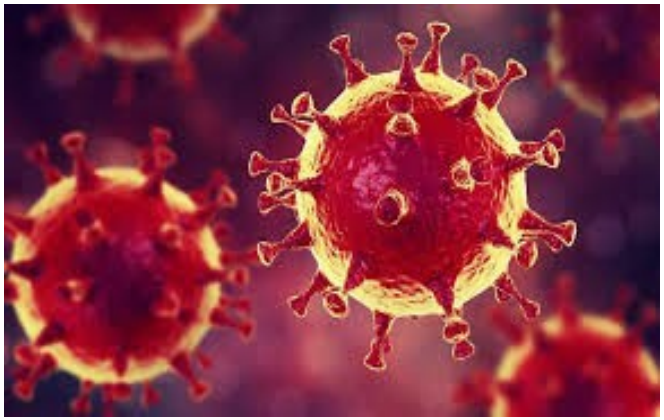
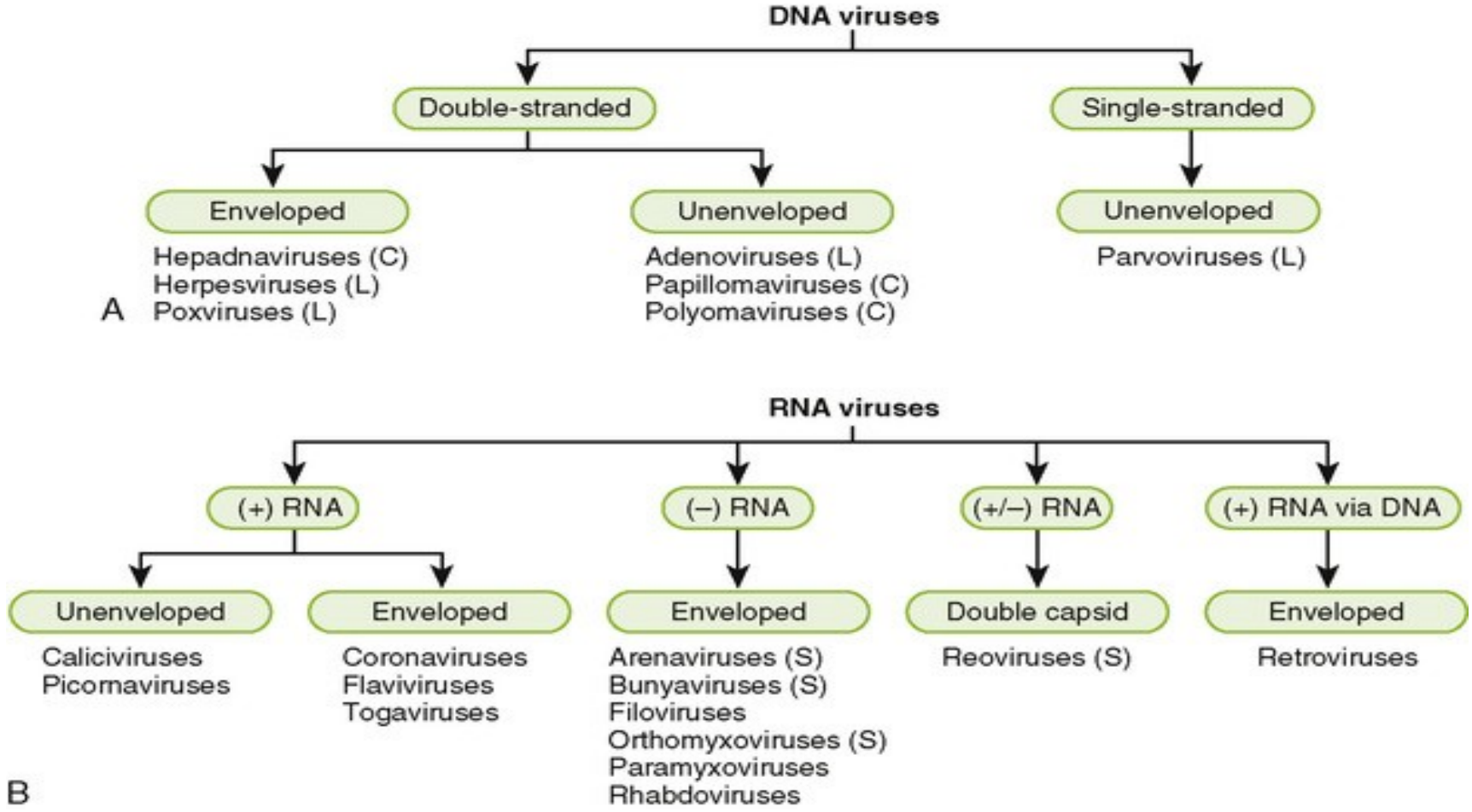
Corona virus Infections—More Than Just the Common Cold



Dr Zahid Khattak
Assistant Professor
Microbiology

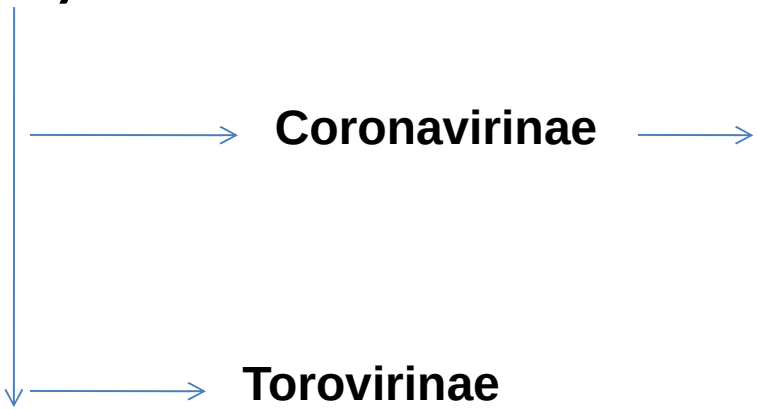
- Emergent zoonotic infection
- Documented human-to-human transmission
- Significant pathogenicity
- Limited options for treatment

