# History Taking for Pharmacist


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# Outline

- URI symptoms
- Headache
- Abdominal pain
- Diarrhea
- Fever

# History Taking – Overview

- History
- Physical examination
- Lab and radiological investigation

- Diagnosis

- Management

# History Taking – Overview

- **Introduction (WIIPP)**
  - **W**ash your hands
  - **I**ntroduce yourself
  - **I**dentity: confirm you're speaking to the correct patient
  -
  - **P**ermission: confirm the reason for seeing the patient
  - **P**ositioning: patient sitting in chair approximately a metre away from you

# History Taking – Overview

- **Presenting Complaint**

  "expressed in the patient's own words"

  "Try to elicit the patient's ideas, concerns and expectations (ICE)"

- **History of Presenting Complaint**
  - **S**ite
  - **O**nset
  - **C**haracter
  - **R**adiation
  - **A**lleviating factors
  - **T**iming
  - **E**xacerbating factors
  - **S**everity (1-10)

**Anatomical localization**

**Etiology**

# History Taking – Overview

- **Past Medical History**

- All previous medical problems (they may forget some)

- Top ensure none are missed ask about these important conditions specifically **(mnemonic: "MJTHREADS Ca")**

**M**yocardiac infarction
**J**aundice
**T**uberculosis
**H**ypertension and **HIV**
**R**heumatic fever
**E**pilepsy
**A**sthma
**D**iabetes and **D**yslipidemia
**S**troke
**C**ancer (and treatment if so)

# History Taking – Overview

- **Risk factors**

- **Clarification of past medical history**
  - COPD; diagnosis, severity, treatment
  - Myocardial infarction; previous heart attacks, any previous angiograms , previous stenting
  - Diabetes: treatment, insulin and usual control of diabetes
  - HIV: medication, CD4

# History Taking – Overview

- **Drug History**
  - **All medications** that they take for each medication ask them to specify:
  - Dose, frequency, route and compliance (i.e whether they regularly take these medication).
  - **Recreational drugs**
  - **Intravenous drug use** (current or previous)
  - **Over the counter (OTC) medications**


http://www.oxfordmedicaleducation.com

# History Taking – Overview

- **Allergies**
  - Does the patient have any allergies?
  - If allergic to medications, clarify the type of medication and the exact reaction to that medication.
  - Specifically ask about whether there's been a history of ***anaphylaxis*** e.g. "throat swelling, trouble breathing or puffy face"

## Allergy vs. Side Effects

# History Taking – Overview

- **Social History**
  - **Alcohol intake**
  - **Tobacco use**
  - **Employment history**
  - **Home situation**
  - **Travel history**



# Upper Respiratory Tract Symptoms

- Common cold
- Pharyngitis
- Sinusitis
- Bronchitis

**Fever**
**Cough**
**Runny nose**
**Sore throat**

# Common Cold

- Clinical manifestations
  - Onset: 1 to 3 days after viral infection
  - First symptom noted is frequently a sore or ***"scratchy" throat***
  - ***Nasal obstruction*** and ***rhinorrhea***
  - Sore throat resolves quickly and ***nasal symptoms predominate***
  - ***Cough*** is associated with approximately 30% of colds and usually begins after the onset of nasal symptoms
  - ***Systemic symptoms*** are uncommon
  - The usual cold persists about 1 week, although ***25% last 2 weeks***
  - A ***change in the color or consistency*** of the secretions is common during the course of the illness and is ***not indicative of sinusitis or bacterial superinfection***

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# Common Cold: Etiology

**TABLE 58-1 Viruses Associated with the Common Cold**

| VIRUS GROUP | ANTIGENIC TYPES | PERCENTAGE OF CASES |
|---|---|---|
| Rhinoviruses | >100 types | 40-50 |
| Coronaviruses | 5 types | 10-15 |
| Parainfluenza virus | 5 types | 5 |
| Respiratory syncytial virus | 2 types | 5 |
| Influenza virus | 3 types* | 25-30 |
| Adenovirus | 57 types | 5-10 |
| Metapneumovirus | 2 types | 5 |
| Other viruses: enteroviruses, bocavirus | | |

*Multiple subtypes.

Ronald B. Turner. Mandell, Douglas, and Bennett's Principles and Practice of Infectious Diseases, 8th Edition, 2015

# Differential Diagnosis

- Allergic rhinitis; nasal or conjunctival itching
- Foreign body
- Streptococcosis
- Catarrhal phase of pertussis
- Complication of common cold; sinusitis
  - Bacterial sinusitis is more likely to be present if symptoms persist for ***more than 10 days***, if severe illness is present, or ***if symptoms worsen after improvement >> occur 8%***

Ronald B. Turner. Mandell, Douglas, and Bennett's Principles and Practice of Infectious Diseases, 8th Edition, 2015

# Treatment

- ***Symptomatic Therapies***

- Given the absence of demonstrated benefit and the potential for toxicity, ***symptomatic common cold therapies are not recommended for children younger than 4 years.***

Ronald B. Turner. Mandell, Douglas, and Bennett's Principles and Practice of Infectious Diseases, 8th Edition, 2015

# Treatment

- **Nasal congestion**
  - Topical and oral adrenergic agents
  - Prolonged use of the topical adrenergic agents should be avoided to prevent the development of ***rhinitis medicamentosa (use longer than 2 weeks)***
- **Topical**
  - Imidazoline derivatives
  - Beta phenylethylamine derivatives: ephedrine, phenylephrine
- **Oral**
  - Pseudoephedrine, phenylephrine, phenylpropanolamine

**Side effects: central nervous system stimulation, hypertension, and palpitations**

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# Treatment

- **Rhinorrhea**
  - Blockade of cholinergic stimulation of glandular secretion

- Ipratropium
- First-generation antihistamines

- Second-generation or “nonsedating” antihistamines have had no effect on common cold symptoms in a limited number of studies

**Side effects: sedation and drying of the eyes, mouth, and nose**

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# Treatment

- **Sneezing** >> antihistamine
- **Sore Throat** >> acetaminophen, NSAIDS
- **Cough** (caused by nasal secretion or virus-induced reactive airway) >> anti histamines and bronchodilator
  - Codeine or dextromethorphan hydrobromide >> no benefit

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# Treatment

**TABLE 58-2 Effective Treatments for Symptoms of the Common Cold**

| SYMPTOM | TREATMENT |
|---|---|
| Nasal obstruction | Topical adrenergic agents, oral adrenergic agents |
| Rhinorrhea | First-generation antihistamines, ipratropium bromide |
| Sneezing | First-generation antihistamines |
| Sore throat | Acetaminophen, ibuprofen, and other NSAIDs |
| Cough | First-generation antihistamines; bronchodilators (?) |

NSAIDs, nonsteroidal anti-inflammatory drugs.

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# Pharyngitis

- Triad of ***sore throat, fever, and pharyngeal inflammation*** characterized by erythema and edema, although exudates, vesicles, or ulcerations may also be present

Anthony R. Flores. Mandell, Douglas, and Bennett's Principles and Practice of Infectious Diseases, 8th Edition, 2015

# Pharyngitis: Etiology

- ***Viruses*** are the single most common cause of pharyngitis
- ***What virus?***
- ***Some clinical clues***

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## TABLE 59-1 Microbial Causes of Acute Pharyngitis

| PATHOGEN | ASSOCIATED DISORDER(S) |
|---|---|
| **Viruses** | |
| Rhinovirus | Common cold |
| Coronavirus | Common cold |
| Adenovirus | Pharyngoconjunctival fever |
| Herpes simplex type 1 and 2 | Pharyngitis, gingivostomatitis |
| Parainfluenza | Cold, croup |
| Enteroviruses | Herpangina, hand-foot-mouth disease |
| Epstein-Barr virus | Infectious mononucleosis |
| Cytomegalovirus | CMV mononucleosis |
| Human immunodeficiency virus | Primary HIV infection |
| Influenza A and B | Influenza |
| Respiratory syncytial virus | Cold, bronchiolitis, pneumonia |
| Human metapneumovirus | Cold, bronchiolitis, pneumonia |

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# Pharyngitis: Etiology

- ***Bacteria***

- *Streptococcus pyogenes*, group A *Streptococcus* (GAS)
  - GAS and acute rheumatic fever (ARF)
  - GAS is responsible for ***approximately 10% to 15%*** of cases of pharyngitis ***in adults*** >> no association in non-group A streptococci

- *Fusobacterium necrophorum*, 10% of cases of pharyngitis
  - 23% of cases of peritonsillar abscess
- *Arcanobacterium haemolyticum <1%*
- *Corynebacterium diphtheriae*
- *Mycoplasma* and *Chlamydia*
- Syphilis, Gonococci

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## TABLE 59-1 Microbial Causes of Acute Pharyngitis

| PATHOGEN | ASSOCIATED DISORDER(S) |
|---|---|
| **Bacteria** | |
| *Streptococcus*, group A | Pharyngitis, tonsillitis, scarlet fever |
| *Streptococcus*, groups C and G | Pharyngitis, tonsillitis |
| Mixed anaerobes | Vincent's angina |
| *Fusobacterium necrophorum* | Pharyngitis, tonsillitis, Lemierre syndrome |
| *Neisseria gonorrhoeae* | Pharyngitis, tonsillitis |
| *Corynebacterium diphtheria* | Diphtheria |
| *Arcanobacterium haemolyticum* | Pharyngitis, scarlatiniform rash |
| *Yersinia pestis* | Plague |
| *Francisella tularensis* | Tularemia, oropharyngeal form |
| *Treponema pallidum* | Secondary syphilis |
| **Mycoplasma** | |
| *Mycoplasma pneumoniae* | Pneumonia, bronchitis, pharyngitis |
| **Chlamydia** | |
| *Chlamydia psittaci* | Acute respiratory disease, pneumonia |
| *Chlamydia pneumoniae* | Pneumonia, pharyngitis |

