MID Exam 1 - Bacteriology
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Infective Endocarditis

Clinical Presentation	Test Findings	Pathogenesis	Predisposing Factors/ Epidemiology	Likely Pathogens
Common: fever, chills and sweats, heart mummurs. **Less common**: myalgias, arthralgias, arterial emboli, neurologic manifestations, splenomegaly. **Three classic presentations**: **(Native Valve) Older patient with damaged native valve presents with low-grade fever and flu like illness** that persists for several weeks. Patient treated for recurrent bronchitis with short course antibiotics. **IV drug user with acute pulmonary infection**, pleuritic chest pain, hemoptysis (from **pulmonary emboli** from infected TRICUSPID valve – happens in IV drug users mostly). **Prosthetic valve patient** with **abrupt onset of heat failure** (from loosening of prosthetic ring or disruption of sutures.	**Most important:** positive blood culture (2-3 cultures collected over 24 hour intervals in patients that have not received eceived bial therapy in previous two weeks. 60% of cultures will be eceived in those that have eceived antimicrobial therapy). **Common:** anemia (70-90%), leukocytosis (20-30%; 15,000-25,000), elevated ESR (90%), **Less common:** hematuria (30-50%), proteinuria.	**Sterile Vegetation** Platelet and fibrin aggregation = sterile vegetation. These form at areas of altered endothelium. The endothelium can be altered at: 1) Interface of high to low pressure area caused by structural intercadiac lesion that creates turbulent flow. Examples: **Mitral insufficiency**: L. ventricle = high pressure, L. atrium = low pressure → vegetation on atrial surface of mitral valve. **Aortic insufficiency**: Systemic circ. = high pressure; L. ventricle = low pressure → vegetation forms on ventricular side of aortic valve **Ventricular Septal Defect**: L. ventricle = high pressure; R. ventricle = low pressure → vegetation on right ventricular septum. 2) Point of impact of jet flow caused by structural changes. Example: **Ventricular Septal Defect** → free right ventricular wall. **Bacteremia** Bacteremia with organism capable of adhering to vegetation. Ex. Via trauma to mucosal surfaces → GI/GU, dental, respiratory. Extracellular polysaccharides such as dextran increases adherence. **Therefore Gram (-) are generally rare causes of endocarditis.**	**Native Valve:** **Most Common:** old age leading to degenerative valve disease**.** **Less common:** past rheumatic fever. **IV Drug User:** Talc causes injury to endothelial surfaces, esp. tricuspid valve prior to introduction of bacteria to blood stream. **Prosthetic valve:** **Early: (w/I 60 days post-op)** contamination of operative site with organisms normally found on skin of patient or surgeon, or from organisms in irrigation fluid at time of valvular insertion. **Late: (after 60 days postop):** similar to native valve damage	**Native Valves:** **Most Common:** Streptococci (viridians and Group D), Enterococci, and Staph. Areus. **Also**: Staph. Epi (Coagulase-negative. **Rare**: Gram (-) including E. Coli, Klebsiella, and HACEK group. **IV Drug Users**: **Most Common:** Staph. Areus **Less Common:** Gram (-) including Pseudomonas aeroginosa, B. cepicia, and Serratia. Fungal including Candida. **Prosthetic valve** **Early: Most common:** Staph. Coagulase (-), ex. Staph. Epi. **Also**: Staph. Aureus, Psuedomonas aruginosa, Klebsiela. Fungal – Candia and Asperigillus. **Late:** same as fo native valvular infection except both Staph. Aureus and coagulase (-) Staph. are more common.

Definitive Diagnosis	Complications	Treatment	Prevention
Clinical Major: 1) 2 positive blood cultures 2) endocardial involvement (via echo or auscultation of new murmur) Minor: Several which generally include predisposing factors and symptoms of infection. **Pathological** What you would expect to see under microscope: microorganisms and vegetations.	**Persisting of Relapsing Infection** **Native:** unusual. **IDU:** Not uncommon, usually Psuedomonas or Candida. **Prosthetic: Early** = very common, due to nature of organism and suture involvement. **Late** = any organisms other than Strep. **Congestive Heart Failure** Any time with any presentation, esp. with aortic valve involvement. **Major Organ Emboli** Spleen, kidney, and brain and heart.	**Anitbiotic** 1) tailored to organism 2) needs to be long enough 3) low toxicity S. areus → if penicillin resistant → go to vancomycin → if resistant → streptogramin, or lenazolid **Surgical Valve Repair/Replacement Indications:** 1) relapsing infection 2) antibiotic therapy not available 3) new CHF 4) more than one embolization	**Antibiotic prophylaxis** for congenital and valvular disease in order to: 1) decrease numbers of microorganisms 2) inhibit binding Dental procedures → amoxicillin GI/GU procedures → ampicillin In penicillin allergic patients → erythromycin, clindamycin, or in some case IV vancomycin **Major Risk Factors:** • Prosthetic Heart Valves • Most Congential Heart Defects • Rheumatic or other heart dysfunction • Mitral valve prolapse • Redundant valve

Infectious Diarrheas - Secretory

Clinical Presentation	Test Findings	Pathogenesis	Predisposing Factors/ Epidemiology	Likely Pathogens	Definitive Diagnosis	Complications	Treatment	Prevention
Secretory: **No fever,** leukocytosis, volume depletion prominent **Stools:** high volume, **watery**	**Stool Sample**: No fecal WBC's	Disruption of water/electrolyte secretion by GI mucosal cells, no inflammation **Enterotoxin mediated**	**Exposure:** ▪Ingestion of contaminated seafood or water ▪Food handling	**Vibrio cholerae** ▪In water or food ▪Flagella motility, Pili, accessory colonization proteins all help colonize GI tract ▪**Cholera toxin:** subunit A activates adenylate cyclase by adding ADP-ribose to stimulatory G-protein ▪**Increase in cAMP** results in outflow of Cl- ions and water ▪**Subunit B of toxin** binds to cell surface receptors ▪**Zot toxin**: disrupts tight junctions or zona occludens	**Antibody to toxin** **Gram stain:** comma shaped gram-negative rods **Stool culture:** ▪Oxidase-positive (distinguishes them from other Enterobacteriaceae)		Fluid and electrolyte replacement	Sewage disposal, chlorination of water supply, hand washing. Tetracylcine for close contacts.
			Exposure: ▪Travel in tropical climates, developing countries – "traveler's diarrhea" ▪Various foods and water	**Enterotoxigenic E. coli (ETEC)** ▪Preferentially bind to differentiated GI mucosal cells with microvilli vs. other bacteria ▪**Adherence**: aided by Type 1 pili, Colonization factor antigens, bundle forming pili (resembles those of cholera) ▪**Heat labile toxin (LT):** same mech as cholera toxin ▪**Heat stable toxin (ST):** same mech but with cGMP instead of cAMP	Not normally identified in routing stool culture because normal inhabitant, but on **MacConkey Culture:** ▪facultive ▪ferments lactose ▪turns pink **Request serotyping** **Slant test:** ▪acid slant ▪acid butt with gas ▪no H2S Facultive, gram-negative rod		Fluid and electrolyte replacement	Prevent traveler's diarrhea by eating only cooked food and drinking boiled water in countries where disease is endemic.

