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:
a) basal metabolic activity
b) muscle movement

Lost by:
1) Conduction
2) Convection (which is increased by wind or fanning)
3) 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 ± 0.5°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 stimulate the synthesis and release of various *pyrogenic cytokines* including:
  1)interleukin-1, interleukin-6
  2)TNF-α, and
  3)IFN-γ.

- 1) Exogenous : stimuli from out side the host
  Like : microorganism, their products, or toxins and it is called Endotoxin
- Endotoxin : lipopolysaccharide (LPS)
- LPS: is found in the outer membrane of all gram negative organism
- Action :
- 1) through stimulation of monocytes and macrophages
- 2) direct on endothelial cell of the brain to produce fever

- 2) 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 are called pyrogens

- What are these pyrogens:
  Cytokines:
- Definition:
- Cytokines are regulatory polypeptides that are produced by
- 1) monocytes / macrophages
- 2) lymphocytes
- 3) 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 centre.

- Diurnal variation
- 6 am : 37.2 &4pm : 37.7
- Rectal temperature>0.6^{0C} oral temperature
- Fever: Morning : AM >37.2^{0} C
  Evening : PM >37.7^{0} 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 :
  1) brucellosis and malaria
  2) sepsis with abscess
  3) 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 headache.
  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 such as influenza
  Malaria and brucellosis

- Hyperthermia
- Is an elevation of core temperature without elevation of the hypothalamic set point.
- Cause: inadequate heat loss
- Examples:
- 1) Heat stroke
- 2) Drug induced such as tricyclic antidepressant
- 3) Malignant hyperthermia. associated with psychiatric drugs

Fever: Beneficial/Dangerous?

- Elevation of body temperature increases chance for survival
- Temperatures appear to increase

  1) The phagocytic and Bactericidal activity of neurtrophils, and

  2) The cytotoxic effects of lymphocytes

  3)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

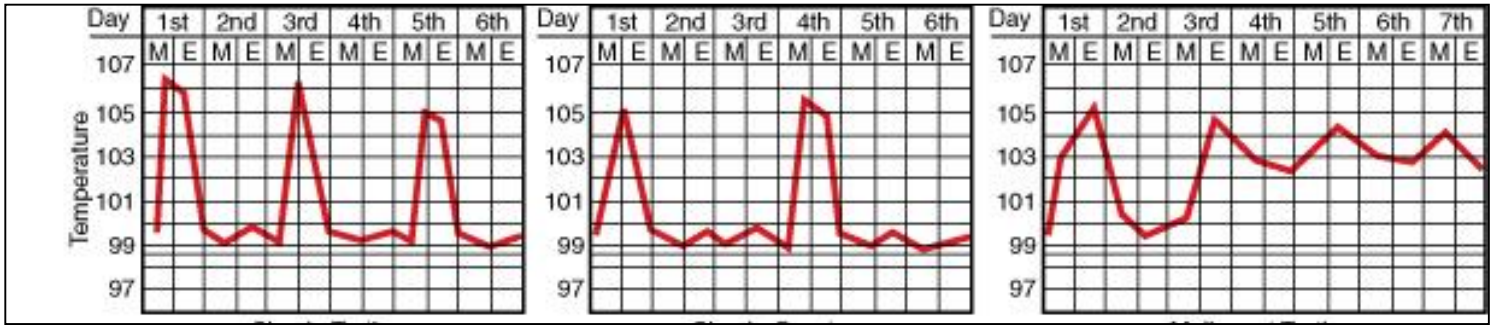
- Intermittent fever: exaggeration of the normal circadian rhythm,& temp. falls daily to normal, when the variation is large it is called hectic

  Cause: a) Deep seated infection
  b) Malignancy
  c) Drug fever

  Quotidian fever: hectic fever that occur daily.

- Remittent fever: Temperature falls daily but not to normal.

