

# Infectious Diseases

**Jessica L. Spruit, DNP, CPNP-AC**

Assistant Clinical Professor, College of Nursing  
Wayne State University, Detroit, MI

Pediatric Bone Marrow Transplant Nurse Practitioner  
Children's Hospital of Michigan, Detroit, MI  
C.S. Mott Children's Hospital, Ann Arbor, MI

# Disclosures

No relevant financial disclosures



# Learning Objectives

- Describe typical infections in children based on the age of the child and organ system involved
- Discuss the presentation and diagnostic evaluation strategies of acute bacterial, viral, fungal, and parasitic infections in children
- Review management strategies for acute bacterial, viral, fungal, and parasitic infections in children

# Infectious Disease

- Fever in the Neonate
- Fever without a Source / Fever of Unknown Origin
- Neonatal Sepsis
- Systemic Inflammatory Response (SIRS)
- Septic Shock
- DIC
- Bacterial infections - age dependent
- Viral Infections
- Fungal Infections
- Sexually Transmitted Infections
- Parasitic/Vector infections
- Travel Organisms



# Fever

# Fever in the Neonate

- Neonates are at greater risk for significant bacterial infection (SBI)
- Maternal IgG cells present at birth, however, absence of immunologic memory and adaptive immunity
- B and T cells are normal in quantity, however, less efficient than adult cells
- Immune system rapidly develops in first 3 months of life

# Neonatal Sepsis

- Presentation

- Infant <28 DOL, rectal fever of >38° C/hypothermia, lethargy, poor feeding, respiratory distress, irritability, jaundice

- Etiology

- Common: urinary tract infection (UTI), bacteremia, meningitis, pneumonia

- Evaluation

- CBC with diff, urinalysis/culture (cath'd specimen), blood culture, lumbar puncture, chest x-ray for upper respiratory symptoms

Normal WBC does not  
exclude infection

# Neonatal Sepsis

- Common organisms

- *Group B strep, Listeria monocytogenes, E. coli, Enterococcus, S. aureus, HSV, CMV, VZV, RSV, Candida*

- Management

- Treat for 48 – 72 hours with broad spectrum antibiotics while cultures mature
- Gentamicin and ampicillin **or** ampicillin and cefotaxime; other supportive therapies as needed
- Meningitic dosing until CSF results obtained
- Add acyclovir for CSF pleocytosis, maternal prolonged rupture of membranes, primary maternal HSV infection, seizures, fetal scalp electrode use, seizures or mucocutaneous lesion
  - Continue acyclovir until HSV results are available
- Tailor antibiotics as cultures mature

IF RSV positive or +UTI, risk for SBI does not change; full evaluation needed



## Fever Without a Source

- Presence of fever without localizing signs on physical examination
- Classified into 4 categories: neonate, young infant, older infant, toddler
- Higher risk of SBI in younger infants and children
- \*Most infants/children with FWS will have an underlying, self-limited viral infection

# Fever Without a Source

- Epidemiology:
  - Dramatic decreases in *Haemophilus influenzae* type B and *streptococcus pneumoniae* due to vaccines
  - Serious bacterial infections causing fever without other symptoms:
    - Bacteremia
    - Urinary tract infection
    - Pneumonia

Young Infant	Older Infant/Toddler
Group B streptococcus, Listeria monocytogenes, Salmonella, Escherichia coli, Neisseria meningitides, Streptococcus pneumonia, Haemophilus influenza B, Staphylococcus aureus	Salmonella, Neisseria meningitides, Streptococcus pneumonia

# Fever Without a Source

- Evaluation:
  - Physical examination
  - Diagnostic studies if young infant or toxic appearance
    - CBC, urinalysis/culture, blood culture, lumbar puncture
    - Additional studies based on symptoms (stool specimen, chest x-ray)
- Management:
  - Empiric antibiotics
  - Consider admission
  - Re-evaluation plan

Teething is not likely to cause fever  $>38.5^{\circ}\text{C}$ , and height of temperature is associated with increased risk of occult bacteremia in older toddlers & children

# Fever of Unknown Origin

- Definition
  - Fever  $> 101^{\circ}\text{F}$  or  $> 38.3^{\circ}\text{C}$  lasting for at least 8 days and up to 3 weeks with no apparent clinical diagnosis
- Etiology
  - Most common are infectious disease and connective tissue diseases
  - Neoplastic disorders: less common, often have manifestations other than fever
  - Often caused by common disorder with unusual presentation

# Systemic Infections most commonly associated with FUO in Children

- Salmonella
- Tuberculosis
- Rickettsial disease
- Syphilis
- Lyme disease
- Cat-scratch disease
- Atypical prolonged common viral diseases
- Infectious mononucleosis
- Cytomegalovirus (CMV)
- Viral hepatitis
- Coccidioidomycosis
- Histoplasmosis
- Malaria
- Toxoplasmosis

# Infectious Disease

- **Common Diagnostic Testing**

- **C-Reactive Protein**

- Nonspecific, indicates inflammation or bacterial infection
    - Normal: <1.0mg/dL or <10.0mg/L

- **Erythrocyte Sedimentation Rate**

- Nonspecific, detects acute/chronic infections, inflammation, advanced neoplasm, and tissue necrosis
    - Normal values depend on gender and age

- **D-Test**

- Detects presence of macrolide-inducible resistance to clindamycin

- **Polymerase Chain Reaction**

- Rapid detection of pathogens, especially clinical virology and mycobacteriology

# Fever and Neutropenia

- Definition

- Fever with neutropenia in an oncology patient secondary to chemotherapy or hematologic disease
- 1/3 of children treated with chemotherapy or stem cell transplant develop a fever
- Criteria: Single temperature  $> 38.3^{\circ}\text{C}$  or  $> 38.0^{\circ}$  for  $> 1$  hour with an ANC  $< 500$  cells/ $\mu\text{L}$  or an ANC expected to decrease to  $< 500$  cells/ $\mu\text{L}$  within the next 48 hours