Classification



Taxonomy

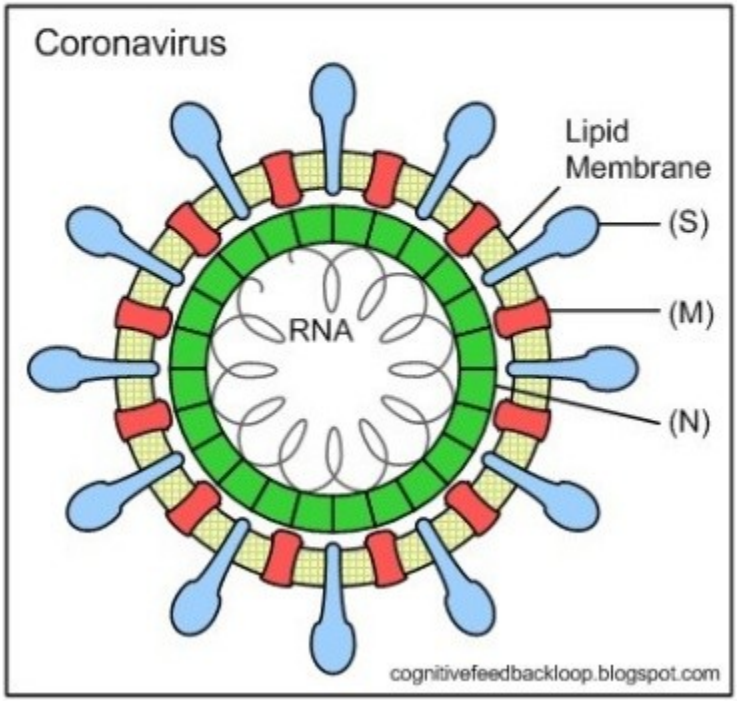
- Family Coronovirdae



- Common human coronaviru
  - 229E (alpha coronavirus)
  - NL63 (alpha coronavirus)
  - OC43 (beta coronavirus)
  - HKU1 (beta coronavirus)
- Other human coronaviruses (Zoonotic)
  - MERS-CoV(beta coronavirus)
  - SARS-CoV(beta coronavirus)
  - 2019-nCoV(beta coronavirus)
- Gammacoronavirus
- Deltacoronavirus

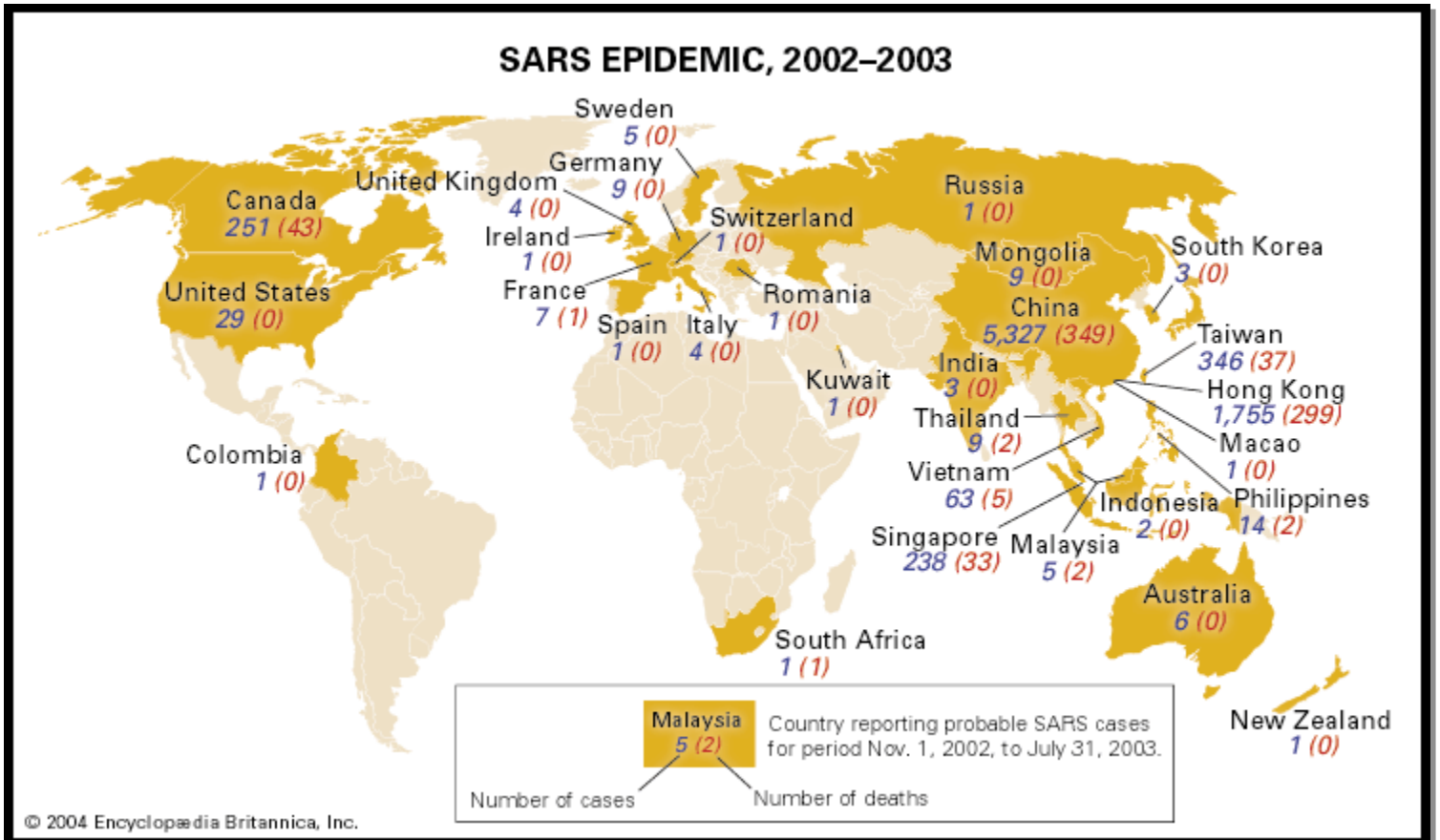
Morphology & Structure

- Pleomorphic
- Enveloped
- 60-220nm diameter
- Non segmented SS + RNA
- Nucleoprotein (N)
- Transmembrane protein (M)
- Spike (S) glycoprotein
- HE Glycoprotein

