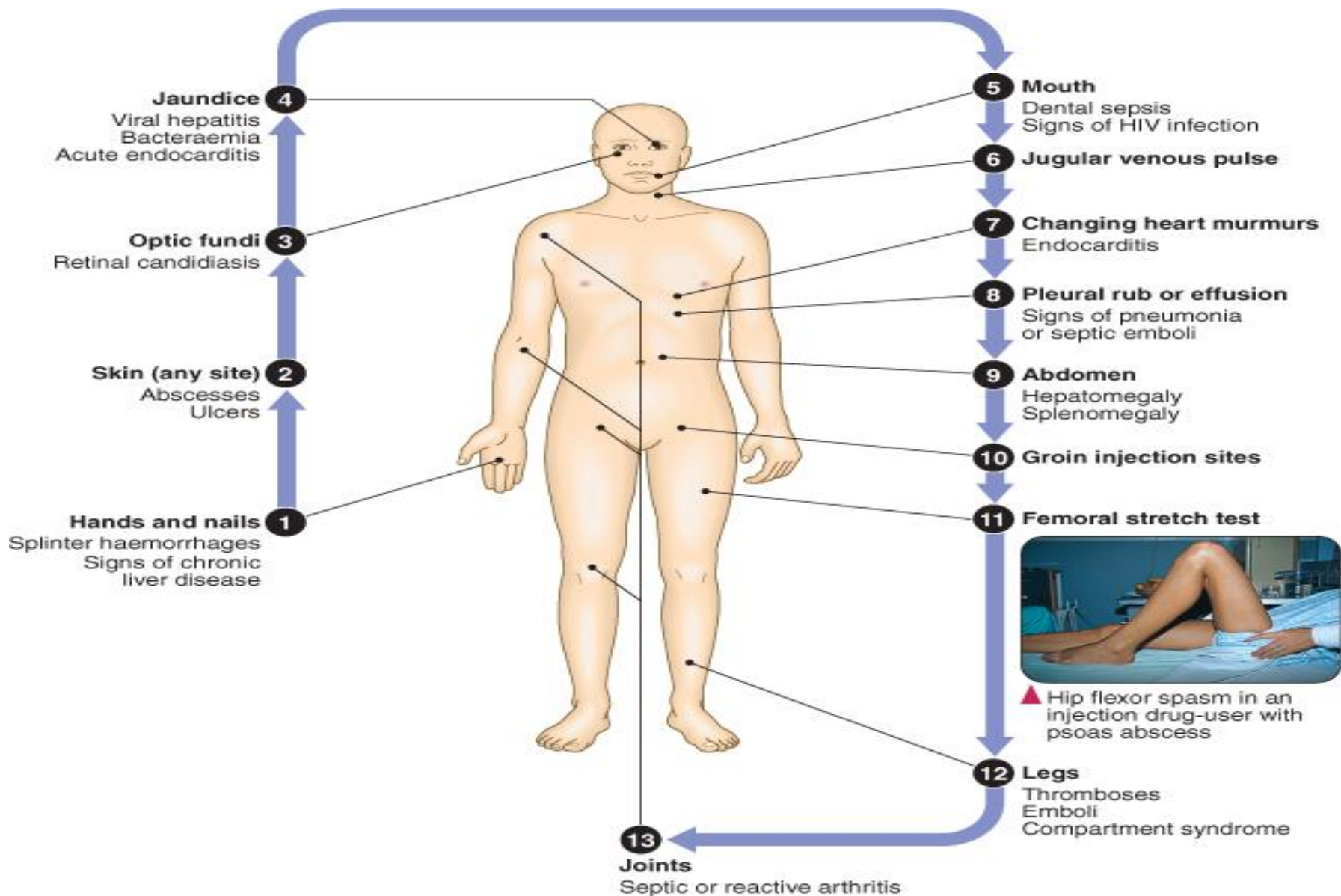
- Recent consumption of hot or cold drinks.
- Smoking.
- Hyperventilation.

Document the presence of fever.

A careful examination is vital and must be repeated regularly.

Particular attention should be paid to:

- The skin for rash.
- Throat for pharyngitis.
- Eyes for jaundice, scleritis.
- Nail bed for clubbing, splinter hemorrhage.
- lymph nodes for enlargement.
- abdomen for ascites or sign of peritonitis.
- heart for murmurs indicating endocarditis.