  Causes: a) tuberculosis
  b) viral infection
  c) many bacterial infections



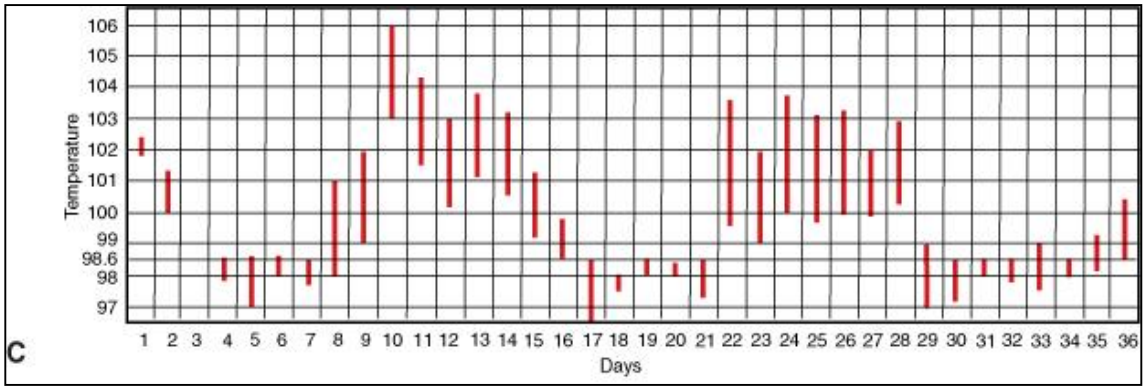
- Relapsing fever: febrile episodes are separated by intervals of normal temperature

  a) Malaria fever every 3days (tertian).plasm. falciparam.

  or every 4 days (quartan) ..plasm .vivax

  b) Borrelia ..Days of fever followed by days of no fever.

Fever Pattern



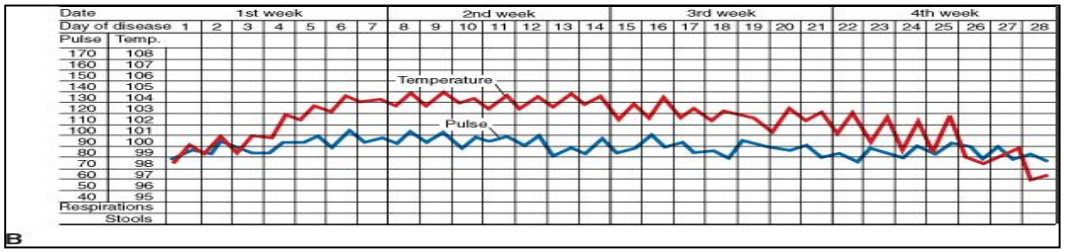
- Pel-Ebstein fever : fever for 3 to 10 days followed by no fever for 3 to 10 days

Causes : a) Hodgkin lymphoma

b) Tuberculosis

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 :
    1) Antipyretics
    2) Steroids
    3) Antibiotics



- Temperature – pulse dissociation (Relative bradicardia)
- is seen in

A) Typhoid fever

B) Brucellosis

C) leptospirosis

D) factitious fever

E) acute rheumatic fever with cardiac conduction abnormality

F) Viral myocarditis

G) Endocarditis with valve ring abscess affecting conduction .

Fever Patterns..Degree

- Fever with extreme degree:
- gram-negative bacteremia,
- Legionnaires‘ disease, and
- bacteremic pyelonephritis
- Noninfectious cause of extreme pyrexia:
- heat stroke, intracerebral hemorrhage

Physical Examination

- Fever may sometimes be absent:
- Seriously ill newborns
- Elderly patients,
- Uremic patient,
- Significantly malnourished individuals,
- Receiving corticosteroids or
- Continuous treatment with anti-inflammatory or antipyretic agents

Approach to the Febrile Patient

The most important step is

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:

1) *chronology of symptoms*

Detailed complain of the patient with the symotoms arranged chronologically

2) *Use of drugs*

- Drug fever is uncommon and therefore easily missed.
  The culprits include:
  penicillin and
  cephalosporin
  sulphonamide
  anti tuberculous agents
  anticonvulsants particularly phenytoin

3) Surgical or dental procedure

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

4) Nature of any prosthetic material or implanted devices prosthesis implant for: the knee joint prosthetic valve replacement

5) Occupational history including:

Exposure to animals: brocellosis & Q fever

exposure to infected person at home ..tuberculosis or infleunza.

Geographic Area of Living

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

- Malaria
- Typhoid fever
- Viral hepatitis

Dengue fever & other haemrrhagic fevers:

- Ebola
- CORONA(MERS-COV)
- ZIKA 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

History-Taking in Febrile Patients

Symptoms of common respiratory infections.

