The Annual General Pediatric Review & Self-Assessment

Nicklaus Children's Hospital

Infectious Diseases - II

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Dr. Kowalsky has not had (in the past 24 months) any relevant conflicts of interest or relevant financial relationship with the manufacturers of products or services that will be discussed in this CME activity or in his presentation.

Dr. Kowalsky will support this presentation and clinical recommendations with the "best available evidence" from medical literature.

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VACCINES

Immune Globulin and Live Vaccines

- IG, IVIG, blood, plasma interfere w MMR and Varicella vaccines
  - PRBC's 10ml/kg: wait 6 mo
  - VariZig: wait 5 mo
  - Kawasaki IVIG 2gm/Kg: **wait 11 mo**

- If IG is received within 14 days after live vaccine is given (MMR or V):
  - Repeat vaccine dose

Pregnancy

- Inactivated vaccines: no contraindications

- Live vaccines: Contraindicated
- -Includes MMR, Varicella, LAIV

  -YF vaccine is a precaution

  -If Rubella vaccine inadvertently given: Not a indication for termination of pregnancy

- Pregnancy in household member: Not a contraindication to any vaccine (i.e. VZV, LAIV)

Immunodeficiency in Household Contact

- Contraindication: Smallpox, OPV.
- Varicella vaccine: Indicated. If recipient develops rash:
  - Avoid direct contact if possible
  - VariZIG (IVIG) is not indicated
- MMR, Rotavirus, LAIV: Indicated

Live Viral Vaccines and Steroids

- Should not be administered if receiving:
  - >2mg/kg/day prednisone daily or alternate days
  - >20mg/day if weight > 10kg
- If above dose given for > 14 days wait at least 1 month after last dose to give vaccine
  - Shorter duration: OK to give vaccine
  - Lower doses: not a contraindication
  - Aerosol and topical steroids: Not a contraindication

Management of Exposures to Measles

- Routine MMR or MMRV 12-15 mo, 4-6 yrs
- Pre and Post Exposure Prophylaxis:
  - Community Outbreak @6-11 mo*
  - Travel to endemic area @6-11 mo*
  - School or Day-care If <2 doses MMR w/i 3d
  - < 6 mo IG w/i 6 days
  - 6-12mo MMR w/i 72 hrs *
  - Pregnant, HIV, IC IVIG w/i 6 days

*If MMR vaccine given <12 m/o doesn't count toward series

MMR Adverse Events

- **Fever (6-12 days)** 5 to 15%
- Rash 5%
- Arthralgia 0.5% (25% women)
- Arthritis 0.1% (10% women)
- Febrile Sz's 1 in 3000 to 4000
- Thrombocytopenia 1/22,000 to 1/40,000

[AE's mainly due to the Rubella component]

Allergies and Vaccines

Hypersensitivity to eggs

- Influenza (IIV)
  - no contraindication (even with anaphylaxis)
- MMR
  -no contraindication

Neomycin

- Measles
  - non anaphylaxis = immunize
  -anaphylaxis = allergy consultation

-If live viral vaccines not given at same time wait 28 days in between doses (MMR, V, PPD/IGRA)

VIRUSES

HERPES SIMPLEX VIRUS

- HSV Type-1
  - Herpetic gingivostomatis: Grouped vesicles at "vermilion border"
  - **Eczema herpeticum**
  - Erythema multiforme
  - Encephalitis: mental status changes, **Seizures**; temporal lobe predilection.
    CSF pleocytosis with lymphocytosis and RBC's (late with necrosis)

HERPES SIMPLEX VIRUS (HSV)

- Genital Infection: >50% cases by HSV type I
- Neonatal: Primary infxn - risk 25 to 60%
  Recurrent - risk <2%

  Disseminated- Freq. 25%
  - High mortality 30%

  CNS - Freq. 30%
  - High mortality 30%

  SEM - Freq. 45%
  - Low mortality 5%
- Dx: Surface HSV Cx/PCR of NP, conjunctiva, anus; Serum PCR, **CSF HSV-PCR;** MRI and EEG **(CNS);** dec PLT, elevated ALT (Dissem.dz)
- Tx: Acyclovir (20mg/kg/dose) q 8 hrs IV (14-21 days)
- Suppressive Tx: PO Acyclovir x 6 months

Varicella Zoster Virus (VZV)

