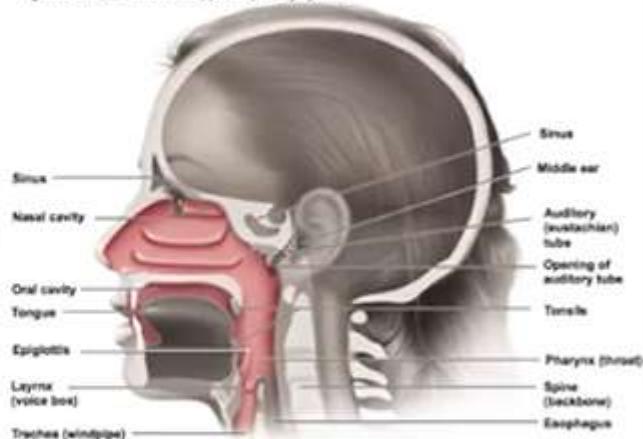


Respiratory System

- Upper respiratory system
 - Nose, pharynx (throat), eustachian tubes
 - Pathogenic microorganisms present as normal microbiota
 - But suppressed by other microorganisms.

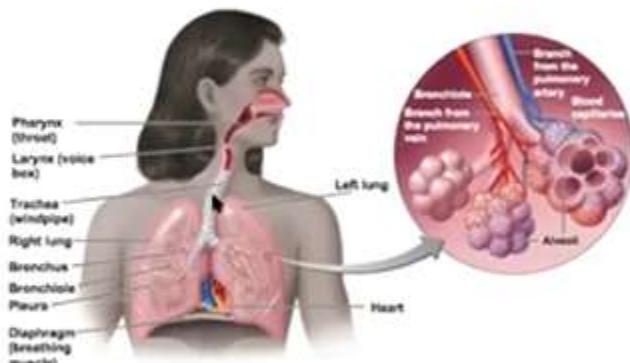
Figure 24.1 Structures of the upper respiratory system.



Respiratory System

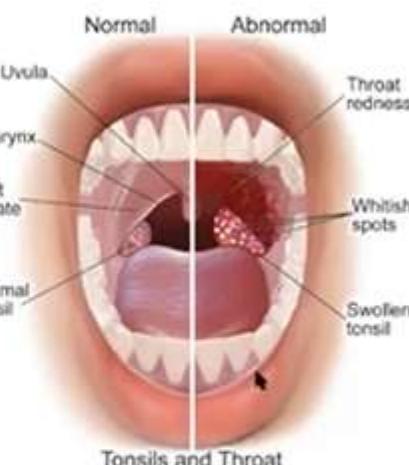
- Lower respiratory system
 - Larynx (voice box), trachea (windpipe), bronchial tubes, and alveoli (air sacs)
 - Ciliated mucous membrane lining
 - Nearly sterile due to ciliary escalator.

Figure 24.2 Structures of the lower respiratory system.



Streptococcal Pharyngitis

- Strep throat
- Upper respiratory infection
- Caused by GAS
 - *Streptococcus pyogenes*
- Gram positive
- β-hemolytic on BAP
- Pharyngitis characterized by local inflammation and fever.



Scarlet Fever

- When *Streptococcus pyogenes* infected by bacteriophage (lysogeny)
- Produces erythrogenic toxin
- Causes pinkish-red skin rash, fever
- Strawberry tongue.



Diphtheria

- Upper respiratory infection
- Leading infectious killer of children in US (until 1935)
- Caused by *Corynebacterium diphtheriae*
- Gram positive bacillus, frequently club-shaped
- Disease characterized by tough grayish membrane on throat
 - Contains fibrin, dead tissue, and bacterial cells
 - Can block passage of air into lungs
- Transmitted by droplets
- DTaP vaccine
 - Diphtheria toxoid
 - Inactivated toxin causes body to produce Abs.



The Common Cold

- Upper respiratory infection
- Caused by rhinovirus (30-50%), coronavirus (10-15%)
- RNA virus
- Thrive at slightly lower temps (33-35°C) (nose)
- Transmitted via airborne droplets
- Symptoms
 - Excessive nasal secretions
 - Congestion
- Antibiotics are useless.



Pertussis

- Whooping cough
- Lower respiratory infection
- Caused by *Bordetella pertussis*
- Obligate aerobe
- Gram negative coccobacillus
- Virulent strains have capsule.



**Not Vaccinated?
No Kisses!**

Get the adult whooping cough vaccine.