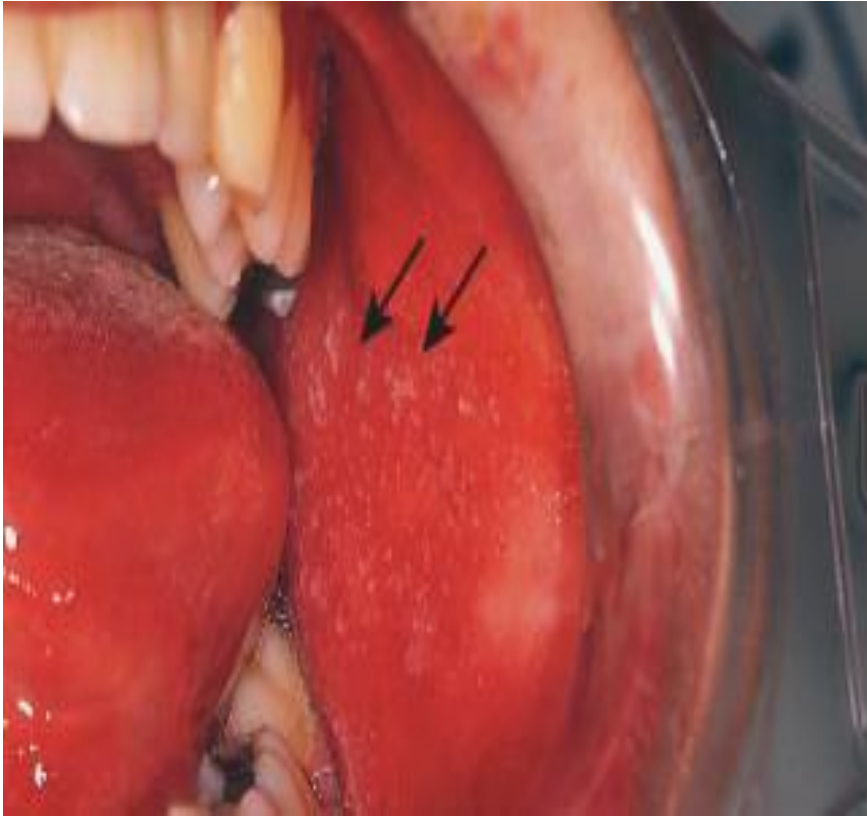
SKIN

Look for rash.

Erythematous rash (rash that blanch on pressure):

Causes:

- Measles: often accompanied by upper respiratory tract symptoms and conjunctivitis.
- Other viral infection like: rubella, scarlet fever.



Purpuric or petechial rash (do not blanch on pressure):

- May suggest meningococcal septicemia.



Vesicular rash:

May be caused by chickenpox or shingles.



MOUTH AND OROPHARYNX

Vesicular lesions, tonsillar exudate suggest Infectious etiology:

- Streptococcal pharyngitis.
- Coxsackie infection.



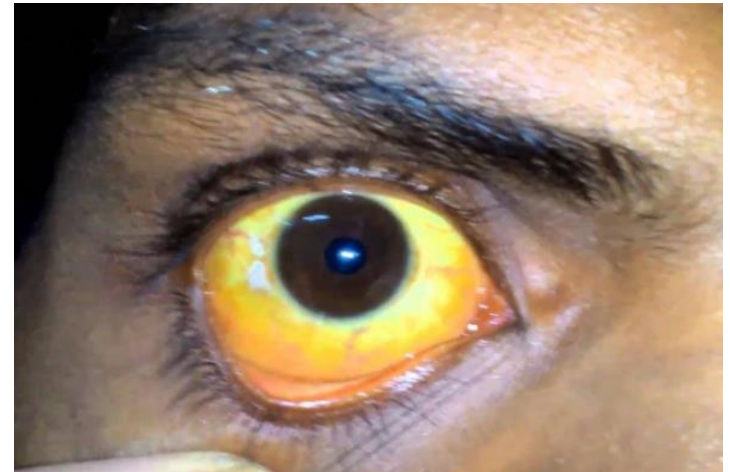
Hairy leukoplakia or oropharyngeal candidiasis suggest:

- HIV /AIDS



EYES

- Conjunctival petechiae may suggest meningococcal meningitis.
- Jaundice may suggest acute hepatitis A.