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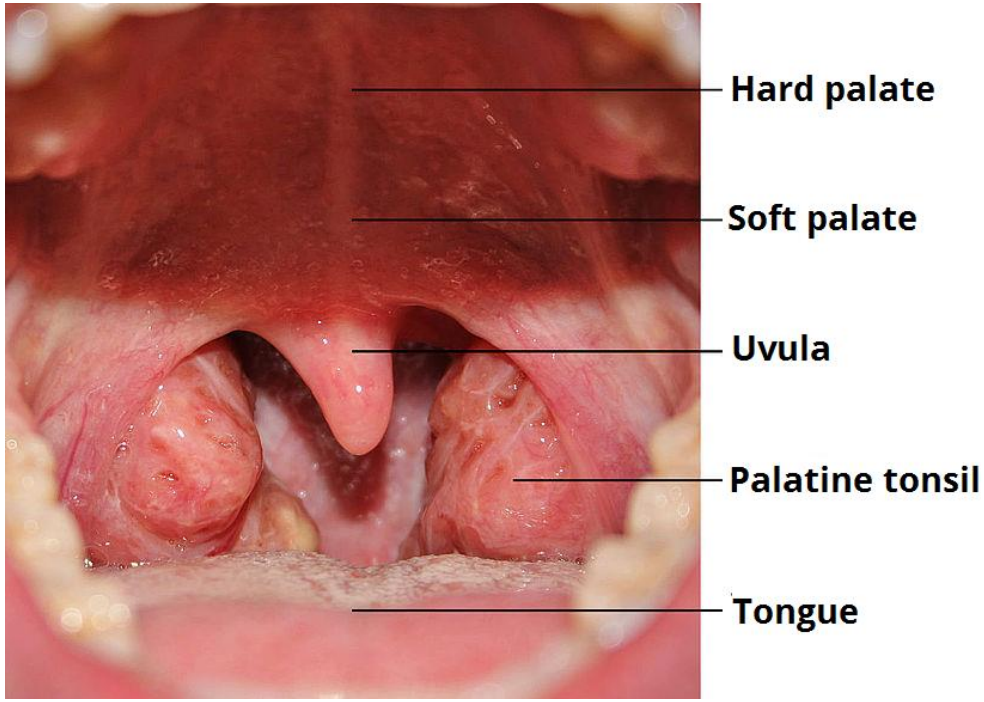
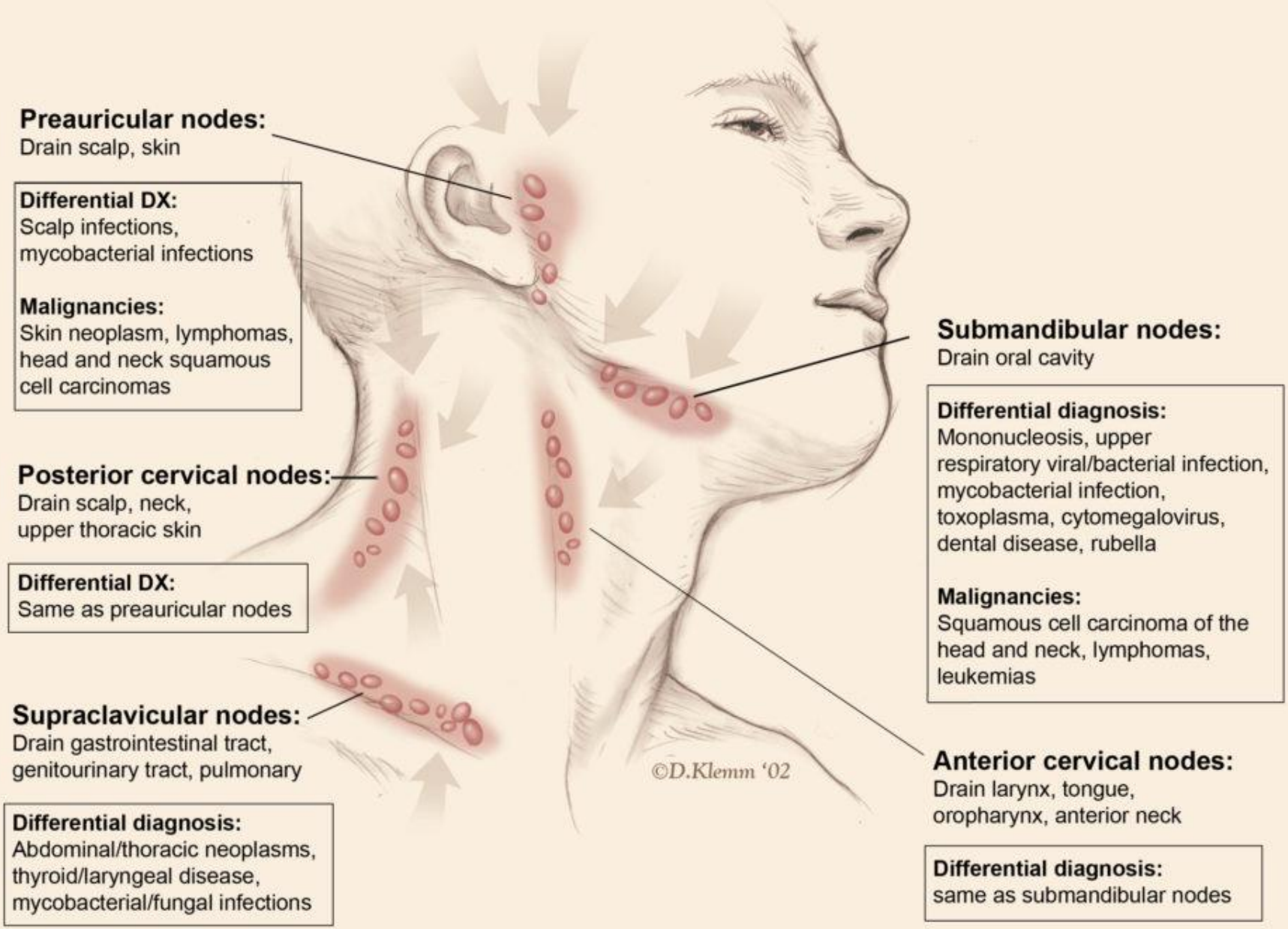
# Throat Examination




Preauricular nodes:
Drain scalp, skin
Differential DX:
Scalp infections, mycobacterial infections
Malignancies:
Skin neoplasm, lymphomas, head and neck squamous cell carcinomas
Posterior cervical nodes:
Drain scalp, neck, upper thoracic skin
Differential DX:
Same as preauricular nodes
Supraclavicular nodes:
Drain gastrointestinal tract, genitourinary tract, pulmonary
Differential diagnosis:
Abdominal/thoracic neoplasms, thyroid/laryngeal disease, mycobacterial/fungal infections
©D.Klemm '02
Submandibular nodes:
Drain oral cavity
Differential diagnosis:
Mononucleosis, upper respiratory viral/bacterial infection, mycobacterial infection, toxoplasma, cytomegalovirus, dental disease, rubella
Malignancies:
Squamous cell carcinoma of the head and neck, lymphomas, leukemias
Anterior cervical nodes:
Drain larynx, tongue, oropharynx, anterior neck
Differential diagnosis:
same as submandibular nodes

# Clinical Manifestations

- **Group A *Streptococcus***
- ***Sudden in onset, fever, headache***, and gastrointestinal symptoms (nausea, vomiting, abdominal pain)
- ***Pharyngeal erythema***, tonsillar enlargement, and a gray-white ***exudate*** covering the posterior pharynx and tonsillar pillars
- ***Petechiae*** are sometimes observed on the soft palate, with erythema and edema of the uvula
- Anterior cervical lymphadenopathy
- Scarlatiniform rash

Signs and symptoms most indicative of GAS pharyngitis are tonsillar or pharyngeal ***exudates***, tender anterior cervical ***nodes***, ***fever*** or history of fever, and ***absence of cough***

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# Clinical Manifestations

- ***Fusobacterium necrophorum***, 10% of cases of pharyngitis
  - 23% of cases of ***peritonsillar abscess >> severe complication***

- ***Arcanobacterium haemolyticum*** *<1%*
  - ***Rash is more common*** than GAS
- ***Corynebacterium diphtheriae***
  - Membrane on the tonsil or pharyngeal
  - ***White early*** in the course of the illness, becomes ***dark gray***, and ***leather-like***, with attempts to dislodge the membrane potentially ***causing bleeding***
  - Swelling of the neck
- ***Mycoplasma*** **and** ***Chlamydia***
  - Lower respiratory tract infection
- **Syphilis** >> chancre
- **Gonococci** >> mild symptom

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# Bull neck in diphtheria patient

# Clinical Manifestations

- **Epstein-Barr Virus >> Infectious Mononucleosis**
  - Fever, pharyngitis, and adenopathy
  - Other symptoms included cough, myalgia, arthralgia, and nausea
  - Rash was uncommon and is typically described as a diffuse maculopapular eruption in patients given ***ampicillin or related compounds***
  - Painful anterior and posterior ***cervical lymphadenopathy***
  - ***Hepatosplenomegaly***
  - Mild-to-moderate enlargement of the tonsils as well as ***exudates and palatal petechiae***

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# Clinical Manifestations

- **Human Immunodeficiency Virus >> acute HIV infection**
  - Occur in 40% to 90% of primary infection
  - 5 to 29 days after infection
  - Fever, rash, pharyngitis, fatigue, weight loss, myalgia, arthralgia, headache, night sweats, cervical adenopathy, nausea, vomiting, or diarrhea
  - Pharyngitis is recognized in 50% to 70% of patients, whereas cervical adenopathy is noted in 25% to 50%
  - Low incidence of exudate
  - Ulceration

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# Clinical Manifestations

- **Enterovirus**
  - Herpangina
  - Hand foot mouth syndrome


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# Clinical Manifestations

- **Adenovirus**
  - Pharyngoconjunctival fever is a specific syndrome caused by adenovirus infections, often occurring in outbreaks and associated with swimming or bathing

- **Herpes Simplex Virus**
  - Fever, pharyngeal erythema, exudates, and enlarged tender cervical adenopathy
  - Gingivostomatitis

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# Pharyngitis

- **Group A *Streptococcus is the most improtant pathogens***
- ***10 to 15% in adults***

Signs and symptoms most indicative of GAS pharyngitis are tonsillar or pharyngeal ***exudates***, tender anterior cervical ***nodes***, ***fever*** or history of fever, and ***absence of cough***

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# White patch on tonsils ?

## viral

**Infectious mononucleosis**
(90% EBV, 10% CMV and others)

enlarged red tonsils, thick WHITE coating
Check : LN, LoSo, lymphophytes

## bacterial

Patch may extend beyond tonsils/pharyngeal wall, stick tightly to base

Easily removable patch

### GAS


may be part of **Scarlet fever**
Check : white → red strawberry tongue, sandpaper-like exanthem, Pastia's line

### Diphtheria


Mortality 10-30%

Comp. : myocarditis, polyneuritis, renal tubular necrosis, etc.