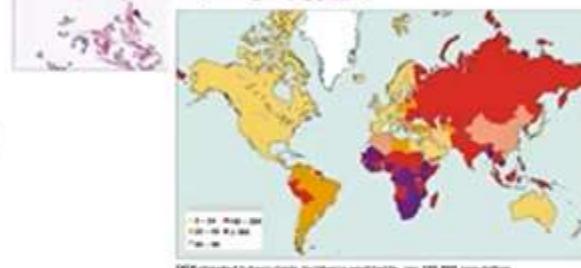
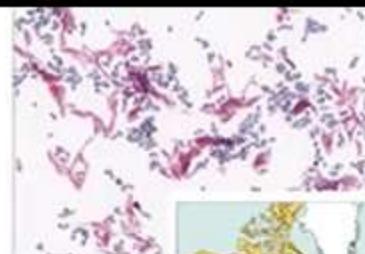
Pertussis

- Bacteria attach to ciliated cells of trachea
 - Impeding ciliary action and destroying cells
 - Ciliary escalator fails to move mucus
- Tracheal cytotoxin
 - Damages ciliated cells
- Mucus accumulation leads to violent coughing
- Gasping for air in between coughs (whooping)
- Broken ribs and irreversible brain damage can occur in small children
- DTaP vaccine

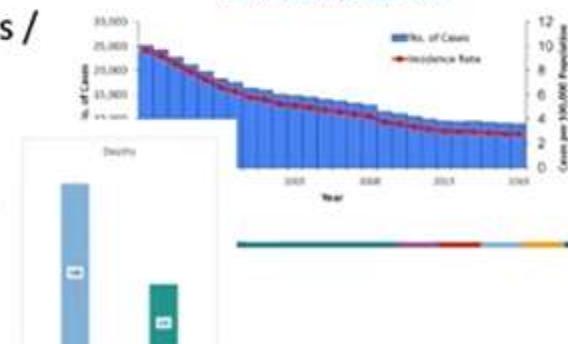


Tuberculosis

- Lower respiratory infection
- Caused by *Mycobacterium tuberculosis*
- Obligate aerobe
- Mycolic acids in cell wall; acid-fast
 - Makes cell resist desiccation
- Acquired by inhalation
- 30% of the world's population is infected
- 9M people develop active infections / year
 - 8916 cases in US (2019)
- 1.5M worldwide deaths (2018)
 - More deaths than any other single microbial agent
 - 542 deaths in US (2018).

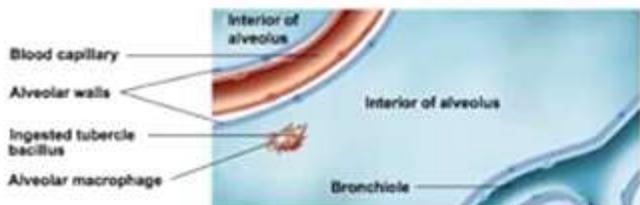


Estimated Tuberculosis Incidence worldwide, per 100,000 population



Tuberculosis

- Mycolic acid stimulate inflammatory response
- Bacteria reach alveoli, ingested by macrophages
- Multiply in macrophage.



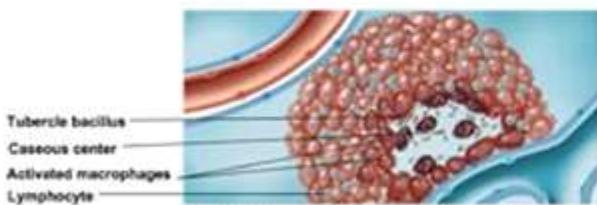
① Tubercle bacilli that reach the alveoli of the lung (see Figure 24.2) are ingested by macrophages, but often some survive. Infection is present, but no symptoms of disease.



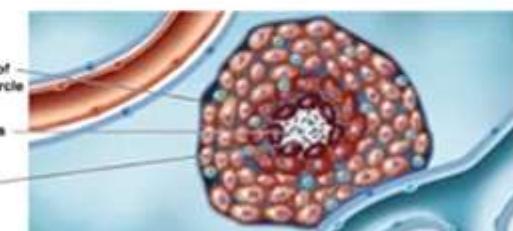
② Tubercle bacilli multiplying in macrophages cause a chemotactic response that brings additional macrophages and other defensive cells to the area. These form a surrounding layer and, in turn, an early tubercle. Most of the surrounding macrophages are not successful in destroying bacteria but release enzymes and cytokines that cause a lung-damaging inflammation.