# Fever and Neutropenia

- Etiology

- Bacteremia is the most common form of infection
- Other common sites include the GI tract (oral or intestinal mucositis, diarrhea), upper and lower respiratory tract infections, urinary tract infection
- Diarrhea most commonly caused by Clostridium Difficile and Salmonella
- Consider both gram positive and gram negative organisms

Gram Positive (60-70%)  
Coag neg staph,  
Streptococcus Viridans,  
Staph Aureus (inc. MRSA)

Gram Negative  
Gram neg bacilli,  
Escherichia coli, Klebsiella,  
Pseudomonas, Acinetobacter,  
Enterobacter



# Fever and Neutropenia

- Etiology (continued)
  - Fungi are also a threat to this population (i.e. Candida, Mucor)
  - Other opportunistic fungi include Aspergillus, Cryptococcus, pneumocystis jiroveci (formerly carinii) pneumonia
  - Viral etiologies including herpes simplex, varicella zoster, respiratory viruses

# Fever and Neutropenia

- Diagnostic Evaluation
  - CBC with differential, complete metabolic panel, blood and urine cultures
    - If central catheter present, blood culture from each lumen
  - Consider CT/ultrasound imaging for fluid collections or effusions
  - Chest radiograph if respiratory symptoms
  - Respiratory virus panel if symptomatic
  - Lumbar puncture if altered mental status
  - C. difficile toxin assay if diarrhea

# Fever and Neutropenia

Remember to discontinue double coverage when clinically stable. Continue discontinuing double coverage or empiric therapy if no microbiologic indication to continue after 24-72 hours and afebrile for 24 hours

- Management

- Low-risk: consider oral, outpatient therapy
  - Fluoroquinolone monotherapy or fluoroquinolone and amoxicillin-clavulanate
- High risk: cover gram negative organisms, strep viridans, and pseudomonas aeruginosa
  - Hospital admission and antibiotic monotherapy (antipseudomonal beta lactam, fourth-generation cephalosporin, or carbapenem) if stable
  - Add gram-negative agent or glycopeptide if unstable, resistant pathogen suspected
  - Also consider adding gram-positive and anaerobic coverage for resistant organisms
  - If minimal response or signs of decline, therapy should be adjusted for clinical, radiographic, and/or culture data
- Tailor to microbiology results

# Fever and Neutropenia

- Management (continued)
  - Do not add therapy due to fever alone in stable patient
  - If the patient becomes unstable, escalate to include coverage of gram-negative, gram-positive, and anaerobic bacteria
  - Vancomycin or Linezolid should be used for cellulitis or pneumonia
  - An aminoglycoside and carbapenem should be used for pneumonia or a gram-negative bacteremia
  - Flagyl should be used if the patient has abdominal symptoms or suspected C. difficile infection
  - Consider anaerobic coverage in the setting of mucosal impairment
  - Antifungal therapy is reserved only for neutropenic patients with a fever persisting for 4-7 days after starting broad-spectrum antibiotics

# Sepsis Continuum



# Systemic Inflammatory Response Syndrome (SIRS)

- SIRS is non-specific inflammatory process
- Sepsis is SIRS with a known or suspected infection
- Risk factors
  - Immune problems, prematurity, musculoskeletal or neurologic disease, chromosomal or genetic disease, chronic disease state
- Example of pathology
  - Toxins are released with a Gram + infection that initiates a cytokine cascade resulting in fever, vasodilation, and hemodynamic instability
  - Lobar infiltration, petechiae, purpura, purulent drainage, WBCs in normally sterile bodily fluid (blood/CSF)

# SIRS Diagnosis

Two or more of the following:

- Temperature  $>38^{\circ}\text{C}$  **OR**  $< 36^{\circ}\text{C}$
- Tachycardia  $>2$  SD above age norm not induced by external stimuli, drugs or pain for 0.5-4hrs **OR** in children  $<1\text{yr}$  bradycardia ( $<10^{\text{th}}$  percentile for age)
- Mean respiratory rate  $>2$  SD above age norm **OR** mechanical ventilation for an acute process not related to neuromuscular disease or anesthesia
- Leukocyte count elevated **OR** depressed for age or  $> 10\%$  immature (band) form

# Severe Sepsis & Septic Shock

## Severe Sepsis:

- Sepsis plus one of the following:
  - Cardiovascular organ dysfunction OR
  - Acute Respiratory Distress Syndrome (ARDS) OR
  - Two or more other organ dysfunctions

## Septic Shock:

- Adults: Severe sepsis with refractory hypotension
- Children: Sepsis in the presence of cardiovascular dysfunction



# Septic Shock Presentation

- Fever or subnormal temperature
- Irritability, lethargy
- Tachypnea with respiratory distress
- Tachycardia, gallop rhythm with myocarditis, poor perfusion, hypotension
- Hepatomegaly or jugular vein distention
- Shock – warm or cold
- Oliguria
- Rash
- Multiple organ dysfunction syndrome – 2 or more systems involved

# Infectious Disease

- Septic work-up
  - Blood cultures (peripheral and central)
  - Urinalysis/urine culture
  - Lumbar puncture (LP)
  - Endotracheal sputum, if airway in place
  - CBC with differential
  - Electrolytes, glucose, BUN/creatinine
  - Culture of wounds/other bodily fluids, if appropriate
  - Chest radiograph if + respiratory symptoms
  - Ultrasound or CT scan of involved body organ

# Management-PALS

- ABC's
- Fluid resuscitation - goal CVP 10-12
- Inotropic support - cold/warm shock
- Septic work-up
- Antimicrobial therapy – initially broad spectrum
- If concern for fungal disease (immunocompromised) - ECHO, ophthalmology exam, evaluation of sinuses

# Disseminated Intravascular Coagulation



# Disseminated Intravascular Coagulation

- Alteration in clotting triggered by tissue injury
- Bleeding is initial symptom, thrombosis with tissue ischemia
- Prolonged bleeding studies
  - D-dimer is diagnostic
- Manage shock
- Address coagulation:
  - Vitamin K
  - Cryoprecipitate
  - FFP
  - Platelets

