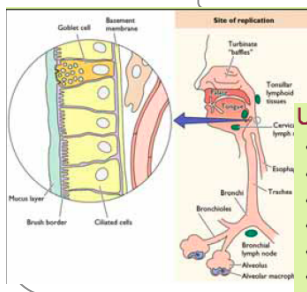


## viral respiratory infections



**Overview-** + most are **virally** induced [bacterial superinfxn. may follow]. most are fairly mild, self-limiting/ confined to the URT. URT infxns may spread downwards and cause more severe infxn/death [infants/kids esp.]. LRT infxns typically have more severe clinical outcomes.

### Upper Respiratory Tract: Lower Respiratory Tract:

- |   |   |
|---|---|
| <ul style="list-style-type: none"> <li>• Rhinitis (common cold)</li> <li>• Pharyngitis ('sore throat')</li> <li>• Laryngitis</li> <li>• Tonsillitis</li> <li>• Sinusitis &amp; Otitis Media</li> <li>• Influenza</li> </ul> | <ul style="list-style-type: none"> <li>• Laryngo-Tracheo Bronchitis (Croup)</li> <li>• Bronchitis</li> <li>• Bronchiolitis</li> <li>• Pneumonia</li> <li>• Influenza</li> </ul> |
|---|---|

- + different pathogens = one syndrome e.g.- rhino/coronaviruses = common cold.
- + any one pathogen = more than one disease RSV=croup/pneumonia
- + bugs below can cause disease without URT infxn, & viruses can infect through the URT, but can cause disease at other sites- measles/mumps, herpes, VZV CMV
- + **polarized virus spread**- direction of release can determine outcome of infxn
- release at apical membranes**- localized infxn [influenza, rhino,RSV,corona
- release at basal membrane**- disseminated/systemic [measles/mumps]

### clinical signs/symptoms

#### URT

1. **rhinitis**- common cold, watery-mucoid nasal discharge 'coryza'. sneezing sore throat, fever sinusitis/O.M. often followed by bact.infx
2. **pharyngitis**-sore throat. generalized erythema of pharynx. not localized to tonsils/ no coryza. fever/cough
3. **laryngitis**-inflamm of vocal cords, hoarse lost voice, sore throat. viral/bact/enviro.
4. **tonsillitis**-local infxn. of tonsils- red surface exudate. may start as pharyngitis bacterial is common.
5. **sinusitis& O.M.**- painful inflamm. sinuses/ middle ear.
6. **Influenza**- fever, myalgia, sore throat, cough, HA, fatigue. usually NOT much nasal discharge. frequent LRT involvement (pneumonia)

#### LRT

1. **laryngo-Tracheo bronchitis [croup]**- acute inflamm of larynx and trachea. often preceded by a "cold". fever, hoarseness, cough, inspiratory stridor. can be **life threatening in kids**.
2. **bronchitis**- inflamm. of **bronchi** [larger airway passages in lungs]. fever, cough, wheezing [expiratory sound produced by airflow through bronchioles]
3. **bronchiolitis**-inflamm of terminal **bronchioles**. usually preceded by cold- like symptoms- later develop into major pulmonary illness. fever, rapid respiration, exhausting cough and wheezing. very common in kids in developing world.
4. **pneumonia**- acute respiratory disease w/fever, restlessness, cyanosis. **can be life-threatening**.
5. **influenza**- URT and systemic symptoms OR LRT (pneumonia) as a frequent complication

#### URT

- Rhinitis:
  - Rhinovirus
  - Coronaviruses
  - Enteroviruses

- Pharyngitis:
  - Adenoviruses
  - Epstein-Barr virus (EBV)

- Laryngitis, tonsillitis, sinusitis, otitis media:
  - all viruses listed

- Influenza
  - Influenza virus

#### LRT

- Croup & Bronchitis:
  - Parainfluenza virus
  - Respiratory syncytial virus
  - Influenza

- Bronchiolitis
  - Respiratory syncytial virus
  - Parainfluenza virus

- Pneumonia
  - Influenza virus
  - SARS Coronavirus
  - Respiratory syncytial virus

- Influenza
  - Influenza virus

#### rhinoviruses

**general- major cause of common cold** over 100 serotypes. ~50% of all colds. **picornavirus family** ["small RNA"]-related to enteroviruses [poliovirus, coxsackievirus\*, echovirus\*] and hepatoviruses [ hepatitis A] \*cause colds too.

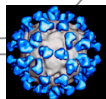
**structure/replication**- non-enveloped icosahedral. **genome**- + mRNA. **cell Receptor**- ICAM-1 on epi cells. not suited to GI tract- too hot and too acidic. these properties distinguish rhinoviruses from enterovirus.

**clinical**- inhalation- infxn. of URT. **short incubation**- 2-4 days → HA, sore throat. profuse watery discharge from nose. acute O.M./sinusitis may occur. **acute disease period**- 3-7 days/ **infx. resolves**- 1-2 weeks [unless secondary infxn.] **symptoms** largely caused by immune response.

