

Acute (Transient) Infections

Virologic mechanisms · organ pathology · clinical interpretation

COVID-19 • Measles • Mumps • Poliomyelitis

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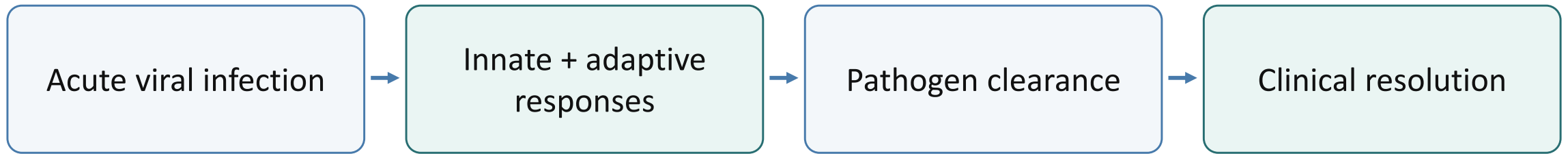
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Learning outcomes

- Explain why most acute viral infections resolve yet reinfections differ among viruses.
- Trace key cellular events in SARS-CoV-2, measles, mumps and poliovirus infections.
- Recognize the characteristic tissue injury and major clinical complications.
- Connect clinical syndromes and pathology with targeted diagnostic approaches.

Transient infection: An immunologic outcome



- “Transient” describes usual pathogen clearance, not uniformly mild clinical disease.
- Severe organ damage may occur before the infection is controlled.

Schematic temporal sequence, not a quantitative time course

Why reinfection risks differ

Virus-related features

- Limited antigenic diversity can support durable protection against repeat infection.
- New genetic variants can reduce recognition of prior immune responses.

Host-related features

- Waning protection is especially relevant to some respiratory and gastrointestinal viruses.
- Effective clearance of one episode does not guarantee lifelong protection.

Different viruses, different patterns of repeat infection

Illustrative virus	Source emphasis	Clinical implication
Mumps	One genetic subtype	Usually durable protection after infection
Influenza	New variants arise periodically	Repeat infection can occur
Respiratory / GI viruses	Immunity may decline with time	Reinfection despite previous exposure

Four archetypes within acute viral disease

Infection	Usual entry / spread	Principal teaching pathology
COVID-19	Respiratory	Alveolar injury; Inflammation; Thrombosis
Measles	Airborne; Lymphatic / hematogenous	Rash, giant cells, immune suppression
Mumps	Respiratory; Hematogenous	Parotitis; Orchitis; Pancreatitis
Poliomyelitis	Fecal–oral; Possible CNS spread	Motor-neuron injury and paralysis

COVID-19 illustrates acute cytopathic viral infection

- SARS-CoV-2 infection ranges from asymptomatic infection to life-threatening organ injury.
- The respiratory tract is a major portal of entry and site of clinically important disease.
- Outcome depends on viral replication, immune containment and inflammatory injury.
- Severe disease can include coagulation abnormalities and extrapulmonary manifestations.

SARS-CoV-2 genome and structural components

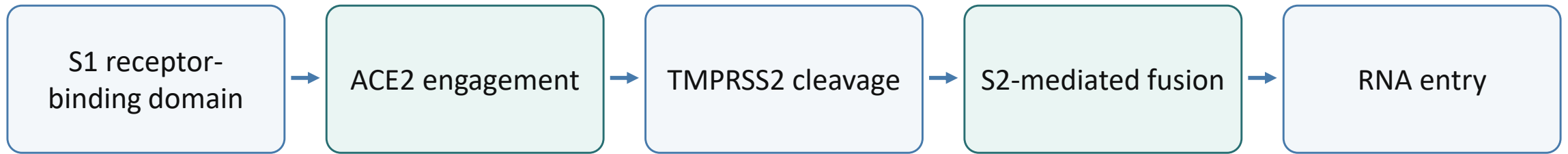
Genome

- Single-stranded, positive-sense RNA genome; Approximately 30 kilobases.
- Viral RNA is translated by host ribosomes after cell entry.

Structural proteins

- Spike and membrane proteins are located in the lipid envelope.
- Nucleocapsid protein associates with viral RNA.
- Spike protein mediates host-cell entry and is a central target of neutralizing antibodies.

Spike-mediated entry: Receptor to fusion



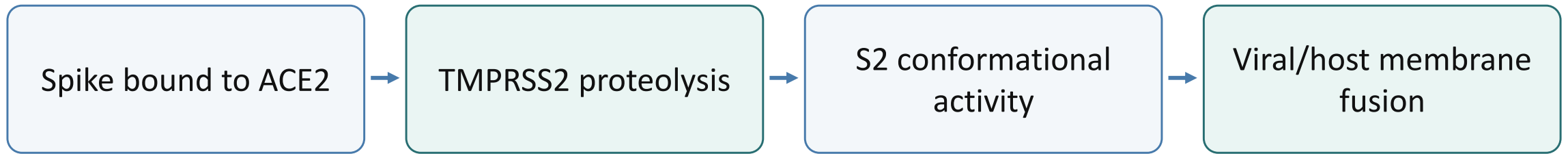
- ACE2 is expressed by epithelial cells, including respiratory epithelium.
- The spike subunits perform distinct receptor-binding and fusion functions.