# DIC



# Meningococcal Infections



## Meningococccemia: *Neisseria meningitidis*

- Acute fulminant bacterial illness that follows viral illness
  - Gram-negative encapsulated organism
  - 9 serogroups: A, B, C and W135 are the most common
  - Serogroups B and C most common in U.S.
  - May produce isolated meningitis or meningococccemia
  - 50-100 times the endotoxin load of other gram-negative bacteria
  - Level of endotoxin correlates with severity of disease
  - Newer vaccine available for serogroup B meningococcal



# Meningococemia

- Diagnosis:
  - The presence of *N. meningitidis* in the systemic circulation
- Rapid onset of symptoms
  - Fever
  - Altered mental status
  - Poor perfusion
  - Tachycardia
  - Hypotension
  - Tachypnea
  - Irritability
  - Purpura



# Meningococccemia

- Management

- Labs: CBC with diff, complete sepsis workup, liver enzymes, renal function, and LP
- Droplet isolation of patient, immediate resuscitation with ABC, fluids, antibiotics, blood products, ventilation, broad spectrum antibiotics such as third generation cephalosporins-either ceftriaxone or cefotaxime
- Close contacts and health care workers will need prophylaxis-single dose ciprofloxacin or rocephin IM

# Healthcare Associated Infections



# Healthcare Associated Infections

- Definition
  - Infection not present at admission that develops within 48hrs OR not present at discharge but develop within 10 days
- Top Infection Sites
  - Catheter related (CLA-BSI, CAUTI), ventilator-associated pneumonia (VAP), and surgical site infections (SSI)
- Symptoms
  - New fever, temperature instability, increased O2 need, wound purulence

# Healthcare Associated Infections

- Risk Factors
  - Invasive lines, endotracheal tube/ventilator, immunocompromised host, foley, PRBC transfusion, ECMO, dialysis, parenteral nutrition
- Diagnostic Evaluation
  - Blood cultures (peripheral & central)
  - Urinalysis and culture
  - Sputum gram stain and culture
  - CBC with diff (leukocytosis & anemia)
  - May have elevation of inflammatory markers (CRP/ESR)

# Health Care Associated Infections

- Prevention is key with bundled approach
- Treatment:
  - CLA-BSI: Bundled care of lines-insertion, access and maintenance
    - No evidence to remove if difficult access
  - VAP: Empiric broad-spectrum antibiotics
    - Anaerobic coverage for aspiration concerns
  - SSI: prevention focused on antibiotic prophylaxis and good skin prep
    - Drain and debride all wounds
    - Antibiotics as second tier therapy

# Common Infections and Antimicrobial Choices

# Common Organisms

- Gram Positive

- Streptococcus
- Staphylococcus
- Enterococcus
- Listeria
- Mycobacteria
- Pneumococcus
- Corynebacteria
- Bacillus
- Nocardia

- Gram Negative

- E. coli
- Pseudomonas aeruginosa
- Klebsiella sp
- Acinetobacter sp
- Neisseria sp
- Enterobacter sp
- Haemophilus influenzae
- Legionella
- Salmonella



# Antimicrobial Drug Classes

- Beta-Lactams: Penicillins
  - Bactericidal
  - Gram positive organisms, gram negative cocci, non-beta-lactamase-producing anaerobes
  - Uses: bacterial prophylaxis, UTIs, sinusitis, otitis media, lower respiratory tract infections

# Antimicrobial Drug Classes

- Beta-Lactams: Cephalosporins
  - Bactericidal
  - Coverage increases with each generation, gram positive and gram negative organisms including pseudomonas covered in 4th generation
  - Uses: many uses, vary by generation
  - Examples: 1st generation surgical prophylaxis, 3rd generation meningitis/sepsis (crosses BBB), 4th generation sepsis and febrile neutropenia

# Antimicrobial Drug Classes

- Beta-Lactams: Monobactams
  - Gram negative coverage
  - No gram positive or anaerobic coverage
- Beta-Lactams: Carbapenems
  - Gram positive, gram negative (including pseudomonas), and anaerobic coverage
  - Used for mixed aerobic/anaerobic infections, ESBL-producing gram negative infections, febrile neutropnia

# Antimicrobial Drug Classes

- Glycopeptides
  - Gram positive organisms (MRSA, MRSE), anaerobes
  - No gram negative activity
- Lipopeptides
  - Gram positive organisms (including VRE)
  - No gram negative or anaerobic activity

# Antimicrobial Drug Classes

- Tetracyclines
  - Gram positive, gram negative, some anaerobic coverage
- Macrolides
  - Gram positive (pneumococci, staph, strep, corynebacteria), gram negative, atypical (mycoplasma, legionella, etc) coverage
- Lincomycins
  - Gram positive, anaerobic coverage

# Antimicrobial Drug Classes

- Aminoglycosides
  - Gram negative coverage
  - Used for sepsis, endocarditis, UTIs
- Sulfonamides
  - Gram positive, gram negative organism coverage
  - Poor anaerobic activity

# Antimicrobial Drug Classes

- Fluoroquinolones
  - Gram positive, gram negative, atypical organism coverage
  - Limited anaerobic coverage (moxifloxacin only)
  - Used in UTIs, bacterial diarrhea, soft tissue/bone infections

# Community Acquired Pneumonia

- Most common bacterial cause: *S. pneumoniae*
- Management
  - High-dose amoxicillin, ampicillin if admitted
  - Add staph coverage if MRSA is suspected (consider Vancomycin or Clindamycin pending local susceptibilities)
  - Consider atypical organisms in children > 5 years
    - Add macrolide for this, but remember that azithromycin does not cover *S. pneumoniae* adequately



## Otitis Media

- Antibiotics recommended if severe signs/symptoms or 6-23 months with bilateral disease
- Pathogens: *S. pneumoniae*, nontypable *H. influenzae*, *M. catarrhalis*
- High-dose amoxicillin is first-line therapy per AAP 2013 guideline

# Skin and Soft Tissue Infection

- Organisms
  - S. aureus, group A strep
- Treatment
  - 1st generation cephalosporin (will not cover MRSA), clindamycin, sulfamethoxazole-trimethoprim, vancomycin/linezolid
  - May be able to treat topically or with incision and drainage
  - Remember to always consider local susceptibility trends