Infectious Diarrheas - Inflammatory

Clinical Presentation	Test Findings	Pathogenesis	Predisposing Factors/ Epidemiology	Likely Pathogens	Definitive Diagnosis	Treatment	Prevention
Inflammatory: Fever, leukocytosis, volume loss less prominent **Stools:** dysentery-frequent, small volume stools **containing blood and mucus**	**Stool Sample:** + for WBC's (PMN's)	**Invasion and destruction of mucosal cells with inflammation** **Cytotoxin mediated**	**Exposure:** ▪Habitat **= human colon only** → fecal-oral transmission ▪**Direct contact** with someone who has it: ▪Institutionalized setting ▪Day care centers ▪Seen in developing countries **Low infectious dose** compared to most GI pathogens (10-100 vs. 100,000+)	**Shigella** ▪Invades mucosa of colon ▪**M-cells:** take up Shigella, it trancytoses, adheres, and invades neighboring GI mucosal cells from basolateral surface and avoids being phagocytosed by Mac's ▪**Invasion plasmid antigents (Ipa)** – bind integrins → induce acting rearrangement of host cell → uptake of Shigella ▪**Ipb** → allows Shigella to get out of phagocytic vacule so it can replicate ▪**IcsA** → allows Shigella to propel through host cell using actin ▪**IcsB** → allows Shigella to lyse and enter neighboring cell ▪**Tissue** → immune response ▪**Produces Shiga toxin** – role in pathogenesis unclear	**MacConkey Culture:** ▪Non-lactose fermenting ▪Colorless ▪**Non-motile** (in contrast to Salmonella) **Shiga toxin test** **Slant test:** ▪Alkaline slant ▪Acid butt with no gas no H2S Facultive gram-negative rods	**Fluid and electrolyte replacement** **Severe cases: ciprofloxacin**	Public health measures, etc. Infected individuals must not return to institutions until 3 negative stool cutlurs, 2 days apart.
	May see Hemolytic-uremic syndrome: ▪hemolytic anemia ▪thrombocytopenia acute renal failure		**Exposure:** ▪Associated with outbreaks of food poisoning in undercooked ground beef in fast food chains ▪Also, contaminated water, unpasteurized juices, use of recreational waters, contact with farm animals	**Shiga toxin producing E. coli (STEC)** ▪Adherence via intimin to host cell ▪Shiga-like toxin (AB exotoxin): causes diarrhea, interferes with host cell protein synthesis → death, involved in hemolytic-uremic syndrome (Not a superantigen)	Clinical: high morbidity, mortality Not normally identified in routing stool culture because normal inhabitant, but on **MacConkey Culture:** ▪facultive ▪ferments lactose ▪turns pink **Request serotyping** Facultive, gram-negative rod	Antibiotic use may actually induce toxin production and increase risk of hemolytic-uremic syndorme	
	Colonoscopy: Reveals "pseudomembranous colitis" – yellowish plaques on mucosal surface of colon		**Host:** ▪Antibiotic use (in hospitalized patients risk increases 25-70%)	**Clostridium deficile** ▪Eradication of normal flora allows for overgrowth ▪**Toxin A**: incubation with any cell type results in retraction and detachment of cells; chemotacttic for PMN → immune response ▪**Toxin B:** only causes cytotoxicity in conjunction with Toxin A (may only work on damaged cells) ▪**Spore formation** – resistant to acid pH of stomach	**ELISA to detect Toxins A, B** Gram-positive, anaerobic, spore forming rod	**Metronidazole** (Vancomycin, although effective, should not be used because it might select for vancomycin-resistant enterococci)	
			Exposure: ▪Various foods	**Campylobacter jejuni**	**Culture on special agar** (42 degrees, high CO2, low O2) Comma shaped gram-negative; microaerophilic	**Symptomatic treatment** **Severe cases: erythromycin**	

Systemic Syndrome Diarrhea

Clinical Presentation	Test Findings	Pathogenesis	Predisposing Factors/ Epidemiology	Likely Pathogens	Definitive Diagnosis	Treatment	Prevention
Systemic syndrome: Early in infection: Nausea, vomiting, diarrhea, and then they resolve **Later on:** Fever, hylar adenopathy, enlarged liver and spleen predominate, hypotension (sepsis) **Stools**: GI symptoms not prominent	**Stool sample:** Variable (mononuclear leukocytes) **Blood Labs:** Anemia, decreased WBC's, elevated liver function tests	**Invasion beyond GI mucosa and dissemination systemically**	**Exposure:** ▪Poultry, meats, eggs **Host:** ▪Immunocompromised ▪Young children ▪Hemolytic anemias ▪Taking antacids or having had a gastroectomy also predisposes to Salmonella (can live down to pH of 3)	**Salmonella** ▪Typhi → causes typhoid fever (humans only reservoir) ▪**Non-typhi** → several species → enteriditis (animals major reservoir) → **causes GI disease** ▪Uptake by **M-cell** ▪Multiplies in Mac's and lymphocytes in submucosa ▪Also **invades Gut mucosa** with its invasions (binds host cell receptors → reorganizing cytoskeleton) ▪**Adapts to intracellular environment** with oxy gene → catalase, etc, → resist O radicals; resistant to low pH; resistant to defensins ▪**Disseminated in blood** ▪**Long O-antigen** resists MAC complex formation; Rck → prevents final steps of complement assembly ▪**Replicates in liver and spleen** ▪**Excreted into bile**, and then goes back into blood → cycle	**MacConkey culture:** ▪Non-lactose fermenting ▪Colorless **Slant test:** ▪Alkaline slant ▪Acid butt with gas ▪H2S + Facultive gram-negative rod	Antibiotics may actually prolong excretion of organisms, therefore not warranted for non-complicated (i.e. non-septic) cases **In the case of systemic symptoms:** **Ceftriaxone** (resistance to ampicillin and chloraphenicol mediated by plasmid encoded B-lacatamases and acetylating enzymes respectively)	Oral vaccine available
			Exposure: ▪Various foods	**Yersinia** (not responsible for exam, but very similar to Shigella, Salmonella)			
		Neurotoxin mediated	**Exposure:** ▪Mushrooms → botox	**Staph. areus** **Clostridium botulinum**			