**If UAO →**
emer. trach
DO NOT intubate

GREY patch necrosis ≠ pus

To detect the bacteria → scrape at erythematous rim NOT the plaque

* DO NOT try to remove the plaque, bleeding lead to toxin entering bloodstream

### Vincent's angina


Check : gingivitis, immunocompromised

&

Other bacteria

One Slide ID

## TABLE 59-4 Antimicrobial Therapy for Group A Streptococcal Pharyngitis

| DRUG | DOSE | DURATION |
|---|---|---|
| **Oral Regimens** | | |
| Penicillin V | Children: 250 mg bid or tid<br>Adolescents and adults: 250 mg tid or qid or 500 mg bid | 10 days |
| Amoxicillin | 50 mg/kg once daily (maximum 1000 mg) Alternative: 25 mg/kg bid (maximum 500 mg) | 10 days |
| **For Penicillin-Allergic Patients** | | |
| Erythromycin | Varies with formulation | 10 days |
| First-generation cephalosporins | Varies with agent | 10 days |
| **Intramuscular Regimens** | | |
| Benzathine penicillin G | 600,000 units for patients <27 kg | 1 dose |
| | 1.2 million units for patients ≥27 kg | 1 dose |
| Mixtures of benzathine and procaine penicillin G | Varies with formulation | 1 dose |

*Modified from Alcaide ML, Bisno AL. Pharyngitis and epiglottitis.* Infect Dis Clin North Am. *2007;21:449-469, vii; with permission.*

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# Sinusitis

- Most cases of acute bacterial sinusitis are secondary to viral upper respiratory infection (URI) or allergic inflammation

- The first pattern is that of **persistent symptoms** characterized by nasal discharge and/or cough that last more than 10 days without improvement

  – Lack of improvement that is a sign of an acute bacterial process. Accompanying symptoms may include periorbital edema, malodorous breath, or low-grade fever.

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# Sinusitis

- The second presentation is characterized by the onset of severe symptoms. Fever will accompany purulent nasal discharge that is present over a 3- to 4-day period

- The third presentation; “double sickening”

- Pain, tenderness, swelling and pressure around your eyes, cheeks, nose or forehead that worsens when bending over

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www.mayoclinic.org

# Clinical Diagnosis

- (1) onset with **persistent** symptoms or signs, lasting at least 10 days without evidence of clinical improvement

- (2) onset with ***severe symptoms*** or signs of ***high fever (≥39° C)*** and purulent nasal discharge lasting for 3 to 4 consecutive days

- (3) onset with worsening symptoms or signs characterized by the new development of fever, headache, or increased nasal discharge after a typical viral URI that lasted 5 to 6 days with initial improvement ***("double sickening")***

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# Sinusitis: Pathogens

**TABLE 63-3 Bacterial Etiology of Acute Sinusitis**

| | ADULTS ( *N* = 339) | | CHILDREN (*N* = 30) | |
|---|---|---|---|---|
| **ORGANISM** | **No. of Isolates** | **% of Isolates** | **No. of Isolates** | **% of Isolates** |
| *Streptococcus pneumoniae* | 92 | 41 | 17 | 41 |
| *Haemophilus influenzae* | 79 | 35 | 11 | 27 |
| Anaerobes | 16 | 7 | | |
| Streptococcal species | 16 | 7 | 3 | 7 |
| *Moraxella catarrhalis* | 8 | 4 | 9 | 22 |
| *Staphylococcus aureus* | 7 | 3 | | |
| Other | 8 | 4 | 1 | 2 |

*From references 11, 29, and 30-34.*

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# Invasive fungal sinusitis

- Serious underlying diseases, such as diabetes mellitus, malignancy and associated neutropenia, or those using high-dose corticosteroids

**TABLE 63-4 Types of Fungal Sinus Disease**

| | INVASIVE |
|---|---|
| Underlying Condition | Immunocompromise<br>Diabetes |
| Histopathology | Mucosal hyphal invasion |
| Etiologic Agents | *Mucor, Rhizopus, Fusarium, Pseudallescheria boydii, Alternaria, Bipolaris, Cladophialophora, Curvularia* |
| Therapy | Surgery<br>Systemic antifungal |

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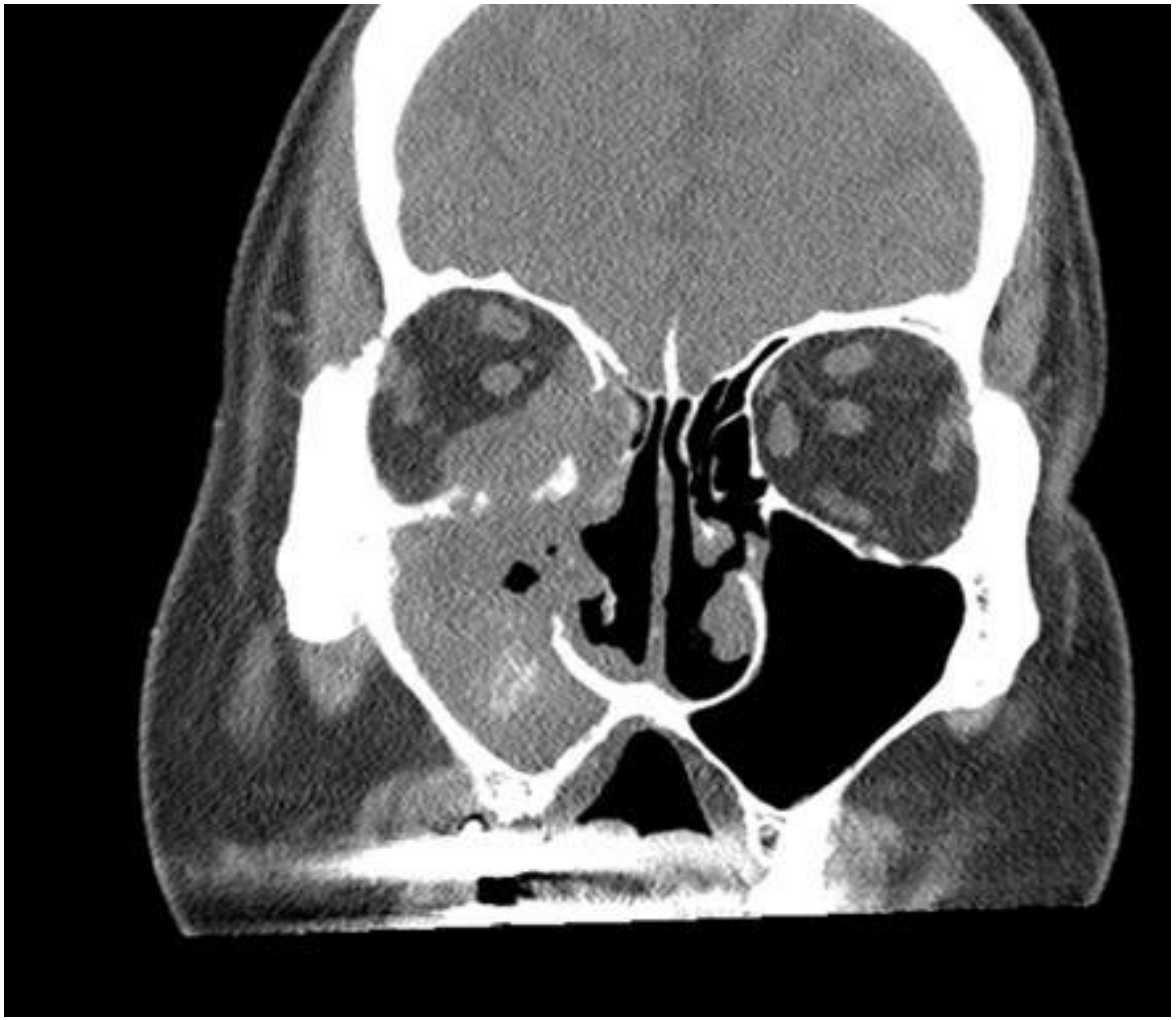
# Invasive Fungal Sinusitis



# Sinusitis: Treatment

- High rate of spontaneous improvement within 2 weeks of presentation
- Overall, antimicrobial agents reduce the rate of clinical failure 25% to 30% within 7 to 14 days of initiating therapy
- Some guidelines give an option to observe signs and symptoms before starting treatment

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# Sinusitis: Treatment

**TABLE 63-9 Oral Antimicrobial Agents for Acute Bacterial Sinusitis**

| ANTIMICROBIAL | ADULT DOSAGE | PEDIATRIC DOSAGE |
|---|---|---|
| Amoxicillin | 500-875 mg q12h | 40-80 mg/kg/day divided q12h |
| Amoxicillin/clavulanate* | 875 or 2000 mg q12h | 40-80 mg/kg/day divided q12h |
| Cefpodoxime proxetil | 200 mg q12h | 10 mg/kg/day divided q12h |
| Cefixime† | 400 mg q12-24h | 8 mg/kg/day divided q12-24h |
| Cefdinir | 300 mg q12h or 600 mg q24h | 14 mg/kg/day divided 12-24h |
| Cefprozil | 250-500 mg q12h | 15-30 mg/kg/day divided q12h |
| Levofloxacin | 500 mg daily | 16 mg/kg/day divided q12h† |
| Moxifloxacin | 400 mg daily | 400 mg daily for adolescents† |

*Dosages specify amoxicillin component.
†Not U.S. Food and Drug Administration–approved for this indication.

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# Acute Bronchitis

- Dry or productive cough of less than 3 weeks' duration
- Acute bronchitis begins with signs and symptoms typical of the common cold syndrome
- Followed shortly by the onset of cough, which becomes the dominant sign in acute bronchitis

Edward E. Walsh. Mandell, Douglas, and Bennett's Principles and Practice of Infectious Diseases, 8th Edition, 2015

# Acute Bronchitis: Microbiology

**TABLE 66-1 Viral and Bacterial Causes of Acute Bronchitis**

| PATHOGEN | SEASONALITY | COMMENTS |
|---|---|---|
| Influenza viruses | Winter | Local epidemics last 6-8 wk during which clinical illness of cough and fever has high predictive value; laboratory diagnosis readily available; early neuraminidase inhibitor therapy effective |
| Rhinoviruses | Fall and spring | Most frequent cause of common cold syndrome; immunity is serotype specific |
| Coronaviruses | Winter to spring | Causes common cold syndrome; newer strains are difficult to culture and require RT-PCR for diagnosis |
| Adenoviruses | Year-round, winter epidemics | High attack rates in closed populations such as persons living in military barracks or college dormitories; serotype-specific immunity |
| Respiratory syncytial virus (RSV) | Late fall to early spring | Attack rates approach 75% in neonates, 3%-5% in adults; associated with wheezing in all age groups; rapid antigen test accurate in children but requires culture or RT-PCR to diagnose in adults |
| Human metapneumovirus (hMPV) | Winter to early spring | Associated with wheezing in adults and in infants; difficult to isolate in tissue culture and often requires RT-PCR |
| Human metapneumovirus (hMPV) | Winter to early spring | Associated with wheezing in adults and in infants; difficult to isolate in tissue culture and often requires RT-PCR |
| Parainfluenza viruses | Fall to winter | Similar to RSV and hMPV, parainfluenza viruses primarily pediatric pathogens but can cause severe acute disease in some adults |
| Measles virus | Year-round | Can cause respiratory disease in malnourished children; illness causes transient immune suppression |
| *Mycoplasma pneumoniae* | Year-round, fall outbreaks | Long incubation period (10-21 days) results in staggered epidemic pattern in families; nonproductive persistent cough typical; diagnosed by IgM serology; treated with macrolide, quinolone, or tetracycline antibiotics |
| *Chlamydia pneumoniae* | Year-round | Associated with sinusitis; diagnosis by RT-PCR not readily available |
| *Bordetella pertussis* | Year-round | Severe illness in nonimmunized children; illness milder in partially immune adults can be associated with prolonged cough; adults often reservoir for epidemics; early therapy with antibiotics can reduce spread |

RT-PCR, reverse-transcriptase polymerase chain reaction.