- Primary: Varicella (chicken-pox)
  - Very infectious: 1 to 2 days before rash until crust over (7-10 days)
  - Incubation period: 14 to 16 days (10 to 21days)
  - Rash: lesions are in different stages
  - **Complications: secondary bacterial Infxn (Grp A Strep) and Bullous impetigo (S aureus): Prevent via hand washing with soap and water.**
    - Reye syndrome with aspirin use.
    - Encephalitis; Cerebellar ataxia.
    - **Postinfectious Arthritis** 2 to 3 weeks after VZV infection

Varicella Zoster Virus (VZV)

- Recurrent: herpes zoster (shingles)
  - Grouped vesicles that cross 1-3 dermatomes
  - Frequent in IC but can be seen in normal host

- Dx: clinical, PCR, Cx, DFA, serology
- Tx: Acyclovir; foscarnet for acyclovir resistant
- If Exposed/Prevent: vaccine if given w/i 72 hrs
- In susceptible host: VariZIG w/i 10 days of exposure
- Treatment: only indicated if IC, >12 and unvaccinated, chronic cutaneous/pulm d/o, receiving ASA or steroids

VariZIG

- Indications:
  - Exposed IC Pt's
  - Non-immune pregnant women
  - Neonate born to mother with Varicella infxn 5 days before delivery to 2 days after delivery

[Varicella]

- Isolation: Standard, airborne and contact
  - Minimum 5 days after onset of rash to crusting-over
  - Exposed Pt: 8 to 21 days (28 days if VariZIG)

Cytomegalovirus (CMV)

- Acquired
  - Largely asymptomatic
  - Mononucleosis-like syndrome: (heterophile Ab negative)
  - Lymphadenopathy, hepatitis, pneumonitis
- Congenital
  - Most common congenital infection
  - 90% asymptomatic (shed in urine and saliva mainly)
  - Main sequela: **sensorineural hearing loss in 15 -50%**
  - Growth retardation, microcephaly, periventricular Ca, **chorioretinitis**, HSM, jaundice, thrombocytopenia, petechiae, rash (blueberry muffin)

  Dx: **PCR w/i 3 weeks of birth**: Urine, saliva, blood or CSF

  Tx: PO Valganciclovir in neonates for 6 months; IV ganciclovir if does not tolerate oral

Epstein-Barr virus (EBV)

- Infectious Mononucleosis
  - Fever, exudative pharyngitis, Bilat LN, HSM, atypical lymphocytosis, **PCN rash (1 week later)**
  - Complications: **splenic rupture**, hemolytic anemia, thrombocytopenia, agranulocytosis, HLH.
- Lymphoma (Burkitt), Nasopharyngeal CA
- X-linked Post-transplant Lymphoproliferative D/O
- Encephalitis, aseptic meningitis, myelitis, GBS
- Dx: Heterophile Ab pos. (Neg. < 4 yrs); PCR
  Serologies: VCA IgM, IgG; EBNA
- Tx: **Supportive**; Steroids (airway obstruction)
- Counsel:No contact sports while with splenomegaly

Measles (Rubeola)

- Highly contagious: 4 days before S&S to 4 days post rash (KS3)
- Fever, cough, coryza, conjunctivitis; photophobia; Koplik spots (pathognomonic)
- Rash: maculopapular from face-trunk-extremities:(Last symp)
  - Spreads cephalocaudally
- Complications: otitis media, pneumonia, croup, encephalitis; SSPE 7 to 11yrs after infection
- Dx: Serologies; NP, Serum and urine PCR
- Tx: Supportive; Vitamin A
- Isolation: standard + airborne for 4 days after rash

Slide 21

KS3 would just say 4 d before to 4d after onset of rash. easy to remember 4 and 4. plus the "M "is 4 lines thats how I remember. Can mention URI symptoms present befpre rash onset

Kowalsky, Shanna, 4/15/2020

Rubella

- Acquired
  - 25% asympt; generalized fine maculopapular rash
  - Fever, suboccipital, postauricular cervical LN
  - Polyarthralgia/polyarthritis, (adolescent and adult)
- **Congenital (CRS)**
  - Risk: 85% if acquired at < 4 weeks to 5% during 3rd to 4th mo of gestational age
  - HSM, thrombocytopenia, purpura, blueberry muffin rash
  - Eye: **cataracts**, retinopathy (salt and pepper), glaucoma
  - Cardiac: **PDA, peripheral pulmonary stenosis**
  - Neuro: behavioral D/O, MR, meningoencephalitis
  - Dx: Serology (TORCH); PCR
  - Tx: Supportive
  - Isolation: standard and droplet precaution for 7 days after rash for postnatal infxn