Urinary Tract Infections

Clinical Presentation	Test Findings	Pathogenesis		Predisposing Factors/ Epidemiology	Likely Pathogens	Definitive Diagnosis	Treatment
Females and Males **<u>Adults:</u>** Cystisis (bladder infection): dysuria, frequency, urgency, suprapubic pain **Urine:** cloudy, malodorous, bloody. Usually no fever or systemic symptoms. **Rule out in sexually active adults, especially males:** acute urethritis (from Chlamydia, gonococci, or herpetic infection) and vaginitis in women **Plus Fever and flank pain = acute pylonephritis** **<u>Children under 2:</u>** irratibility	**<u>Females</u>** **Voided urine sample:** Generally count above 10^5 indicates bacteuria (not contamination) However, in some symptomatic women (20%) count of 10^2 to 10^4 indicates infection, not contamination. **Difficult to determine location of infection.** ▪Can try giving antibiotic dose → wait 48h → if bacteria persist = kidney infection	**<u>In general, 2 mechs:</u>** **Ascending:** ▪Most infections ▪Urethra→ bladder → kidney **Hematogenous:** ▪S. areus bacteremia; ▪Candida can be ascending or descending **Bacteria Factors:** ▪**Type 1 fimbriae:** allow adherence to uroepithelial cells (blocked by mannose – cranberry juice) ▪**P-fimbrae:** not blocked by mannose → cause pylonephritis ▪**Phase variation** ▪These factors more important for pathogenesis in non-predisposed individuals (sexually active women)	**<u>Host Factors:</u>** E.coli gets into bladder through **"urethral massage" during sex** **<u>Host factors:</u>** **Obstructions**→ incomplete emptying, reflux **Catheters** → bacteria use biofilm to adhere to smooth surface, track up into bladder **Immuno-compromised,** diabetics → predisoped to Candida	**<u>Females:</u>** ▪**Sexually active:** intercourse, diaphragm use, spermicidal jelly (raises pH → toxic to normal flora), failure to void after intercourse. ▪Don't have urinary tract abnormality (uncomplicated UTI) **<u>Females, Age:</u>** ▪>65: All of below, incontinence, chronic catheterization ▪36-65: Gynecologic surgery, bladder prolapse ▪6-15: vesicouretal reflux ▪1-5: Congenital abnormalities, vesicouretal reflux ▪<1: anatomic or functional urologic abnormalities	**E. coli (80%)** **Staph. saprophyticus (10%)** **Occasionally:** **Klebsiella** **Others** **Staph. saprophyticus –** more important **E. coli (35%) –** less important **Klebsiella –** more important **Enterococcus –** more important **Candida** – in immunocompromised	**<u>Diagnostic Criteria for UTI:</u>** **WBC count in unpsun urine using hemocytometer** **Luekocyte esterase test** **Nitrate test (gram (-)'s** convert nitrate → nitrite **Gram stain** **<u>Evaluation of Pylonephritis</u>**: Radiographic imaging Bacterial susceptibility testing should be conducted	**<u>Females: Uncomplicated cystitis</u>** ▪Brief course (3 days) of Antibiotics for healthy, young female ▪5-7 day course for all other women ▪**Target E.coli: Trimethorpin, co-trimoxazole, and floroquinolones** (ideal, don't interrupt anaerobic GI/GU flora and b/c they achieve good urine concentrations) **<u>Acute pylonephritis:</u>** ▪IV therapy when patient is febrile, oral when afebrile ▪Longer course 10-14 days ▪Repeat urine cultures to check for relapse **<u>Asymptomatic bacteuria:</u>** ▪Tx is controversial ▪Cultures definitely need to obtained before treatment ▪Patients with indwelling catheter should not be treated
	<u>Males</u> **Voided urine sample** Technique to locate site of infection: ▪VB1: 1st 10 ml = urethral ▪VB2: midstream = bladder, kidney or both ▪EPS: prostate fluid ▪VB3: 1st 10 ml after prostate massage Check for STD's, prostatic hypertrophy			**<u>Males, Age:</u>** ▪>65: All of below, incontinence, long-term catheterization, condom catheters ▪36-65: Prostatic hypertrophy, obstruction, catheterization, surgery ▪16-35: Homosexual anal intercourse ▪1-5: congenital abnormalities, uncircumcised penis ▪<1: urologic abnormalities (fairly common)	**Staph. saprophyticus** – more important **E. coli** (35%) – less important **Klebsiella** – more important **Enterococcus** – more important **Candida** – in immunocompromised		**<u>Males: Uncomplicated cystitis</u>** ▪7-10 of treatment Acute proctitis ▪6-12 WEEKS of treatment of antibiotics ▪may also be Chlamydia or ureaplasmata → give tetracylins, erythromycins, or fluoroquinolones

Prevention
<u>Pregnant women:</u> ▪High risk of pylonephritis; fetus risk of neonatal meningitis ▪Should be cultured and treated in 1st trimested and 3rd trimester ▪Change catheters frequently ▪Address urological abnormalities, sexual behaviors **<u>Men:</u>** ▪Address urological abnormalities, ▪sexual behaviors, ▪prostate problems, Change catheters frequently.

Meningitis

Clinical Presentation	Test Findings	Pathogenesis	Predisposing Factors/ Epidemiology	Likely Pathogens	Definitive Diagnosis	Complications
Neonates: ▪fever often, but not always present ▪lethargy ▪irritability ▪eventually vomiting and seizures	**Blood tests:** - Elevated peripheral WBC's **Lumbar puncture:** - Cloudy (PMNs > 200) - Elevated protein (from edema; normal <50 mg/dl) - Low glucose (from O2 depletion; normal ratio to glucose in blood = 0.6; below .5 = meningitis)	**General:** 2 Routes of reaching CNS: ▪**Hematogenous** ▪**Extension from infection adjacent to nervous system** (ex. trauma to head that causes leakage of spinal fluid through nose) **Colonization:** ▪Binding to epithelial cells via specific adherence molecules (ex. **pili**) ▪pathogenic **IgA proteases** ward off mucosal immune response ▪Reach blood stream (**capsules** resist complement, PMNs) **Invasion of Subarachnoid Space:** ▪Bacteria bind to receptors in choriod plexus and cerebral capillaries ▪**Unstopped proliferation** (No Ab's, complement, or resident Mac's in CSF) and outer membrane proteins (LPS, techoic acids) initiate host immune response in CSF ▪**Selectins, ICAM-1, CD14 upregulated** → PMN migrate across BBB ▪Gram (-)'s stimulate → lots of **TNF**, **IL-1 production**, even more inflammation ▪**Activated PMNs** → ROI's → **tissue damage**, further breakdown of BBB ▪**Edema (**increased cells and protein into CSF) → **increase in intercranial pressure** ▪**Glucose falls** (due to O2 depletion and neuronal lactate production) not b/c bacteria consume it ▪**Vascular changes** in subarachnoid space: vasculitis, narrowing, thrombosis, ischemia, infartion. ▪**Outflow impeded** → further increase in intercranial pressure	**Neonates** **Exposure:** **Vetrical transmission** (mother to child) - especially with birth complications - aspirate genital flora in birth canal - or mother has high grade bacteremia prior to or at the time of birth **Nosocomial** in premature infants (ventilators) **Host:** **Weak immune system**	**Neonates:** **Group B strep. Agalactiae** ▪Gram-positive cocci, encapsulated ▪**Common commensal flora** ▪Neonates weak defenses (absence of IgG) following complications in delivery predispose to this infection **E. coli K1** ▪Gram-negative rod ▪**Many adults lack IgG to K1 antigen**, therefore colonization of this strain has high incidence of bacteremia and meningitis **Listeria monocytogenes** ▪Gram-positive rod, catalase positive, tumbling motility ▪**Food born transmission to mother** (Mexican style soft chesses, dairy, and poultry products) **Premature (less developed immune system):** **Coagulase negative staph (Staph. epi)** ▪Part of normal mucosal flora ▪Also from ventilators Candida Enterococci (if antibiotics were taken and selected for them)	**Based on CSF analysis:** Elevated WBC cell count in CSF: - PMNs - Decrease sugar concentration - Increased protein - **Gram stains and oxidase test** If N. memingidits suspeceted: - should be transported to lab immediately under ambient conditions - **Culture on Thayer-martin medium**	**Complications from inflammation,** parenchymal damage, vascular insults even if bacteria susceptible to Antibiotics **Waterhouse-Friedrichsen** syndrome (destruction of adrenals with N. meningitidis) **Infants and Children** at highest risk for developmental, hearing, learning disorders, hemiplegias, deafness, blindness
Infants: (Sx often start out looking like otis media → but gets progressively worse) ▪fever often, but not always present ▪lethargy ▪irritability ▪eventually vomiting and seizures			**Infants** Exposure: **Direct contact** **Host:** infants lose maternal IgG b/w 6 months to 1 yr of age. Window b/w then and 2 yr of age. - increased risk to common encapsulated bacteria	**Infants:** **S. pneumoniae** ▪gram-positive dipplococci, encapsulated ▪oral mucosa colonizer (**IgA protease**) ▪leads to meningitis after antecedent infection: pneumonia, otitis, sinusitis ▪cell wall **peptidoglycan fragments → highly immunostimulatory** → most likely pathogen to lead to neurological complications once in CSF **N. meningiditdis** ▪gram-negative diplococci, encapsulated ▪colonizes nasopharngeal cells (**IgA protease, pili**), transported to blood stream ▪**capsules**, type B capsule especially, mimic neuronal adhesion molecules → **fails to activate host's protective Ab response** **H. influenza type B** (in unvaccinated) ▪gram-negative rods, encapsulated ▪respiratory colonizer (**IgA proteaste, pili**)		
Older Children and Adults: (Sx: may start off looking like pneumonia, otitis, or sinusitis if exposed to S. pneumonia) ▪Fever ▪Headache (often severe) ▪Vomiting ▪Stiff neck ▪Kernig and Brudzinski signs (indicate meningeal irritation) ▪Altered mental status			**Exposure:** - **Direct contact** - Crowded living conditions (meningicoccus); military, dorm setting **Host:** - **Humoral deficiency (IgG)** - **Lack of splenic function** (splenctomy) - Complement deficiency (genetic or liver damage) - **Inhibited respiratory function:** clearance (smokers, etc.); antecedent viral infection - **Aspiration (**in intoxicated drinkers, etc)	**Adults:** 1. **N. meningitidis** (most common in college kids) 2. **S. pneumoniae**		

