Organism	Classification (Gm + Metabolism)	Human Pathology and Natural History	Specialized Virulence	Diagnosis and Notes	Treatment Vaccination
GRAM-NEGATIVE BACILLI : THE ENTEROBACTERIACEAE causing NON-ENTERIC DISEASE					
General Characteristics Facultative anaerobes Most are introduced into the GI tract at birth They are the major organisms until outcompetition by obligate (strict) anaerobes Somatic O Ag (LPS) This is a prominent ENDOTOXIN → (bacterial lysis and Ag exposure) → activation of complement → massive release of IL-1 and TNF Gm +ve bacteria do not have ENDOTOXIN (LPS) Gm –ve bacteria also produce EXOTOXIN Flagellar H Ag (some, with flagella) Capsular K Ag (most) Type 1 Pili PAP (uropathogenic strains) Siderophores					
Uropathogenic *Escherichia coli* **(UPEC)**	Gm neg *facultative* anaerobes (thus, **aerobic**) All are NF of the GI tract	Cystitis (bladder infection) Ascending UTI **Urosepsis** in elderly patients	**Pyelonephritis-asscociated pili (PAP)** Bind to host Gal-Gal in the renal pelvic epithelium (P group antigen) **Formation of biofilms** on urinary catheters and other foreign bodies		
Proteus		*P. mirabilis* causes community-acquired ascending UTIs Other species cause nosocomial infection	**Urease** Hydrolyzes urea → CO2 + NH3. This causes alkalinization of the urine and precipitation of struvite calculi → UT ibstruction		
Providincia		Noscomial UTI in catheterized patients			
Neonatal meningitis *Escherichia coli* **(NMEC)**		**Bacterial Neonatal Meningitis** Hematogenous dissemination into the CSF after oropharyngeal uptake of normal maternal vaginal flora. No maternal antibody protection	**K1 Capsule Antigen** Polysaccharide is an repeating oligomer of sialic acid. Conceals surface antigens, low immunogenicity → not opsonized by anticapsule Ab		

Klebsiella pneumonia		**Bacterial pneumonia** Causes necrotizing hemorrhagic lung abscesses. Characteristic currant-jelly sputum. *Typically in a background of decreased pulmonary function*	**Polysaccharide Capsule** α-phagocytic function	Mucoid colonies (capsule) Ferments lactose	
Serratia		**Nosocomial pneumonia** (typically opportunistic infection)			

GRAM-NEGATIVE MICROBES causing ENTERIC DISEASE

General Characteristics
Transmission of all pathogens can occur via the fecal/oral route
Minimal infective incoculum is determined by sensitivity to gastric HCl
Cyototoxic gastroenteritis (e.g. hemorrhagic colitis) should not be confused with dysentery

Dysetery is caused by deep invasion
EIEC, Shigella, Campylobacter (late dysentery)
Mucosal colonization and destruction results in simple gastroenteritis (bloodless diarrhea + fever)
EPEC, Campylobacter (early simple gastroenteritis)

Enteric fever is rare, and typically associated with *S. typhi*
Also *Campylobacter, Yersinia, non-cholera Vibrio*

Reactive arthritis is aseptic, and follows enteric and UT infection
Salmonella, Shigella, Campylobacter, Yersinia

Enterotoxigenic *Escherichia coli* **(ETEC)**	Gm neg *facultative* anaerobes (thus, **aerobic**)	**Secretory Diarrhea** Produces cholera-like toxins that are heat-stable and labile (ST and LT). Encoded by plasmids Profuse diarrhea without fever "Travel's Diarrhea"	**ST and LT** cholera-like toxins Plasma-coded **colonization factors**	ETEC and EPEC are endemic among humans	
Enteropathogenic *Escherichia coli* **(EPEC)**		**Necrotizing gastroenteritis** The pathogen causes destruction of the mucosal epithelium of the small bowel Non-bloody diarrhea + fever			Infantile diarrhea in underdeveloped countries