# Acute Bronchitis: Treatment

- Narcotic cough suppressants, expectorants, antihistamines, decongestants, and $\beta_2$-agonists

- Not clear benefits

- Infectious Diseases Society of America, ***do not recommend the routine use of antibiotics*** for uncomplicated acute bronchitis in otherwise normal persons.

# URI

- Common cold: nasal discharge
- Pharyngitis: sore throat
- Sinusitis: complicated nasal discharge
- Bronchitis: cough
- Clinical spectrum
- Few cases need antibiotic

# Headache

- Primary headache
  - Patients with a history of headache who ***do not have red flag signs*** and symptoms are at low risk of serious headache
  - Migraine, Tension-type, Cluster, Other (e.g., cold stimulus headache)

- Secondary headache
  - Headache attributed to any of the following: head or neck trauma, cranial or cervical vascular disorder, nonvascular intracranial disorder, substance use or withdrawal, infection, disturbance of homeostasis, psychiatric disorder
  - Headache or facial pain attributed to ***disorder of the cranium***, neck, eyes, ears, nose, sinuses, teeth, mouth, or other facial or cranial structures

# TENSION-TYPE HEADACHE

- Bilateral mild to moderate pressure without other associated symptoms

**Table 2. ICHD-2 Diagnostic Criteria for Episodic Tension-Type Headache**

**Infrequent**

At least 10 episodes occurring fewer than one day per month on average (fewer than 12 days per year) and fulfilling the following criteria:

- Headache lasts 30 minutes to seven days
- Headache has at least two of the following features: bilateral location, pressing or tightening (nonpulsating) quality, mild or moderate intensity, not aggravated by routine physical activity such as walking or climbing stairs
- Both of the following: no nausea or vomiting (anorexia may occur), either photophobia or phonophobia

Headache is not attributed to another disorder

**Frequent**

At least 10 episodes occurring on more than one but fewer than 15 days per month for at least three months and fulfilling all of the criteria for infrequent episodic tension-type headache

*ICHD-2 = International Classification of Headache Disorders, 2nd ed.*

*Adapted with permission from the American Academy of Neurology: Lipton RB, Bigal ME, Steiner TJ, et al. Classification of primary headaches.* Neurology. *2004;63(3):431. Table 4. ICHD-2 criteria for episodic tension-type headache (TTH). http://www.neurology.org/content/63/3/427.abstract.*

www.aafp.org

# Migraine Headache

- Nausea, photophobia (sensitivity to light), and phonophobia (sensitivity to sound)
- Physical activity often exacerbates migraine headache
- Pulsatile quality, duration of four to 72 hours, unilateral location, nausea or vomiting, and disabling intensity
- Aura may be present in some cases of migraine

# Migraine without Aura

**Table 4. ICHD-2 Diagnostic Criteria for Migraine Without Aura**

At least five episodes fulfilling the following criteria:

- Headache episodes lasting four to 72 hours (untreated or unsuccessfully treated)
- Headache has at least two of the following characteristics: unilateral location, pulsating quality, moderate or severe pain intensity, aggravated by (or causes avoidance of) routine physical activity such as walking or climbing stairs
- During the headache, the patient experiences at least one of the following: nausea or vomiting; and photophobia and phonophobia

Headache is not attributed to another disorder

www.aafp.org

# Migraine with Typical Aura

**Table 3. ICHD-2 Diagnostic Criteria for Migraine with Typical Aura**

| |
|---|
| At least two episodes fulfilling the following criteria: |
| Aura consisting of at least one of the following, but no motor weakness: fully reversible visual symptoms including positive features (e.g., flickering lights, spots or lines) and/or negative features (i.e., loss of vision); fully reversible sensory symptoms including positive features (i.e., pins and needles) and/or negative features (i.e., numbness); fully reversible dysphasic speech disturbance |
| At least two of the following: homonymous visual symptoms and/or unilateral symptoms; at least one aura symptom develops gradually over five or more minutes and/or different aura symptoms occur in succession over five or more minutes; each symptom lasts at least five minutes, but no longer than 60 minutes |
| A headache that fulfills the criteria for migraine without aura (Table 4), and begins during the aura or follows the aura within 60 minutes |
| Headache not attributed to another disorder |

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# Case

- A 47-year-old HIV-infected woman was on TDF, 3TC and SQV/r
- She presented with necrosis of the left foot and generalized peripheral cyanosis
- She having had severe headache and a pharmacist at her local drugstore advised her to take ***ergotamine*** for the relief of her migraine

Figure 1. Peripheral ischemia of the left forefoot

Avihingsanon A. et al. Top Antivir Med. 2014

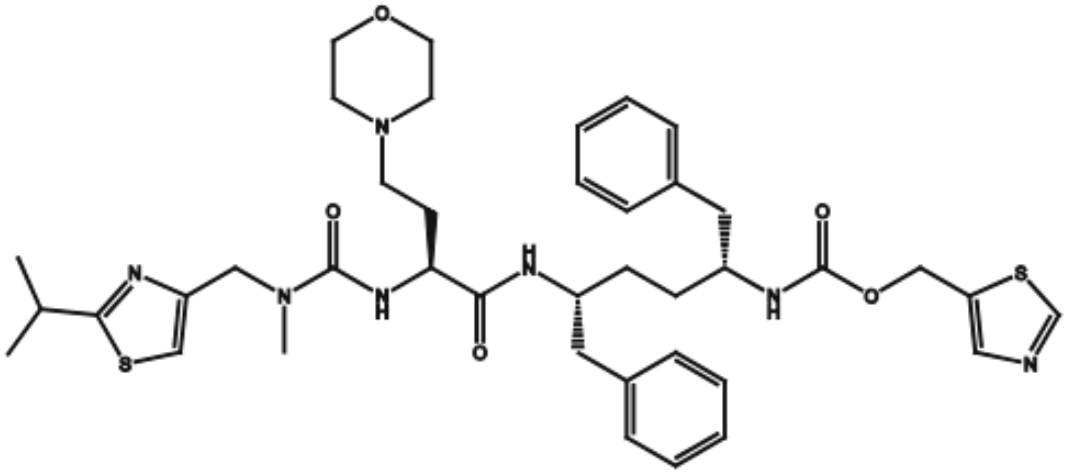
# Ergotism and Antiretrovirals

- Ergotamine, typically used to treat migraine, has less than 5% bioavailability due to extensive first-pass metabolism by cytochrome ***P450 3A4 (CYP3A4)***
- Concurrent intake of ergotamine and strong CYP3A4 inhibitors, such as the HIV protease inhibitors (PIs), can lead to clinical ergotism
- Peripheral vasoconstriction
- Pain, cyanosis, gangrene

Avihingsanon A. et al. Top Antivir Med. 2014

# Cobicistat

- Selective, mechanism-based inhibitor of CYP3A enzymes
- Not active against HIV



Emma D. Deeks. Drug, 2014

# Ergotism and Antiretrovirals

- Use of ***cobicistat, a CYP3A inhibitor*** prescribed as an alternative boosting agent to ritonavir, is contraindicated in patients taking ergot alkaloids

Avihingsanon A. et al. Top Antivir Med. 2014

# CLUSTER HEADACHES

- Brief (15 to 180 minutes) episodes of severe head pain with associated autonomic symptoms
- Most commonly describe the pain as sharp, but some report that it can also be pulsating and pressure-like
- Can occur on both sides of the head, most patients report unilateral pain
- Retro-orbital area, followed by the temporal region, upper teeth, jaw, cheek, lower teeth, and neck
- Ipsilateral autonomic symptoms such as eyelid edema, nasal congestion, lacrimation, or forehead sweating

# CLUSTER HEADACHES

At least five episodes fulfilling the following criteria:

- Severe or very severe unilateral orbital, supraorbital, or temporal pain lasting 15 to 180 minutes if untreated
- Headache is accompanied by at least one of the following ipsilateral autonomic symptoms: conjunctival injection or lacrimation, nasal congestion or rhinorrhea, eyelid edema, forehead and facial sweating, miosis or ptosis, restlessness or agitation
- Headache episodes occur from one every other day to eight per day

Not attributable to another disorder

**Episodic cluster headache**

Fulfills all of the above criteria

At least two cluster periods lasting seven to 365 days and separated by pain-free remissions of more than one month

**Chronic cluster headache**

Fulfills all of the above criteria

Episodes recur for more than one year without remission periods or with remission periods lasting less than one month

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| *Danger sign or symptom* | *Possible diagnoses* |
|---|---|
| First or worst headache of the patient's life | Central nervous system infection, intracranial hemorrhage |
| Focal neurologic signs (not typical aura) | Arteriovenous malformation, collagen vascular disease, intracranial mass lesion |
| Headache triggered by cough or exertion, or while engaged in sexual intercourse | Mass lesion, subarachnoid hemorrhage |
| Headache with change in personality, mental status, level of consciousness | Central nervous system infection, intracerebral bleed, mass lesion |
| Neck stiffness or meningismus | Meningitis |
| New onset of severe headache in pregnancy or postpartum | Cortical vein/cranial sinus thrombosis, carotid artery dissection, pituitary apoplexy |
| Older than 50 years | Mass lesion, temporal arteritis |
| Papilledema | Encephalitis, mass lesion, meningitis, pseudotumor |
| Rapid onset with strenuous exercise | Carotid artery dissection, intracranial bleed |
| Sudden onset (maximal intensity occurs within seconds to minutes, thunderclap headache) | Bleeding into a mass or arteriovenous malformation, mass lesion (especially posterior fossa), subarachnoid hemorrhage |
| Systemic illness with headache (fever, rash) | Arteritis, collagen vascular disease, encephalitis, meningitis |
| Tenderness over temporal artery | Polymyalgia rheumatica, temporal arteritis |
| Worsening pattern | History of medication overuse, mass lesion, subdural hematoma |
| New headache type in a patient with: | |
| Cancer | Metastasis |
| Human immunodeficiency virus infection | Opportunistic infection, tumor |
| Lyme disease | Meningoencephalitis |