Meningitis (cont)

Treatment	Prevention
Corticosteroids: ▪Quick dose before giving antibiotics decreases secondary increase in TNF leading to better clinical outcomes Antibiotics (need prolonged therapy 3 wks): ▪**Penicillin G (IV) for N. meningidits, S. pneumonia, Group B strep** ▪**3rd or 4th generation cephlasporins for E. Coli, H. influenza** ▪**Ampicillin, trimethoprim / sulfamethoxazole for Listeria** **Vancomycin for Staph. Epi**	**Prevent vertical transmission** ▪taking cultures in prenatal care **Rifampin for close contacts** (secreted into nasal mucosa) **Meningococcal vaccine** (except doesn't protect against B subgroup which is most common in US, and perhaps most virulent) **S. pneumonia vaccine:** Against the 23 most popular capsular Ag's

Sepsis/Septic Shock

<table>
<tr><th>Clinical Presentation</th><th>Test Findings</th><th>Pathogenesis</th><th>Predisposing Factors/ Epidemiology</th><th>Likely Pathogens</th><th>Treatment</th></tr>
<tr>
<td><u>Classic presentation</u>
▪Fever
▪Shaking chills or rigors
▪Nausea, emesis, and diarrhea may occur

<u>Physical exam:</u>
▪Pulse – bounding
▪BP – normal/ low normal
▪Temp – elevated, normal, or below normal (more common in newborn)
▪RR – rapid
▪MSE – confused, agitated
▪Skin- warm flushed
▪Urine volume – down

Later on….

<u>Shock</u>
▪Pulse – becomes rapid, “thready”
▪BP – becomes low <90 systolic
▪Temp – elevated, normal, or down
▪MSE – confused, agitated
▪Skin – becomes cool, clammy
▪Urine – way down</td>
<td><u>Labs:</u>
▪pH up
▪Low pCO2
▪Modestly low pO2
▪Bood lactate
▪WBC elevated
▪Prothrombin clotting time prolonged – platelets down

Later on…

▪pH down
▪pCO2 low
▪pO2 down
▪Blood lactate up
▪WBC’s up or down
▪Pt time prolonged</td>
<td><u>Microbial Initiation (2 mechs):</u>
▪Cell lysis (complement fixation or by antibiotics) → LPS or peptidoglycans and techoic acids get out
▪Exotoxin elaboration (Superantigens) by S. areus or Group A strep → T cell proliferation → release of cytiokines

<u>TNF Release:</u>
▪LPS binds to Mac, endothelial cell → (s)CD14 → (TLR4 for gram (-) or TLR 2 for gram (+)) → activation of kinase cascade → NFkB → TNF transcription

<u>Endotoxin mediated effects:</u>
1. Activation of clotting cascade:
▪Tissue factor + (collagen exposure → Factor XII) → thrombin, fibrin deposition → DIC
2. Activation of Kinin system
▪Factor XII → bradykinin → potent vasodilator
3. Complement activation
▪C5a → PMN recruitment → tissue injury
4. AA metabolism
▪Complement activation → phospholipase activation → PGE2 → fever. (IL-1 release stimulates this pathway)
5. NO release by endothelial cells
▪Vasodilation
6. PAF release
▪By Mac’s → stimulates cell adhesion and amplifies action of cytokines

<u>Transition from sepsis → septic shock mediated by:</u>
▪Decrease in intravascular volume
▪Decrease in cardiac function (decreased afterload, increased compliance – baggy ventricles, decreased contractility)

<u>V-Q mismatch early in lung:</u>
▪Agglutination of white cells and platelets in pulmonary vasc. → alter perfusion
▪Extravasation of fluid in lung → triggers “J” stretch receptors → increases RR → respiratory distress</td>
<td>Skin catheter – IV</td>
<td>Staph areus
Staph coagulase neg
P. auregenosa
Acinetobacter</td>
<td rowspan="6">Removal of infecting agent

Empiric Ab therapy

ABC’s
▪Intubation
▪Volume resuscitation: fluids, pressor agents (Dopamine, NE, dobutamine)

Pulmonary catheterization

Vasopressin

Coticosteroids for W-F syndrome

Experimental:
▪Ab to LPS, TNF, IL-1
▪Activated Protein C (stops thrombosis and inhibits inflammatory cascade)</td>
</tr>
<tr>
<td>Respiratory tract – Aspiration</td>
<td><u>Community:</u>
S pneumoniae
S pyogenes

<u>Nosocomial:</u>
P auruginosa
Enterobacter</td>
</tr>
<tr>
<td>GU tract – bladder catheter, uretal obstruction</td>
<td>E. coli
Klebsiella
P aeruginosa</td>
</tr>
<tr>
<td>GI/biliary tract – cholangitis, bilary tract stent</td>
<td>E. coli
Klebsiella</td>
</tr>
<tr>
<td>Bowel abscess – perforation</td>
<td>E. coli
Klebsiella
Salmonella
Bacteroides</td>
</tr>
<tr>
<td>Reproductive system – post partum</td>
<td>Strep
E. colia
Bacteriodes</td>
</tr>
</table>