Enterohemorrhagic *Escherichia coli* **(EHEC)**		**Hemorrhagic Colitis** Requires a very small inoculums (<100 organisms) Shiga-like verotoxins Bloody diarrhea + severe abdominal pain **Hemolytic Uremia Syndrome (HUS)** Intravasation of the veratoxin → thrombotic microangiopathy, *hemolytic anemia*, thrombocytopenia (secondary to diathesis), *renal lesions* due to direct cytotoxicity	**Veratoxin**	EHEC is found in cow intestines (main reservoir) but can be undergo horizontal transmission	
Salmonella typhi	**Simple Gastroenteritis** Similar to infection due to EPEC. Characteristic rotten egg odor of stool sdue to bacterial SH metabolites. **Bacteremia** *Invasion* through submucosa → *phagocytosis* by macrophages → intracellular *replication* →transport of pathogen load to mesenteric lymph nodes → *hematogenous dissemination* → colonization of reticuloendothelial system → colonization of *gallbladder* → *reinfection* of small bowel though the bile duct **Enteric Fever** Multifocal disease (splenic abscesses + osteomylitis + atheroma infection) Conversion to carrier state (constant pool in gallbladder) **Reactive Arthritis**		Sensitive to gastric acid Requires large inoculum *Salmonella* selectively incubates in eggs and poultry **Dx** Stool culture is negative < 2 wks BUT blood cultures positive < 1 wk	
Shigella	**Dysentery > Gastroenteritis** Necrosis of the colonic mucosa, largely inflicted by deep invasion and cytotoxicoty of the *shiga* toxin (Similar to EIEC + EHEC) **Reactive Arthritis**		*Shigella* does not have an animal reservoir Is highly resistant to gastic acid: small incoculum (<100 cells) sufficient for infection	
Campylobacter jejuni	**Early gastroenteritis + Late dysentery** Early disease is due to mucosal colonization and destruction (similar to EPEC) Late dysentery is due to submucosal invasion (similar to EIEC) **Reactive Arthritis** **Enteric Fever**	Polar flagella	*Campylobacter* is found in raw poultry and unpasteurized milk Requires large inoculum	

			Dx Characteristic darting motility	
Yersinia enterocolitica	**Evolving Gastroenteritis** Progresses to terminal ileitis, mesenteric lymphadenopathy, and finally pseudoappendicitis **Reactive Arthritis** **Enteric Fever** No bacteremia These organisms are distinct from *Y. pestis*		*Yersnia* is endemic to domestic livestock	
Vibrio cholerae	**Gastroenteritis** Secretory diarrhea (similar to ETEC)	Colonization of the small bowel mucosa and secretion of the cholera toxin →	*Vibro* infection requires a massive inoculum. Thus, it requires a highly contaminated water source	IV rehydration is necessary and sufficient
Vibrio vunificans	**Gastroenteritis** **Enteric Fever** **Reactive Arthritis**		Reservoir is shellfish and salt water bodies	Seen in alcoholism and background of immunosuppression
Vibrio parahemolyticus	**Bullous Lesion in Wound Infection** **Sepsis** 50% mortality **Reactive Arthritis**			
Helicobacter pylori	Gastritis Dastric + duodenal ulcers Gastric neoplasma, MALT lymphoma	Tropism for the mucosal slime layer (lower acidity and proximity to host cells) Urease: alkalinization		2 antibiotics + PPI (direct bacteriocidal activity; add only with positive Dx) Do not use H2 antagonists or antacids

GRAM-POSITIVE COCCI

General Principles of Diagnosis and Classification

Staph is catalase +ve

S. aureus is coagulase +ve. The coagulase +ve organisms include *S. epidermdis*

Strep is catalase –ve

Antibiotic Resistance

Staph aureus resistant to methecillin and β-lactams

Pneumoccocus is exhibiting increasing frequency of resistance to PCN

Enteroccocus can be resistant to vancomycin (CRE) and ampicillin (VAREC)

Hemolysis

α-hemolytic: green radius on agar. *Strep pneumonia, viridans,* **and** *enterococcus*

Differentiate *pneumonia* from *viridans* and *Group D* via **optochin** test (+ve)

S. pneumoniae is also soluble in bile

β-hemolytic*:* lucent radius. *Strep pyogenesl* (Group A) **and** *agalacticae* (Group B) + Groups C, F, G

Differentiate *pyogenes* from *agalacticae* via **bacitracin** (+ve, susceptible)

Use the Lancefield **groupings**, followed by **typings**

γ-hemolyitc: *Strep viridans* **and** *enterococcus*

Differentiate *viridans* from *Group D* via **Bile Esculin** (-ve growth), **6.5% saline** (-ve growth), and **PYR** (susceptible)