Selected molecular steps in viral entry

SARS-CoV-2 receptor-binding domain

- The receptor-binding domain (RBD) is part of spike subunit S1.
- RBD engagement of ACE2 is the first depicted step in cellular attachment.
- Neutralizing antibodies against spike—especially RBD—can block infection of host cells.
- Antigenic changes affecting spike help explain some patterns of immune escape.

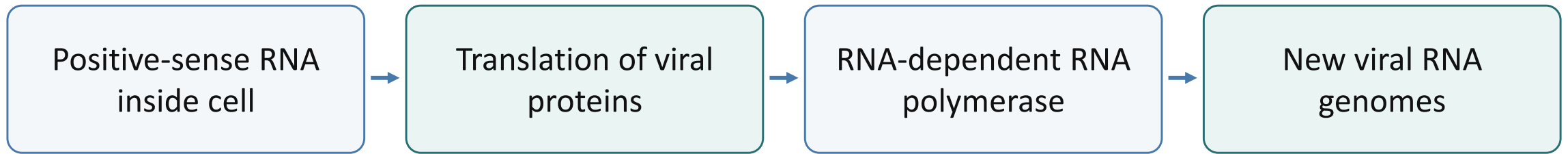
After attachment: Membrane fusion is activated



- Entry requires more than simple receptor attachment.
- The host protease-dependent activation step links the surface receptor to RNA delivery.

Mechanistic schematic; Cell membrane not drawn to scale

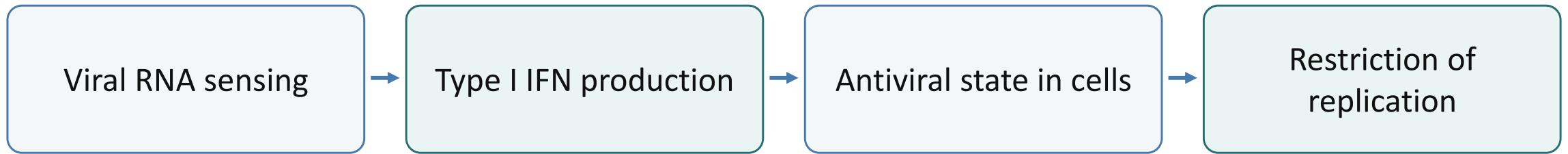
Intracellular RNA replication



- Replication involves a double-stranded RNA intermediate.
- Viral RNA and replication intermediates are potential innate immune stimuli.

Selected steps; Does not depict the complete replication cycle

Type I interferon: An early restriction mechanism



- Interferon activity limits replication in infected and neighboring cells.
- Severe disease may follow impaired production or signaling of type I IFN.

Simplified antiviral response

Innate sensing creates evolutionary pressure

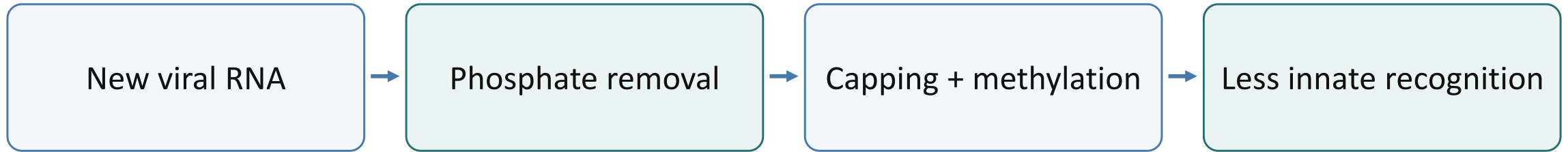
Host detects

- Viral RNA structures can activate innate RNA receptors.
- Double-stranded RNA intermediates are an important signal of replication.

Virus counters

- Viral RNA can be modified to resemble host RNA.
- Replication intermediates can be hidden within membrane-bound compartments.
- Viral proteins interfere with interferon-generating pathways.

RNA capping and methylation reduce sensing



- These modifications help viral RNA resemble cellular RNA.
- Reduced recognition favors viral survival during early infection.

Mechanistic simplification of one immune-evasion route

Membrane sequestration of viral RNA

Protected replication environment

- Host endoplasmic reticulum membranes form double-membrane vesicles around viral RNA.
- Replication intermediates remain sequestered in these compartments.