STDs – "non-ulcerative" infections

Clinical Presentation	Test Findings	Likely Pathogens	Definitive Diagnosis	Complications	Treatment
Urethritis in Men: ▪Sexually active ▪Purulent discharge that can be expressed by milking of urethra ▪Often associated with dysuria and frequent urination	**Discharge/urine test:** ▪PMNs	N. gonorrhea Chlamydia trachomatis HSV	**Microscopy:** ▪Examine discharge or first 20-30 ml of urine with gram-stain ▪**Look for gram-negative diplococci within PMNs** ▪Culture for Chlamydia and gonorrhea **Serology:** ▪If difficult to culture Chlamydia, DFA test immunofluorescence or ELISA **Clinical:** ▪Rule out Herpes if no ulcerative lesions	**Epididymitis** (more commonly associated with Chlamydia than gonorrhea) **Proctitis** **Disseminated Gonococcal infection**	**Gonorrhea: Ceftriaxone. If penicillin allergic: Spectinomycin or ciprofloxacin.** **Chlaymdia: Doxycycline or tetracyline**
Epididymitis in Males ▪Sexually active ▪Unilateral testicular pain of acute onset ▪Intrascrotal swelling ▪Tenderness ▪fever	**Discharge/urine test:** ▪PMNs	**Chlamydia trachomatis (more common)** **N. gonorrhea**	Same as above **Rule out testicular torsion**		Same as above
Cysititis/ urethrtiris in Females ▪Sexually active ▪Purulent discharge ▪Dysuria and frequent urination	**Discharge/urine test:** ▪<10^2 E. coli or other common UTI pathogens	**Chlamydia trachomatis** **N. gonorrhea** **HSV**	Same as above **Rule out: UTI**	**Extension to cervix** **Salpingitis** (PID = major complication of gonorrhea) Transmission to fetus for pregnant women	Same as above
Mucupurulent Cervicitis in Females ▪symptomatically silent Gynecollogical exam : ▪yellow mucupurelent discharge	**Discharge test** : ▪PMNs	**Chlamydia trachomatis** **N. gonorrhea**	Same as above	Extension to fallopian tubes (**PID salpingitis**,)	Same as above
Pelvic Inflammatory Disease -ascending infection Oocurs in about 15% of women with gonorrhea Females : ▪Proceeds from mucupurlent discharge → ▪Endometritis (midline abdominal pain and abnormal vaginal bleeding) → ▪Salpingitis (bilateral lower abdominal pain and pelvic pain) → ▪Peritonitis (nausea, vomiting, increased abdominal tenderness)	**Blood test :** ▪ESR elevated **Discharge :** ▪PMNs **Preganancy test :** negative	**N. gonorrhea** **Chlamydia trachomatis** **Group B Strep (from alteration in vaginal flora)**	Same as above	If not treated soon enough → **infertility**	**Doxcycline plus cefetan or clindamycin plus gentamycin**

Gonococcal and Chlamydial Infections

Clinical Presentation	Pathogenesis	Predisposing Factors/ Epidemiology	Likely Pathogens	Definitive Diagnosis	Complications	Treatment	Prevention
Males: ▪mostly uethera affected ▪proctitis, pharyngitis (homosexual men) **Females** In decreasing order of frequency: 1 Endocervix 2 Urethra 3 Anal canal 4 pharnyx also during pregnancy → child	**Gonoccocal Infection** ▪Transimitted sexually ▪**Pili** – mediate attachment (to mucosal cells) and are also antiphagocytic ▪**LOS** → inflammation ▪**IgA protrease** → allows for colinazation of mucosa ▪**Phase variation** – allows them to switch OPA and pili genes on and off → selection for best binding strains and resistance to immune response	**Exposure:** ▪Usually spread by ASYMPTOMATIC carriers ▪High rate of transmission per encounter ▪Can also be transmitted through birth canal **Host** ▪Peak incidence occurs from age 20-24 ▪Age, sex, race, socioeconomic status → sex behaviour, illness behavior, accessibility to health care	**N. gonorrhea** ▪gram-negative diplococci ▪**oxidase-positive** colonies ▪**ferments glucose,** not maltose, sucrose, or lactose (differentiates from other Nisseria) ▪In vitro: **T1, T2 virulent**, T3, T4 not virulent due to loss of pili ▪Outer membrane: lipopolysaccharide, phospholipids, OMPs ▪**Variation of pili, OMPs** = reason why there is no vaccine	**Microscopy** ▪Look for **gram-negative diplococci** within PMNs (less sensitive in female) Culture all sited of infection on **Thayer-Martin medium** (which contains inhibitory antibiotics for everything except gonorrhea) ▪**Oxidase positive**	**Females:** ▪**Uthrethritis, proctitis (anal canal), pharyngitis** ▪Pelvic inflammatory disease **(PID)** ▪**Disseminated gonoccocal infection** ▪**Transmission to children:** conjunctiva, pharynx, respiratory tract, anal canal **Males:** ▪Rare complications: **epididymitis, prostatitis, inguinal lymphadenopathy**	**Ceftriaxone or Ciprofloxacine + azytrhomycin for possible concominat Chlamydia infection** In Wash. Heights, 40% of N. gonoorrhea are beta-lactam resistant **If treament of gonococcal infection persists even after beta-lactam antibiotic, then chlamydial infection. Treat chlamydia with azythromycin or tetracycline → protein synthesis inhibition.**	**No vaccine –** b/c variable pilin genes that can recombine with the active pilE locus creating new pili.
▪**Fever** ▪**Polyarthralgias** (limited to tenosynovitis asymetrically – wrists, fingers, knees, and ankles most often involved) ▪Papular, petechial, pustular, hemorrhagi, or necrotic **skin lesions** (about 3-20 of them on distal extremities) ▪**Serious cases** → septic arthiritis	**Disseminated Gonococcal Infection** ▪Strains are uniquely resistant to complement ▪ Circulating immune complexes	**Exposure**: ▪gonoccocal infection **Host:** ▪complement deficiencies are common ▪2/3 are women	**N. gonorrhea**	Same as for gonococcal infections	▪**Myopericarditis** ▪**"toxic" hepatitis** ▪Endocarditis and meningitis (less frequent	**Ceftriaxone; for penicillin allergic, ciprofloxacine**	
Males: ▪Urethra ▪Epdidymiis ▪Anal canal **Females:** ▪Urethra ▪Cervix ▪Endometrium ▪Fallopian tubes ▪During pregancy → child	**Chlamydial infection** Primarily infect epithelial cells ▪**Rarely cause invasive, disseminated infections** ▪**Immunotypes D-K** are the ones that cause gential infection ▪**Immunotypes L1-L3** cause (**lymphagranuloma venereum**) – the ulcerative genital lesion version of Chlamydia	**Exposure:** ▪Most common bacterial STD in U.S. ▪Sexual transmission or through birth canal ▪Often co-infection with gonorrthea **Host:** ▪Nongonoccola uthrethritis occurs more in higher socioeconomic groups	**Chlamydia trachomatis** ▪obligate **intracellular** parasite ▪rigiid cell wall ▪Have a replicative life unlike any other bacteria: ▪**Elementary body:** extracellular, metabolically inert infectious particle. ▪**Reticulate body:** intracellular, metabolically active → binary fission to produce more elementary bodies (uses host machinery; occurs in phagosome)	**Male:** ▪**Urinary antigen test** – which detects chlamydial DNA by PCR **Female:** ▪Flourescent Ab test (**ELISA**) on urethral or cervical secretions Culture not often used	**Males:** ▪**Urethritis** ▪**Epdidymitis** ▪**Proctiitis** (in homosexual men) ▪**Reiter's symdrome** **Females:** ▪**Urethritis** ▪**Cervicitis** ▪**Salpingitis** ▪**During pregancy → child**	**azythromycin or doxycline or tetracyline**	