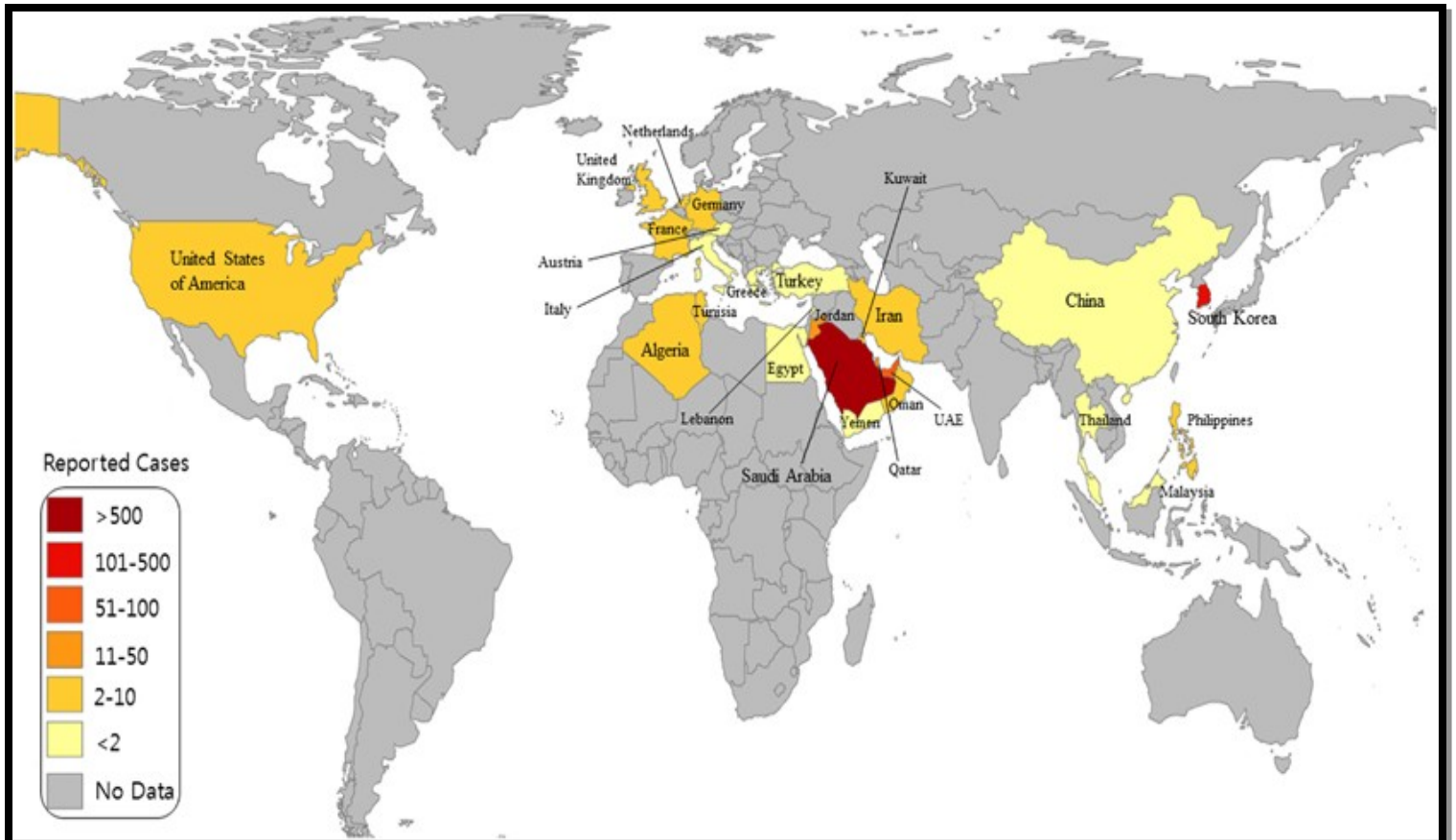


Coronavirus Outbreaks

- Severe Acute Respiratory Syndrome – SARS-CoV (2002)



- Middle East Respiratory Syndrome – MERS-CoV (2012)



MERS vs SARS

- **Origin**
- First reported in 2012 in Saudi Arabia.
- First reported in 2002 in southern China.
- **Transmission**
- Often from touching infected camels or consuming their milk or meat. Limited transmission between humans through close contact.
- Believed to have spread from bats, which infected civets. Transmitted mainly between humans through close contact.
- **Cases**
- 2,494 confirmed cases; 858 deaths (as of Nov. 30, 2019). Mortality rate of 34%.
- 8,098 cases; 774 deaths. Mortality rate of about 10%.
- **Current status**
- All cases linked to Arabian Peninsula, with 80% in Saudi Arabia. Others in about two dozen countries, including U.S. Cases and deaths have been declining since 2016.
- No new cases reported since 2004.

Coronavirus Outbreaks (2019-nCoV

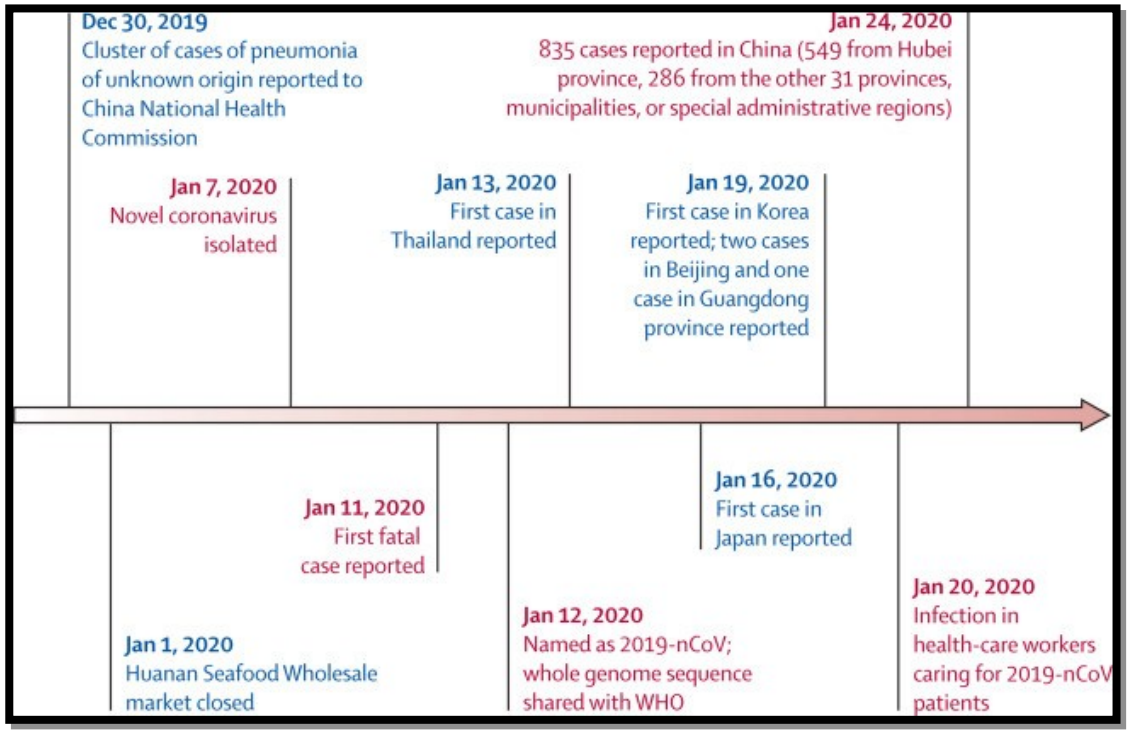
- On **31 December 2019**, cases of pneumonia of unknown etiology detected in **Wuhan City**, Hubei Province of China
- CDC identified **a seafood market suspected to be at the center of the outbreak.**
- A **new type of coronavirus** was isolated on **7 January 2020**
- A **novel Beta-coronavirus** has reportedly been cultured and characterized by electron microscopy and genome sequencing and **has been detected by PCR**

Coronavirus Outbreaks (2019-nCoV)

- Link to a large **seafood and animal market**, **suggesting animal-to-person spread.** number of patients reported not exposure to animal markets, suggesting **l person-to-person spread.**

Coronavirus Outbreaks

Timeline of early stages of 2019-nCoV



What are the symptoms?