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# Headache

- Primary or Secondary
- Beware of Red Flag Signs
- Consult doctor

# Abdominal pain

- Visceral pain: internal organ, dull aching, difficult to localized
  - Epigastrium >> foregut: stomach, duodenum, liver, pancreas, biliary
  - Periumbilicus >> midgut: jejunum, appendix, cecum, ascending colon
  - Hypogastrium >> hindgut: transverse colon to rectum

- Somatic pain: abdominal wall or peritoneum, sudden, severe, localized

CONDITIONS ASSOCIATED WITH

# ABDOMINAL PAIN

| RIGHT | CENTER | LEFT |
| --- | --- | --- |
| Gallstones<br>Cholecystitis<br>Stomach Ulcer<br>Duodenal Ulcer<br>Hepatitis | Heartburn/ Indigestion<br>Hiatal Hernia<br>Epigastric Hernia<br>Stomach Ulcer<br>Duodenal Ulcer<br>Hepatitis | Functional Dyspepsia<br>Gastritis<br>Stomach Ulcer<br>Pancreatitis |
| Kidney Stones<br>Kidney Infection<br>Inflammatory Bowel Disease<br>Constipation | Umbilical Hernia<br>Early Appendicitis<br>Stomach Ulcer<br>Inflammatory Bowel Disease<br>Pancreatitis | Kidney Stones<br>Kidney Infection<br>Inflammatory Bowel Disease<br>Constipation |
| Appendicitis<br>Inflammatory Bowel Disease<br>Constipation<br>Pelvic Pain (Gyne) | Bladder Infection<br>Prostatitis<br>Diverticulitis<br>Inflammatory Bowel Disease<br>Inguinal Hernia (Groin Pain)<br>Pelvic Pain (Gyne) | Constipation<br>Irritable Bowel Syndrome<br>Inflammatory Bowel Disease<br>Pelvic Pain (Gyne)<br>Inguinal Hernia (Groin Pain) |

# Abdominal pain

- Duration, onset and severity
  - Acute and severe >> acute abdomen:
  - Acute appendicitis, cholecystitis, gut obstruction, pancreatitis, ureteric stone, peptic perforation, diverticulitis, complication of pregnancy, Gynae condition

- Consult doctor

# Dyspepsia

- Epigastric discomfort
- Lasting at least 1 month
- Can be associated with any other ***upper gastro intestinal symptom*** such as epigastric fullness, nausea, vomiting, or heartburn, provided epigastric pain is the patient's primary concern.

The American Journal of GASTROENTEROLOGY, 2017

# Dyspepsia: DDx

- ***Functional dyspepsia***
- Presence of at least one of the following:
- Bothersome postprandial fullness
- Early satiation
- Epigastric pain
- Epigastric burning and

- No evidence of structural disease (including at upper endoscopy) that is likely to explain the symptoms

**Table 2. Differential Diagnosis of Dyspepsia**

| *Diagnostic category* | *Approximate prevalence** |
|---|---|
| Functional (nonulcer) dyspepsia | Up to 70 percent |
| Peptic ulcer disease | 15 to 25 percent |
| Reflux esophagitis | 5 to 15 percent |
| Gastric or esophageal cancer | < 2 percent |
| Abdominal cancer, especially pancreatic cancer | Rare |
| Biliary tract disease | Rare |
| Carbohydrate malabsorption (lactose, sorbitol, fructose, mannitol) | Rare |
| Gastroparesis | Rare |
| Hepatoma | Rare |
| Infiltrative diseases of the stomach (Crohn disease, sarcoidosis) | Rare |
| Intestinal parasites (*Giardia* species, *Strongyloides* species) | Rare |
| Ischemic bowel disease | Rare |
| Medication effects (Table 3) | Rare |
| Metabolic disturbances (hypercalcemia, hyperkalemia) | Rare |
| Pancreatitis | Rare |
| Systemic disorders (diabetes mellitus, thyroid and parathyroid disorders, connective tissue disease) | Rare |

*—*Based on the occurrence of the disorders in patients with dyspepsia who are evaluated with endoscopy.*

*Information from references 15 through 18.*

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# Dyspepsia: DDx

| TABLE 2. Alarm features for dyspeptic patients |
| --- |
| Age ≥50 years |
| Family history of upper GI malignancy in a first-degree relative |
| Unintended weight loss |
| GI bleeding or iron deficiency anemia |
| Dysphagia |
| Odynophagia |
| Persistent vomiting |
| Abnormal imaging suggesting organic disease |

The American Journal of GASTROENTEROLOGY, 2017

# Dyspepsia: DDx

**Table 3. Agents Commonly Associated with Dyspepsia**

| | |
|---|---|
| Acarbose (Precose) | Metformin (Glucophage) |
| Alcohol | Miglitol (Glyset) |
| Antibiotics, oral (e.g., erythromycin) | Nonsteroidal anti-inflammatory drugs, including cyclooxygenase-2 inhibitors |
| Bisphosphonates | Opiates |
| Corticosteroids (e.g., prednisone) | Orlistat (Xenical) |
| Herbs (e.g., garlic, ginkgo, saw palmetto, feverfew, chaste tree berry, white willow) | Potassium chloride |
| Iron | Theophylline |

*Adapted from Dickerson LM, King DE. Evaluation and management of nonulcer dyspepsia.* Am Fam Physician. *2004;70(1):109.*

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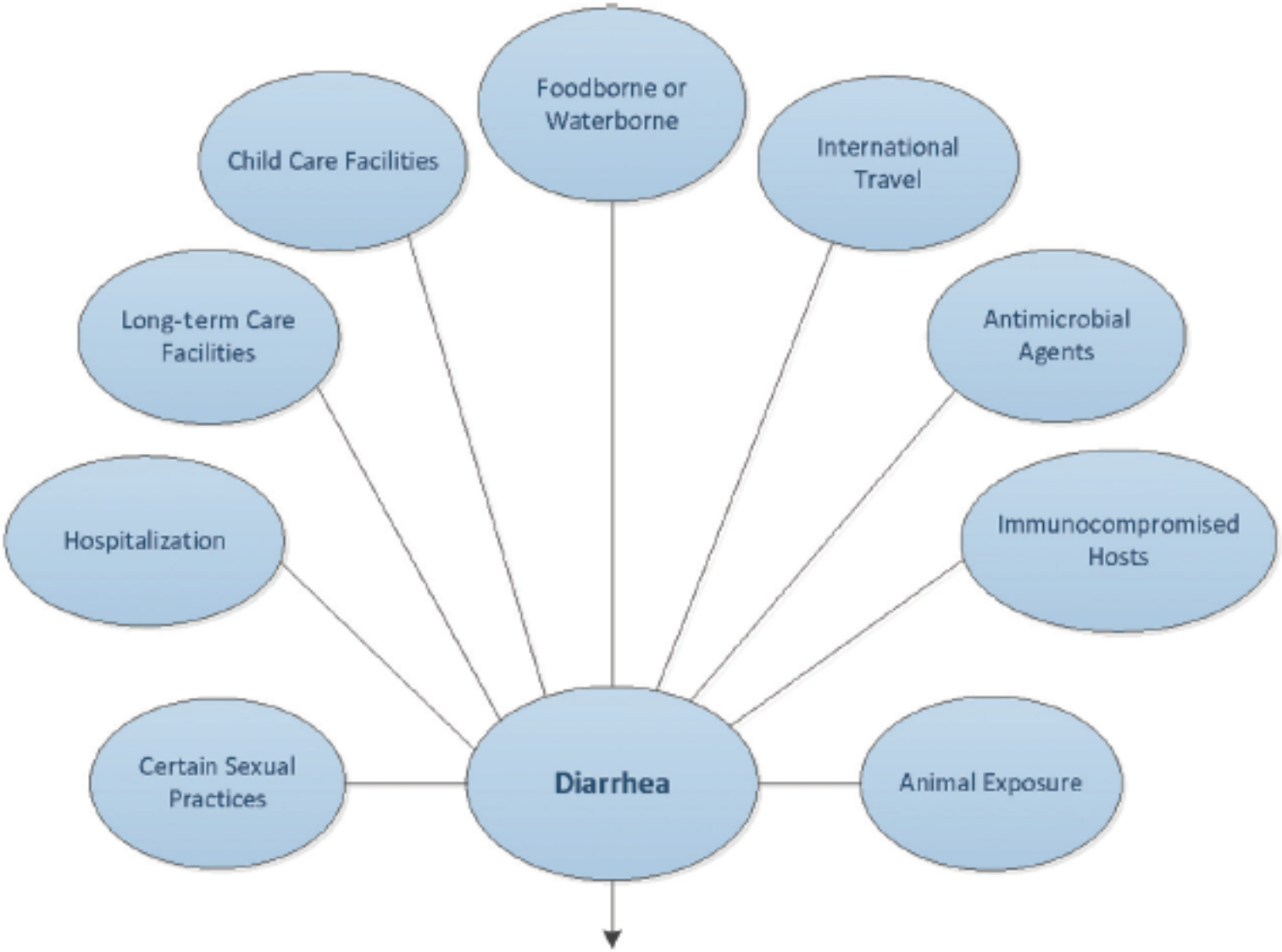


Clinical Manifestations

- Acute Diarrhea (0 through 13 days)
- Persistent diarrhea (14 through 29 days)
- Chronic Diarrhea (≥30 days)

IDSA, 2017

# Acute Mucus Bloody Stool

- CMV
- *Shigella*
- *Salmonella*
- *Vibrio parahaemolyticus*
- *Plesiomonas*
- *Yersinia enterocolitica*
- EHEC
- EIEC
- *C. difficile*
- *Campylobacter*
- *Entamoeba histolytica*
- *Balantidium coli*

***Need W/U***

# Clinical Clues

**Table 3. Clinical Presentations Suggestive of Infectious Diarrhea Etiologies**

| Finding | Likely Pathogens |
|---|---|
| Persistent or chronic diarrhea | *Cryptosporidium* spp, *Giardia lamblia*, *Cyclospora cayetanensis*, *Cystoisospora belli*, and *Entamoeba histolytica* |
| Visible blood in stool | STEC, *Shigella*, *Salmonella*, *Campylobacter*, *Entamoeba histolytica*, noncholera *Vibrio* species, *Yersinia*, *Balantidium coli*, *Plesiomonas* |
| Fever | Not highly discriminatory—viral, bacterial, and parasitic infections can cause fever. In general, higher temperatures are suggestive of bacterial etiology or *E. histolytica*. Patients infected with STEC usually are not febrile at time of presentation |
| Abdominal pain | STEC, *Salmonella*, *Shigella*, *Campylobacter*, *Yersinia*, noncholera *Vibrio* species, *Clostridium difficile* |
| Severe abdominal pain, often grossly bloody stools (occasionally nonbloody), and minimal or no fever | STEC, *Salmonella*, *Shigella*, *Campylobacter*, and *Yersinia enterocolitica* |
| Persistent abdominal pain and fever | *Y. enterocolitica and Y. pseudotuberculosis*; may mimic appendicitis |
| Nausea and vomiting lasting ≤24 hours | Ingestion of *Staphylococcus aureus* enterotoxin or *Bacillus cereus* (short-incubation emetic syndrome) |
| Diarrhea and abdominal cramping lasting 1–2 days | Ingestion of *Clostridium perfringens* or *B. cereus* (long-incubation emetic syndrome) |
| Vomiting and nonbloody diarrhea lasting 2–3 days or less | Norovirus (low-grade fever usually present during the first 24 hours in 40% if infections) |
| Chronic watery diarrhea, often lasting a year or more | Brainerd diarrhea (etiologic agent has not been identified); postinfectious irritable bowel syndrome |

Abbreviation: STEC, Shiga toxin–producing *Escherichia coli*.