Innate immune consequence

- Double-stranded viral RNA becomes less accessible to cytoplasmic RNA sensors.
- The viral RNA endonuclease additionally limits accumulation of immunostimulatory intermediates.

Impaired type I interferon defense and severity

- The source describes multiple viral proteins that reduce IFN generation or signaling.
- Autoantibodies directed against type I IFNs are associated with increased risk of severe COVID-19.
- Inherited abnormalities of IFN production or signaling provide a parallel susceptibility mechanism.
- The link illustrates the importance of early innate restriction.

Respiratory exposure and transmission

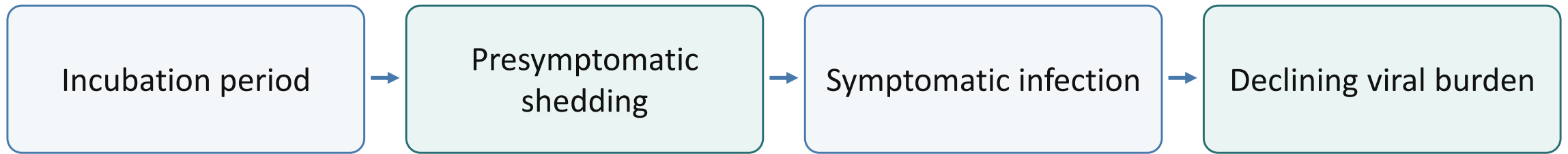
Transmission routes

- Virus moves person-to-person via respiratory particles, including droplets and aerosols.
- Inhalation exposure is relevant, including at longer distances in poorly ventilated environments.

Conditions increasing exposure

- Indoor gatherings and prolonged close contact favor transmission.
- Shared living settings and institutions can facilitate spread.
- Transmission may precede symptom onset.

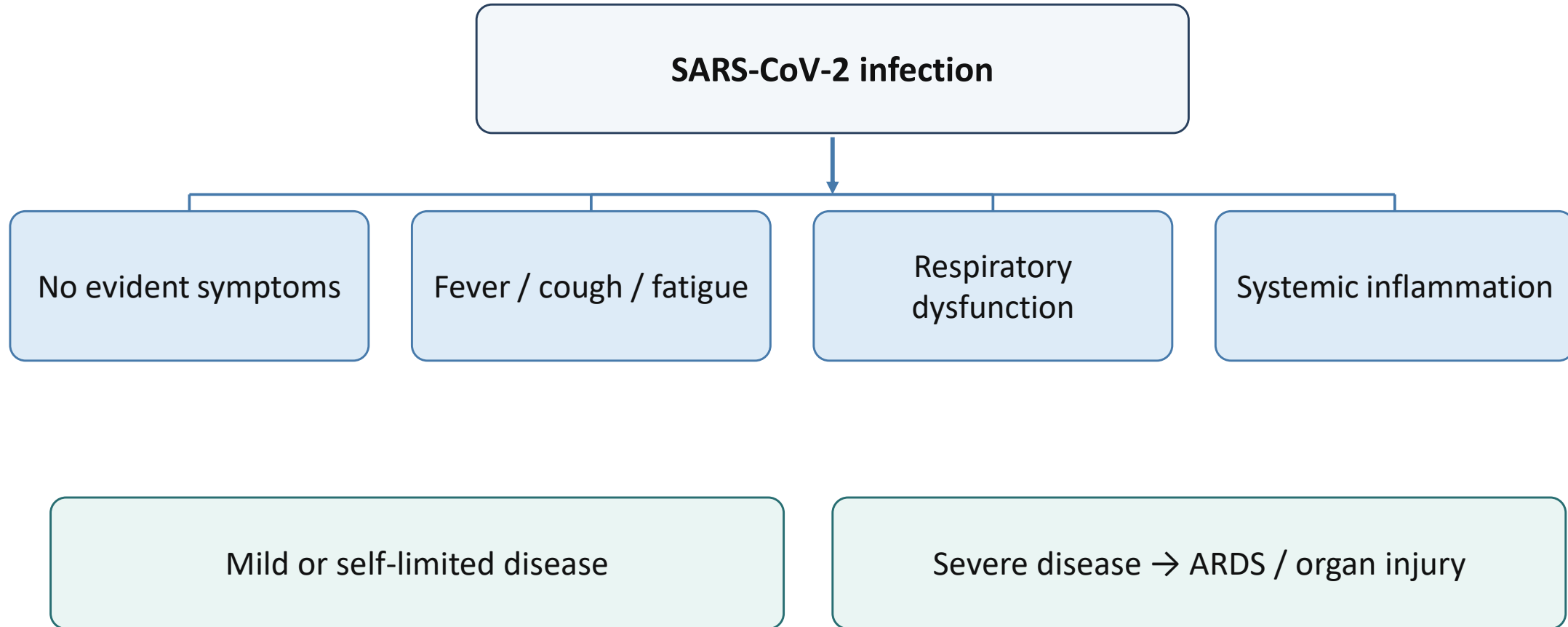
Infectiousness is not synonymous with symptoms



- The excerpt associates highest upper respiratory viral levels with early infection.
- Individuals without symptoms may transmit SARS-CoV-2.