1) Sore throat, nasal discharge, sneezing …?URTI (VIRAL)

2) Sinus pain and headache…..? Suggesting A sinusitis

3) 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
  a) Urinary tract infection,
  b) Pelvic inflammatory disease and
  c) Sexually transmitted infection (STI)

- *Abdominal symptoms*

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

  a) Gastroenteritis,

  b) Intra-abdominal sepsis,

  c) Inflammatory bowel disease,

  d) Malignancy

- *Joint symptoms*

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

A) distribution: mono, oligo or poly arthritis

B) appearance: fleeting or additive

It suggests:

1) infective arthritis…oligo

2) collagen vascular disease…..fleeting

3) reactive arthritis

- *Drug history*
- Drug fever is uncommon and therefore easily missed.

The culprits include :

penicillin and
cephalosporin
sulphonamide
anti tuberculous agents
anticonvulsants particularly phenytoin

- *Alcohol consumption*

  Alcoholic hepatitis,

  hepatocellular carcinoma

  are all recognized causes of fever.

- *Family history of:*

a) Tuberculosis
b) Arthritis
c) Other infectious diseases
d) Any one with symptoms of Polyserositis or bone pain

- Ethnic origin of the patient
  is important. Example:

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

Physical examination/important points:

REPEATED METICULOUS EXAMINATUION on a regular basis(better by diff.colleagues) until diagnosis is reached.

Temperature should be taken

1) Orally ..or

2) Rectally ....

Axillary temperature is notoriously unreliable .

- Cautions while taking oral temperature
  1) Recent consumption of hot or cold drinks
  2) Smoking
  3) Hyperventilation

Examination

Document the presence of fever

- A careful examination is vital and must be repeated regularly
- Particular attention should be paid to :

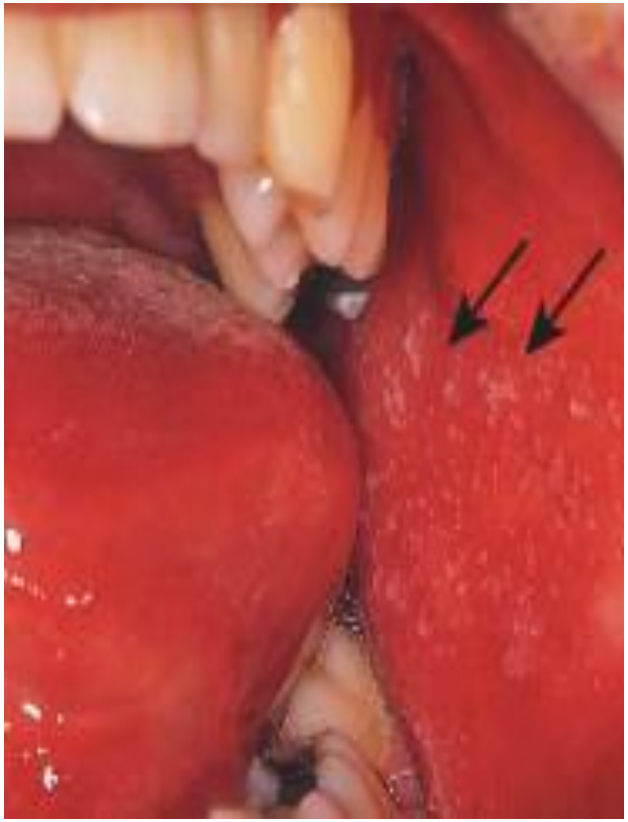
The skin .....for skin rash
Throat.....for pharyngitis
Eyes.....for jaundice , scleritis.
Nail bed .....for clubbing, splinter hemorrhage.
lymph nodes..... for enlargmant
abdomen .....for ascitis or sign of peritonitis
heart .....for murmurs indicating endocarditis.