Tuberculosis

- Chemotactic response that recruits more macrophages
- Forms tubercle (lump, knob)
- Disease is arrested, lesions heal and become calcified
- Visible on X-rays.



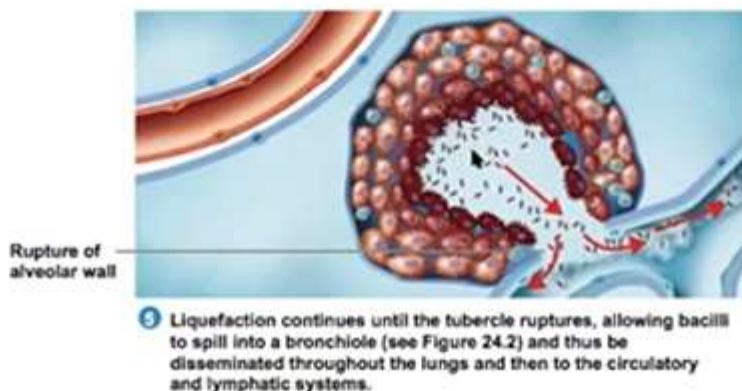
③ After a few weeks, disease symptoms appear as many of the macrophages die, releasing tubercle bacilli and forming a caseous center in the tubercle. The aerobic tubercle bacilli do not grow well in this location. However, many remain dormant (latent TB) and serve as a basis for later reactivation of the disease. The disease may be arrested at this stage, and the lesions become calcified.



④ In some individuals, disease symptoms appear as a mature tubercle is formed. The disease progresses as the caseous center enlarges in the process called liquefaction. The caseous center now enlarges and forms an air-filled tuberculous cavity in which the aerobic bacilli multiply outside the macrophages.

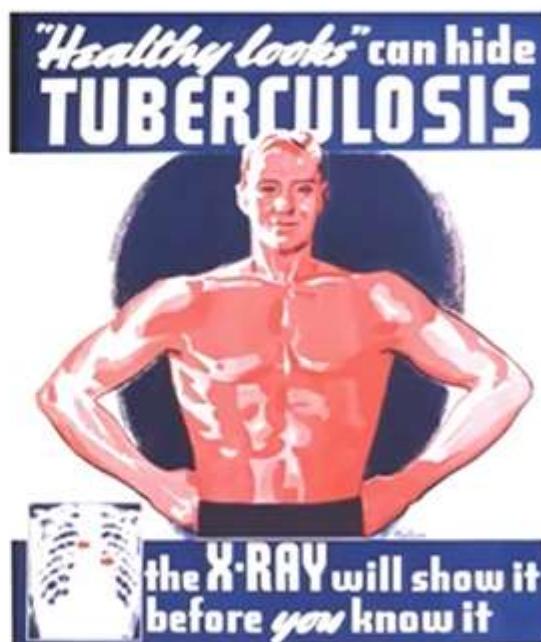
Tuberculosis

- If immune system fails, tubercle ruptures
- Releasing virulent bacilli in to lungs and circulatory system.



Tuberculosis

- Coughing spreads the aerosolized bacteria
- Blood vessels erode and rupture
- Resulting in fatal hemorrhaging.



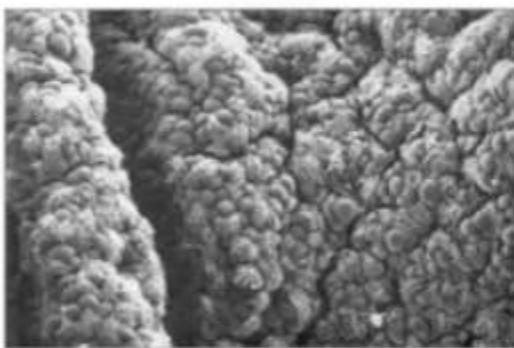
Tuberculosis

- Diagnosis
- Mantoux Tuberculin Skin Test
 - Purified protein derivative from *M. tuberculosis*
 - Injected cutaneously
 - If person infected with TB in the past, memory T cells react
 - Read 48-72 hours after injection
 - Measure induration (hardening) of area around injection site
- Chest X-ray if necessary
- BCG vaccine (not used in US), not effective on adults.