Group A and B strep are β hemolytic

Strep pneumonia is purely α-hemolytic

Strep viridans is mixed α + γ

Enterococcus is also mixed α + γ

Staphylococcus aureus	Gm Pos facultative anaerobe	Commensal colonization of anterior nares, skin, and mucosa **Cutaneous abscess** The most frequently seen lesion **Impetigo** Localized cutaneous infection in face and limbs of pediatric patients. Forms crusting abscesses. **Folliculitis** Typically self-limiting **Furunculitis** Involvement of the skin and subcutaneous soft tissue; formation of a boil. **Carbuncles** Coalescence of furncles and further extension of infection into deep soft tissue. May erode into cutaneous vessels and lead to bacteremia. **Mastitis** Transferof *S. aureus* to the mother during breastfeeding after nosocomial infection of infant **Enterotoxicity** Typically self-limiting disease. Bacterial grow at room temperature and produce a heat-stable toxin.	**Techoic Acid** Binds to fibronectin and is involved in mucosal attachment **Protein A** Finds to Fc IgG and inhibits humoral immunity (coating of capsule by antibody) **α – γ cytotoxins** Cause damage to the plasma membrane; cause generalized necrosis **PV leukocidal toxin** Highly associated with community-acquired MRSA **Exfoliative toxin** Disrupts the adhesion zone within the stratum granulosum, leading to desquamation and SSS **Heat-stable enterotoxins** Cause a transient gastroenteritis **Toxic Shock Syndrome Toxin (TSST-1)** Massive indiscriminate activation of T cells via superantigens → release of cytokines → increased vascular permeability →	**Treatment** Methacillin Oral Dicloxacillin Vancomycin (use with MRSA) Linezolid (MRSA pneumonia) Penicillin (use in strains that are susceptible; < 10%) Clindamycin (if allergic to penicillin) Penicillinase → resistance to penicillin (most strains) *mec* gene → MRSA Encodes the altered methicillin binding protein *vanA* → Vancomycin-resistance

		Toxic Shock Syndrome (TSS) Associated with tampon use and surgical insulation. TSST-1 toxin is only produced by 1% of all staph. Fever + diffuse erythema + hypotension + desquamation **Scalded Skin Syndrome (SSS)** Triggerd by exfoliative toxin. Abrupt erythema and desquamation. Usually seen in infants and pediatric patients. **Bacteremia + Endocarditis** Valvular colonization occurs after prolonged bacteremia. Formation of vegetations. **Pneumonia** Co-morbid with bacteremia and endocarditis. Risk groups include patients with CD, COPD, or who are elderly. **Osteomyelitis** Hematogenous seeding into the bone. **Septic Arthritis**	hypovolemia **Coagulase** Proteolysis of fibrinogen → fibrin. Forms a fibrin plug around bacterium, inhibiting phagocytosis **Catalase** Neutrlaizes h202 **Hyaluronidase** Allows invasion and spread through tissue **Dx** Gm + cocci in clusters Mostly β-hemolytic, but hemolysis is not used in diagnosis Growth on mannitol salt agar Ferments mannitol (color change in media) Catalase +ve (degredation of H202) Differentiate staph from strep Coagulse +ve (clots plasma) Normal flora in anterior nares, skin, muscosa. Horizontal transmission.	
Staphylococcus epidermidis and other coagulase-negative staph		Commensal colonization of the skin and mucosa **Endocarditis** Adhesion to prosthetic valves; inoculation occurs during placement. **Catheter Infection** Causes prolonged bacteremia and increases risk of endocarditic. **Joint Prosthesis Infection** Localized pain and eventual prosthetic failure. **Post-Surgical Infection** THIS IS THE LEADING CAUSE OF NOSOCOMIAL INFECTION!	**Adherence to foreign bodies** **Formation of Biofilms** Increases adhesion, blocks antimicrobial therapy and host immune cells **Dx** Gm +ve cocci in clusters γ-hemolytic Growth of mannitol salt agar Does not ferment mannitol (no color change) Catalase +ve Coagulase –ve	Typically resistant to β-lactams, TMP, clindamycin, and macrolides. **Treatment** Vancomycin (firstline), linezolid, or daptomycin Remove infective source