## Bone and Joint Infection

- Most common organism is *S. aureus*
- May also be secondary to group A strep, *kingella kingae*, *S. pneumoniae*, *H. influenzae*, salmonella (esp in sickle cell anemia), *N. gonorrhoeae*
- Consult infectious disease
- Often starts with cefazoline or clindamycin given preference for eventual oral therapy
  - May use vancomycin (+ ceftriaxone) if very sick or positive cultures

# Methicillin-resistant *S. aureus* (MRSA)

- Treatment options:
  - Based on local susceptibility rates (highly variable)
  - Trimethoprim-sulfamethoxazole
  - Clindamycin
  - Doxycycline
  - Vancomycin

# Multi-Drug Resistant Organisms



# Multi-Drug Resistant Organisms

- When bacteria that are present are able to evade antibiotic activity
- Produce an enzyme that changes antibiotic to less active form
- Alter the target site of the antibiotic
- Change the drug entry or removes drug from the bacterial cell

# Drug Resistance

- Most common in pediatrics
  - CA-MRSA: Community Acquired Methicillin Resistant Staph Aureus
    - Resistant to beta lactams
    - Treat with Clindamycin or vancomycin or Septra or Linezolid
  - DRSP: Drug-resistant strep pneumoniae
    - Resistant to Beta-lactams
    - Treat with Clindamycin or vancomycin or high dose Beta-lactams

# Meningitis



# Meningitis

- Definition:
  - Infection of the meninges, usually bacterial, can be viral
- Medical emergency if bacterial
- 100% fatal if untreated
  - Cerebral (vasogenic, cytotoxic and interstitial) edema ensues
    - May lead to coma, increased intracranial pressure, herniation

# Meningitis

- Presentation
  - Fever, chills, headache, nausea and vomiting, lethargy, photophobia, altered neurological status, poor feeding, agitation, bulging fontanel in infant
- Diagnostic Evaluation
  - Physical examination, typically with meningeal signs
- Complications
  - Hearing loss, neurologic impairment, seizures, death

Remember the  
meningeal signs: Kernig  
and Brudzinski

# Meningitis

## • Evaluation

### • Lumbar Puncture

- Elevated opening pressure
  - Ratio of RBC's and WBC's should be the same as serum ratio
  - If contaminated with blood, interpretation can be difficult
  - If significant RBCs: suspect Herpes Simplex Virus
- CBC w/diff, blood culture, urinalysis/culture, erythrocyte sedimentation rate (ESR), c reactive protein (CRP), comprehensive metabolic panel
  - Consider chest radiograph

If concern of increased ICP, obtain head CT prior to LP



# Meningitis – CSF Results

Type	WBC (cells/mm <sup>3</sup> )	Protein	Glucose	Gram Stain	Misc.
Normal	Neonate: 0-30 1-5yrs: 0-20 6-18yrs: 0-10 Adult: 0-5	15-45 mg/dL	50-75 mg/dL	Negative	Clear, colorless, negative for blood
Viral	<500	Elevated	Normal to low	Negative	Send viral studies (i.e. HSV PCR)
Bacterial	>1000, predominant leukocytes	Elevated	Low	80-90% positive if no treatment	Cloudy to purulent color

# Viral Meningitis

- Most common organism is Enterovirus (80 serotypes)
- Mild and self-limiting to severe with seizures, encephalitis and death
- Neonates: HSV may have RBC's in tap
- Summer: arboviruses
- Hallmark triad of symptoms in older kids without nuchal rigidity:
  - Fever
  - Headache
  - Altered LOC

# Bacterial Meningitis

- Organisms and Symptoms by Age

- Neonates: Group B streptococcus, E. coli, Listeria monocytogenes
  - Fever, lethargy, bulging fontanel, poor feeding, jaundice, decreased muscle tone
- Young children (>2 – 23 months): streptococcus pneumoniae, N. meningitides, group B streptococcus, Haemophilus influenzae
  - Fever, headache, nuchal rigidity, + Kernig & Brudinski signs, poor feeding, decreased muscle tone
- >2 Years of age: N. meningitides, S. pneumoniae, H. influenzae
  - Altered mental status, hypertension, bradycardia, petechiae, exanthems

# Meningitis

- Management

- Based on age and presentation
- Neonates
  - Ampicillin and gentamicin or cefotaxime, with acyclovir
- Infants
  - Vancomycin and ceftriaxone, with acyclovir
- Older child:
  - Ceftriaxone and vancomycin
- Do NOT delay antibiotics for > 1 hour after presentation!

# Meningitis

- Supportive care
  - Anticonvulsant therapy as indicated
  - Increased intracranial pressure management as indicated
  - Long term follow-up to include hearing and developmental evaluation (learning and behavioral issues)



# Toxic Shock Syndrome



# Toxic Shock Syndrome

- Background

- Multisystem febrile illness caused by staph. aureus and Strep. Pyogenes
- Toxin production triggers massive activation of host cellular immune response

- Presentation

- Begin with non-specific symptoms, progress quickly to fever and hypotension, severe organ dysfunction

# Toxic Shock Syndrome

- Clinical Criteria:

- Fever > 39°C
- Rash: diffuse macular erythroderma
- Desquamation: palms and soles, 1-2 weeks after onset
- Hypotension
- Multisystem involvement (at least three of the following):
  - GI: vomiting, diarrhea
  - Muscular: severe myalgias, CK at least twice upper limit of normal
  - Mucous membranes: hyperemia of conjunctiva/oropharynx/vagina
  - Kidney: BUN or creatinine at least twice upper limit of normal, urinary sediment with pyuria
  - Liver: TBili, ALT, AST twice upper limit of normal
  - Hematologic: platelets <100,000
  - Neurologic: altered mental status without focal signs (absence of fever, hypotension)

# Toxic Shock Syndrome

- **Laboratory Criteria:**

- Negative cultures from blood, throat, CSF (*S. aureus* may be detected in blood)
- No elevation in serum titers for Rocky Mountain spotted fever, leptospirosis, or measles