STDs – "ulcerative" infections

Clinical Presentation	Test Findings	Pathogenesis	Predisposing Factors/ Epidemiology	Likely Pathogens	Definitive Diagnosis	Complications	Treatment
Patient infected with Chlamydia ▪**PAINFUL inguinal lymphadenopathy** (2-6 weeks after exposure) – most common presentation (2/3 of case = unilateral) ▪ 1/3 of men, only a few women show genital lesion (**small, PAINLESS**, usually heals in few days without scarring		**Lymphagranuloma Venereum** ▪L1-L3 immunotypes of chlamydia		**Chlaymdia trachomatis**	Male: ▪**Urinary antigen test** – which detects chlamydial DNA by PCR **Female:** ▪Flourescent Ab test (**ELISA**) on urethral or cervical secretions		**azythromycin or doxycline or tetracyline**
1st phase: ▪**Chancre** – single, indurated **PAINLESS** ulceration in genital area some 10-90 days after sexual contact (~20 days) ▪Painless enlargement of lymph nodes ▪**Males** – located on coronal sulcus or prepuce. Homosexuals – may find lesions on anus. ▪**Females** – located on labia, but chancre on cervix not uncommon ▪May also have: lesions on lips, breasts, mouth.	**Serologic:** negative during first presentation	**Syphilis = Chronic systemic infection** ▪invades via sexual contact ▪leads to **PAINLESS lesion** ▪heals spontaneously in 3-6 weeks ▪**Infects the endothelium of small blood vessels → endarteritis → especially important in third stage** ▪Late lesions (which are rare) have granulamatous appearance	Primary → Secondary syphillis is fairly common At this stage: ▪1/3 cure ▪1/3 remain latent ▪1/3 progress to tertiary syphillis	**Trepona pallidum (Syphilis)** ▪Spirochete ▪Cannot be grown in vitro ▪Not seen in gram stain	**Serological:** ▪**VDRL** – sensitive, not specific ▪**FTA** – specific There may be false positives following: mono, leprocy, hepatitis, immunizations, lyme disease	Secondary and Tertiary syphillis	**Penicillin** – long lasting **Penciillin G (IV)** for neurosyphilis **Ceftriaxone, Doxycylcine, erythromycins also work**
2nd phase (2-6 weeks after the primary lesion): ▪**flu-like illness:** headache, malaise ▪**lymphadenopathy, arthralgias** ▪**rash** (bilateral, copper-colored, **covers PALMS and SOLES)** ▪annular, pustular, or follicular lesions ▪mucusal genital lesions – broad wart like, moist, referred to as condylomata lata ▪edema (nephrotic involvement) ▪jaundice (hepatic involvement)	**Labs:** ▪nephrosis with: hyperchlosteremia, proteinuria ▪abnormal liver function tests **Serologic tests:** ▪always positive						
3rd phase: **Neurological disease:** ▪Find Argyll-Robertson pupil and Romberg sign in PE ▪hemipareris, aphasis, and seizures (from endarteritis producing infarcts aka. Meningovascular syphillis) ▪psychiatric symptoms, tabes dorsalis (loss of deep pain, prorpioception, shooting pareshesias) – Parenchymatous syphillis **Cardicvascular disease:** ▪dilated aortic root with aortic insufficiency – from endartritis damage to elastic layer Gumma disease: granulamatous like lesions (rare)	**CSF abnormal** **Aortic insufficiency**						
▪**Multiple, bilateral grouped umbilicated vesicles which become postular and coalece into large PAINFUL ulcers ("shaggy")** ▪severe painful vulvovaginits or balantis ▪with or without urthritis ▪pain, itching, dysuria with or without urethral discharge ▪tender inguinal lymphadenopathy	In 80% of females, virus recovered from uterus	▪Transmitted via sexual contact ▪Invades local cell → causes local inflammatory response ▪Spreads to other cells locally ▪**Moves aliong sensory**	▪Virus can be shed by symptomatic and asymptomatic individuals ▪Most common STD in higher socioeconomi	**Herpes Simplex Virus (1, 2)**	**Clinical:** ▪ulcerate leaving a shaggy ulcer ▪lymph node involvement **Microscopic:** ▪Wright-stained or Tzank stained: see multinucleated	Associated with primary disease: ▪**Aseptic meningitis** ▪**Transverse myelitis** ▪**Sacral radiculopathy** ▪**Can be transmitted** to newborn resulting in	**Acyclovir**

In 1/3 of patients, symptomatic complaints: ▪headache, fever, malaise, and myalgia		**nervers (Schawn cells) to ganglia** ▪Becomes latent, reactivates	c groups		giant cell in Herpes (cytopathic involvement) Serology: ▪Rise in anitbody titers Rule out syphilis, chancroid, LGV.	serious organ damage	
▪After 2-5 days **SOLITARY macule (papule) appears, develops into pustule, then becomes a PAINFUL ulcer** → sharply circumscibed with minimal inflammation that bleeds easily ▪**Regional lyphadenopathy develops**. In some patients they may become so big that they rupture.			▪Infrequent in New York ▪Frequent in Africa and in developing countries	**Hemophilus ducreyi** ▪small gram negative rod ▪difficult to culture	Culture ▪need special chocolate agar supplemented with calf serum	Major risk factor for HIV infection	Many strains carry plasmin-mediated penicillinase **Therefore give: beta-lactamase stable beta-lactam (ceftriaxone) or floroquinolone (ciprofloxacin)** **Erythromycin also works.**