Mumps

- Swelling of salivary glands: parotitis (most common)
- Transmission: infectious secretions 1-2 days before to 5 days after parotid swelling
- Complications in older children/adults:

  orchitis (post-puberty); pancreatitis, meningoencephalitis
- Dx: serology; Cx or PCR of NP
- Tx: Supportive
- Isolation: droplet until 5 days after parotid swelling (no longer infectious)

Parvovirus B19

- Erythema Infectiosum (Fifth Disease)
- High fever (40.0C)
- **Rash (slapped cheeks and lace-like/evanescent): trunk and spreads peripherally**; circumoral pallor
- Arthralgia and arthritis (esp. adults)
  - This is the immune phase: not contagious
  - Acute phase 7 to 10 days prior
- **Complication: Erythroid hypoplasia in IC, aplastic crisis in pts with hemoglobinopathies**
- Congenital: fetal death/hydrops in 5 to 10%
- Dx: serology; PCR. Tx: IVIG for IC
- Isolation: none with rash

Influenza

- Infectious period 24 hrs before S&S to 7days
- Sudden high fevers, malaise, myalgias, HA, dry cough, sore throat, rhinitis, conjunctival injection, abd pain, N/V
- Incubation: 1 to 4 days
- Complications: Bac pneumonia, sepsis-like picture, Reye syndrome, parotitis, myositis, encephalitis
- Dx: Antigen detection EIA (rapid); PCR NP
- Tx:Oseltamivir and Zanamivir x 5 days for types A & B
  Peramivir IV and Baloxavir PO x1dose for types A & B
- Prevention: annual vaccine > 6 mo; High risk groups
- Isolation: Droplet precaution

Respiratory Syncytial Virus (RSV)

- Age < 2 yrs
- Viral shedding: 3-8 days; (3-4 wks in neonates)
- Low/No Fever, tachypnea cough, wheezing, rales
- URI, bronchiolitis, pneumonia; apnea (neonates)
- **CXR: perihilar vascular cuffing; hyperinflation**
- Increase M&M: Cardiopulmonary comorbidities, prematurity/low birth weight, IC
- Dx: NP PCR, Ag detection (DFA) via NP Aspirate;
- Tx: **supportive mainly**; Ribavirin to IC
- Prevention: Hand washing; **Contact precautions**.

SARS-CoV-2 (COVID-19)

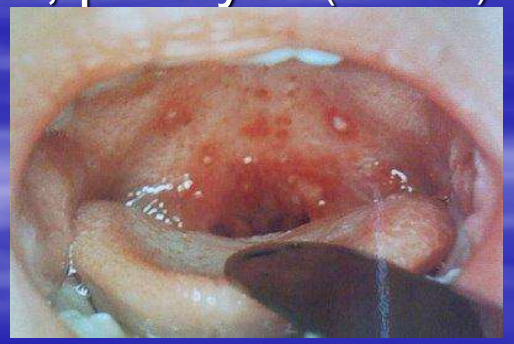
- Emerged in China late 2019
- Most common symptoms children: Fever, cough
- Other symptoms: anosmia, ageusia. Conjunctivitis, rash, flu-like, GI
- Mild or asymptomatic illness
- Racial ethnic minority groups Inc. risk severe dz.
- Complications: resp. failure, acute cardiac injury, AKI, shock, coagulopathy, MOF
- Labs: lymphopenia, leukopenia, incr. CRP/procal, elevated ALT/AST
- CXR: normal, (uni)bilateral infiltrates, ground glass opacities
- Diagnosis: viral RNA or direct antigen testing from resp. source. Serological testing not helpful
- Transmission: small and large resp. droplets. Crowded, poorly ventilated spaces
- Incubation period: 2-14d. Contagious 2d before -10d after symptoms
- Treatment: changing, antivirals, steroids, Moab
- Isolation: standard, droplet, contact, airborne