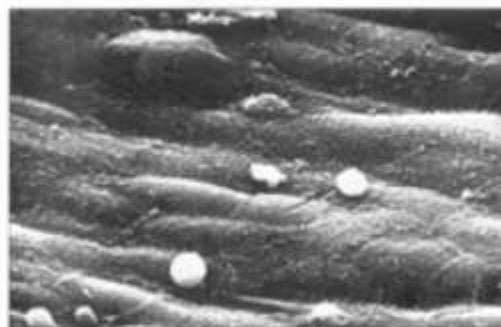
Influenza (The Flu)

- Virus infects cells of lower respiratory tract.



4. A dense jungle-like growth of epithelial cells covers a healthy mouse trachea.

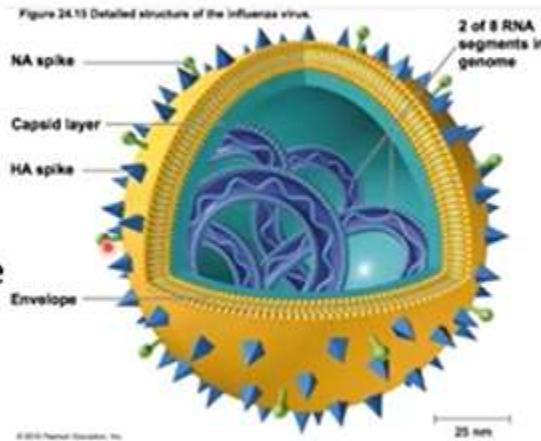
3. Only seventy-two hours after infection the influenza virus transforms the same area into a barren and lifeless desert. White blood cells are patrolling the area, too late.



The Great Influenza by John M. Barry

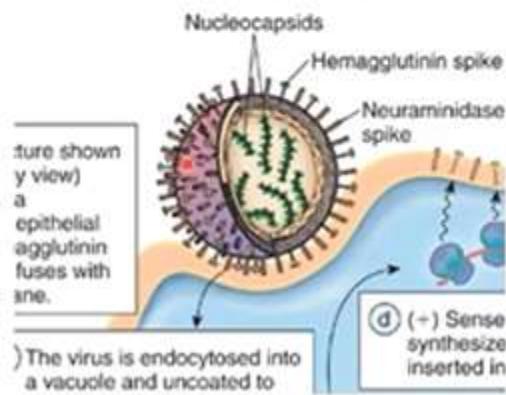
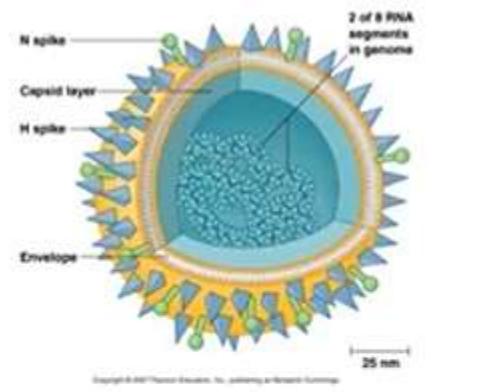
Influenza

- Influenzavirus
 - 4 types (A, B, C, D)
 - A, B – seasonal flu
 - C – mild illness
 - D – primarily affect cattle
 - 8 separate RNA strands
 - Capsid enclosed by envelope
 - Studded with spikes.



Influenza (The Flu)

- Infection dependent on glycoprotein spikes
 - Hemagglutinin (H)
 - H1, H2, H3... (18 subtypes)
 - Binds respiratory mucosal receptors
 - Induces viral entry
 - Abs directed against H
 - Neuraminidase (N)
 - N1, N2... (11 subtypes)
 - Helps release progeny virus from cell
 - Enzyme that degrades respiratory mucous.