- Incubation period: 4 to 7 Days
- Similar symptoms to previously identified coronaviruses
- Mild pneumonia-like symptoms
- Elevated body temperature
- A dry cough
- Shortness of breath or breathing difficulties

- *As the disease progresses patients may also present with pneumonia which can be detected via X-ray*

Mode of Spread

- Infected animals (alive or dead) to animal
- Infected person-to-person
- Infected animal to person

Route of Transmission

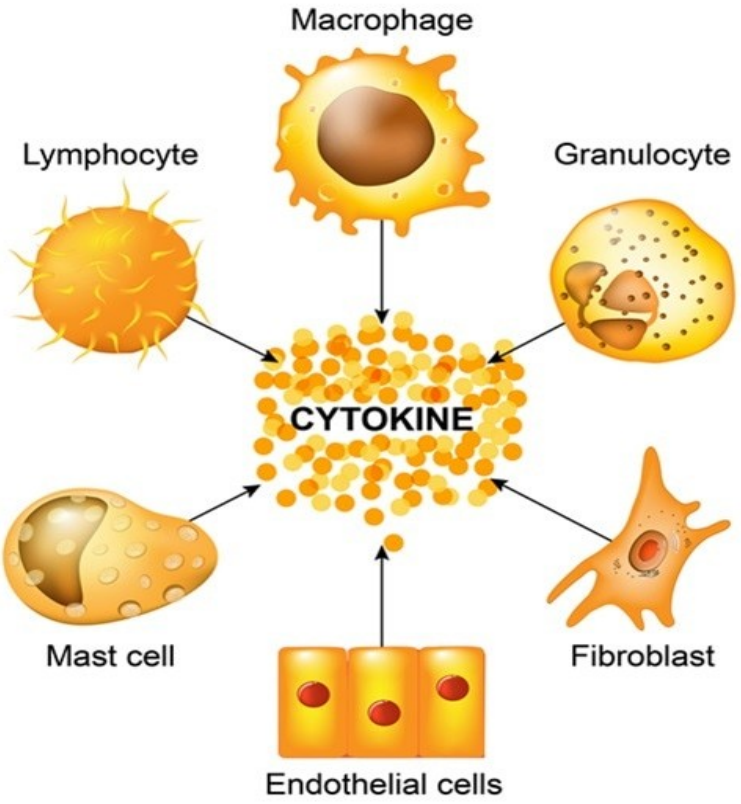
- Through the air by coughing and sneezing
- Close personal contact, such as touching or shaking hands
- Touching an object or surface with the virus on it, then touching your mouth, nose, or eyes before washing your hands

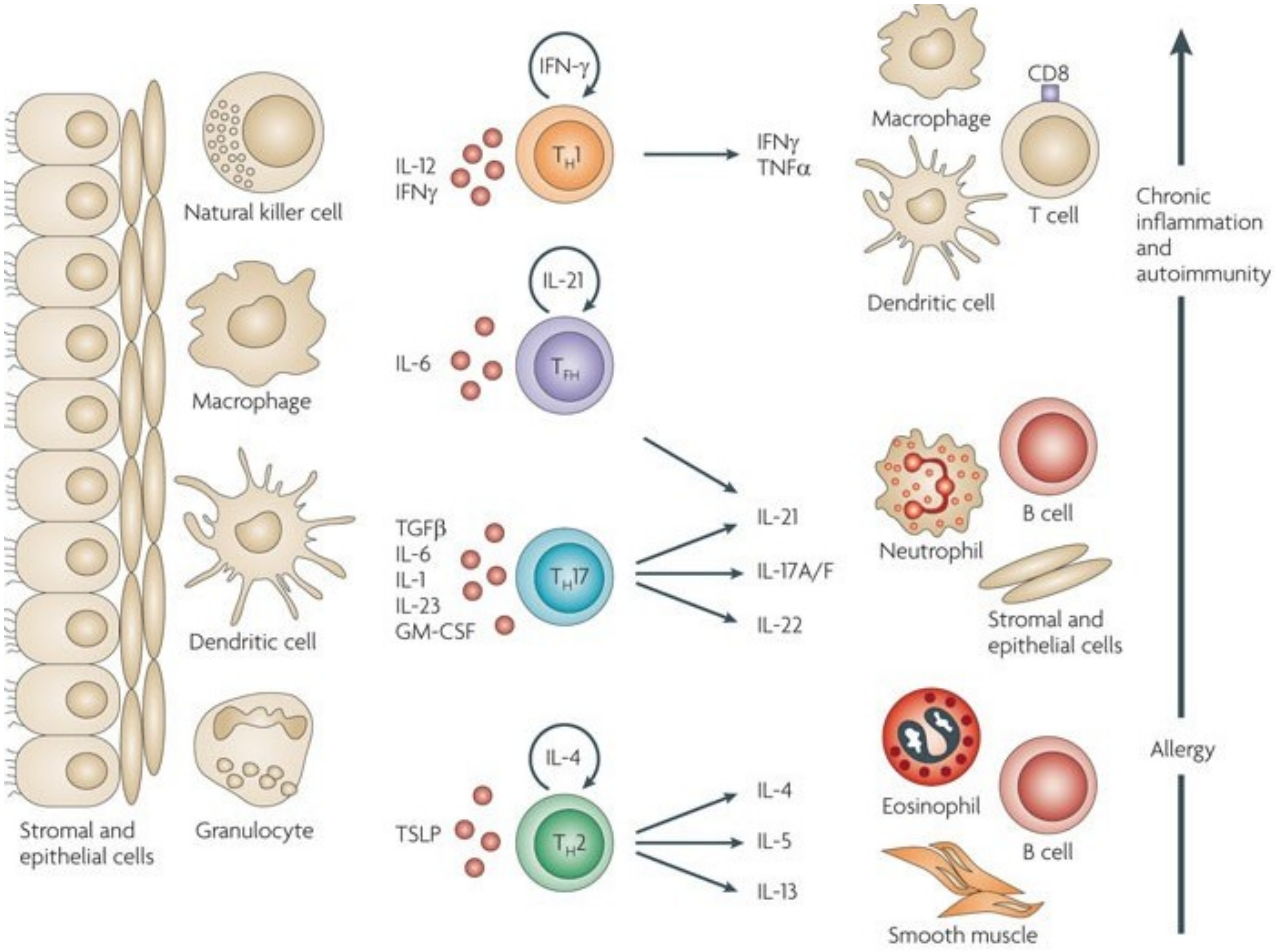
Implementation of IPC measures

- Application of Standard Precautions
  - Hand Hygiene
  - PPE
  - Respiratory hygiene
  - Safe injection practices
  - Disposal of sharps
  - Routine environmental
  - Cleaning