Rotavirus

- Age <2 yrs
- Fecal-Oral transmission; Day-care attendance
- AGE: vomiting followed by diarrhea for 3-7 days; fever
- Complication: Dehydration, electrolyte ABNL, acidosis
- Dx: PCR, Stool EIA
- Tx: supportive
- Isolation:Contact for diapered and Incontinent children
- Vaccine: Do not begin in older than 15 wks of age
  - Give final dose no later than 8 m/o age

Enterovirus

- Coxsackieviruses, echoviruses, enteroviruses, polioviruses, parechovirus
- Fever, rash: Hand-foot-mouth Disease
- Resp: common cold, pharyngitis, herpangina, stomatitis, parotitis, bronchiolitis, pneumonia.
- Neuro:aseptic meningitis, encephalitis, paralysis(EV-D68)
- GI: AGE, abd pain, hepatitis
- Eye: hemorrhagic conjunctivitis
- Heart: myocarditis (Coxsack-B)
- Neonate: severe disseminated Dz



- Dx: PCR: CSF and serum Cx: throat, stool, rectum
- No treatment; IVIG in IC, myocarditis and Neuro Pts,

Roseola (HHV-6)

- Exanthem subitum or Roseola infantum
- High Fever (>39.5C)[>103.0F]: 3 to 7 days
- Followed by an erythematous maculopapular rash
- Cervical and occipital LN
- Seizures: 10 to 15% during febrile stage
- Dx: Clinical; Encephalitis: Serum and CSF PCR
- Tx: None; For Encephalitis or IC: Ganciclovir

Rabies

- Exposure: secretions (saliva) from infected animal
- Bats, raccoons, skunks, foxes, coyotes, mongoose, woodchuck
- Cattle, dogs, cats, ferrets (less likely)
- Not in rodents or lagomorphs (rabbits)
- Acute, progressive CNS involvement: anxiety, radicular pain, dysesthesia, dysphagia, seizures, hydrophobia; death (100%)
- Dx: Ag in brain tissue (DFA); Negri bodies; Cx/PCR saliva, serum and CSF
- Prevention: **+RIG + Human diploid cell vaccine (HDCV) 4 doses: (Days**
- **0, 3, 7, 14); (If IC give extra dose at 28 days)**

Dogs + Cats can be confined and observed for 10 days

Parainfluenza

- Type 1: most common Fall
- Type 2: Fall and less severe
- Type 3: spring and summer
- Rhinorrhea, fever, wheezing; RSV (-)
- Laryngotracheobronchitis **(croup),** parotitis pneumonia, bronchiolitis, myopericarditis
- Sz, Aseptic meningitis, encephalitis, GBS
- Dx: PCR
- Tx: Supportive; Ribavirin, IVIG for IC

Adenovirus

- Pharyngoconjunctival fever
- Occurs during summer; Asso.camp/swimming
- Common cold, pharyngitis, tonsillitis, OM
- Acute hemorrhagic keratoconjunctivitis, aka“follicular”; hemorrhagic cystitis
- Pertussis-like syndrome, pnuemonia, bronchiolitis
- Gastroenteritis; hepatitis
- Neuro: Meningitis and encephalitis
- Dx: PCR; NP Ag, Cx

HIV
(Acute Retroviral Syndrome)

- Fever 96%
- LN 74%
- Pharyngitis 70%
- Rash 70%
- Myalgias 54%
- Arthralgias 54%
- Diarrhea 32%
- Headaches 32 %
- N/V 27%
- HSM 14%
- Weight loss 13%
- Thrush 12%
- Neuro: 12%;
  - meningitis, encephalitis facial palsy, GBS, etc.

(PT's with zoster, Parotitis,

Chronic thrush, TB, FTT)

HIV
Immune Disregulation

T-lymphocytes	-Decreased CD4+ T cells
	-Increased CD8+ T cells
	(decreased in advanced disease)
Natural killer cells	-Decreased number/cytotoxicity
Monocytes	-Decreased stimulation of T cells
Neutrophiles	-Decreased number/chemotaxis
B-lymphocytes	-Polyclonal activation:
	Increased IgG, IgM, IgA:
	A reduced antigen specific response

HIV Testing

- HIV Antigen/Antibody (4th generation test)
- HIV DNA by PCR (Pro-viral DNA in infected mononuclear cells); < 18 m/o
- HIV RNA quantitation (viral load); viral RNA in plasma
  - Represents viral replication
  - Progression/risk for disease progression
  - Response to therapy
  - Less valuable than HIV DNA by PCR for diagnosis in neonates

HIV

- **CD4+ T-lymphocyte #** and **percentage** is the critical parameter and marker of disease prognosis in pediatrics.