**epi**- ubiquitous world wide. efficient person-to-person transmission via sneezing/physical transfer of secretions- fomites can remain infectious for several hours on fomite...

**prevention**- hand washing etc., vaccine impractical- too many serotypes. 2 ary bact. infxn. treated w/antibiotics

**treatment**- none. symptom treatment. **acquired immunity**- after infxn- short period of immunity to all serotypes. longer to specific one.



#### Coronaviruses

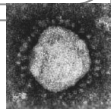
**general- 2nd most common cause of cold**. in 50s- found rhinoviruses, couldn't account for ~50% of colds.=20-30% of colds **order nidovirales**- can also infect cattle, pigs, rodents, cats, dogs, birds

**morphology**- enveloped w/ club-shaped spikes, crown like appearance. ss+ RNA

**pathogenesis**- infect a variety of mammals/birds. cannot be grown in culture- don't know how many there are.

humans- resp. infx. like SARS, enteric infxn in infants, neuro syndromes [rare]. **transmission**- resp. secretions, fecal-oral. greatest incidence in winter. **re-infxn** indicates most. serotypes. mild/self-limiting illness usually. in URT- localized. SARS-viral pneumonia of LRT

**SARS**- outbreak from china 2003. novel human coronavir. death = resp. failure from alveolar damage. by July of same year- contained. latest infxn from china, but from laboratory exposure. currently no known SARS transmission in the world.



#### adenoviruses

**general-non-enveloped**, linear **ds DNA**. 20 triangular surfaces w/penton fibers projecting from each vertex [fibers= attachment to host cell]

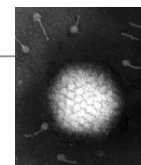
**clinical**- infect mammals. 5% resp infxn. in kids. **transmission**- droplet/fomite/ingestion. infect **epi. cells of resp. tract**, frequently **asymptomatic**. can cause inflamm/necrosis- acute resp. syndromes local **LAD**. some serotypes also infect epi cells of GI/bladder/eye.

**syndromes**- 1. **acute pharyngitis w/ fever**. 2. **pneumonia/pneumonitis** [in kids]. 3. **Acute resp disease ARD**- epidemic form of acute pneumonia- crowded living conditions like the military. 4. **pharyngo-conjunctival fever**- acute conjunctivitis w/ sore throat and fever other serotypes- pink eye, cystitis, gastroenteritis, adenitis [abd. pain]

**diagnosis**- culture, serology, ELISA for viral antigens. **PCR**.

**treatment**- none, most infxn. mild. symptom treatment.

**prevention**- vaccine- used to prevent ARDS, live adenovirus- 3 serotypes. ran out 1999, 2009 should be more for military. good hygiene



#### paramyxoviruses-

family contains resp. pathogens [below] as well as measles and mumps virus

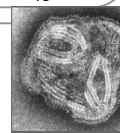
#### parainfluenza virus

**general-enveloped** -ssRNA, nonsegmented genome, 4 serotypes, env glycoproteins-attachment, fusion/HA properties

**clinical-croup** most common. found in 30% of croup cases. [others include influenza/RSV]. can also cause pharyngitis cold-like, LRT-bronchiolitis/pneumonia. virus replicates locally in resp tract lining of URT- may spread to lungs

**diagnosis**- ELISA detection of PIV antigen from nasopharyngeal/throat swabs. **serology**- 4fold or greater rise in titer

**treat/prevention**- no treatment. severe cases of croup =hospitalized/O2 tents. **vaccine**- killed virus tried- no success Medimmune currently working on live attenuated intranasal vaccine against 1 serotype.and a combo RSV/PIV one.



#### respiratory syncytial virus

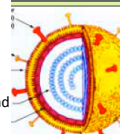
**general**- genus **pneumovirus** of **paramyxovirus** family. **enveloped. ss- RNA**. structure similar to PIV. two subgroups- a and w/ variation between the two. both create sizable epidemics/yr. cause cells to create- syncytium- clump together

**clinical- most common cause of bronchiolitis** in children in northern hemisphere.- 50% infected by 1 year/ all by 2. **most common cause of bronchiolitis and pneumonia in infants**. also = croup/bronchitis/O.M. **infant mort.** 5-1%- most at risk are preemies/peeps w/heart or lung conditions. in older- much milder symptoms [cough/wheeze/resp.distress]. duration 10-14 days. death = heart/resp failure often from bacterial superinfxn.

**pathogenesis**- **transmission**- resp. droplet or direct contact- mouth/hand. infects epi cells of U/M/Lower resp. tracts. infants have **no passive immunity**. re-infection happens, but mild.

**diagnosis**- exclude other paramyxos's, adenoviruses, influenza, chlamydia, mycoplasma- use **viral isolation/serology/PCR**

**treat/prevention**- **ribavirin good but causes liver damage/B.M. toxicity**. immunoglobulin and mAb also good especially for kids. **vaccine**- in clin trials- live attenuated RSV and combo RSV/PIV.