Respiratory Infections

Clinical Presentation	Test Findings	Pathogenesis	Predisposing Factors/ Epidemiology	Likely Pathogens	Definitive Diagnosis	Complications	Treatment	Prevention
▪**Sore throat** ▪Inflammation ▪Exudates ▪Fever ▪Leukocytosis ▪Tender cervical lymph nodes **May extend to:** ▪Otitis ▪Sinusitis ▪Mastoiditis ▪Meningitis **Sometimes presents with:** ▪Scarlet fever **Sometimes after pharyringits goes away:** ▪Fever ▪Migrating polyarthritis ▪carditis		**Pharyngitis** **Pyogenic inflammation via:** ▪**M protein** – interferes with phagocystosis (KO: results in avirulent strain). Mediates type specific immunity. Adherence factor. Some types cause rheumatic fever. ▪**Preotein F1** and **lipoteichoic acid** – mediates GAS binding to fibronectin on endothelial cells ▪**Protein G** – binds FC portion of IgG ▪**Hyaluronic capsule** – interferes with phagocytosis ▪**Surface proteins** – attachment ▪**Enzymes**: hyaluronidase, DNAse, Stretokinase **Toxin mediated:** ▪**Streptolysin O** (exotoxins SPE, A, B, C in syllabus) → antigenic → ASO antibody → rheumatic fever. Also responsible for hemolysis on blood agar plates. ▪**Erythrogenic toxin** – superantigen → scarlet fever ▪**Pyrogenic exotoxin A** → causes toxic shock syndrome	**Exposure:** Droplets produced by sneezing or coughing, direct contact with secretions **Host:** Children especially, ages 5-15 Asymptomatic carriage in nares, pharynx	**Streptococcus pyogenes (Group A)**	**Microbiologic** ▪Gram-positive, cocci ▪Swabs from cultured on blood agar: **Beta-hemolysis** in 18-48 hours ▪If **inhibited by bacitracin disk,** likely to be Group A strep ▪**Rapid test:** bacterial antigens – ready in 10 minutes **Serologic:** ▪Elevated ASO titer in patients suspected to have rheumatic fever	**Rheumatic Fever** **Acute Glomerulonephritis (rarer) → more likely with skin infections**	**Penicillin** (all group A strep are sensitive) **In penicillin allergic: erythromycin**	**Rheumatic fever can be prevented with prompt treatment of pharyngitis** **No vaccines**
Sudden onset: ▪Fever ▪Chills ▪Pleuritic chest pain ▪**Cough with rusty colored sputum** **May extend to:** ▪Otitis ▪Sinusitis ▪Bronchitis ▪Sepsis ▪Arthritis ▪Endocarditis	**Chest X-ray:** ▪**Lobar infiltrate** **Blood tests:** ▪Bacteremia (up to 1/3 of time)	**"Typical" Pnuemonia** **Virulence:** ▪**Polysaccharide capsule** ▪Cell wall **peptidoglycan** → inflammatory response ▪**Adherence** – increased quantities of phosphoryl choline → more binding to nasopharyngeal cells ▪**IgA protease** **Aspiration** → allows infection to occur (not hematogeneous spread) Once in alveoli: ▪Adhere to Type II alveolar cells ▪**Evade phagocytosis** (b/c of capsule) → infection persists ▪**Inflammation (from peptidoglycan) → fluid consolidation** ▪**Resolution** occurs only with type specific antibody production	**Exposure:** ▪respiratory droplets **Host** ▪20-40% of children colonized at any one time ▪**Infection occurs at extremes of age** ▪**Defects in humoral immunity** predispose (including sickle cell) ▪**Splenectomy** ▪**Factors that decrease respiratory clearance** predispose (ex. smoke)	**Streptococcus pneumonia**	**Microbiologic:** ▪Sputum sample ▪Gram-stain – predominant organisms – **gram positive cocci** ▪Blood agar culture: **alpha-hemolysis** ▪**Inhibited by optochin disks**	Bacteremia related complications	**Penicillin** About 25% resistant, therefore for these use **Vancomycin** **Penicillin allergic patients: erthryomycin**	**Polysaccharide vaccine –** polyvalent to 23 types – 5 years of protection
Age group: **Children (5-9 y.o), young adults** **Symptoms:** **Low grade fever**, headache, **dry non-productive cough**, sore throat general malaise. Mild upper respiratory tract illness (cold in young children)	**Chest X-ray:** **Bilateral infiltrates. Appears worse than the patient looks clinically**.	**"Atypical" Pneumonia** **PI protein** – attachment to sialic receptors of the respiratory epithelium and to red blood cells. **Extracellular** – interacts with cilia of the respiratory tract **causing both the cilia and epithelia to be destroyed** → loss of normal airway clearance → contamination of airway with microbes → chronic cough **Superantigen** → stimulation of	**Living in close quarters:** Infection is spread in droplets. Cause of 50% of pneumonia's in college age kids. **Incubation period:** 2-3 weeks **Shedding:** 2-8 days prior to developing symptoms	**Mycoplasm pnumoniae**	**Lab Confirmation**: **Serology or PCR based** – **Cold agglutinins** (IgM Ab's that bind to the I antigen of the red blood cells) → positive 65% of time.	**otis media, erythema multiforma** (red and white patchy rash often on hands), hemolytic anemia, **myocarditis, pericarditis, neurological abnormalities**	**Erythromycin or tetracylcin.** **Resistant to "cell wall" antibiotics such as penicillins, cephlasporings, vancomycin and others.**	Prevention is difficult since spread by droplets. Isolation isn't feasible. No vaccine.

Lower tract infection more common in young adults (walking pneumonia). **PE:** **Mild fine inspiratory rales**		PMN's and Mac's to release → TNF, IL-1, IL-6 **Immunity** – local and systemic. IgA appears early and disappears by 4 weeks, IgG at 3-4 weeks.						
Age group: **Neonate** (1-3 months old – usually 6 weeks) **Symptoms:** **Staccato-like cough** (very sharp), **rapid respiratory rate, and do not have fever**. **PE:** **Wheezing is rarely heard.**	**Chest X-ray:** **Hyperinflation and diffuse infiltrates** on chest radiographs. See **"perivascular cuffing."** **Blood test:** Peripheral **eiosinophelia.**	**"Atypical Pneumonia"** Intracellular (two phase life cycle) - infects non-ciliated epithelial cells in respiratory tract. Symptoms due to host response - infiltrate. Immunity is not long lasting.	**Mother: lack of prenatal care and the possibility that she carried a chlamydial infection.**	**Chlamydia tracomatis**	**Detection depends on serology or antigen tests (DFA, ELISA) and PCR.** IgM Ab test for C. trachomatis with titer >1:32 is strongly suggestive. Organisms not readily cultured. Culture or non-culture tests of the nasopharynx (non-culture tests have a lower sensitivity and may yield negative results).		**Erythromycin.**	**Eye drops may prevent conjunctivitis but not pneumonia.** No vaccine.
Age group: **School age to young adult** **Symptoms:** Non-specific upper respiratory tract infection such as **rhinnorea or sore throat progressing to chronic cough that may persist for weeks** despite appropriate antibiotic therapy. **Patient usually afebrile.**	**Chest X-ray:** **Often show lobar consolidation but also may be diffuse interstitial pattern, or with bilateral involvement with pleural effusions and lymphadenopathy.** **Blood test:** **Normal WBC count.**	**"Atypical Pneumonia"** intracellular (two phase life cycle) - infects non-ciliated epithelial cells in respiratory tract. Symptoms due to host response - infiltrate. Immunity is not long lasting.	**Incubation period:** ~3 weeks **28% of school aged pneumonias** **<10% of adult outpatient cases of pneumonia.**	**Chlamydia pneumonia (TWAR strain responsible for disease)**	**Serologic or antigen tests, PCR** IgM (in 4 weeks), IgG (in 6 weeks)	Atherosclerosis?	**Azitrhomycin or clarithromycin**	No vaccine.
Age group: **Older than 55 y.o**. **Symptoms**: **High fever**, **non-productive cough, chills, diarrhea, abdominal pain, nausea, mental confusion or delirium**.	**Chest X-ray:** **Multilobular with microabcesses.** **Blood test:** **High WBC count** (10,000-20,000) with a left shift. Liver and renal function may be affected.	**"Atypical Pneumonia"** **Bacillus** is inhaled and **multiplies within mac's and monocytes in alveoli**. **Binds complement receptor** → enters cells via endocytosis **Prevention of phagosome-lysosome fusion** → promotes survival Bacilli proliferate, produce → several enzymes which kills cell when vacuole is lysed. **CMI response needed**.	**Incubation period:** ~10 days **Abrupt onset.** **Immuno/Pulmonary compromised represent greatest risk** **Occupational exposure: Construction, working in moist environments and water systems** 15-20% mortality	**Legionella** (small gram (-) rod)	**Serology – most often used**. Ab titer (1:128 greater = +) **DFA** → rapid (70% sensitive) **Culture:** special, buffered charcoal-yeast extract agar. Ag detection (urine test) for detection of serogroup 1 only.		**Macrolide antibiotic (azithromycin, erythromycin) or levoflaoxaxin (a quinilone).**	**Hyperchlorination and super-heating to eliminate from water supply.**
Age group: **Children under 1 year of age (unvaccinated) or in adults with waning immunity.** **1st stage:**	During 2nd Stage: **Blood tests** → reveal **leukocytosis**	**"Whooping Cough"** Disease caused by **toxins** 1 **Binding and uptake by phagocytic cells:** **Attaches to CILIATED epithelial cells via action of pertussis toxin**	**Declined after vaccine in 1949.** **Incubation period:** 7-10 days Habitat = human resp. tract	**Bordetella pertussis** (small gram (-) rod)	Gram-stain **Special culture – Bordet-Gengou agar**		**Succeptible to erythromycin, however, this only decreases communicability, not course of infection**.	**Whole-cell inactivated vaccines and multivalent acellular vaccines (DPT).**