Schematic course; Timing varies between patients and variants

Clinical spectrum of acute COVID-19



Clinical categories are illustrative; Boxes are not proportional

Risk of severe COVID-19 is heterogeneous

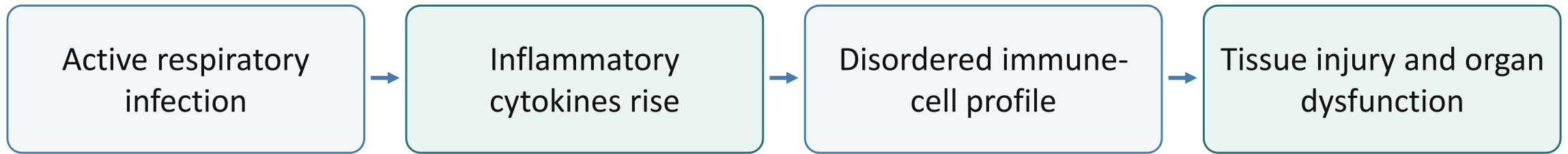
Host characteristics

- Older age is emphasized as the strongest risk factor in the text.
- Pregnancy and immunocompromise can increase vulnerability.
- Unequal access to prevention and care influences observed risk.

Comorbid conditions

- Lung and cardiovascular disease.
- Diabetes, obesity and smoking.
- Cancer and chronic kidney or liver disease.

Severe COVID-19: Excessive inflammatory response



- TNF and IL-6 are emphasized in the source.
- Lymphopenia and abnormalities of myeloid cells accompany severe disease.

Conceptual sequence; Multiple feedback pathways exist

Lymphopenia and immune dysregulation

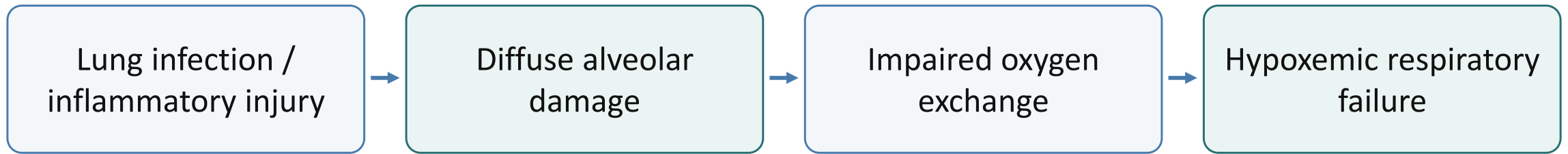
Described cellular findings

- Reduced T-cell and NK-cell numbers occur in severe cases.
- Myeloid cell populations may be dysregulated.

Pathologic significance

- Antiviral defense may be compromised even while inflammatory responses are amplified.
- This combination distinguishes immune dysregulation from a simple “strong” response.

Pulmonary injury: From inflammation to ARDS

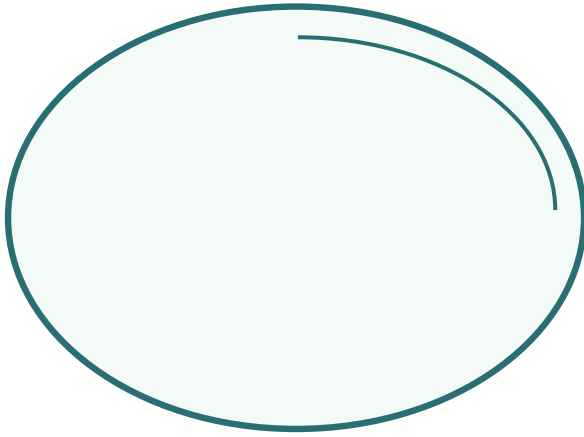


- Alveolar-capillary dysfunction links histologic lesions to dyspnea and hypoxia.
- Severe respiratory failure can progress to multiorgan dysfunction.