**Probable TSS:** 4 clinical criteria +  
laboratory criteria

**Confirmed TSS:** 5 clinical +  
laboratory criteria

# Toxic Shock Syndrome

- Evaluation
  - Blood cultures, CSF, urine, sputum, throat culture, vaginal culture
- Treatment
  - Supplemental oxygen
  - Fluid resuscitation
  - Immediate antibiotic therapy
    - Broad spectrum (Ceftriaxone + Vancomycin, add Clindamycin if high suspicion for TSS)
  - Aggressive hemodynamic and respiratory support according to PALS
  - Removal/debridement of site of infection
  - Consider IVIG

# Dental Issues



# Dental Issues – AAP Guidelines

- Etiology & Pathogenesis
  - Aciduric and acidogenic bacteria predominate in dental plaque (streptococcus mutans)
  - Dietary sugar intake allows to additional bacteria → decreased pH at tooth surface → demineralization of enamel → cavitation
  - Saliva buffers low pH, flushes oral cavity of food → rich calcium/phosphate environment → remineralization
  - Flouride inhibits demineralization, enhances remineralization, and inhibits bacterial enzymes

# Dental Issues – AAP Guidelines

- Primary Prevention
  - Risk assessment
  - Avoidance of sugar intake and reduction of time in mouth
  - Primary caregiver oral hygiene
  - Consider chronic diseases and medications



# Dental Issues – AAP Guidelines

- Anticipatory Guidance
  - Dietary counseling
  - Fluoride
  - Oral hygiene
  - Pacifiers and bottles
  - Dental injury

# Fungal Infections



# Fungal Infections

- Common pathogens include histoplasmosis, candida species, pneumocystis (carinii) jiroveci (PJP)
- Common in immunocompromised hosts, neonates and critically ill children on long term antibiotics
- Typical therapy consists of fluconazole, voriconazole, amphotericin B complex, TMP-SMX for PCP prophylaxis

# Sexually Transmitted Infections



# Sexually Transmitted Infections – Human Papillomavirus

- Background
  - Double-stranded DNA, genital or recurrent resp papillomatosis
- Symptoms
  - Typically asymptomatic, may present with genital or throat warts
- Diagnostics
  - Visual inspection, pap with HPV testing
- Treatment
  - No pharmacologic treatment in absence of warts
  - Cryotherapy/surgical removal, laser surgery

Prevention is key!

# Sexually Transmitted Infections - Gonorrhea

- Background
  - 2nd most common STI in US
  - Caused by *N. gonorrhoeae* (gram -)
- Symptoms
  - Dysuria, frequency/urgency, discharge
- Diagnostics
  - Bacterial culture with Gram stain, NAATs
- Treatment
  - Intramuscular ceftriaxone + azithromycin or doxycycline

# Sexually Transmitted Infections - Chlamydia

- Background
  - Most common STI in US, obligate intracellular bacteria
- Symptoms
  - Typically asymptomatic
  - Women may present with vaginitis, urethritis, endometriosis, PID
- Diagnostics
  - Swabs, NAATs is test of choice, cell culture, EIA, screening recommended
- Treatment/Prognosis
  - Azithromycin or doxycycline per CDC guidelines

# Sexually Transmitted Infections - Syphilis

- Background
  - Caused by spirochete *Treponema pallidum*
- Symptoms
  - Depends on primary, secondary, or tertiary presentation
- Diagnostics
  - Darkfield examinations, DFA for *T. pallidum*, serologic testing
- Treatment/Prognosis
  - Benzathine penicillin G



# Vector & Tick Borne Illnesses



# Vector Borne Disease – West Nile Virus

- Viremic inflammation
  - WNV enters the brain through an alteration in the blood brain barrier (BBB)
- Symptoms
  - Abrupt fever, myalgias, headache, malaise, diarrhea, and a maculopapular rash
- Management
  - Supportive care

# Tick Borne Disease – Lyme Disease

- Divided into 3 categories:
  - Early dissemination
  - Late disease
  - Latent dissemination
- Peaks: Summer early fall
- May present as an erythematous macule with clearing of the center → target lesions (erythema migrans)
- Fever, arthralgia, headache, facial palsy
- Treatment:
  - Amoxicillin for children younger than 8 years
  - Doxycycline for children  $\geq$  8 years

Antibiotic duration for early localized disease is 14-21 days. Extended to 21-28 days for mult. Erythema migrans, isolated facial nerve palsy, and arthritis

# Erythema Migrans



# Tick Borne Disease – Rocky Mountain Spotted Fever

- Background
  - Systemic vasculitis that incubates for 2-14 days
- Presentation
  - Fever, severe headache, myalgia followed by vomiting, and decreased PO
  - 2-5 days after fever, rash develops on the wrist, ankles, palms and soles that spreads to trunk
- Diagnostic Evaluation
  - Rickettsial serologic assay
- Management
  - Do not delay treatment with doxycycline while awaiting testing
  - Untreated patients are at risk for DIC and septic-shock-like picture with CNS sequelae

# Rocky Mountain Spotted Fever



# Malaria

- Background
  - Endemic in tropical regions
  - Almost all US cases are among emigrants or travelers returning from endemic regions
- Definition
  - Mosquito-transmitted parasitic infection
- Etiology
  - Five known Plasmodium species cause malaria

# Malaria

- Pathophysiology

- Infective sporozite transmitted via mosquito bite
- Parasites travel to liver where they develop and multiply over next 7-10 days
- Erythrocytes become infected and begin symptomatic phase of disease

- Presentation

- Paroxysmal fever
- Chills, headache, malaise, cough
- Hemolytic anemia with thrombocytopenia
- Proteinuria and hemoglobinuria
- Severe disease: Hypotension, renal dysfunction, hypoglycemia, metabolic acidosis



# Malaria

- Diagnostic Evaluation

- Thick and thin blood smears to identify parasites, repeat every 12 – 24 hours when test negative
- Clinical presentation and characteristic laboratory findings

- Management

- Severe: intravenous artesunate or quinidine with doxycycline, tetracycline, or clindamycin
- Uncomplicated cases: oral therapy selected by geographic area of resistance
- Prophylaxis recommended prior to travel: tailored to patient risk factors and location of travel
  - Most US cases are travelers not following CDC recommendations for prophylaxis
  -