- 2) Look for RASH
- a) Erythmatous rash (rash that blanch on pressure)

  Causes:

  1) Meseals: often accompanied by upper respiratory tract symptoms and conjunctivitis

  2) other viral infection like : rubella , scarlet fever



- B) a purpuric or petechial rash: (do not blanch on pressure)
- May suggest meningococcal septecemia

- Vesicular rash: may be caused by
- chickenpox or shingles

- Mouth and oropharynx
- Vesicular lesions, tonsillar exudate: suggest
  Infectious etiology:
  1) streptococcal pharyngitis
  2) coxsakie infection

- Hairy leukoplakia. OR oropharyngeal candidiasis suggest:
  HIV /AIDS

- Oropharyngeal candidiasis.. suggest
  Immunodefficiency syndrome

- Eyes
- Conjunctival petechiae….
- …may suggest …..meningococcal meningitis
- Jaundice ……may suggest acute hepatitis A
- Cervical lymphnodes enlargment :
  Tonsillar LN enlargmant ….suggest :
  Acute pharyngitis or tonsillitis

  Posterior lymphadenopathy…suggest :
  1) Infectious mononucleosis
  2) HIV infection

- Axillary lymph node enlargement ….may suggest:
  1) Sepsis
  2)leukemia
  3) lymphoma

Joints (any joint but commonly the knee and ankle)

Look for swelling, redness, hotness and effusion suggesting active arthritis ..? infective/septic arthritis

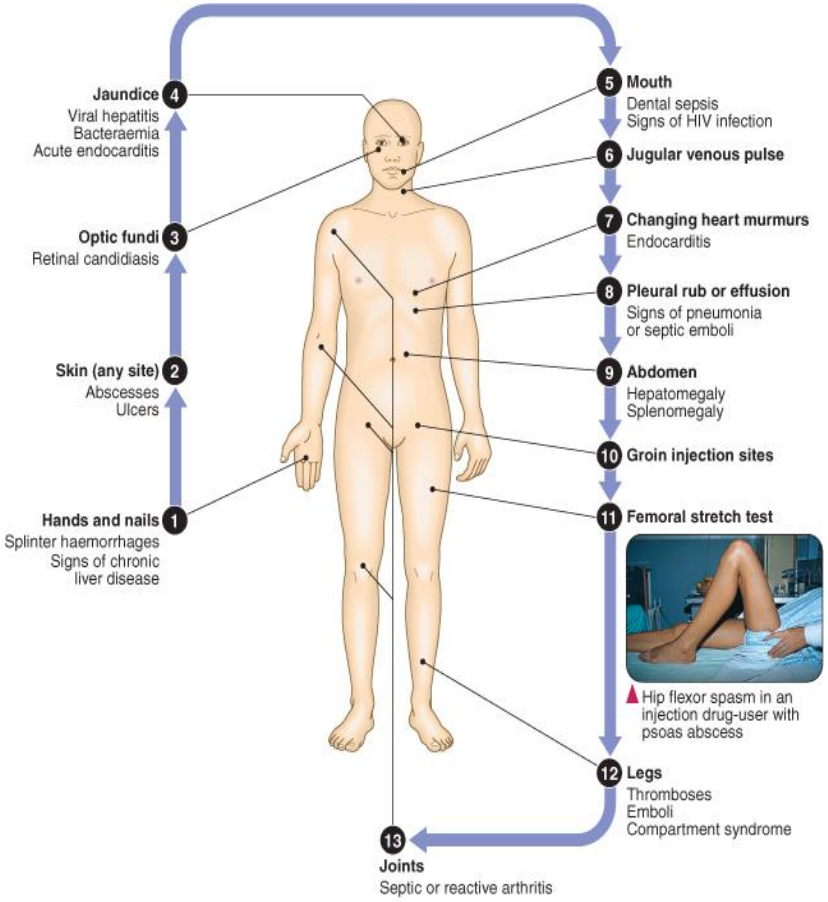
- Neck ..look for stiffness ..may suggest meningitis
- Abdomen:
- Look for : Tenderness(especially in the RIF)...& ac.append./other types of ac abdomen

Chest and heart

1) Sign of consolidation
2) Pleural effusion
3) Pericardial rub
4) Cardiac murmur.....Endocarditis or acute rheumatic fever

- Rectal examination: look for
- 1) perianal abscess
- 2)acute prostatitis

Drug-IV user



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

- The answer :

- Hip flexor spasm due to psoas abscess
- Secondary to staphylococcus septicemia with seeding into the muscle

REMEMBER; 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°C
- Absence of sweating during defervescence
- Normal ESR and CRP despite high fever

Useful methods for the detection of factitious fever include
1) Supervised (observed) temperature measurement
2) Measuring the temperature of freshly voided urine

Laboratory Tests

- Laboratory investigation is indicated if
- presentation suggests more than Simple viral infection or acute phartngitis in children

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

1) Investigations:

- complete blood count with differential,

** band forms and toxic granulation ..suggest bacterial infection

** Neutropenia : may be seen with:

Infection : Typhoid,brucellosis ,viral infection

vasculitis : systemic lupus erythromatosis

** lymphocytosis : may be seen in:

a) Tuberculosis, brucellosis, Viral disease.