LYMPH NODES

Cervical lymph node enlargement and tonsillar enlargement suggest:

- Acute pharyngitis or tonsillitis.

Posterior lymphadenopathy suggest:

- Infectious mononucleosis.
- HIV infection.

Axillary lymph node enlargement may suggest:

- Sepsis.
- Leukemia.
- Lymphoma.

JOINTS

Any joint but commonly the knee and ankle.
Look for swelling, redness, hotness and effusion
suggesting active arthritis ..? infective/septic arthritis



Neck: look for stiffness. may suggest meningitis

Chest and heart:

- Sign of consolidation.
- Pleural effusion.
- Pericardial rub.
- Cardiac murmur: Endocarditis or acute rheumatic fever.

Abdomen: Look for tenderness (especially in the RIF) acute appendicitis and other types of acute abdomen.

Rectal examination: look for

- Perianal abscess.
- Acute prostatitis.

20 years male who is a heroin drug abuser for a long time,
came to ER c/o left thigh pain and fever.

Look at the picture and guess what is his problem



Hip flexor spasm due to psoas abscess secondary to staphylococcus septicemia with seeding into the muscle.

FACTITIOUS FEVER

This is defined as fever created by the patient by manipulating the thermometer and/or temperature chart apparently to obtain medical care.

uncommon and typically presents in young women who work in paramedical professions.

Examples include the dipping of thermometers into hot drinks to fake a fever.

The factitious disorder is usually medical but may relate to a psychiatric illness with reports of depressive illness.

Clues to the diagnosis of factitious fever:

- A patient who looks well.
- Absence of temperature-related changes in pulse rate.
- Temperature $> 41^{\circ}\text{C}$.
- Absence of sweating.
- Normal ESR and CRP despite high fever.

Useful methods for the detection of factitious fever include:

- Supervised (observed) temperature measurement.
- Measuring the temperature of freshly voided urine.

LABORATORY TESTS

Laboratory investigations are indicated if the presentation suggests more than a simple viral infection or acute pharyngitis in children.

Lab test can be focused if the history is suggesting a certain diagnosis.

CBC with differential:

Band forms(%of neutrophils), and toxic granulation(periph.B.F) suggest bacterial infection.

Neutropenia may be seen with:

- Infection: Typhoid, brucellosis ,viral infection.
- Vasculitis: systemic lupus erythematosus.

Lymphocytosis may be seen in:

Tuberculosis, brucellosis and viral disease.

Monocytosis is seen with:

- Tuberculosis, typhoid and brucellosis.
- Lymphoma.

Eosinophilia is seen in:

- Hypersensitivity drug syndrome.
- Hodgkin disease.
- Adrenal insufficiency.

Blood films to exclude Malaria.

Urinalysis.

Sample any fluid and examine: pleural, peritoneal, joint.

Bone marrow aspirate & biopsy for microbiologic & histopathology.

Stool exam for occult blood, O, C & parasites.

Chemistry: electrolytes ,glucose, urea , and liver function.

Microbiology:

Samples from sputum, urethra, joint aspirates, pleural fluid, ascetic fluid and send for smears and culture.

Sputum evaluation:

- Gram staining.
- Z-N staining for acid fast bacilli.

Cultures for: blood, abnormal fluid collection and urine.

CSF: if meningitis is suspected do gram stain and culture.

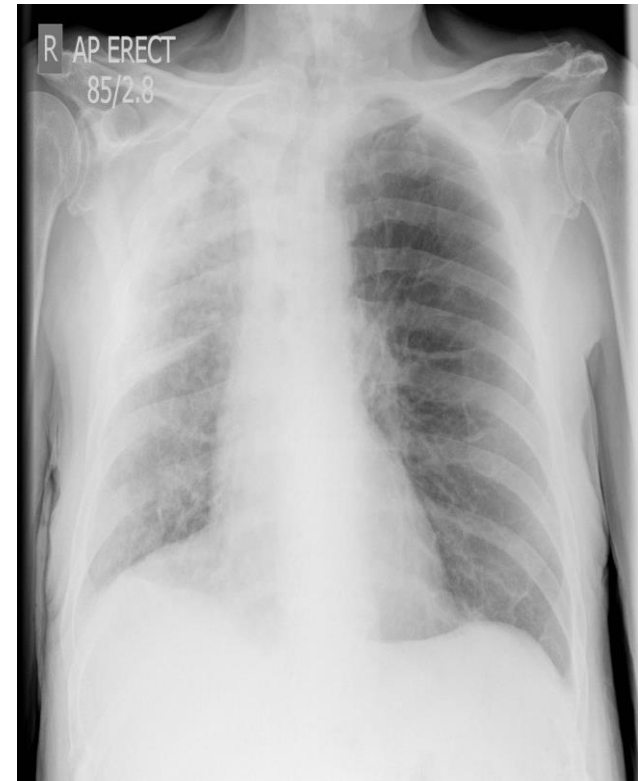
Special blood tests:

HIV screening for patient who has risk factor (high risk behaviors):

- Recent travel with high risk behaviors.
- Injection drug user.
- Sex workers.
- Blood transfusion recipient.

Radiology:

Chest x ray is indicated for any patient with significant febrile illness.



OUTCOME OF DIAGNOSTIC EFFORTS

Patient recover spontaneously suggesting:
viral illness or some of the spontaneously recovering
bacterial infection (mainly intracellular organism like
typhoid or brucellosis).

If fever persist for more than 2-3 weeks with no diagnosis is
reached by repeated physical examination and laboratory
tests then it's:

PYREXIA OF UNKNOWN ORIGIN(PUO,FUO)

TREATMENT OF FEVER

Is it fever or hyperthermia?

Hyperthermia:

1. Heat stroke.
2. Drug-induced hyperthermia.
3. Malignant hyperthermia.

Heat stroke:

Thermoregulatory failure in association with a warm environment.

- **Exertional:** young person exercising at ambient temperature and or humidity that is higher than normal.
- **Non Exertional:** typically occur in the elderly.

Hyperpyrexia: more than 40 should be treated with antipyretics and physical cooling.

While resetting the hypothalamic set point with antipyretic will speed the process. Antipyretics also help treating headaches, myalgia and chills.

Low grade or moderate fever is not harmful; so no antipyretics use except for:

- Pregnant women.
- Child with febrile seizures.

Why no antipyretics for mild fever?

- Obscure the natural history of the patient disease or syndrome.
- Gives false feeling of well being. may miss/mask meningitis which may be imminently life-threatening.

ANTIBIOTICS USE IN ER

Pathogens

Infection focus

host factors (Immune factors)

Common infection in ER:

- UTI
- Respiratory tract infection
- CNS infection
- Cellulitis

ANTIBIOTICS USE IN UTI

Upper urinary tract infection

Symptoms: Fever, flank pain, dysuria

lab test: Pyuria, bacteria

Treatment: cotrimoxazole , cephalosporin or aminoglycoside (duration: 7-10 days)

ANTIBIOTICS USE IN-RESPIRATORY TRACT INFECTION

Pneumonia:

Cough, fever, sputum or not.

Clinical manifestations: consolidation.

CXR: opacity with air bronchogram interstitial infiltrate.

Sputum: gram's stain.

Treatment: 3rd generation cephalosporins and macrolides.

ANTIBIOTIC USE IN-RESPIRATORY TRACT INFECTION

Nosocomial fever:

Fever acquired after 48 hours of admission to the hospital.

Maybe:

- Pneumonia.
- Catheter related infection.
- UTI.

Consider hospital pathogen while selecting antibiotics.

ANTIBIOTICS USE IN-CNS INFECTIONS

Bacterial meningitis:

Use aggressive antibiotics-due to prognosis and sequence.
cephalosporin ±Vancomycin.

Viral meningitis:

Observation, s/s Tx.

Herpes meningitis: acyclovir.

TB meningitis:

Anti-TB agents.

Prognosis: variation.

Fungal meningitis: antifungal agents.

ANTIBIOTICS USE IN-CELLULITIS

Pathogens: common streptococcus, or staphylococcus.

Antibiotics: PCN G or oxacillin/synthetic penicillin's

PITFALLS

- Depend on laboratory data.
- Incomplete history and examination.

Atypical presentation:

- Immunocompromised patient.
- Newborn.
- Early sign.
- Dehydration.



Thank you