Causal interpretation of the source-described morphology

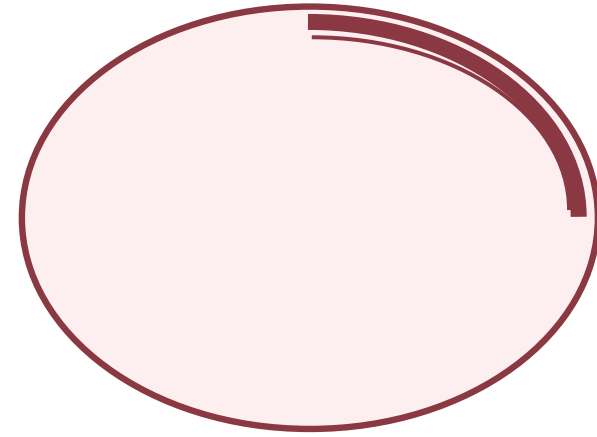
Diffuse alveolar damage in severe COVID-19

Normal gas-exchange surface



Thin alveolar barrier

Diffuse alveolar damage



Hyaline membrane

- Alveolar edema and fibrinous hyaline membranes impair diffusion.
- Congested capillaries, type II pneumocyte hyperplasia and microthrombi compound dysfunction.

Why hyaline membranes compromise gas exchange

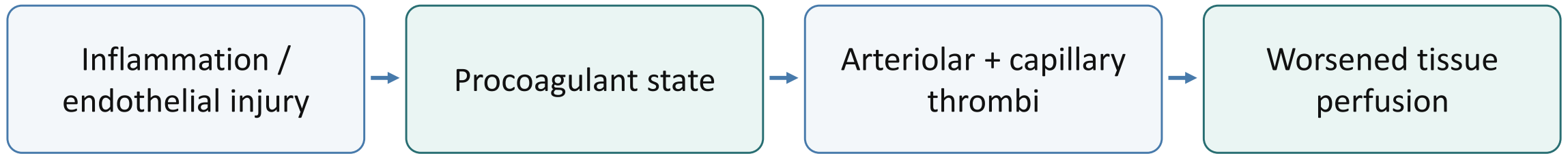
Observed lesion

- Edema fluid accumulates in alveolar spaces.
- Fibrinous material lines alveolar walls as hyaline membranes.
- Some alveoli collapse and alveolar ducts dilate.

Physiologic effect

- Air–blood diffusion is impeded.
- Functional gas exchange surface is reduced.
- Hypoxemia develops as injury becomes extensive.

Microvascular thrombosis compounds lung injury



- Thrombi are reported in pulmonary arterioles and alveolar capillaries in severe cases.
- Thrombosis and alveolar injury can jointly aggravate respiratory dysfunction.

Schematic; Magnitude and timing are not quantified

Coagulopathy: Increased clot formation

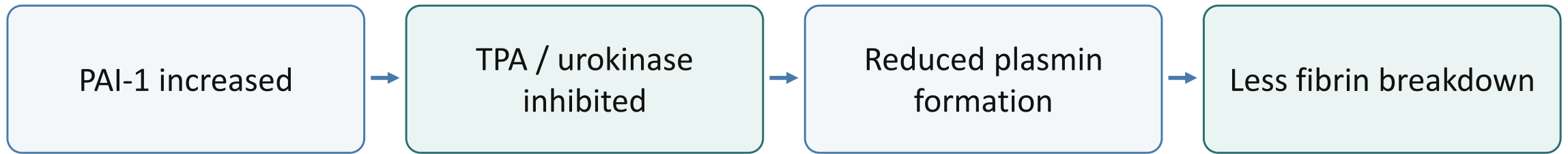
Potential activating factors

- Endothelial injury can expose tissue factor.
- Inflammation favors coagulation activation.
- Antiphospholipid antibodies are described in some severe cases.

Disease expression

- Shift toward thrombosis rather than normal hemostatic equilibrium.
- Thrombi may affect small and larger blood vessels.
- Coagulopathy is one component of systemic severe COVID-19.

Impaired fibrinolysis sustains thrombi



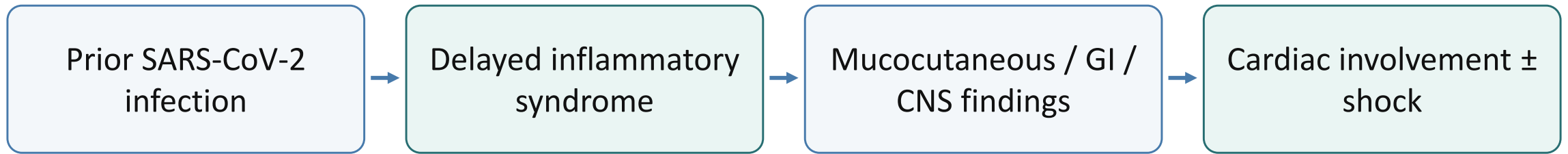
- The source describes reduced fibrinolytic activity in severe disease.
- Inhibiting fibrin clearance augments the prothrombotic shift.