Staphylococcus saprophyticus		NF around urethra **UTI** in sexually active females		
Streptococcus pyogenes		Colonization of the skin and upper respiratory tract (nasal and pharyngeal mucosa) **NOT** considered NF! **Supperative Disease** **Streptococcal Pharyngitis** **Exotoxic Fever** Occurs with lysogenic transformation of infecting strain by bacterophage and upregulated secretion of exotoxin. Pharyngitis is followed by a diffuse erythematous rash and strawberry tongue. **Impetigo** Colonization of skin and trauma introduces the organism into the dermis. Formation of purulent vesicles, rupture, and crusting. Can occur in superinfection with *Staph.* **Erysipelas** Well-delineated areas of erythema and edema. Spreads with time. Usually affects the lower limbs. **Cellulitis** Infection of skin and superficial fascia. Distinguished from erysipelas by poorly defined margins. **Necrotizing Fasciitis** Deep infection and liquifactive necrosis of tissue along the investing fascial planes. **Streptococcal Toxic Shock Syndrome (Strep TSS)** Occurs universally with strep bacteremia and necrotizing fasciitis. Control requires debridement of amputation. Incited by streptococcal purogenic exotoxin (superantigen). **Non-Supperative Disease** **Acute Rheumatic Fever (ARF)** Cross-reactivity of antibodies against *S. pyogenes*. Seen in Group A strep infections, predominantly in M types. Associated	**Lipteichoic Acid + Protein F** Binding to epithelial cells via fibronectin (similar to techoic acid) **M protein** Cell wall antigen involved in increased adherence and α-phagocytosis. Isolated in strains causing ARF and PSGN. **Capsule** Hyaluronic acid; α-phagocytic function **Streptococcal Pyrogenic Exotoxin** Causes exotoxic fever. Superantigen mechanism can also cause strep TSS. **Hemolysin** Streptolysin O and S. Lysis of all formed elements. Confer β-hemolytic properties. Streptolysin O used in the ASO antibody detection test for recent infections. **Streptokinase** **Hyaluronidase** **Dx** Gm+ve cocci in chains ASO test → rheumatic fever due to prior infection Rapid strep test: agglutination of pharyngeal swab with group Abs β-*hemolysis* **Catalase –ve** **Bacitracin +ve** (sensitive) Agglutination of Group A antisera *Confirmation via PYR and serology* PYR positive LPAse hydrolyzes PYR, causing a color	Extremely susceptible to penicillin. Erythromycin if allergic

		with strep pharyngitis. Affects valves + subcutaneous CT. Untreated ARF develops into chronic rheumatic valvulopathy. **Post-Streptococcal Glomerulonephritis (PSGN)** This is a Type II hypersensitivity reaction. Ag-Ab complexes are deposited in the basal laminae of glomeruli. Seen with nephritogenic strains of M-type Group A strep. Associated with pharyngitis + cutaneous lesions.	change ASO test Detect Abs against streptolysin O Analyze acute and convalescent titers for recent infection and ARF	
Streptococcus agalacticae		Asymptomatic colonization of GU tract **Neonatal Bacteremia, Pneumonia, and Meningitis** Mutli-systemic with fever, RDS, and sepsis. Vertical transmission during delivery. Leading cause of neonatal meningitis **Pospartum Maternal Infection** Asymptomatic residence in the GU and lower GI tracts.	**Capsule** α-phagocytic function Inhibition of complement **Dx** Gm+ve coci in chains *ß-hemolysis* Catalase w–ve Agglutination in Group B antiserum	Same Tx and Group A Severe infections: use β-lactam + aminoglycoside Chemoprophylaxis > 4 hrs before delivery Screen for organism during third trimester
*Streptococcus pneumonia (*also, *pneumococcus)*		Colonization of the nasopharynx and oropharynx Active disease requires susceptible host (e.g. post-viral infection) **Acute Otitis Media (AOM)** **Sinusitis** Leading cause. Involves sinus outflow obstruction and replication **Community-Acquired Pneumonia** Leading cause of CAP. Presentation: fever + hemoptysis. Lobar lung consolidation. **Bacteremia** Hematogenous spread from the nasopharynx, ear, lungs, and sinuses. **Systemic Inflammatory Response Syndrome (SIRS)** Progresses to lobar pneumonia and respiratory failure, or meningitis and increased ICP **Meningitis** Among the three leading causes.	**Capsular Polysaccharide** Inhibits opsonization by complement (C3b) → inhibit phagocytosis. Can incites an excessive inflammatory response → septic shock. Encoded by plasmid The capsule is highly immunogenic and elicits a massive inflammatory response **Altered Penicillin Binding Protein (PBP)** (Major host defense is opsonophagoytosis via IgG) **Dx** Gm –ve diplococcic with capsular lucency Lancet or ellipsoid morphology α-hemolyic mucoid pattern Capnophile Catalase –ve	Amoxicillin: AOM and sinusitis Macrolides, Cephalasoprins, Flouroquinolone: CAP Vancomycin + cephtriaxone + dexamethasone: meningitis PCN is not effective in sepsis, AOM, and meningitis! **Vaccine** *Adults (Pneumovax):* Multivalent (23 serotypes) vaccine with polysaccharide Ag *Peds (PCV)*: Heptavalent protein conjugate vaccine Immunize all infants < 1 yr + equivalent population for