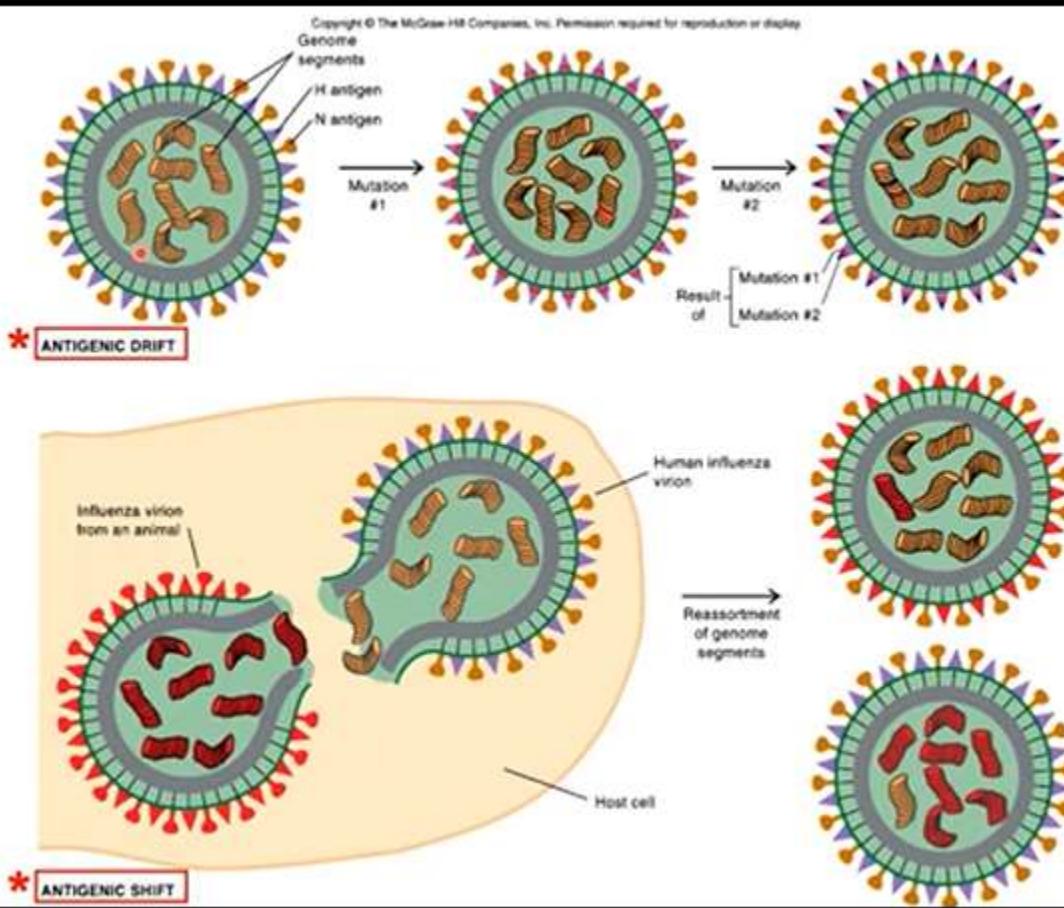
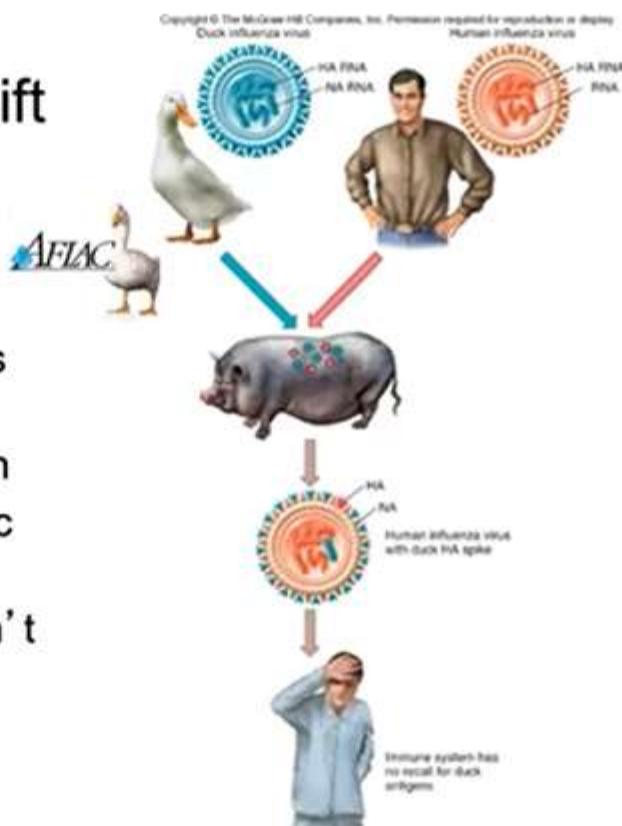
Influenza: Antigenic Drift

- RNA genome undergoes frequent mutations
 - Especially in H and N
 - Antigenic drift
- Decreases host immune recognition.



Influenza: Antigenic Shift

- Genome has 10 genes
 - On 8 RNA strands
- Sometimes they swap!
- Bird virus + human virus infects swine host
- Upon infection of human
- There is no immunologic recognition
- Previous antibodies don't work.