TPA: Tissue plasminogen activator; PAI-1: Plasminogen activator inhibitor 1

Severe COVID-19 is a multisystem disorder

Affected domain	Examples
Respiratory	ARDS with diffuse alveolar damage
Vascular / coagulation	Thrombosis; Systemic vasculitis
Inflammatory	HLH-like features; Elevated acute-phase response
Musculoskeletal	Myositis and arthritis

MIS-C follows acute SARS-CoV-2 infection



- Onset commonly 2–6 weeks after acute disease in children.
- Myocardial dysfunction and coronary artery dilation are among the cardiac manifestations.

HLH-like changes in severely affected adults

- Some adults show hemophagocytic lymphohistiocytosis-like features.
- Cytopenias, hemophagocytosis and elevated acute-phase reactants can occur.
- This inflammatory phenotype is not unique to SARS-CoV-2.
- Associated pathology must be interpreted within the clinical syndrome.

Postacute sequelae: Long COVID

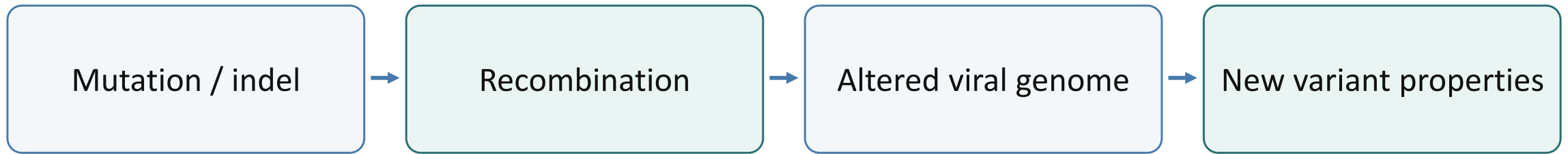
Clinical manifestations

- Persistent fatigue, weakness, dyspnea, chest pain or cough may occur.
- Impaired memory or concentration and psychological symptoms are also described.

Interpretive cautions

- Definitions differ among studies.
- A relapsing–remitting course is described in persistent cases.
- Persistent symptoms alone do not establish ongoing viral replication.

Viral variants arise through genomic change



- Variants may differ in efficiency of transmission or immune escape.
- Spike changes can alter recognition by infection- or vaccine-induced antibodies.

The figure does not imply all variants increase disease severity

Immune escape: Lesson from Omicron

Viral characteristic

- The many spike-protein alterations in Omicron.
- Some changes reduce binding by previously generated antibodies.

Population-level implication

- Prior immunity may not prevent all infections.
- Immune escape is distinct from the intrinsic severity of disease.
- Variant descriptions in this source refer to the 2021–2022 period.

Diagnosis: Viral antigen versus nucleic acid

Principle	Target	Specimen / interpretation
Antigen detection	Nucleocapsid protein	Antibody-based test on nasal material
Nucleic-acid amplification	SARS-CoV-2 RNA	PCR-based detection of viral sequences

Clinical application: Respiratory illness with hypoxia

Illustrative case: A patient with confirmed SARS-CoV-2 infection develops increasing dyspnea, hypoxia and evidence of systemic inflammation.

Interpretation question

Which pulmonary lesion best connects this presentation to severe COVID-19?

Details to integrate

Confirmed infection

Hypoxemia

Systemic inflammation

Case interpretation: Diffuse alveolar damage

Most consistent interpretation

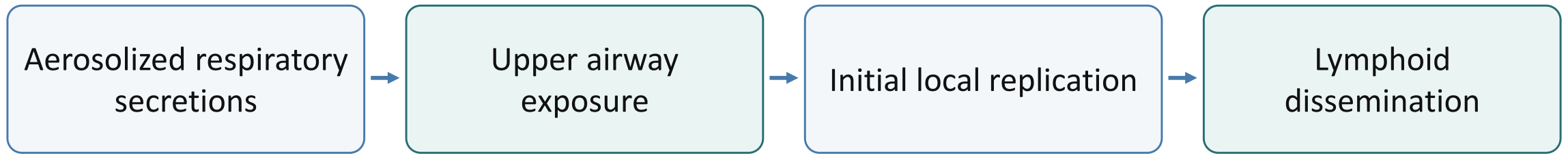
ARDS with diffuse alveolar damage

- Alveolar edema and hyaline membranes reduce effective gas exchange.
- Type II pneumocyte hyperplasia reflects alveolar epithelial injury.
- Pulmonary microvascular thrombi may further impair oxygenation.

Measles: Airborne infection with systemic dissemination

- Measles is an acute systemic infection caused by a Paramyxoviridae RNA virus.
- There is one recognized serotype of measles virus in the source.
- Infection can affect skin, lymphoid organs, lung, intestine and the CNS.
- Severe outcomes are more likely with malnutrition, inadequate access to care or impaired cellular immunity.

Measles is transmitted efficiently by aerosols



- Measles is described as highly efficient at airborne transmission.
- Susceptible unvaccinated persons are prominent in outbreaks.