# Dengue

- Background
  - Primarily present in tropics and subtropics
  - U.S endemic areas: Puerto Rico, Virgin Islands, American Samoa
  - Previous US outbreaks: Texas, Florida, and Hawaii
- Definition
  - Mosquito-transmitted viral illness
  - Typically self-limiting, however, may progress to severe shock

# Dengue

- Etiology

- Caused by 1 of 4 dengue viruses (DEN 1,2,3,4)
- Transmitted through bites of infected mosquitos
- Humans remain viremic for ~7 days and virus may be transmitted through blood products

- Presentation

- Non-specific febrile illness, often with retro-orbital headache, mylagias, maculopapular rash
- Critical phase: defervescence within 2-7 days of onset, most improve although some progress to severe disease
- Severe disease: Vomiting, mucosal bleeding, leukopenia, thrombocytopenia, respiratory distress, shock, plasma leakage (pleural effusion, ascites), DIC

# Dengue

- Diagnostic Evaluation
  - Leukopenia with thrombocytopenia should raise suspicion
  - Serologic testing: ELISA for anti-dengue IgG and IgM antibodies
- Management
  - No specific antiviral
  - Supportive care including hydration
  - Avoid agents contributing to coagulopathy (e.g. aspirin and NSAIDs)

# Zika Virus

- Definition
  - Mosquito (*Aedes* species) transmitted infection
- Transmission
  - Mosquito bites
  - Can be passed from a pregnant woman to her fetus, potentially causing certain birth defects
  - May be transmitted during sex
  - Possible transmission through blood transfusion (likely, but not confirmed)

# Zika Virus

- Presentation
  - Fever, rash, headache, arthralgia, injected sclera, myalgia
- Diagnostic Evaluation
  - Blood or urine test
  - Clinical presentation and relevant/sexual travel history
- Management
  - Supportive care

Symptoms are usually mild and may last for several days to a week

# Travel Infections - Typhoid

- *Salmonella enterica*
- Background
  - Enters the body via the GI tract and is transferred the lymphatics, blood, liver, and spleen
  - Leads to widespread bacteremia and endotoxin release
- Presentation
  - Fever, headache, malaise, abdominal pain, nausea, vomiting, constipation, diarrhea, hepatomegaly, splenomegaly
- Diagnostic Evaluation
  - Most often isolated on blood culture
- Management
  - Ceftriaxone or ciprofloxacin

# Viral Infections



# Common Viral Infections

## Adenovirus

- Double-stranded DNA virus, 51 serotypes
- Incubation 2-14 days for respiratory and 3-10 days for gastrointestinal illness
- Incidence inversely related to age (highest risk <5 years)
- Close contact necessary for spread of infection
- Symptoms
  - Respiratory: common cold, fevers, pharyngitis, tonsillitis, bronchiolitis, cough, crackles, wheezes, tachypnea and dyspnea with more severe cases (associated with serotypes 3, 7, 21)
  - Eyes: erythema, itching, burning, increased lacrimation, foreign body sensation, photophobia, hyperemia
  - GI tract: diarrhea, abdominal pain, vomiting

**\*\*Viral findings concerning in all immunocompromised children**

# Common Viral Infections

## Adenovirus

- Diagnostic tests
  - Identified by cell culture (except serotypes 40 and 41)
  - If present in blood, pleural/pericardial fluid, CSF indicative of disseminated or severe disease
  - Rapid identification using immunofluorescence, ELISA, latex agglutination
  - PCR to quantify viral load in immunocompromised patients
- Plan of care
  - Usually benign and self-limited, requiring supportive care
  - Overwhelming infection may warrant vasopressors/inotropic agents
  - Stop or decrease immunosuppression if possible
  - Consultation to ophthalmology
  - Cidofovir or ribavirin for immunocompromised hosts or disseminated disease, respectively
  - Contact +/- droplet precautions



**\*\*Viral findings concerning in all immunocompromised children**

# Common Viral Infections

## Cytomegalovirus

- Double-stranded DNA virus from the Herpesviridae family
- May cause primary and secondary infection
  - Primary infection: viremia delivers the virus to organs including kidneys, lungs, liver, brain
  - Secondary infection: reactivation seen in the setting of immunodeficiency
- Incubation 3-12 weeks if acquired by blood transfusion and 1-4 months if acquired by tissue transplantation
- Congenital infection seen in 0.2-2.2% of live births
  - 10-20% of affected infants born with a defect (hearing loss, ocular damage, ocular/motor dysfunction)
- Higher prevalence in young children 1-3 years and adolescence (close contact)

**\*\*Viral findings concerning in all immunocompromised children**

# Common Viral Infections

## Cytomegalovirus

- Symptoms

- Congenital CMV: hearing loss, microcephaly, seizures, hepatosplenomegaly, hepatitis, thrombocytopenia, anemia, ascites, cognitive/motor deficiencies, growth retardation, pneumonia/pneumonitis, cutaneous vasculitis, sepsis-like syndrome, “blueberry muffin” lesions
- Older patients are often asymptomatic
- Mononucleosis syndrome: prolonged fever, severe malaise, maculopapular/rubelliform rash, headaches, abdominal pain, myalgias (usually will not present with pharyngitis, tonsillitis, or splenomegaly)
- Pneumonia
- Dysphagia, abdominal pain, nausea, vomiting, diarrhea, feeding intolerance

**\*\*Viral findings concerning in all immunocompromised children**

# Common Viral Infections

## Cytomegalovirus

- Diagnostic tests
  - Identified by cell culture from urine, saliva, nasopharynx, sinus washing, BAL, conjunctiva, tears, middle ear fluid, human milk, peripheral blood, semen, cervical/vaginal secretions, CSF, tissue biopsy, amniotic fluid
  - CMV PCR detects DNA rapidly, is highly sensitive, and allows for quantification of viral load
- Plan of care
  - Usually asymptomatic or benign
  - Overwhelming infection may warrant vasopressors/inotropic agents
  - Ganciclovir is first-line for immunocompromised patients, valganciclovir is the prodrug
  - Good hand-washing
  - CMV seronegative blood products for select patients, leukoreduction techniques