Influenza: Transmission

- Inhalation of virus
 - Respiratory droplets
- Fomites
- Survives for 24 hours on inanimate objects
- Facilitated in
 - Crowded areas
 - Poor ventilation
 - Occupational contact with poultry and swine.



Influenza: Treatment and Prevention

- Drugs that inhibit membrane actions
 - Endocytosis
 - Uncoating
 - Budding (Tamiflu).
- Flu Vaccine
 - A(H1N1), A(H3N2), and 1 or 2 influenza B viruses.



Influenza A(H1N1)pdm09



THE TURKEYS HAVE BIRD FLU. THE COWS HAVE MAD COW DISEASE. I'M TELLING YOU, BOYS... UNLESS WE WANT TO SEE MORE RAM SERVED ON THANKSGIVING, WE'RE GOING TO HAVE TO GET OUR OWN DISEASE! /

- Referred to as swine flu early on
 - Genes similar to influenza virus in pigs in N. America
 - Now shown to be very different
- First detected in US in April 2009
- Signs and symptoms very similar to seasonal flu
- Older adults do not seem to be more at risk
 - About 1/3 had antibodies against it.

Influenza A(H1N1)pdm09

- In the US
 - 60M cases
 - 12,500 deaths
- August 2010
 - WHO declared an end to the pandemic
- It still circulates as seasonal flu.



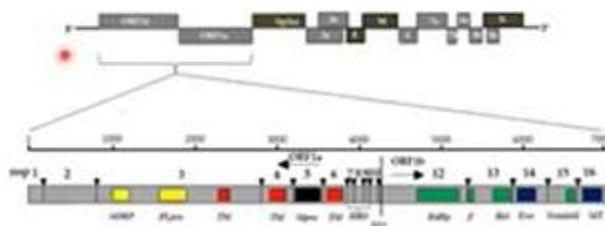
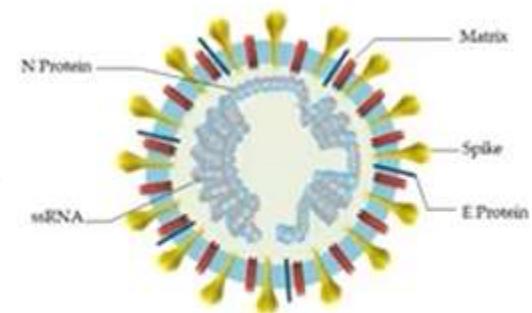
Some perspective

- Every year: 30k-50k people in US die from flu-related complications
 - 34,157 deaths in 2018-19
 - >70% of deaths are people 65+ yrs
- H1N1 not spread by pork or pork products.



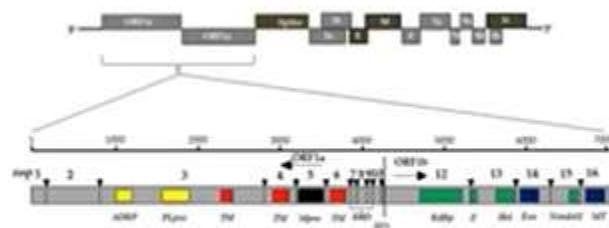
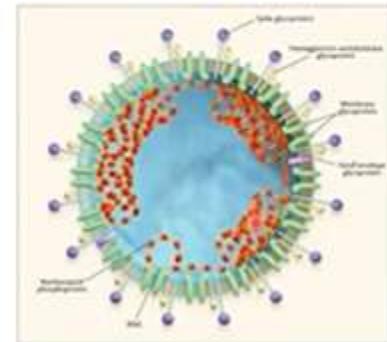
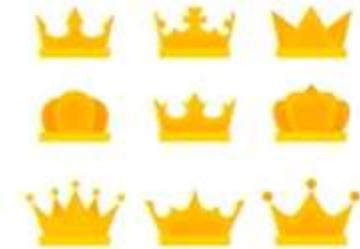
COVID-19

- Caused by novel coronavirus
 - Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2)
 - Humans and other mammals.



COVID-19

- Enveloped RNA virus
 - Genome is 29.9 kb
- Structural proteins
 - Spike (S) glycoprotein
 - Binds protein on lower respiratory tract cells
 - Nucleocapsid (N) protein.



COVID-19

- Structural proteins
 - Membrane (M) glycoprotein
 - Role in shape of viral envelope
 - Can bind other structural proteins
 - Promotes completion of viral assembly
 - Small Envelope (E) glycoprotein
 - Role in production/maturation of virus.