# Hx of Exposure

**Table 2. Exposure or Condition Associated With Pathogens Causing Diarrhea**

| Exposure or Condition | Pathogen(s) |
|---|---|
| Foodborne | |
| Foodborne outbreaks in hotels, cruise ships, resorts, restaurants, catered events | Norovirus, nontyphoidal *Salmonella*, *Clostridium perfringens*, *Bacillus cereus*, *Staphylococcus aureus*, *Campylobacter* spp, ETEC, STEC, *Listeria*, *Shigella*, *Cyclospora cayetanensis*, *Cryptosporidium* spp |
| Consumption of unpasteurized milk or dairy products | *Salmonella*, *Campylobacter*, *Yersinia enterocolitica*, *S. aureus* toxin, *Cryptosporidium*, and STEC. *Listeria* is infrequently associated with diarrhea, *Brucella* (goat milk cheese), *Mycobacterium bovis*, *Coxiella burnetii* |
| Consumption of raw or undercooked meat or poultry | STEC (beef), *C. perfringens* (beef, poultry), *Salmonella* (poultry), *Campylobacter* (poultry), *Yersinia* (pork, chitterlings), *S. aureus* (poultry), and *Trichinella* spp (pork, wild game meat) |
| Consumption of fruits or unpasteurized fruit juices, vegetables, leafy greens, and sprouts | STEC, nontyphoidal *Salmonella*, *Cyclospora*, *Cryptosporidium*, norovirus, hepatitis A, and *Listeria monocytogenes* |
| Consumption of undercooked eggs | *Salmonella*, *Shigella* (egg salad) |
| Consumption of raw shellfish | *Vibrio* species, norovirus, hepatitis A, *Plesiomonas* |

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# Hx of Exposure

| Exposure or contact | |
|---|---|
| Swimming in or drinking untreated fresh water | *Campylobacter*, *Cryptosporidium*, *Giardia*, *Shigella*, *Salmonella*, STEC, *Plesiomonas shigelloides* |
| Swimming in recreational water facility with treated water | *Cryptosporidium* and other potentially waterborne pathogens when disinfectant concentrations are inadequately maintained |
| Healthcare, long-term care, prison exposure, or employment | Norovirus, *Clostridium difficile*, *Shigella*, *Cryptosporidium*, *Giardia*, STEC, rotavirus |
| Child care center attendance or employment | Rotavirus, *Cryptosporidium*, *Giardia*, *Shigella*, STEC |
| Recent antimicrobial therapy | *C. difficile*, multidrug-resistant *Salmonella* |
| Travel to resource-challenged countries | *Escherichia coli* (enteroaggregative, enterotoxigenic, enteroinvasive), *Shigella*, Typhi and nontyphoidal *Salmonella*, *Campylobacter*, *Vibrio cholerae*, *Entamoeba histolytica*, *Giardia*, *Blastocystis*, *Cyclospora*, *Cystoisospora*, *Cryptosporidium* |
| Exposure to house pets with diarrhea | *Campylobacter*, *Yersinia* |
| Exposure to pig feces in certain parts of the world | *Balantidium coli* |
| Contact with young poultry or reptiles | Nontyphoidal *Salmonella* |
| Visiting a farm or petting zoo | STEC, *Cryptosporidium*, *Campylobacter* |

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# Patient Evaluation

- People of all ages with acute diarrhea should be ***evaluated for dehydration***, which increases the risk of life-threatening illness and death, especially among the young and older adults
- Hx of voluminous diarrhea
- Tachycardia
- Hypotension
- Sunken eye ball
- Poor skin turgor

- Adequate Volume Replacemer


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# Infectious Diarrhea Tx

- **In immunocompetent children and adults, *empiric antimicrobial therapy for bloody diarrhea* while waiting for results of investigations is not recommended (strong, low), except for the following**
  - a. Infants <3 months of age with suspicion of a bacterial etiology.
  - b. Ill immunocompetent people with fever documented in a medical setting, abdominal pain, bloody diarrhea, and bacillary dysentery (frequent scant bloody stools, fever, abdominal cramps, tenesmus) presumptively due to *Shigella*.
  - c. People who have recently travelled internationally with body temperatures ≥38.5°C and/or signs of sepsis (weak, low)

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# Infectious Diarrhea Tx

- Fluoroquinolone such as ciprofloxacin, or azithromycin, depending on the local susceptibility patterns and travel history

- Children: third-generation cephalosporin for infants <3 months of age and others with neurologic involvement, or azithromycin, depending on local susceptibility patterns and travel history

- Antimicrobial therapy for people with infections attributed to STEC O157 and other STEC that produce Shiga toxin 2 (or if the toxin genotype is unknown) should be avoided

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## Table 6. Recommended Antimicrobial Agents by Pathogen

| Indication | First Choice |
|---|---|
| Bacteria[a] | |
| *Campylobacter* | Azithromycin |
| *Clostridium difficile* | Oral vancomycin |
| Nontyphoidal *Salmonella enterica*[b] | Usually not indicated for uncomplicated infection |
| *Salmonella enterica* Typhi or Paratyphi[b] | Ceftriaxone or ciprofloxacin |
| *Shigella*[a] | Azithromycin[c] or ciprofloxacin[a], or ceftriaxone |
| *Vibrio cholerae* | Doxycycline[d] |
| Non–*Vibrio cholerae*[d] | Usually not indicated for noninvasive disease. Single-agent therapy for noninvasive disease if treated. Invasive disease: ceftriaxone plus doxycycline |
| *Yersinia enterocolitica* | TMP-SMX |

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## Table 6. Recommended Antimicrobial Agents by Pathogen

| Indication | First Choice |
|---|---|
| Parasites | |
| *Cryptosporidium* spp | Nitazoxanide (HIV-uninfected, HIV-infected in combination with effective cART): |
| *Cyclospora cayetanensis* | TMP-SMX |
| *Giardia lamblia* | • Tinidazole<br>Note: Based on data from HIV-uninfected children<br>• Nitazoxanide |
| *Cystoisospora belli* | TMP-SMX |
| *Trichinella* spp | Albendazole |
| Fungus | |
| Microsporidia | For disseminated (not ocular) and intestinal infection attributed to microsporidia other than *Enterocytozoon bieneusi* or *Vittaforma corneae*:<br>• Albendazole after initiation of cART and resolution of signs and symptoms<br>For *E. bieneusi* or *V. corneae* infections:<br>• Fumagillin recommended for treatment of infections due to *E. bieneusi* in HIV-infected adults |

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# Watery Diarrhea

- In most people with acute watery diarrhea and without recent international travel, empiric antimicrobial therapy is not recommended
  - Except; infant, immunocompromised, ill-appearing

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# Supportive Tx

- Antimotility, antinausea, or antiemetic agents can be considered once the patient is adequately hydrated

- Antimotility drugs (eg, loperamide) should not be given to children

IDSA, 2017

# Acute Diarrhea

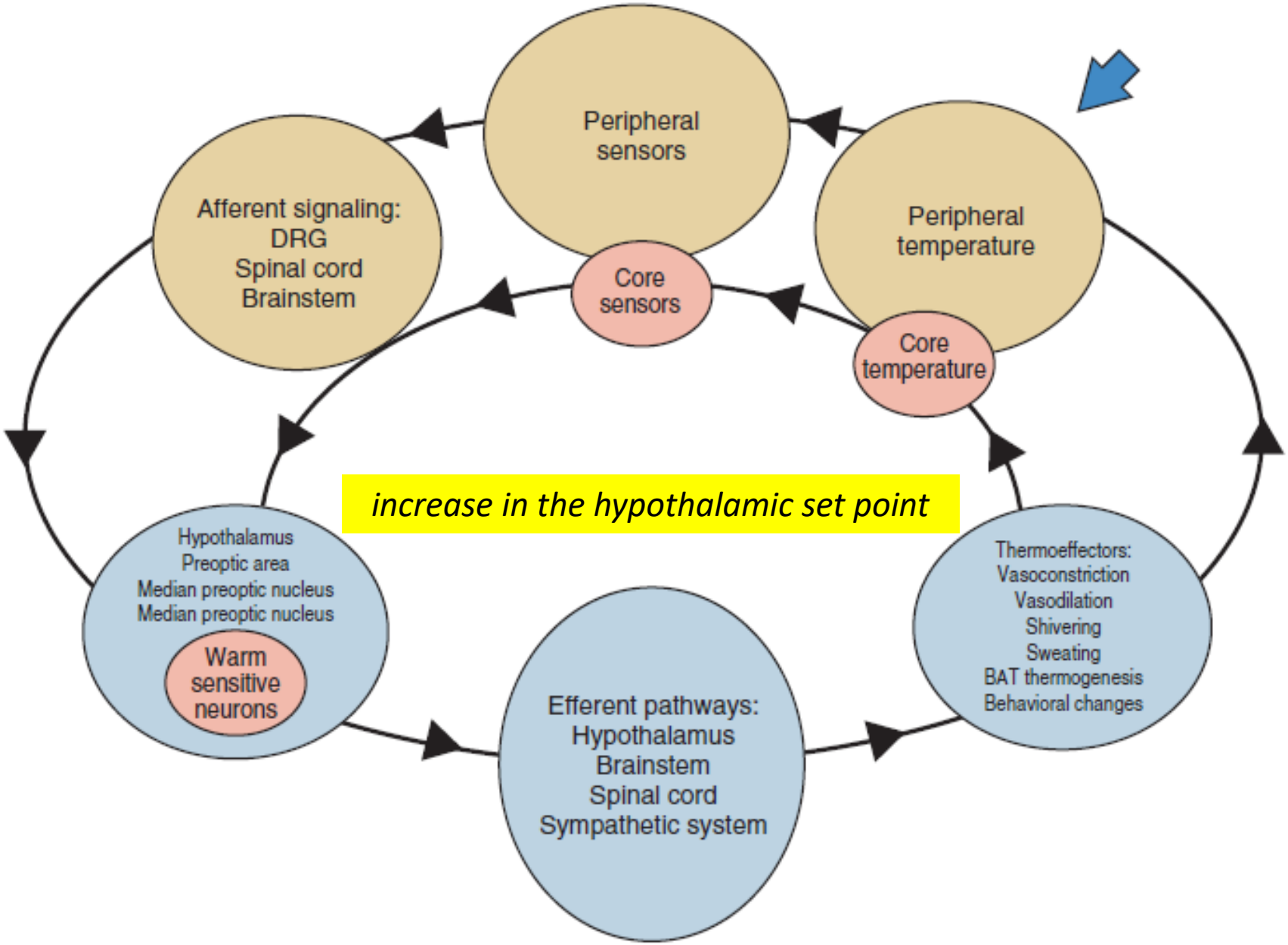
- Mucus Bloody or Watery
- Clinical Clue
- Patient evaluation
- Few cases need ABx