Fungal

Pneumocystis (PCP)

- P. jirovecii (PJP); Atypical Fungus
- In IC pts (**HIV, prolonged steroids**)
- Subacute diffuse **pneumonitis w dyspnea**, tachypnea, **O2 desaturation: Hypoxic**; nonproductive cough, fever and chills.
- **CXR: bilateral diffuse interstitial pattern**
- Dx: methamine silver stain on bronchoscopy
  w BAL or induced sputum; PCR
- Tx: TMX-SMX, IV pentamidine, atovaquone x 21days;
  Steroids for mod. to severe cases x 21 days: if PaO2 < 70 mm Hg or A-a DO2 that is >35 mm Hg

Candidiasis

- Candida albicans
- Thrush, **diaper rash (satellite)**, vaginitis
- Tx Nystatin; If fail, Tx w fluconazole
- Invasive Disease:
  - Risk Factors: Broad spectrum **(Recent) Abx**, immunosuppression, central lines, heavy colonization, hyperalimentation/lipids, ICU care, candiduria; Very low birth wgt/preterm neonates.
  - Tx: removal line; fluconazole (stable Pt)
    amphotericin B (unstable Pt, IC and neonates)

Coccidioidomycosis

- Found in soil; Infxn via inhalation of **dust borne** arthroconidia in **Southwestern US**
- Asymptomatic or self-limited in 60% to 65%
- Fatigue and wgt loss; Fever, cough, rash, erythema multiforme, **e. nodosum**, myalgia, arthralgia, HA
- Resp. infxn: **pneumonia, pleural effusion, pulm cysts, nodule, cavitary lesions, coin lesions CXR:diffuse bilat. infiltrates**
- Disseminated: skin/soft tissue, bone and joints, meningitis.
- Dx: Cx and serology; **Histopathology Bx: Spherule**
- Tx: Fluconazole or Amphotericin B

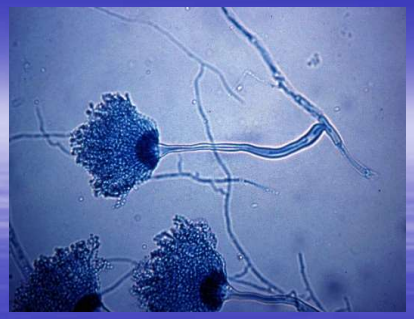
Histoplasmosis

- In soil form bird, bats, chicken feces in Mississippi-Ohio River Valleys
- Asymtomatic-95% of time
- Influenza-like illness, chest pain; hilar adenopathy, mediastinal granuloma and fibrosis, pulm infiltrates; erythema nodosum; disseminated Dz, CNS.
- Dx: Antigen in serum, urine, BAL, CSF; Serology
  Cx of bone marrow, blood, sputum, tissue;
  Skin test is not useful
- Tx: Itraconazole for acute Dz x 6 to 12 weeks
  Amphotericin B for disseminated/severe Dz

Sporotrichosis

- Sporothrix schenckii
- Found in soil: hay, straw, thorny plants (esp. roses), decaying vegetation
- Risk factors: gardening or farming (minor trauma)
- Cutaneous infxn: **painless to slightly tender papule**, subcutaneous firm nodule then ulcerative
- Cx: tissue or wound drainage
- Tx: Itraconazole x 3 to 6 months

Aspergillosis



- Mold
- Transmission by inhalation of conidia (spores)
- Incidence is highest during periods of prolonged neutropenia and fever
- Invasive Dz: IC, GvHD, CGD, T-cell Lymphocyte def.
- Involves: Pulm, sinus, CNS or skin
- Health care associated outbreaks from nearby **construction site** or faulty ventilation system
- Dx: **CT-Scan of chest "halo sign";** Bx of skin, sinus or lung/BAL for Cx and PCR; Serum/BAL antigens
- Tx:Voriconazole+/-Echinocandin; Ampho-B:neonates

Thank You
and
Good Luck!