CYTOKINE STORM IN COVID-19 PATIENTS

- INTRODUCTION – CYTOKINES
- Polypeptides
- Secreted by leukocyt
- Cell signaling
- Examples
  - Interferons
  - Interleukins
  - Growth factors




Natural killer cell
Macrophage
Dendritic cell
Granulocyte
Stromal and epithelial cells
IFN-γ
IL-12
IFNγ
T_H1
IFNγ
TNFα
IL-21
IL-6
T_{FH}
TGFβ
IL-6
IL-1
IL-23
GM-CSF
T_H17
IL-21
IL-17A/F
IL-22
IL-4
TSLP
T_H2
IL-4
IL-5
IL-13
Macrophage
CD8
T cell
Dendritic cell
B cell
Neutrophil
Stromal and epithelial cells
Eosinophil
B cell
Smooth muscle
Chronic inflammation and autoimmunity
Allergy

INTRODUCTION - CRS

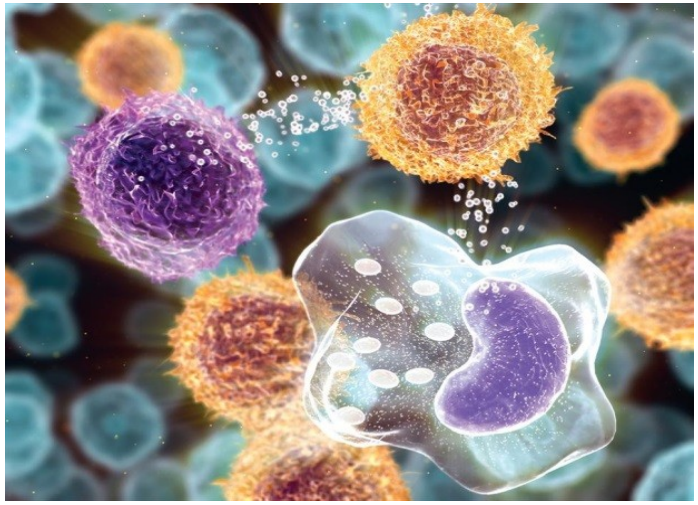
- **Cytokine storm or cytokine release syndrome (CRS):**
  - Acute systemic inflammatory reaction
  - Fever
  - Multi organ dysfunction

- **Causes:**
  - Infections
  - Drugs

- **Associated with**:
  - Increase in inflammatory cytokines
  - Activation of T-lymphocytes and macrophages

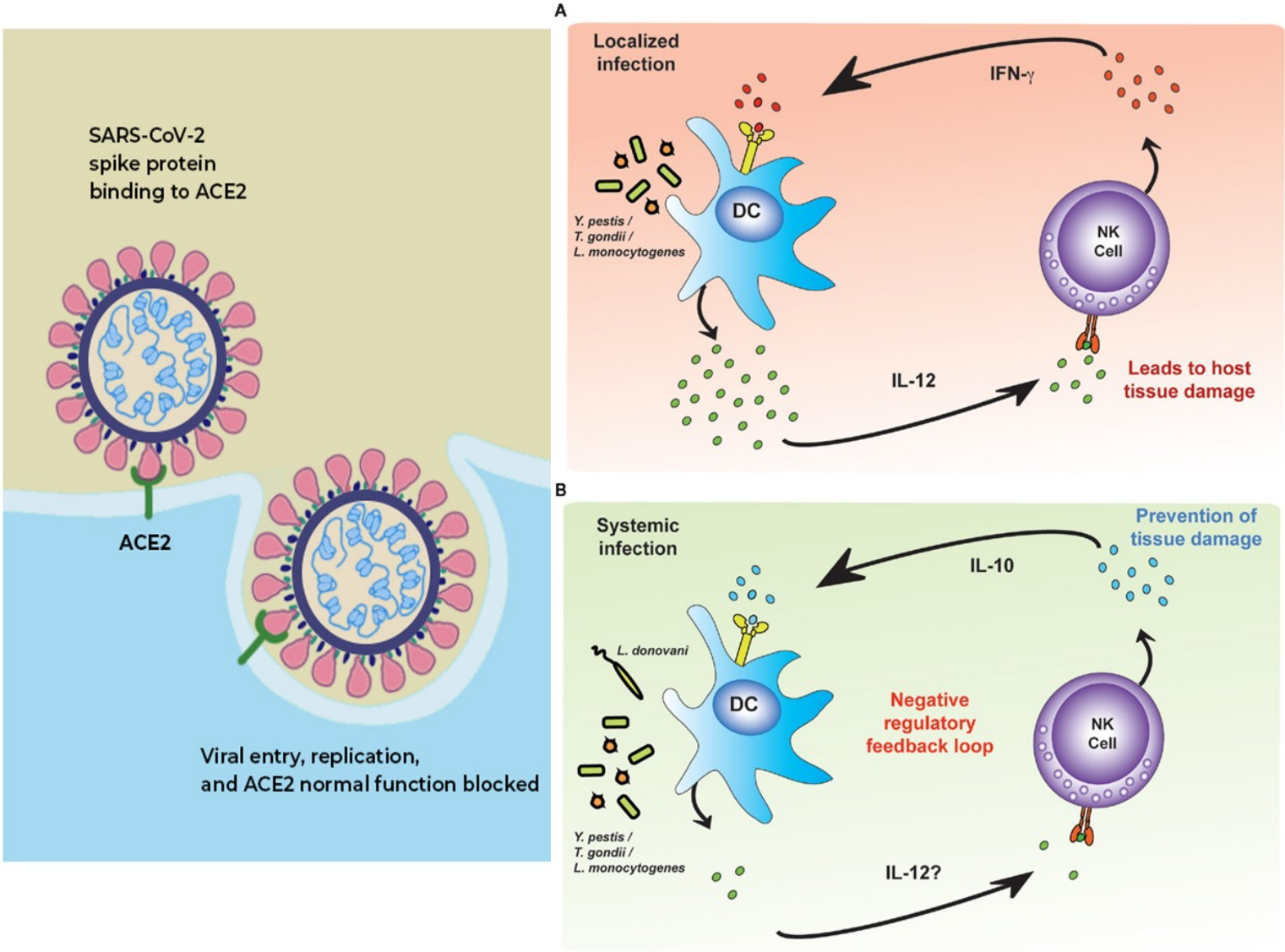
INTRODUCTION - CRS

- Common in:
  - Immune system pathology
  - Immunotherapy
  - Organ transplant sepsis
  - Viral infections