# Common Viral Infections

## Ebstein-Barr Virus

- Double-stranded DNA virus of the Herpesviridae family, two major genotypes
- Invades nasopharyngeal cells and spreads to B cells
- May lead to uncontrolled proliferation of B cells and lymphoproliferative disease if the immune system fails to control the infection
- Infectious mononucleosis 50-100 cases/100,000 people per year

**\*\*Viral findings concerning in all immunocompromised children**

# Common Viral Infections

## Ebstein-Barr Virus

- Symptoms

- Usually asymptomatic or nonspecific
- Classic cause of infectious mononucleosis
  - Fatigue, fever, sore throat, malaise, symmetric lymphadenopathy (especially cervical), exudative pharyngitis
  - Splenomegaly at risk for splenic rupture
  - 10% will evolve in to a chronic, active infection with symptoms > 1 year
- May develop maculopapular, pruritic rash to the face, trunk, and extremities if treated with ampicillin/amoxicillin
- Symptoms may persist for 3-4 weeks
- Associated with malignancies: Burkitt's lymphoma, B-cell tumors, Hodgkin lymphoma, T-cell lymphoma
- Neurologic manifestations: headache, fever, nuchal rigidity, encephalitis

Patients with splenic rupture may present with positive Kehr's sign

# Common Viral Infections

## Ebstein-Barr Virus

- Diagnostic tests
  - Atypical lymphocyte count >10%
  - Detection of viral antigen, viral DNA/RNA, serology
  - Quantification by PCR
  - Rapid assays for Paul-Bunnell heterophile antibodies (Monospot, Mono-Test, Mono-Diff)
- Plan of care
  - Supportive care including rest, hydration, antipyretics
  - Antivirals usually not effective, may require steroids for severe complications
  - Emergent stabilization for splenic rupture
  - Education to reduce transmission, standard precautions in the hospital
  - Avoid contact/wheeled sports

**\*\*Viral findings concerning in all immunocompromised children**



# Common Viral Infections

## Enterovirus

- Single-stranded RNA virus (include polioviruses, coxsackieviruses, echoviruses, enteroviruses)
- Enters via the nasopharynx or GI tract and attaches to host cell surface
- Lymph nodes infected by the second day, blood stream by the third day
- Distribution to other tissues → secondary infection (source of symptoms)
- Highest incidence in youngest patients (< 1 year)
- Majority spread fecal-oral route

**\*\*Viral findings concerning in all immunocompromised children**

# Common Viral Infections

## Enterovirus

- Symptoms
  - Highly variable based on type of infection, majority are asymptomatic or nonspecific febrile illness
- Diagnostic tests
  - Identified by cell culture, obtain several sources simultaneously
  - Viral nucleic acid detected by PCR
  - Serologic detection possible, but requires serial sampling (therefore, impractical)
- Plan of care
  - Supportive care based on involved systems
  - Standard and contact precautions in the hospital
  - Inactivated polio vaccine for prevention in the US

**\*\*Viral findings concerning in all immunocompromised children**

# Common Viral Infections

## Herpes Simplex Virus

- Double-stranded DNA virus
- Invades through mucous membranes or skin
- Incubation 2 days to 2 weeks
- HSV-1 usually acquired in childhood, HSV-2 transmitted sexually
- Neonatal infections present in 1 per 3000 live births
  - 20% will have disseminated disease, 30% with CNS disease
- Intermittent viral shedding in symptomatic/asymptomatic patients

**\*\*Viral findings concerning in all immunocompromised children**

# Common Viral Infections

## Herpes Simplex Virus

- Symptoms

- Gingivostomatitis
  - Multiple, grouped vesicles on the lips, tongue, gingiva, hard palate, mucous membranes
  - Concurrent fever, lymphadenopathy (submandibular nodes), malodorous breath
  - Lesions ulcerate and bleed over 5 days and usually resolve over the next 7 days
- Vesicles to genital organs and perineum, possibly accompanied by pain, pruritis, lymphadenopathy of the inguinal nodes, and discharge
- Skin manifestations: eczema herpeticum (Kaposi varicelliform eruption)
- Keratoconjunctivitis: corneal injection, lacrimation, pruritis, fever
- Meningitis: nuchal rigidity, headache, photophobia
- Neonatal disease may be severe, rapidly progressing, disseminated

**\*\*Viral findings concerning in all immunocompromised children**



# Common Viral Infections

## Herpes Simplex Virus

- Diagnostic tests
  - Cell culture is study of choice, acquired by swabbing lesions or aspirating fluid
  - Direct immunofluorescent staining , antigens, ELISA, PCR, serologic testing
- Plan of care
  - Acyclovir is first-line therapy
  - Supportive care (hydration for gingivostomatitis)
  - Wound care
  - Contact precautions in the presence of mucocutaneous lesions and neonatal patients born to women with active genital herpes
  - Avoid topical analgesics with oral lesions due to risk of overdose with ingestion

**\*\*Viral findings concerning in all immunocompromised children**

# Common Viral Infections

## Influenza

- Single-stranded RNA virus, three major types (A, B, C)
- Incidence highest in children < 4 years
- Seasonal epidemics during winter months
- Risk for mortality increased in chronically ill or immunocompromised patients
- Symptoms
  - Sudden fever, headache, myalgia, malaise
  - Respiratory symptoms usually appear two days later (cough, sore throat, nasal congestion)
  - Bronchiolitis, croup
  - Encephalitis
  - Septic-like presentation

**\*\*Viral findings concerning in all immunocompromised children**

# Common Viral Infections

## Influenza

- Diagnostic tests
  - Identified by viral culture
  - Rapid detection results available within 30 minutes
  - Immunoassays, PCR
- Plan of care
  - Supportive care based on involved systems
  - Avoid salicylate-containing medications (risk of Reye's syndrome)
  - Treatment with adamantanes and neuraminidase inhibitors
  - Vaccine administration for prophylaxis