# Fever

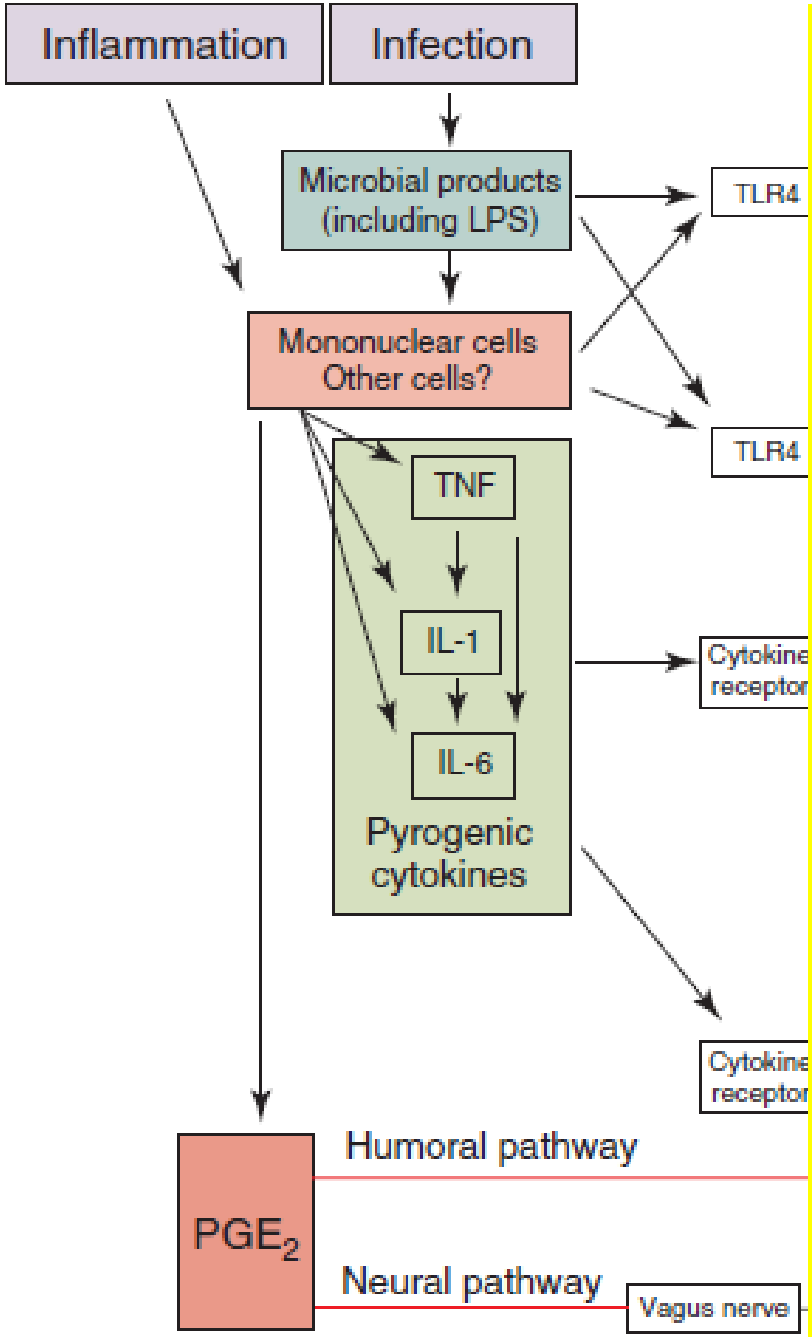
- "A state of ***elevated core temperature***, which is often, but not necessarily, part of the defensive responses of multicellular organisms (host) to the ***invasion of live*** (microorganisms) or ***inanimate matter*** recognized as ***pathogenic or alien*** by the host."

- Find the causes of fever

Sajadi et al. Mandell, Douglas, and Bennett's Principles and Practice of Infectious Diseases, 8th edition, 2015




Sajadi et al. Mandell, Douglas, and Bennett's Principles and Practice of Infectious Diseases, 8th edition, 2015




# Pyrogens

- ***Pyrogen*** (Greek *pyro*, "fire") is used to describe any substance that causes fever.

- **Exogenous pyrogens** are derived from outside the patient; most are ***microbial products, microbial toxins, or whole microorganisms (including viruses)***

- Examples:
  - ***lipopolysaccharide (endotoxin)*** produced by all gram-negative bacteria
  - ***Pyrogenic products of gram-positive*** organisms include the ***enterotoxins*** of ***Staphylococcus aureus*** and the ***groups A and B streptococcal toxins***, also called ***superantigens***
  - One staphylococcal toxin of clinical importance is that associated with isolates of *S. aureus* from patients with toxic shock syndrome

Sajadi et al. Mandell, Douglas, and Bennett's Principles and Practice of Infectious Diseases, 8th edition, 2015

# Very High Fever

- A fever of >41.5°C (>106.7°F) is called ***hyperpyrexia***
  - This extraordinarily high fever can develop in patients with severe infections but most commonly occurs in patients with central nervous system (CNS) hemorrhages

- In rare cases, the hypothalamic set point is elevated as a result of local trauma, hemorrhage, tumor, or intrinsic hypothalamic malfunction >> ***hypothalamic fever***

Dinarello at al. Harrison's Principles of Internal Medicine, 19th edition, 2015

# Hyperthermia

- An uncontrolled increase in body temperature that exceeds the body's ability to lose heat
- The setting of the hypothalamic thermoregulatory center is unchanged

Dinarello at al. Harrison's Principles of Internal Medicine, 19th edition, 2015

# Fever > 40 Celsius
# R/O life-threatening non-infectious cause first

| Condition | Clinical clue | Hx clue | Treatment |
|---|---|---|---|
| **Heat Stroke** | NO SWEAT (hot but dry skin)<br>N/S: Ataxia/confusion/irritability convulsion/coma, hyperven., arrhythmia, pulm edema, AKI, shock<br>⇒ mimic sepsis | - Exertional vs Non-exertional (classic, by environmental temp.)<br>*More @ http://www.aafp.org/afp/2005/0601/p2133.html | Prompt reversal of hyperthermia<br>Supportive Rx<br>+ - BDZ, chlorpromazine to inh.shivering and prevent seizure |
| **Adrenergic fever** | Sympathetic hyperactivity | - Recreational drugs: phenylamines eg. amphetamine, meth., ecstasy; cocaine<br>- MAOI | |
| **NMS (Neuroleptic malignant syndrome)** | Agitated, muscle rigidity | - Haldol use<br>- Parkinson's disease medication discontinuation<br>*Usually 1-3 d after trigger | Stop medication causing the condition<br>Dantrolene, BDZ<br>Supportive care |
| **Serotonin syndrome** | Agitated, hyperreflexia, N/V | - SSRI, TCA, antiemetics, anti-migraine, linezolid, amphetamine and derivatives , etc.<br>*Usually within 24 hr after trigger<br>* More @ http://www.aafp.org/afp/2010/0501/p1139.html | Stop medication causing the condition<br>BDZ, cyproheptadine<br>Supportive care |
| **Malignant hyperthermia** | Drowsy, lead-pipe rigidity | - Halothane, succinylcholine<br>- Family Hx<br>*Usually onset within 1 hr after trigger | Stop medication causing the condition<br>Dantrolene, BDZ<br>Supportive care |

# Etiology of Fever

- Infection
  - Bacteria;
    - Pyogenic bacteria; *Staphylococcus aureus*, *Streptococcus pneumoniae, E. coli*
    - Higher order bacteria; mycobacteria, *Nocardia*, *Rhodococcus*
    - Others: rickettsioses, *Chlamydia*, *Mycoplasma,* Leptospirosis
  - Fungus;
    - Mold; Aspergillosis, Mucormycosis
    - Yeast; Cryptococcosis, Candidiasis
    - Dimorphic fungi: Histoplasmosis, Talaromycosis
  - Virus
  - Parasite;
    - Helminths; Cestodes, Nematodes, Trematodes
    - Protozoa; Coccidia, Ciliate, Flagellate, Amoeba

- Inflammation; autoimmune disease, tissue inflammation
- Malignacies; hematologic, solid organ
- Miscellaneous; drugs, factitious

# Clinical Approach

- Fever ***with*** systemic symptoms or organ-specific symptoms
- For organ-specific >> anatomical localization
- Use all clues to predict the most likely cause of fever
  - History; ***clinical course***, ***clinical manifestation (some clues for some pathogens)***, risk factor (patient information, habitat, occupation, recreational activity, sexual behavior, traveling, pets etc.), incubation peroid, previous medical condition and drugs
  - Physical examination
  - Laboratory and imaging
  - Epidemiology; common pathogens for the disease community acquired or hospital acquired infection
- Choose the proper management
  - Antibiotics, surgery, immunosuppressive agents etc.