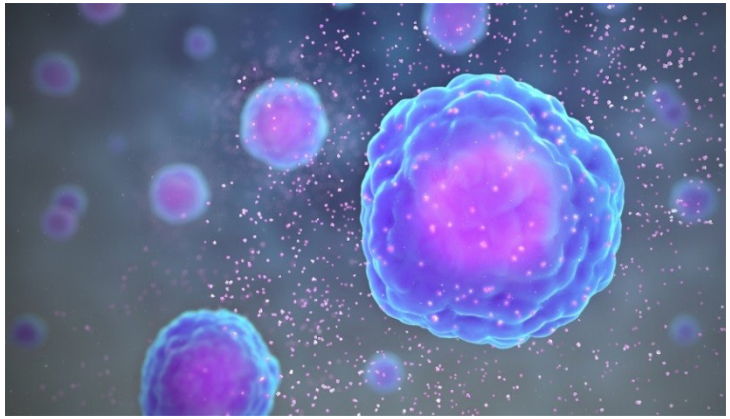
- Severity:
  - Mild – Flu like symptoms
  - Moderate – Fever ≥ 105º
  - Severe – SIRS, multi organ failure

PATHOGENESIS

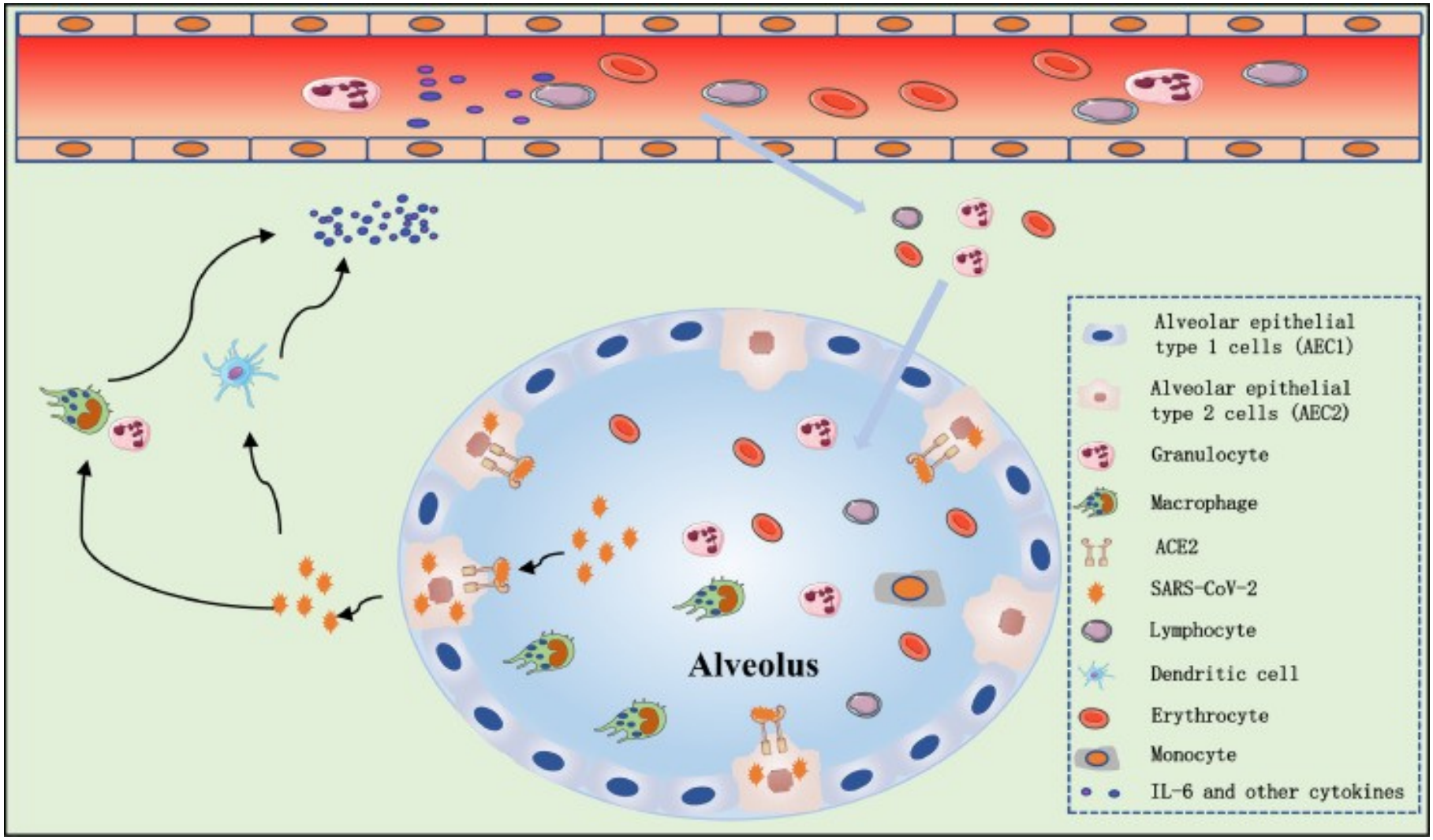


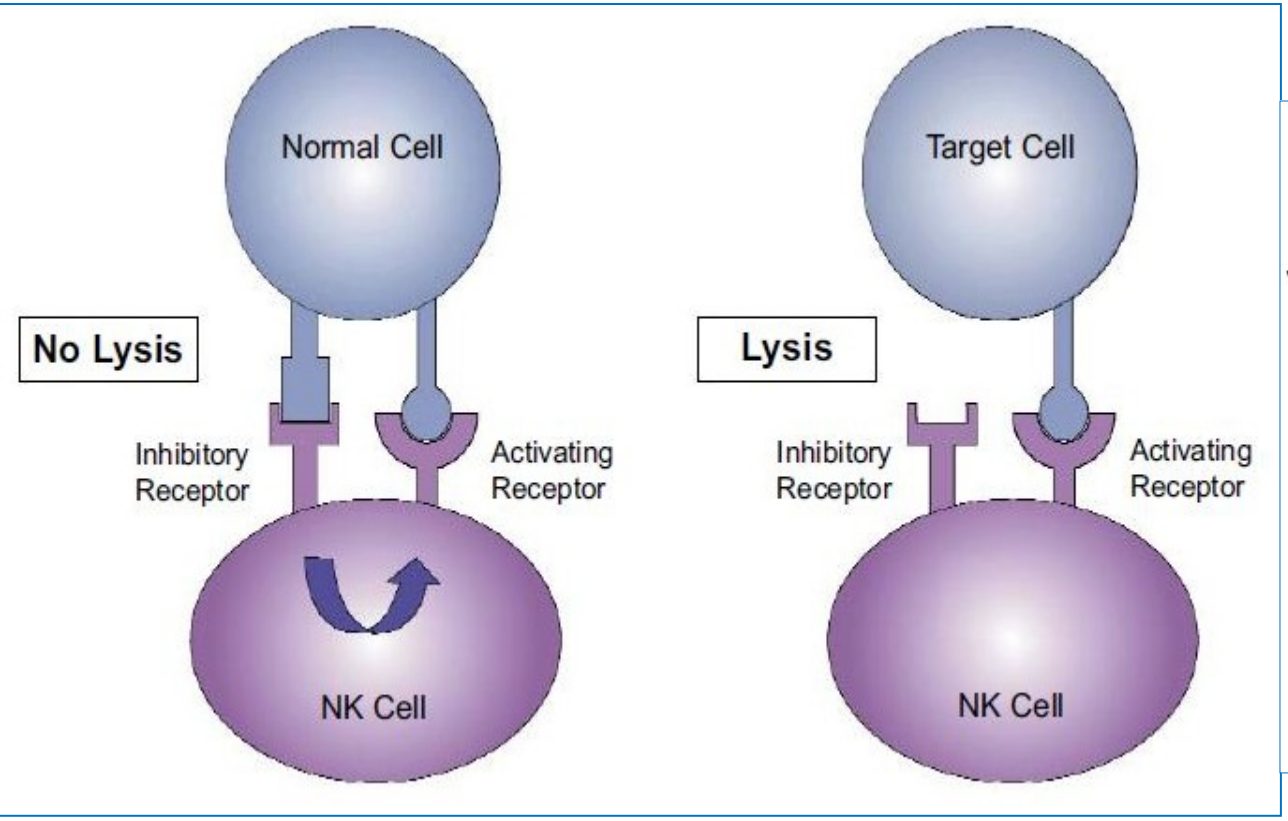
PATHOGENESIS

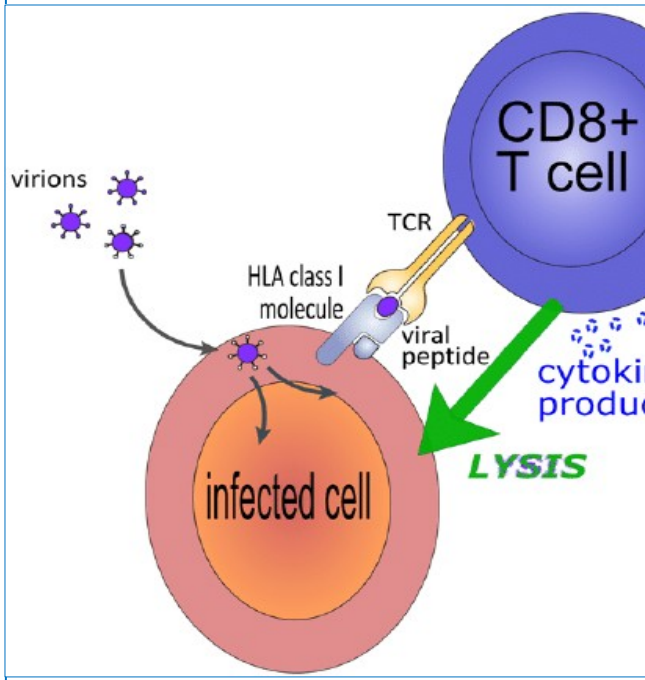
- Cytokines involved:
  - Interleukins 1, 2, 6, 10
  - GM-CSF
  - IP-10
  - MCP-3