**\*\*Viral findings concerning in all immunocompromised children**

# Common Viral Infections

## Parvovirus B19

- Single-strand DNA virus
- Invades respiratory tract, replicates only in actively dividing cells
- Half of children are infected by the age of 15
- Increased incidence in the winter and spring
- Increased risk of transient aplastic crisis in patients with underlying RBC destruction (sickle cell anemia, spherocytosis, G6PD deficiency)
- Symptoms
  - Fifth disease (erythema infectiosum to cheeks with circumoral pallor, arthritis, arthralgia)
  - Fever, headache, myalgias, malaise
  - Lacy, maculopapular pruritic rash that starts on the trunk and spreads to extremities
  - Transient aplastic crisis
  - Decreased reticulocyte count, anemia

**\*\*Viral findings concerning in all immunocompromised children**



# Common Viral Infections

## Hepatitis

- Background
  - Associated with liver inflammation (acute/chronic)
  - Many causative factors: medications, toxins, infections, passive congestion, storage diseases, autoimmune injury
- Symptoms
  - Often detected by elevation of labs, incidental finding
  - Acute onset jaundice, abdominal pain, nausea, vomiting, fever, joint pain, weakness, malaise, altered LOC, kidney failure, cardiovascular collapse
  - Hepatosplenomegaly, pain upon palpation, ascites, peripheral edema
  - Ecchymosis, petechiae
  - Altered mental status

**\*\*Viral findings concerning in all immunocompromised children**

# Common Viral Infections

## Hepatitis

- Diagnostic Tests

- Elevated transaminases (ALT, AST), bilirubin (direct), alkaline phosphatase
- Tests of factors produced in the liver: coagulation studies (PT, PTT), albumin, ammonia, factors VII/VIII, vitamin K, glucose
- CBC with differential
- Abdominal ultrasound with Doppler

- Treatment

- Based on type and symptoms, supportive care
- Consult GI/Hepatologist
- Anticipatory guidance to prevent spread during acute viral shedding, chronic management



**\*\*Viral findings concerning in all immunocompromised children**

## Question

What is the organism that must be covered in high-risk patients with febrile neutropenia? Antibiotics that will cover this organism include fourth-generation cephalosporins, carbapenem, and certain beta lactams.

- a. Staphylococcus aureus
- b. Streptococcus viridans
- c. Pseudomonas aeruginosa
- d. E. coli

## Answer:

What is the organism that must be covered in high-risk patients with febrile neutropenia? Antibiotics that will cover this organism include fourth-generation cephalosporins, carbapenem, and certain beta lactams.

C. *Pseudomonas aeruginosa*

## Question

A patient presents with fever, myalgia, and a rash that started on the wrists, ankles, palms, and soles before spreading to the trunk. You appropriately initiate what treatment?

- a. High-dose amoxicillin
- b. Doxycycline
- c. Linezolid
- d. Ceftriaxone

## Answer:

A patient presents with fever, myalgia, and a rash that started on the wrists, ankles, palms, and soles before spreading to the trunk. You appropriately initiate what treatment?

B. Doxycycline

## Question

An eight-year old male presents with fever, guarding and tenderness to the lower extremity, and suspected osteomyelitis. You know the most likely organism causing this infection in an otherwise healthy child is:

- a. *Klebsiella kingae*
- b. *Salmonella*
- c. *Staphylococcus aureus*
- d. *Moraxella catarrhalis*

## Answer:

An eight-year old male presents with fever, guarding and tenderness to the lower extremity, and suspected osteomyelitis. You know the most likely organism causing this infection in an otherwise healthy child is:

C. Staphylococcus aureus



## Question

You evaluate a three-year old child with community acquired pneumonia. Appropriate antimicrobial therapy may include:

- a. Cefepime
- b. High dose amoxicillin
- c. Sulfamethoxazole trimethoprim
- d. Azithromycin

## Answer:

You evaluate a three-year old child with community acquired pneumonia. Appropriate antimicrobial therapy may include:

B. High dose amoxicillin

## Question

The results of a spinal tap completed on a previously healthy 6 year old with fever, severe headache and malaise with low grade fever reveals opening pressure of 12, WBC count of 13mm<sup>3</sup>, mildly elevated protein and normal glucose. The MOST likely diagnosis is:

- a. Viral meningitis
- b. Bacterial meningitis
- c. Meningococemia
- d. Fungal meningitis

## Answer:

The results of a spinal tap completed on a previously healthy 6 year old with fever, severe headache and malaise with low grade fever reveals opening pressure of 12, WBC count of 13mm<sup>3</sup>, mildly elevated protein and normal glucose. The MOST likely diagnosis is:

- a. Viral meningitis

## Question

A child presents with erythema infectiosum to the bilateral cheeks, a lacy maculopapular rash that started on the trunk, and decreased reticulocytes. You suspect this patient has:

- a. Rocky mountain spotted fever
- b. Parvovirus B19
- c. Cytomegalovirus
- d. Pneumocystis jirovechi

# Answer:

A child presents with erythema infectiosum to the bilateral cheeks, a lacy maculopapular rash that started on the trunk, and decreased reticulocytes. You suspect this patient has:

B. Parvovirus B19

## Question

The recommended therapy for a 10-year old child with a target lesion is which of the following?

- a. Amoxicillin
- b. Clindamycin
- c. Doxycycline
- d. Cefdinir

Answer:

The recommended therapy for a 10-year old child with a target lesion is which of the following?

C. Doxycycline



## Question

You suspect a patient has meningococemia secondary to *N. meningitidis*. You immediately order which of the following antimicrobials?

- a. Cefotaxime
- b. Acyclovir
- c. Tobramycin
- d. Azithromycin

## Answer:

You suspect a patient has meningococemia secondary to *N. meningitidis*. You immediately order which of the following antimicrobials?

A. Cefotaxime

## Question

This viral infection is the classic cause of infectious mononucleosis and is associated with malignancies including lymphoma:

- a. Parvovirus B19
- b. Cytomegalovirus
- c. Adenovirus
- d. Epstein Barr Virus

## Answer:

This viral infection is the classic cause of infectious mononucleosis and is associated with malignancies including lymphoma:

D. Epstein Barr Virus

# Conclusions

- Many infectious diseases affect children
- Some are self-limiting and some require significant interventions/therapies
- With appropriate identification and evaluation, proper management strategies can improve outcomes