		RFs: age, SCD, splenectomy, hypogammaglobulinemia (secondary to myeloma or nephritic syndrome), CSF fistulae, cochlear implants, post-viral infection	Optochin +ve *and* Bile-soluble Differentiate form other α-hemolytics (Group D and viridans) Urine culture for pneumonia and sepsis	influenza vaccine + post-splenectomy
Enterococcus faecalis + faecium		NF of the GI and GU tract (females) **Community-Acquired** Endocarditis UTI **Nosocomial** UTI Bacteremia Surgical Wound Abscess **RFs:** Intravascular catheter, prolonged hospitalization, broad spectrum antibiotics, age > 60, underlying disease	No major virulence factors. Disease is caused by anchoring to host epithelium (**adhesins**), outcompetition of commensal flora (**bacteriocins**), and **antibiotic resistance** (VRE) **Dx** Gm+ve cocci in isolation, pairs, and chains Mixed α + γ hemolytic Catalase –ve Growth in 40% bile + hydrolyzes esculine Growth in 6.5% saline Sensitive to PYR (+ve)	**Treatment** Ampicillin Penicillin + gentamicin Vancomycion **VRE**: linezolid, daptomycin Restrict broad-spectrum antibiotics
Streptococcus viridans		**Dental Caries** **Subacute Bacterial Endocarditis** **Occult colonic malignancy**	Catalase –ve Mixed α + γ hemolytic Optochin –ve (resistant) Insoluble in bile (-ve)	
GRAM-NEGATIVE MICROBES causing RESPIRATORY DISEASE				
Neisseria meningitides	Gm –ve diplococcus	Transient colonization of nasopharynx (10% carrier frequency) **Meningococcal Sepsis** DIC, gangrene, adrenal insufficiency **Meningitis** Cranial nerve defects (particular sensorineural hearing loss), neurologic deficits Host defense is acquired AMI This is protective against invasive disease, NOT asymptomatic nasopharyngeal colonization Immunity is transiently conferred to neonates via maternal	**Pili** Binding of bacterium to nonciliated epithelial cells of the nasopharynx **LOS + Peptidoglycan** Cause direct injury to host mucosa and are involved in intravasation **Polysaccharide Capsule** Antiphagocytic **Immune Evasion via Antigenic AND Phase Variation** Pilin and Opa undergo significant recombination (antigenic variation) and expression patterns (phase variation)	PCN or cephalosporin is sufficient However, **initial TX** is *broad-spectrum therapy* until identification **Prophylactic therapy** with rifampin, FQ, or cephalosporin TX shock with IV fluid, glucocorticoid replacement, anticoagulation, ventilation,