  - MIP 1-α
  - TNF-α



- Effects:
  - Increased vascular permeability
  - Inflammatory exudate
  - Involvement of erythrocytes and platelets

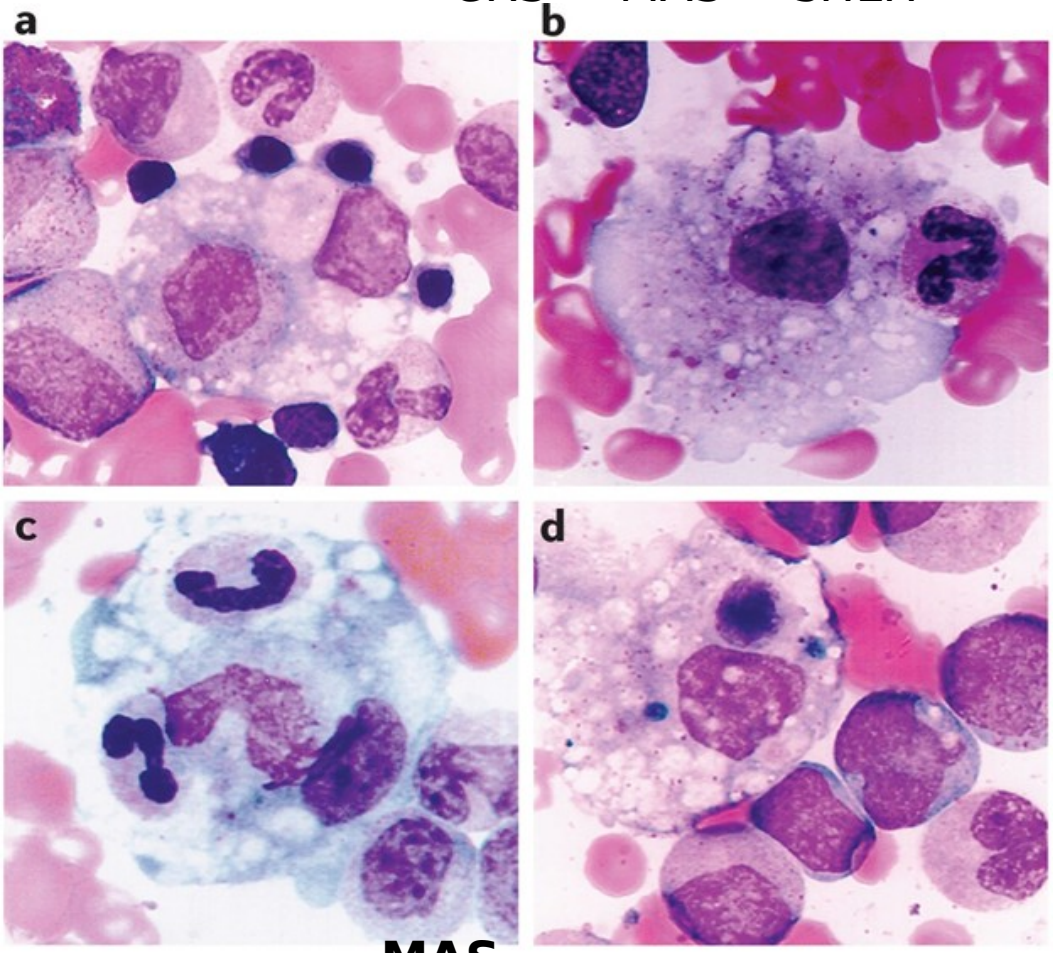

Alveolus
Alveolar epithelial type 1 cells (AEC1)
Alveolar epithelial type 2 cells (AEC2)
Granulocyte
Macrophage
ACE2
SARS-CoV-2
Lymphocyte
Dendritic cell
Erythrocyte
Monocyte
IL-6 and other cytokines