Common cold symptoms: rhinnorhea, sneezing, malaise, anorexia, low-grade fever. (Children slightly irritable). **2nd stage: (1-2 weeks later) cough then "whoops". "paroxysmal coughing"** Vomiting after coughs is common. Baby may turn blue. **3rd stage:** (after 2-4 weeks) **cough subsides however complications are present such as: pneumonia** (often due to other organisms), seizures, and encephalopathy.		and **filamentous hemagglutinin** **Pertussis toxin** – A subunit contains toxic subunit (S1); B subunit helps bind (S2 to resp. epi; S3 to phagocytes). **Filamentous hemaglutinin** – binds to resp. epi and PMN's and facilitates uptake Pili and pertactin – also help **<u>2 Toxin role in disease</u>** **Pertussis toxin** – S1 portion phosphorylates ADP for surface G protein → **cAMP levels unregulated → increased resp. secretions** **Adenylate cylcase/hemolysin toxin** – converts ATP → cAMP. **Also inhibits leukocyte chemotaxis, phagocytosis, and killing.** **Heat labile toxin** – local tissue destruction **Tracheal cytotoxin** – destroys ciliated epithelial cells; stimulates IL-1 secretion **Lipid A and X = LPS** → complement activation and complement release					Treatment is usually supportive.	

Rickettsial Diseases

Clinical Presentation	Test Findings	Pathogenesis	Predisposing Factors/ Epidemiology	Likely Pathogens	Definitive Diagnosis	Complications	Treatment
Symptoms: **Sudden onset of fever, headache, malaise, and myalgia**. **Rash** with three stages: ▪ **erythmatous macule** – blanches on pressure ▪ **macular popular** – a result of fluid leakage from infected blood vessels ▪ **hemorrhage** – into center with frank petichiae **Rash initially appears on wrists, ankles, soles, and palms → spreads to trunk (centripetal rash)**		**Rocky Mountain Spotted Fever** ▪ **Vector bites and feeds** ▪ **Regurgitates bacteria** into skin bite site ▪ Bacteria carried via lymph to small blood vessels where they invade endothelial cells ▪ Speads to contigous endothelial cells, smooth muscle cells, and phagocytes ▪ **Causes vasculitis** ▪ Eventually spread to other organ systems No toxins or virulence factors identified.	**Season:** **May-Sept** **Vector: tick** **Endemic regions:** **South Atlantic** and **South Pacific states** (Not Rocky Mountains!) **Incubation period:** 7-14 days	**Ricketssia rickettssi** **Obligate intracellular parasite. Not seen well on gram stain smear.**	**Skin biopsy** **PCR** **Serologies** – ELISA, latex agglutination	**GI disturbances, hepatomegaly, and jaundice can occur in later stages.**	Doxycycline
Symptoms: An **eschar** (initial localized red skin bump (papule)) forms the bite site. The **eschar turns into blister (vesicle),** Around **5th day** of illness, **a papular-vesicular rash** (similar to chicken pox) with fever, headache, lymphadenopathy, chills, myalgia forms.		**Rickettsial Pox** Same as above	**Vector: mite** on house **mice**	**Ricketssia akari** Self-limiting infection.	Many serologies cross react with RMSF **Clinical diagnosis**		**Doxycylcine or tetracycline**
Similar symptoms to RMSF except rash only 30% of time. **Don't see vasculitis.** **Can be severe:** ARDS, septic shock like picture, rhabdomyalsis, neurologic sequelae.	**Labs:** **Leukopenia** (which is rare for RMSF) **Thrombocytopenia** **Elevated LFT.** **Microscopy:** **Morula (clustered) appearance in host cells**	**Human Ganulocytic Ehrlichiosis (HGE)** Same as above	**Vectors:** **Ixodes ticks** **Resevoirs:** White footed **mouse, chipmunks** **Season:** **Year round**, peak in July and Nov. **Geographic:** **Northeast**	**Anaplasma phagocytophilum (Ehrlichia)** Small obligate intracellular, gram (-)	**Clinical**		**Doxycycline or tetracylcine**
Similar symptoms to RMSF except rash is rare. Don't see vasculitis.	**Labs:** **Leukopenia** (which is rare for RMSF) Thrombocytopenia Elevated LFT. **Microscopy:** **Morula (clustered) appearance in host cells**	Human Monocytic Ehrlichiosis (HME) Same as above	**Vectors:** **Lone star tick** **Resvoir:** **Dog** **Seasons:** **May-July** **Geographic:** **Southeastern and Central US**	**Amblyomma americanum (Ehrilichia)** Small obligate intracellular, gram (-)	**Clinical**		**Doxycycline or tetracylcine**
Early localized stage: ▪ **Erythema migrans** **Early disseminated:** ▪ **Mutliple smaller erythema**		**Lyme Disease** Same as a above	Vector: Ixodes ticks (nymphs) Resevoirs: White-footed mouse, white	**Borrelia burgdorferi** Spirochete **similar to syphilis.**	**Clinical** **PCR** **Serologic – ELISA** followed by Western Blot		**Local stage:** **Doxycycline** **Disseminated:** **IV w/ ceftriaxone**

migrans ▪ **Cardiac** – heart block, myocarditis, mypericarditis ▪ **Muscoskeletal** – generalized joint pain, joint effusion (esp in knee) ▪ **Neurological** – meningitis, Bell's palsy, peripheral neuropathy, encephalitis (ext. rare) **Chronic disseminated (10% of untreated patients - months to years after bite):** ▪ Chronic destructive arthritis ▪ End stage cardiomyopathy ▪ Stroke, menigoencephalities, dementia ▪ acrodematitis			tailed dear, cattle horses, dogs				**Treatment of seropositive asymptomatic patients is not indicated**
High fever, chills, headaches, muscle aches. **Resolves after 3-6 days.** **Afebrile for 8 days, relapses again.**		**<u>Relapsing Fever</u>** Antigenic variation Otherwise same as above	**<u>Vector:</u>** **Body louse (soft tick)** **Western U.S., sleeping campers** **<u>Resevoirs</u>: chipmunk, squirrel, rabbit, rat, rodent**	**Borrelia recurrentis**			**Doxycycline, erthromycine**