		antibodies **RFs:** immunoglobulin deficiency, terminal complement complex (C5 – C9, MAC) deficiency, asplenia (splenectomy or SCD), no prior exposure, densely populated conditions, sub-Saharan meningitis belt	**DNA avidity and turnover** Rapid release and uptake allows for sudden spread of virulence **Iron Acquisition** Occurs via surface proteins that sequester transferrin and lactoferrin (do not use siderophores) **Dx** Gm –ve diplococcus	vasopressors **Vaccines** MCV4: A quadravelent conjugate vaccine containing 4 capsular polysaccharides fused to the diphtheria toxoid Vaccinate peds patients > 2 years with RF for infection + ALL at 12 years A, C, Y, W-135 strains Disease virtually eliminated in vaccinated populations NO VACCINE against serogroup B! *Has same non-immunogenic capsule (sialic acid) as KI NMEC*
Haemophilus influenza Type B encapsulated	Gm-ve coccobacillus	Cause of most morbidity before development of HiB conjugate vaccine **Sepsis** **Meningitis** **Buccal, Periorbital, and Orbital Cellulitis** **Epiglottitis**	**Polysaccharide Capsule** Anti-phagocytic activity (type B) Primary host defense is humoral immunity Requires Factor X and Factor V in erythrocytes Grows on chocolate agar + lysed RBCs	
Haemophilus influenza Non-encapsulated and Non-typable (NTHi)		**Noninvasive mucosal syndromes near portal of entry** **Sinusitis** **Conjunctivitis** **AOM** **Bronchitis** **Pneumonia** After *S. pneumoniae*, a prominent cause of CAP **Chioamnionitis** **Postpartum Maternal Sepsis**	Same growth requirements as Type B	

		Neonatal Infections **Penumonia, Sepsis, Meningitis**		
Moraxella catarrhalis	Gm-ve diplococcus	Asymptomatic colonization of the nasopharynx **URI in pediatric patients** Sinusitis + AOM, after pneumococcus and NHTi **Bronchitis + Pneumonia** RF: viral URI, COPD **Sepsis + Meningitis** RF: immunocompromise (CF, neutropenia, SLE, leukemia) **Nosocomial Infection** In pediatric ICUs		
Bordetella pertussis	Gm-ve coccobacillus	**Mucosal infection upper respiratory tract without invasion** **Catarrhal** Organism is culture + ve from swab. Susceptible to antibiotic therapy. Fever, coughing, malaise 1 – 2 weeks **Toxemic, Paroxysmal** Effects triggered by Tracheal Cytotoxin Spasmodic coughs with an inspiratory gasp Organism is culture –ve, since it has been previously cleared Not responsive to antibiotic therapy Ciliary paralysis, necrosis of the ciliated epithelium, loss of the mucociliary ladder	**Filamentous Hemagglutinin (FHA)** Moderates adhesion to the ciliated respiratory epithelium Binds sulfated glycoplipid and CR3 on mucosal phagocytes **Tracheal Cytotoxin** A peptidoglycan. With LPS. Causes damage to epithelium via stimulation of IL-1 and NO production Causes ciliary paralysis and mucosal necrosis **Pertussis Toxin** Adhesin + A/B exotoxin. The toxin causes ADP ribosylation of G-protein →decrease cAMP → inhibition of phagocyte and lymphocyte activity → inhibits primary clearance **Dx** Fastidious: requires rich media Slow-growing colonies (3 – 6 days for visualization)	**Vaccine** DTaP: multivalent vaccine with purified bacterial antigen (PTx, FHA, fimbriae) Or killed cellular vaccine (DTP) **Treatment** Macrolides Trimethoprim/Sulfamethoxazole Supportive care, prophylaxis of exposed < 3 weeks

Pseudomonas auruginosa	Gm-ve bacillus	**Reservoirs in the environment** An opportunistic pathogen that is asymptomatic with normal host defenses **Acute nosocomial pneumonia** **Chronic pulmonary infection in CF** Dysfunctional mucociliary ladder causes stasis Tenacious secretion can incubate the microbe Decrease host phagocytosis Binds to mutated form of CFTR **Folliculits + Otitis Externa after exposure to pools** **Malignant Otitis Externa** **Corneal infection** **Wound infection** **Bacteremia**	**Formation of biolfilms** **Quorum sensing** **Exotoxin A** ADP-ribosylation of elongation factor EF2 (similar to the diphtheria toxoid) **Hydrolytic enzymes** Exoenzyme S, elastase, phospholipase C **Pili** Involved in adhesion **Polysaccharide capsule** Resistant to phagocytosis **Exopolysaccharide alginate** Commonly seen in CF mucoid strains **Resistance to antimicrobials** **Dx** Flagellar motility Oxidase + ve Pyocyanin allows detection via illumination by UV light Sweet grape-like odor Obligate aerobe + facultative anaerobe	
Neisseria gonorrhea		**Urethitis (males)** **Cervicitis (females)** **Pelvic Inflammatory Disease** Occurs with repeated infection in females. Scarring of the fallopian tubes → infertility and ectopic pregnancy **Neonatal Ocular Infection** **Rarely:** hematogenous spread to cause septic arthritis (this is known as disseminated gonoccocal infection, DGI)	Similar virulence profile to *Neisseria meningitides* Non-encapsulated	No vaccine available