Measles receptor usage explains cell tropism

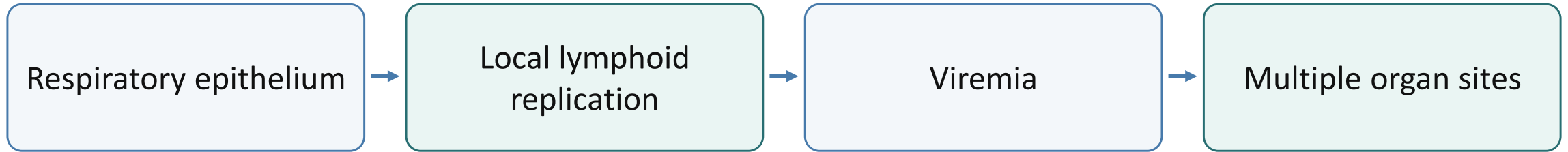
SLAMF1

- Present on activated lymphocytes, dendritic cells and monocytes.
- Supports early infection of immune cells.

Nectin-4

- Located on the basal surfaces of epithelial cells.
- Associated with respiratory epithelial infection and viral shedding.

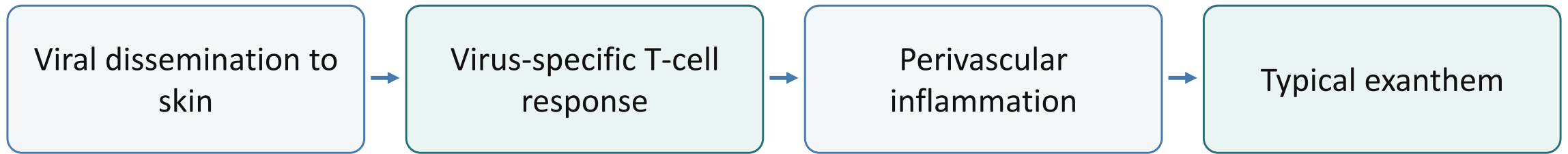
Measles spreads beyond the respiratory tract



- Dissemination reaches conjunctiva, skin, lymphatic system, small vessels and CNS.
- Systemic involvement explains the combination of exanthem and internal-organ complications.

Selected organs; Not exhaustive

The measles rash is immune-mediated



- T-cell responses help contain infection and also contribute to rash formation.
- Rash may be less evident in patients with impaired cell-mediated immunity.

Mechanistic model from source

Measles skin rash: Pathologic substrate

Macroscopic distribution

- Blotchy reddish-brown eruption.
- Affects face, trunk and proximal extremities.

Microscopic pattern

- Dilated dermal blood vessels.
- Dermal edema.
- Mononuclear perivascular infiltrates.

Koplik spots: Diagnostic oral mucosal lesions

Clinical location

- Oral mucosa near openings of Stensen ducts.

- Characteristic finding in measles described as pathognomonic by the source.

Tissue findings

- Mucosal necrosis and neutrophil-rich exudate.

- Associated neovascularization in affected mucosa.

Warthin–Finkeldey multinucleated giant cells

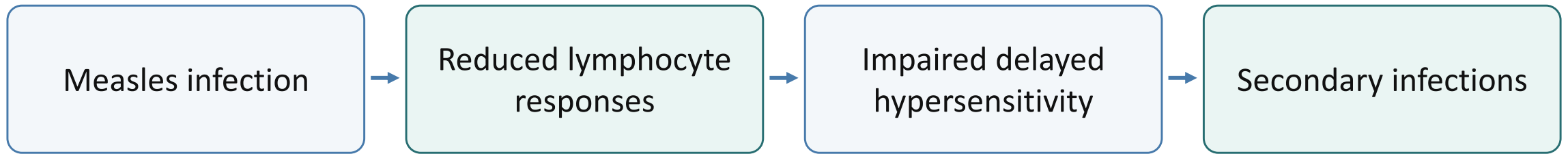
Lymphoid-organ response

- Follicular hyperplasia and prominent germinal centers.
- Multinucleated giant cells within lymphoid tissue.

Distinctive cytology

- Eosinophilic inclusions in nuclei and cytoplasm.
- Similar giant cells may be observed in lung or sputum.

Measles-associated immunosuppression



- Immune suppression may be transient yet profound.
- Secondary bacterial and viral infections account for important morbidity and mortality.

Immune consequences in the source

Severe and complicated measles

Organ system	Examples
Respiratory	Croup and pneumonia
Gastrointestinal	Diarrhea; Protein-losing enteropathy
Ocular	Keratitis, scarring and possible blindness
CNS	Encephalitis; Rare delayed syndromes

Late neurologic complications of measles

Subacute sclerosing panencephalitis

- Rare delayed complication associated with altered viral persistence.
- Source describes defective viral particle formation and cell-to-cell spread.