# Clinical Approach

- A 34-year-old male presented with fever for 4 days
- Please take a history

# Clinical Approach

- 4 วันก่อนมา รพ. ผู้ป่วยมีไข้สูง หนาวสั่น วันละครั้ง ร่วมกับอ่อนเพลีย และปวดหัวมาก ปวดหัวขมับสองข้างและร้าวไปรอบศีรษะ อาการปวดหัวเบาลงเมื่อไม่มีไข้ สามารถไปทำงานได้แต่อ่อนเพลีย มีปวดตามแขนขา เป็นมากเวลาไข้ ปัสสาวะ อุจจาระเหลว 1 ครั้ง

- Physical examination normal

- Problem: acute fever with fatigue and headache for 4 days >> acute undifferentiated fever

# Differential Diagnosis

- Bacteremia; *Staphylococcus aureus*, *E. coli*, Melioidosis etc., *Salmonella*
- Rickettsiosis
- Leptospirosis
- Influenza
- Dengue (plus other virus)
- Malaria

- ผู้ป่วยเป็นตำรวจตระเวณชายแดน อยู่ชายแดนไทยกัมพูชา จังหวัดสุรินทร์ นอนในป่า มานาน 2 เดือน เพิ่งออกจากป่ามา 4 วัน

Rick M. Fairhurst. Mandell Douglas and Benett's Principles and Practice of Infectious Diseases, 2015

# Clinical Approach

- DDx Malaria

  Rickettsial infection

  Meliodosis

- Blood smear: ring form trophozoites of *Plasmodium flaciparum*

**Point of learning: Occupation and Travelling Hx are important**

# Clinical Approach

- A 38-year-old female presented with fever for 10 days
- Please take a history

# Clinical Approach

- 10 วันก่อนมา รพ. ผู้ป่วยมีไข้สูง ไม่หนาวสั่น วันละครั้ง ร่วมกับอ่อนเพลีย และปวดหัวมาก ปวดหัวขมับสองข้างและร้าวไปรอบศีรษะ อาการปวดหัวเบาลงเมื่อไม่มีไข้ สามารถไปทำงานได้แต่อ่อนเพลีย มีปวดตามแขนขา เป็นมากเวลาไข้ น้ำหนักลด 3 กก.

- Problem: acute fever with fatigue and headache for 10 days >> **acute undifferentiated fever**

- Lab: SGOT/SGPT  260/300

# Clinical Approach

- Physical examination showed small painless erythematous plaque with central necrosis >> eschar

- ผู้ป่วยขอบเดินทาง Trekking ล่าสุดเมื่อ 2 สัปดาห์ก่อน

Have central tissue necrosis >> not scab

# Eschars Differential Diagnosis

**Eschar? Other skin lesions?**

**Ecthyma gangrenosum** : mostly *P. aeruginosa* (key : neutropenic hosts, multiple, clinically septicemic)

**Pyoderma gangrenosum** (key : pathergy, neutrophil dysfunction, IBD / RA / MM, etc)

**Ecthyma / Ulcerating impetigo**

- **Rickettsiosis**
  - Tick-borne : most SFG except RMSF (*R. rickettsii*), *R. helvetica* SF, & rarely in Israeli SF (*R. conorii israelensis*)
  - Mite-borne : 10-30% of scrub typhus (*O. tsutsugamushi*), 100% of rickettsialpox (*R. akari*)
  - Flea-borne : *R. felis* SF
- **Non-rickettsiosis**
  - *B. anthracis (key : surrounded by non-pitting edema)*
  - *Bartonella, F. tularensis, C. trachomatis, Y. pestis* (rarely), *P. multicida*
- **Non- infection**
  - Full thickness burn
  - Warfarin and heparin induced necrosis
  - Vasculitis
  - Brown-recluse spider bite

| Pathogens/diseases | Incubation period in range | Usual Incubation period |
|---|---|---|
| Influenza | 1 - 4 days (1) | 2 days (1) |
| RSV | 3 - 7 days (9) | 5 days (9) |
| MERSCoV | 2 – 14 days (1) | 5 days (1) |
| SARS | 2 - 10 days (9) | 5 days (9) |
| Rhinovirus | 2 – 4 days (9) | 2 days (9) |
| Adenovirus | 4 -8 days (9) | 6 days (9) |
| Parainfluenza virus | 2 – 6 days (9) | 4 days (9) |
| Metapneumovirus | 5–6 days (9) | |
| Diphtheria | 1 – 10 days (1) | 2 - 5 days (1) |
| Pertussis | 4 – 21 days (1) | 7 – 10 days (1) |
| EHEC | 1 - 10 days (1) | 3 - 4 days (1) |
| *Shigella* | 1 – 7 days (10) | 0.5 – 4 days (1) |
| *Vibrio cholerae* | 2 h – 5 days (1) | 2 – 3 days (1) |
| *Campylobacter* | 2 – 5 days (1) | 1 – 10 days (11) |
| Norovirus | 12 -48 h (1) | 33 h (1) |
| Rotavirus | 1 – 3 days (2) | less than 48 h (1) |
| Syphilis | 10 – 90 days (3) | 3 weeks (3) |
| Chancroid | 1 – 14 days (13) | 4 – 7 days (12) |
| Acute HIV | 2–6 weeks (15) | 2 – 4 weeks (14) |

| Pathogens/disease | Incubation period In range | Usual Incubation period |
|---|---|---|
| Scarlet fever (Gr. A Strep) | 1 – 7 days (7) | 2 - 5 days (1) |
| Measles | 7 - 21 days (1) | 14 days (1) |
| Rubella | 12 - 23 days (1) | 14 days (1) |
| Chicken pox | 10 - 21 days (1) | 14 - 16 days (1) |
| Roseola infantum (HHV – 6 and 7) | 5 – 15 days (8) | 12 days (8) |
| Erythema infectiosum (Parvovirus B19) | Upto 20 days (6) | 4 – 14 days (6) |
| Mumps | 12 - 25 days (1) | 16 - 18 days (1) |
| Dengue | 3 - 10 days (1) | 5 - 7 days (1) |
| Zika virus | 3 - 14 days (1) | 6 days (5) |
| Ebola | 2 - 21 days (1) | 8 - 12 days (2) |
| Yellow fever | 3 - 6 days (4) | 3 - 6 days (2) |
| Chikungunya | 1 - 12 days (1) | 3 - 7 days (1) |
| Scrub typhus | 5 - 20 days (2) | 10 - 12 days (2) |
| Leptospirosis | 2 - 30 days (2) | 5 - 14 days (1) |
| HAV | 15 - 48 days (3) | 30 (3) |
| HBV | 30 - 180 days (3) | 60 - 90 days (3) |
| HCV | 15 - 160 days (3) | 50 days (3) |
| HEV | 14 - 60 days (3) | 40 days (3) |
| Gonorrhoea | 1 - 10 days (3) | 2 - 5 days (3) |
| Non gonococcal urethritis | 2 – 35 days (17) | 7 - 14 days (16) |
| Herpes simplex | 2 – 12 days (1) | 4 days (1) |

OneSlideID

# Clinical Approach

- Weil-Felix test positive for OX-K 1:160 with 4 fold rising
- Dx: Scrub typhus
- Her fever dramatically responded to doxycycline

**Point of learning: Some Signs are Pathognomonic**

# Clinical Approach

- A 39-year-old female, housewife presented with fever and headache for 5 days

- Please take a history.

# Clinical Approach

- 5 วันก่อนมารพ. ผู้ป่วยมีอาการไข้ ปวดศีรษะ น้ำมูกไหล อาการไข้ไม่มีหนาวสั่น ปวดศีรษะเป็นพร้อมๆ ไข้ดีขึ้นเมื่อไข้ลง มีอาการปวดเมื่อยตามตัว มาห้องฉุกเฉิน ได้รับการตรวจ nasal swab for influenza virus ได้ผล positive for type A Influenza ได้รับการรักษาด้วย oseltamivir แล้วกลับบ้าน
- 3 วันก่อนมารพ. อาการปวดศีรษะไม่ดีขึ้น เป็นตลอดทั้งวัน มีคลื่นไส้อาเจียน ไอจามเบ่งปวดมากขึ้น กลอกตาเจ็บ สู้แสงสว่างไม่ได้ ปวดเมื่อย
- 1 วันก่อนมารพ. เริ่มนอนมากกว่าปกติ ตอบคำถามช้าญาติจึงพามารพ.

# Clinical Approach

- Physical examination showed  high grade of fever
- Slowly responded to one step command
- Nuchal rigidity

- Problem: fever with meningism for 5 days

- Anatomical localization: meningitis with complication

- DDx: Influenza meningitis, acute bacterial meningitis

**Point of learning: Don’t Ignore the Red Flags**

# Clinical Approach

- WBC  more than 20000 cell/µL
- Lumbar puncture
- OP 30, CP 16
- WBC 600, mostly PMN
- Glucose very low
- Protein 250 mg/dL

- **Bacterial meningitis**

# Common Pathogens for Bacterial Meningitis

- *Streptococcus pneumoniae*
  - Typical bacterial meningitis
  - Invasive infection appear as influenza complication
- Group B *Streptococcus;*
  - may be associated with other foci of infection such as skin and soft tissue infection, IE, osteomyelitis
- *Neisseria meningitidis;*
  - very short clinical course, very severe, purpura fulminans may be found
- *Haemophilus influenzae*
  - Uncommon in Thai adult
  - Typical bacterial meningitis
  - Invasive infection appear as influenza complication
- *Listeria monocytogenes*
  - Meningitis with cerebritis or brain abscess
  - Rhombencepahilis
  - Extreme age, neonate, pregnant, immunocompromised pt.

CDC, 2017

# Clinical Approach

- Empirically treated with ceftriaxone 2 g IV q 12 h
- CSF Gram stain showed Gram positive diplococci
- Her hemoculture grew *Streptococcus pneumoniae* for 2 specimens


A 47-year-old male

Progressive dyspnea on exertion for 2 weeks then sudden dyspnea for 2 hours

Low grade fever

Scant sputum

SpO2 80%

*Pneumocystis* pneumonia (PCP)

# PCP: Pathogen

- *Pneumocystis* is closely related ***unicellular fungi*** but ***lacks ergosterol***
- *Pneumocystis* isolated from humans was described as ***P. jirovecii***
  - *P. carinii and P. wakefieldiae* are for rats
  - *P. murina* for mice
  - *P. oryctolagi* for rabbits
- Lack of a reliable *Pneumocystis* in vitro cultivation
- Lifestyles of obligate parasites
- *P. jirovecii* infection is acquired early in life, so by age 2 or 3 years of age most (approximately 80%) children have been exposed

Walzer et al, Mandell, Douglas, and Bennett's Principles and Practice of Infectious Diseases, 2015

# PCP: Clinical Manifestation

- Progressive exertional dyspnea, fever, and a nonproductive cough
- Occasionally sputum is produced; hemoptysis is not a feature
- HIV: 2-4 weeks, non-HIV 5-14 days

- Lung auscultation is usually not helpful
- Impaired oxygenation is frequent

- Elevated LDH
- Extrapulmonary pneumocystosis; lymph nodes, spleen, liver, bone marrow

- The incidence of ***pneumothorax*** in AIDS patients with PCP was ***9.0 percent (8/89)***, compared with 0 percent (0/45) in AIDS patients without PCP ($p<0.03$)

Walzer et al, Mandell, Douglas, and Bennett's Principles and Practice of Infectious Diseases, 2015
Bartlett. Johns Hopkins ABX Guide: Diagnosis & Treatment of Infectious Diseases, 2010
McClellan et al. Chest, 1991

# Summary