ATYPICAL MICROBES causing RESPIRATORY DISEASE

Features of *Chlamydia*
Obligate intracellular Gm-ve bacteria
The defining characteristic is cytoplasmic vesicular inclusion
Do not retain the Gram stain (lack PG layer), and are thus not visible by light-field
Common LPS antigen
The lifecycle (2 – 3 d) consists of intracellular and extracellular phases
- **Elementary Body (EB**) is phagocytosed by a host cell (bacterial heparin sulfate binds the host heparin-R)
- Inhibits lysosomal fusion and thus escapes degradation
- Conversion to a **Reticular Body (RB)** within the phagosome. Uses host ATP to replicate via binary fission
- The RBs recondense to form EBs. Large clusters of EBs agglomerate as inclusion bodies
- The cell lyses and releases EBs into the circulation

EB: infectious, dense, terminal
RB: non-infectious, loose, replicative

Chlamydia trachomatis		**Nonspecific urethritis** **Mucopurulent cervicitis** **Pelvic Inflammatory Disease (PID)** Leads to fibrosis of the Fallopian tubes, infertility, chronic pain, and ectopic pregnancy **Trachoma** **Ophthalmia Neonatorum**	**Dx** Cannot be made on clinical history or sputum sample Series titres with > 4X elevation in Ab over 3 – 4 wks.	Cannot use any antibiotics directed against the cell wall **Treatment** Macrolides, FQ No vaccine **Long-term sequelae of** *Chlamydia* **infection** Trachoma (blindness) Pelvic Inflammatory Disease Reactive Arthritis Cervical Carcinoma
Chlamydophilia pneurminiae		**Community Acquired Pneumonia (CAP)** The leading cause of **atypical CAP** (before *Mycoplasma* and *Legionella*) Typically persistent and indolent illness with pharyngeal pain, non-productive cough, and low-grade fever **Bronchitis** **Sinusitis** **Otitis Media**		

		Atherosclerosis Cellular tropism includes endothelium, macrophages, and vascular SM Antibodies in the background of acute cardiac events Circulating immune complexes seen in a background of confirmed atherosclerosis Organism isolated from plaques Infection stimulates differentiation to foam cell and secretion of cytokines		
Chlymydia psittaci		**Psittacine Pneumonia** TSx via inhalation of EB particles from bird droppings No horizontal TSx. Complications: cardiac and CNS Typically a self-limiting illness Fevers, non-productive cough, headache		
General Features of *Mycoplasma* Strict (*M. pneumonia*) and facultative aerobes Lack PG layer, and thus have pleiomorphic appearance Extremely fastidious: can only be cultured on PPLO agar				
Mycoplasma pneumoniae		**CAP** Endemic adult CAP with seasonal variation, peaking in summer months Non-productive cough, dyspnea, fever **Acute Tracheobronchitis, Sinusitis, Pharyngitis** **Urticaria, Erythema Multiforme, Stevens-Johnson Syndrome (SJS)** **Meningitis, Meningoecephalitis, Cerebellitis, Psychosis, Guillain-Barre Syndome (GBS)** **Pancreatitis** **Pericaditis, Myocarditis, Hemolytic Anemia** The hemolytic anemia is due to cross-reactivity of the CA Abs against RBC antigens (Group I)	**Produce H202 and superoxide** **Inhibit host catalase** These two mechanisms result in host tissue damage due to the accumulation of ROSs **Activation of macrophages and upregulation of cytokine expression** **P1 adhesin** Allows adhesion to the epithelial cells by binding to sialic acid → ciliary paralysis → loss of the mucociliary ladder **Dx** Serology: detection of IgM against the pathogen + cold agglutinin Abs (against Group I erythrocytes)	Cannot use antibiotic directed against cell wall synthesis **Treatment** Doxycycline (tetracycline) Macrolide FQ No vaccine