Normal Cell
No Lysis
Inhibitory Receptor
Activating Receptor
NK Cell
Target Cell
Lysis
Inhibitory Receptor
Activating Receptor
NK Cell

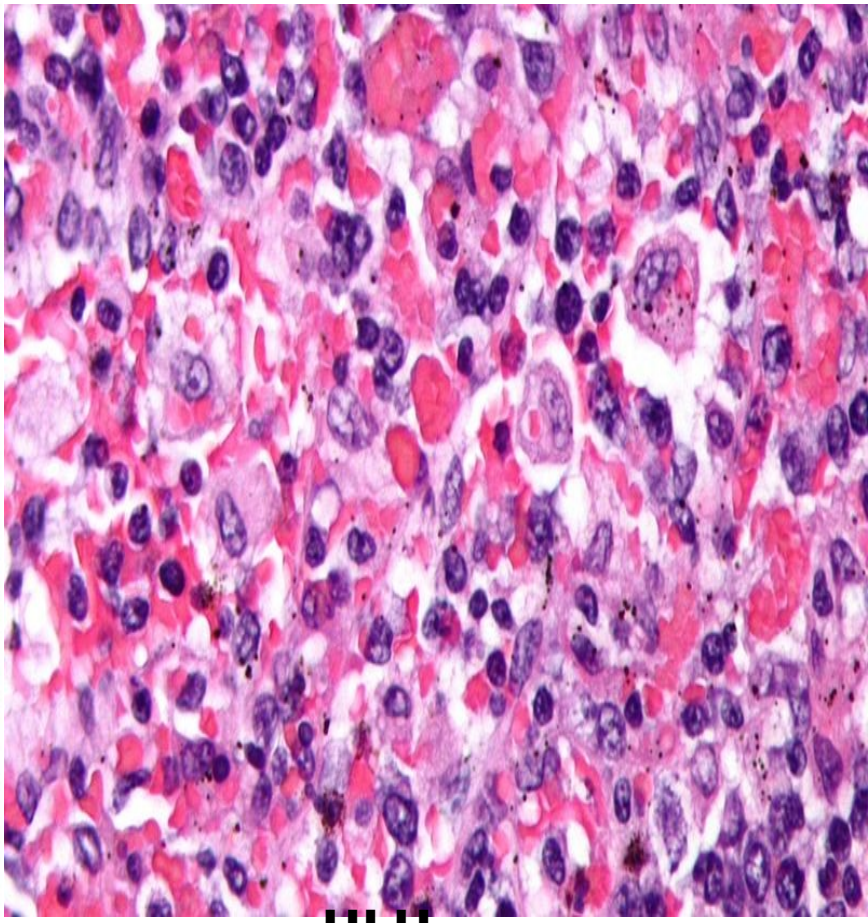

virions
CD8+ T cell
TCR
HLA class I molecule
viral peptide
cytoki
produ
LYSIS
infected cell

PATHOGENESIS

Macrophage activation syndrome
Hemophagocytic lymphohistiocytosis
CRS = MAS = sHLH



MAS



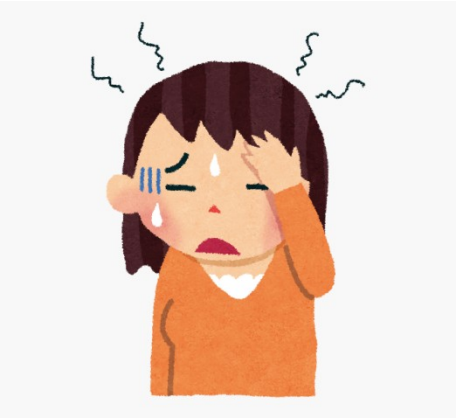
HLH

LITERATURE

- Yang Y. et al
  - Number of cytokines – 48
  - Total COVID–19 cases – 53
  - Severe cases – 34
  - Significant cytokines – 14

  - Cytokines associated with severe CRS:
    - IP-10
    - MCP-3
    - IL-1rα

CLINICAL FEATURES



- Mild – Flu like symptoms
- Moderate – Fever ≥ 105ºF
- Severe – SIRS, multi organ failure
- Associated - Neuropsychiatric findings

LABORATORY FINDINGS

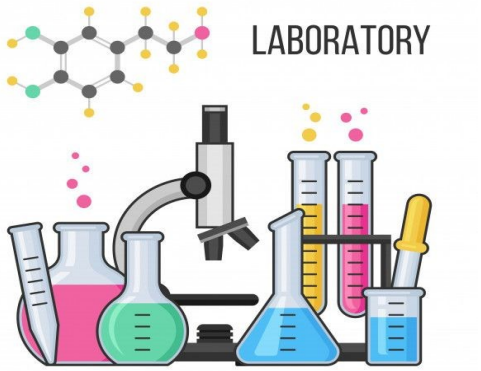
- Elevated markers:
  - CRP
  - Ferritin
  - Interferons
  - Interleukins

- Oxygen saturation:
  - ABGs
  - Pulse oximetry

- Hematology:
  - CBC
  - DLC

LABORATORY FINDINGS

- Coagulation:
  - PT, PTTK
  - Fibrinogen
  - D-dimers
- Chemistry:
  - Serum electrolytes
  - RFTs, LFTs
  - Uric acid
  - Lactate, LDH
- Radiology:
  - Chest X-ray
  - CT scan



DIAGNOSIS

- Fever ≥ 100.4°F
- Hypotension
- Hypoxia
- End organ dysfunction

- Hypercytokinemia
- Leukopenia
- Elevated LFTs
- Elevated ferritin

DIFFERENTIAL DIAGNOSIS

- MAS/ HLH
- Sepsis
- Thromboembolism
- Heart failure
- Allergic reaction

TREATMENT

- Management of COVID-19
  - Antivirals
  - Antipyretics
  - Supportive management

- Immunosuppressive/ immunomodulatory agents:
  - IL-6 receptor antagonists
  - IL-1 receptor antagonists
  - Corticosteroids
  - Intravenous immunoglobulin (IVIG)
  - TNF inhibitors
  - Chloroquine, hydroxychloroquine
  - JAK inhibitors

TREATMENT

- IL-6 blockade:
  - Tocilizumab (8 mg/kg IV daily)

- IL-1 blockade:
  - Anakinra (100-200 mg S/C daily)
  - Canakinumab
  - Rilonacept

TREATMENT

- Corticosteroids:
  - Methylprednisolone (40 mg OD for 4–5 days)
- Intravenous immunoglobulin
- TNF-α inhibitors:
  - Adalimumab
  - Infliximab
  - Etanercept

REFERENCES

- UpToDate
- PubMed
- Research articles

- https://www.uptodate.com/contents/cytokine-release-syndrome-crs?search=cytokine%20storm%20covid&source=search_result&selectedTitle=1~150&usage_type=default&display_rank=1

- https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7118634/
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THANKYOU!