** Monocytosis: is seen with

a) Tuberculosis, typhoid and brucellosis
b) lymphoma

**Eosinophilia is seen in:

a) Hypersensitivity drug syndrome
b) Hodgkin disease
c) Adrenal insufficiency

- blood films to exclude Malaria
- Urinalnalysis
- Sample any fluid and examine: pleural, peritoneal, joint.
- Bone marrow aspirate & biopsy for microbiologic& histopathology.
- Stool exam for occult blood, O, C & parasites.

- 2) chemistry: electrolytes ,glucose, urea , and liver function
- 3) microbiology
- Samples from: sputum, urethra and other sites like joint, pleural fluid, ascetic fluid and send for smears and culture
- Sputum evaluation : a) gram staining
  b) Z-N staining for acid fast bacilli

Culture for: blood, abnormal fluid collection and urine

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

- SPECIAL BLOOD TEST:
- HIV screening for patient who has risk factor (high risk behaviors)

  1) Recent travel with high risk behaviors

  2) Injection drug user

  3) Sex workers

  4) Blood transfusion recipient
- Radiology
- Chest x ray is indicated for any patient with significant febrile illness.

Outcome of Diagnostic Efforts

1) Patient recover spontaneously

suggesting: viral illness or some of the spontaneously recovering bacterial infection: mainly intracellular organism like *typhoid or brucellosis*

2) Diagnosis is reached

3) If fever persist for more than 2-3 weeks with no diagnosis is reached by : a) repeated physical examination.

b) laboratory test ….then

It is *pyrexia of unknown origin(PUO,FUO)*

Treatment of Fever

- Is it fever or hyperthermia
- Hyperthermia

  1. Heat stroke

  Classic heat stroke

  2. Drug-induced hyperthermia

  3. Malignant hyperthermia

- Heat stroke
- Thermoregulatory failure in association with a worm environment
- 1) Exertional: young person exercising at ambient temperature and or humidities that are higher than normal.
- 2)non Exertional: typically occur in elderly.

- Hyperpyrexia: more than 40 should be treated by: anti pyretics and physical cooling
- While resetting the hypothalamic set point with antipyretic will speed the process.
- Antipyretics also help for:
- Headache, myalgia, chills.

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

- 1) Pregnant women
- 2) 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
  1. UTI
  2. Respiratory tract infection
  3. CNS infection
  4. Cellulitis

Antibiotics use in-UTI

Upper urinary tract infection

- Symptoms: Fever, flank pain, dysuria
  lab test: Pyuria, bacteria
- Treatment: cotrimoxasole , Cephalosporin or aminoglycoside …….duration: 7-10 days

Antibiotics use In-Respiratory tract infection

- Pneumonia

  1. Cough, fever, sputum or not

  clinical manifestations: consolidation

  CXR: opacity with air bronchogram interstitial infiltrate

  sputum: gram's stain

  Treatment: 3rd generation cephalsporine and macrolides

Antibiotic use in-respiratory tract infection

- Nosocomial fever
- Fever acquired after 48 hours of admission to the hospital
- 1) pneumonia
- 2) catheter related infection
- 3) UTI

- Consider hospital pathogen while selecting antibiotics

Antibiotics use in-CNS infection

- Bacterial meningitis
  1. Aggressive antibiotics-due to prognosis and sequence
  2. cephalosporin ±Vancomycin
- Viral meningitis
  1. Observation, s/s Tx
  2. Herpes meningitis- acyclovir

continuing

Antibiotic use in- CNS infection

- TB meningitis
  1. Anti-TB agents
  2. Prognosis: variation
- Fungal meningitis: antifungal agents

Antibiotics use In-cellulitis

- Pathogens: common streptococcus, or staphylococcus
- Cellulitis →
- Antibiotics: PCN G or oxacillin/synthetic penicillins

Pitfalls

- Depend on laboratory data
- Incomplete Hx.&EX

- Atypical presentation
  1. Immunocompromised patient
  2. Newborn
  3. Early sign
  4. Dehydration

Thank you