			CA titres rise before IgM! Most cases are subclinical Slow-growing colonies on PPLO agar	
General Features of *Legionella* Motile aerobic bacilli and coccobacilli Fastidious: require BYCE broth for culture Natural reservoir is ubiquitous: fresh water bodies, municipal supplies Requires commensal growth with several other microbes (e.g. intracellular colonization of amoebae) No horizontal TSx Serogroup 1 causes 80% of human disease				
Legionella pneumophilia Serogroup 1 and other *Legionella* species		**CAP (5%) or Legionnaire's Disease** Path: inhaled → phagocytosis by alveolar macrophages via complement-R → inhibit lysosomal fusion → replication within macrophages → lysis → release of cytokines → neutrophil and monocyte recruitment → inflammation → necrotizing pneumonia Muti-lobular involvement Associated with pleural effusion *Natural history*: fevers, myalgia, malaise progressing to dyspnea, non-productive cough, and **GI symptoms** (abdominal pain and diarrhea) **RFs:** age, impaired respiratory function **Nosocomial Infection** **Pontiac Fever** This is a hypersensitivity reaction to the pathogen High attack rate High fever, headache, myalgia, arthralgia **No respiratory symptoms!** A self-limiting disease	Resistant to chlorination Resistant to heat **Dx** Do not sequester the Gram stain, so the organism is not seen on sputum sample Silver stain → visualization Culture in BCYE with increased CO2 Serology: > 4X increase in paired titres over 3 – 4 wks Detect soluble Ag in urine via ELISA Can only detect serogroup 1	**TX** CAP: macrolides, tetracyclines, FQ + rifampin **Prevention** Periodic superheating of water supply + Cu/Ag ionization No vaccine

FUNGI: AGENTS OF SUPERFICIAL, CUTANEOUS, and DEEP MYCOSES

STRUCTURE

The fungal membrane contains: phospholipids + ergosterol (instead of cholesterol)

The fungal cell wall contains: carbohydrate oligomers [chitin, α/β-glucan, α-mannan] + mannoproteins.

Chitin and β-glucan are specific to fungi. DOES NOT contain diamonopimelate (DAP), unlike bacteria.

Most fungi are **free-living** organisms.

Candida albicans and *Malassezia furfur* are NF in humans.

They are non-motile and saprophytic (usually)

Yeast: unicellular morphology, dividing via budding or fission. The yeast morphotype of *Histoplasma capsulatum* is pathogenic. *Cryptococcus neoformans* is only found in the yeast form.

Mold: a synctitium that may grow via apical extension and form branched hyphal networks. The mold morphotype of *Candida albicans* is invasive. *Aspergillus* is only found in the mold form.

Most pathogens involved in superficial, cutaneous, and deep tissue mycoses EXCEPT *Malassezia furfur* and *Sprothrix schenkii*

Pseudohyphae: linear synctitium formed by incomplete septation during budding or fission

Dimorphic: *Malassezia furfur*, *Histoplasma capsulatum*, *Coccidoides, Sporothrix schenkii*, *Candida albicans*

TYPES OF INFECTION

Superficial: confined to the stratum corneum or cuticle of hair shaft

Malassezia furfur, *Exophiala weneckii, Trichosporon beigelli, Piedraia hortai*

Cutaneous: involvement of all epidermal layers, nails, and cortex of hair shafts. Caused by **dermatophytes**.

Trichophyton, Microsporum, Epidermophyton

Subcutaneous: dermis, subcutaneous adipose, fascia, bone

Sporotrichosis, zygomycosis, mycetoma

Systemic: inoculation via RT and metastasis via hematogensous or lymphatic spread.

Histoplasma capsulatum, Blastomyces dermatitidis, Coccidoides

Typically dimorphic. Affect immunocompetent patients.

Opportunistic: require immunocompromised host.

Cryptococcus neoformas, Penicillium marneffei, Candida albicans, *Aspergillus, Pneumocystis jiroveci*

ALLERGIES: *Alternaria, Cladosporum, Aspergillus, Penicillium* (cheese-washers lung)

MYCOTOXICOSIS: *Aspergillus* produces aflatoxin, a potent hepatic carcinogen. *Claviceps pupurea* produces ergot alkaloids, causing peripheral necrosis + gangrene

HOST DEFENSE: Primarily innate immunity and CMI. *Aspergillus* is typically cleared by neutrophils.

SUPERFICIAL MYCOSES

Malassezia furfur				
Exophilia weneckii				
Trichosporon				

beigelli				
Piedraia hortai				