#### influenza

**general- orthomyxoviridae. enveloped- spikes- Hemagglutinin, Neuraminidase. ss- RNA in 8 segments** \*\* important for shift.

NA- activates HA for attachment, HA- attaches to cell receptors. human influenza-2 NA's and 3 HA's- the genetic diversity of HA and NA is responsible for recurring outbreaks.

**clinical**- fever/myalgia/HA/pharyngitis/cough w/prostration. usually **no coryza**. can be mild to severe. **incubation**= 1-3 days.

**transmission**- droplet/fomite from saliva/nasal secretions/feces/blood. can remain infectious at 37 C for a week!! longer if colder.

**complications**- usually in young/elderly/chronic cardio-pulmonary disease. **pneumonia from bacteria** [H. influenzae, S. aureus, Strep. pneumoniae]. **viral superinfection**. **reyes**- after disease onset- esp. kids- fatty acid infiltration of liver CNS, edema. risk enhanced by salicylates [aspirin]

**diagnosis**- nasal swabs/sputum/bronchial wash/serum. then **viral isolation in culture, serology, ELISA, PCR**. rapid diagnostic tests also available- but always confirm w/ one of previous.

**classifications**- three main groups- **A- avian/mammalian, B- sporadic outbreaks in man only, C- uncommon, usually in man [rare-pigs]** named- TYPE/TOWN FIRST ISOLATED/NUMBER OF ISOLATES/YEAR OF ISOLATION/MAJOR HA/NA- A/SINGAPORE/6/1986(H1N1)

**antigenic drift/shift-DRIFT- point mutations**- minor changes to HA [less to NA]- can make new strains and avoid ab recognition.

**SHIFT- recombination**- between different strains. "reassortment". 8 segments allow for easy process. can occur between strains that infect different species- bad news! creation of entirely NEW HA/NA [only in A types so far]

**epidemic/pandemic- EPIDEMIC**- disease outbreak in many people at same time. [A and B] **drift**

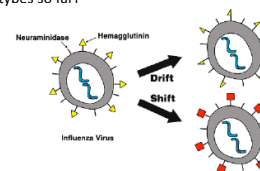
**PANDEMIC**-epidemic over wide area [A, not B- mutates slower] **shift**.

have been 3 pandemics in 20th century- 1919- 20 million died. over time fewer deaths.

**treat/prevention**- antibiotics to prevent/cure bacterial superinfxn. also anti-virals.

**prevent**- good immune response unless drift/shift. now **TIV- trivalent inactivated vaccine** and **LAIV- live attenuated**. have to guess which strains will predominate each year- don't always guess well- 2007/2008. **TIV**- killed virus of currently relevant strains.- for kids/ immunosuppressed/reyes, pregnant, health care workers. **not for**- allergy to eggs, severe prior rxn. to vaccine. **LAIV** live, nasal only for healthy kids/adults **not immunodeficient/active airway disease or asthma**.

**drugs**- amantadine- influenza A, rimantadine- influenza A, Zanamavir- Aand B, oseltamivir- A/B



## Avian Influenza - "Bird Flu"

- The first recorded appearance of Avian influenza H5N1 in humans occurred in Hong Kong in 1997.
- The H5 molecule is common on bird flu strains but has never been seen on epidemic human flu strains.
- Thus, the human population has absolutely no immunity against H5 viruses.
- In October 2003, an epidemic of H5N1 in chickens spread through countries in the Pacific Rim.
- Sporadic human cases of H5N1 have occurred since then, with a high fatality rate of ~60%.
- Most cases thought to have been acquired from close contact with infected birds.
- Rare cases of human-to-human transmission have been reported.
- On April 17 2007, the FDA approved a vaccine for H5N1.
  - Not for commercial sale. Federal government's National Stockpile.

**avian-** first human case 1997. Hong Kong.  
H5 never seen by human immune system.  
2003- spread through chickens. sporadic human cases since w/ 60% mortality.  
most cases = close bird contact. rare = human to human spread.  
vaccine- not available- federal govt Stockpile

## Swine origin Influenza A(H1N1)

- In early 2009, a new influenza A virus emerged and is causing illness and fatality in people.
- The virus is an H1N1 sub-type and was originally called 'swine flu' because it has many similarities with swine influenzas.
- It is now known that the virus contains genes from human and avian species too, and is an entirely new virus.
- The names Swine origin influenza virus (SOIV) or Influenza A(H1N1) are preferred.
- On April 29, the WHO raised the influenza pandemic alert from phase 4 to phase 5.
- As of May 5, 21 countries have officially reported 1490 cases.

**swine-** early 2009- new influenza A = illness/fatality  
H1N1= similar to swine- also contains genes from human and avian species  
phase 5 pandemic alert  
95 deaths/14,000 cases- most deaths assoc. w/ immunocomp. or other illness