Measles inclusion-body encephalitis

- Rare complication particularly noted with immunocompromise.
- Illustrates possible neurologic injury beyond the acute exanthem.

Measles diagnosis: Syndrome and virology

- Clinical findings may suggest the diagnosis, particularly in a compatible outbreak setting.
- Serologic testing provides an additional diagnostic approach.
- PCR can detect measles viral RNA in respiratory secretions or urine.
- Morphologic findings should complement—not replace—appropriate virologic testing.

Clinical application: Febrile exanthem

Illustrative case: A susceptible patient has an acute febrile respiratory illness followed by a widespread rash and characteristic oral mucosal lesions.

Interpretation question

Which mechanisms produce the rash, and why can secondary infections follow?

Details to integrate

Airborne infection

Oral lesions

Systemic exanthem

Case interpretation: Measles immunity and injury

Most consistent interpretation

T-cell-mediated rash with transient immune suppression

- Viremia disseminates the virus to the skin and other organs.
- A cellular immune response contributes to perivascular inflammation and rash.
- Diminished lymphocyte function predisposes to secondary infection.

Mumps: Systemic infection with salivary tropism

- Mumps is a Paramyxoviridae infection characteristically associated with painful salivary gland swelling.
- Viral spread can extend beyond the salivary glands to testis, pancreas, CNS and ovary.
- Infection begins in the respiratory tract and is disseminated via lymphoid tissue and blood.
- The resulting organ pathology often reflects edema and inflammation.

Mumps viral envelope proteins

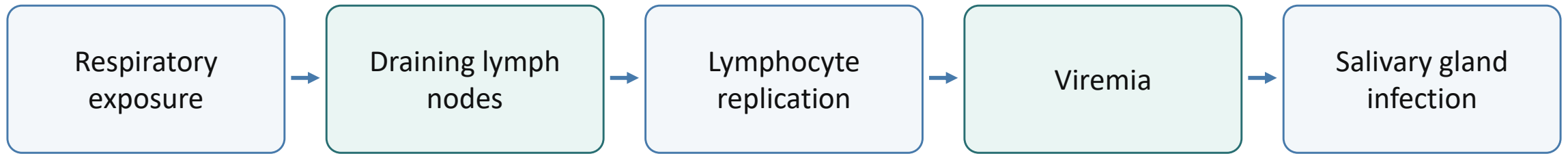
Hemagglutinin–neuraminidase

- One surface glycoprotein combines hemagglutinin and neuraminidase functions.
- Supports interactions required for infection.

Fusion glycoprotein

- The other surface glycoprotein mediates cell fusion.
- Both are part of the description of mumps as an enveloped paramyxovirus.

Mumps: Respiratory entry to salivary gland

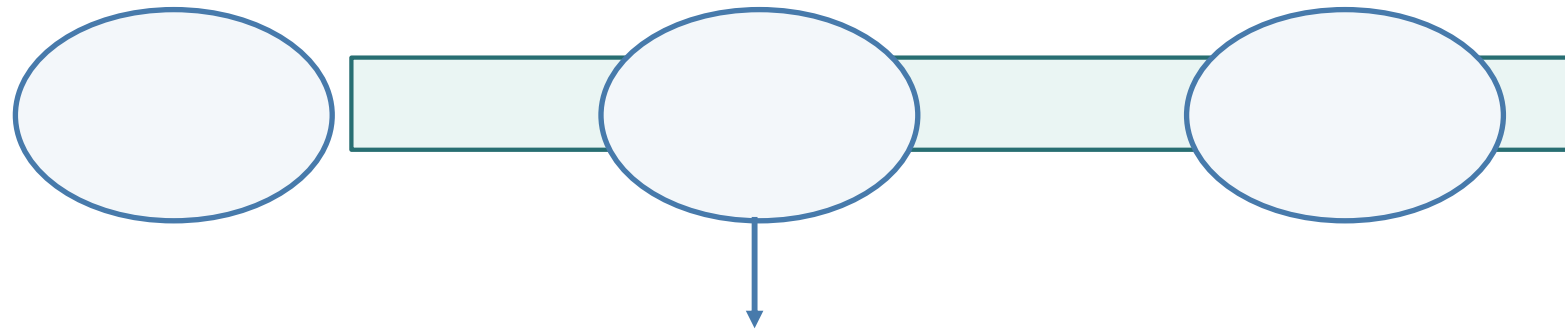


- Activated T cells are highlighted as targets during lymphoid replication.
- Infected duct epithelial cells desquamate and inflame the gland.

Pathogenesis flow

Mumps parotitis: The edema–injury relationship

Parotid duct–acinar unit



Duct epithelial injury + desquamation

Interstitial edema + mononuclear infiltrate

Mechanism of gland enlargement and tenderness

Schematic

Parotid histology: Interstitial inflammation

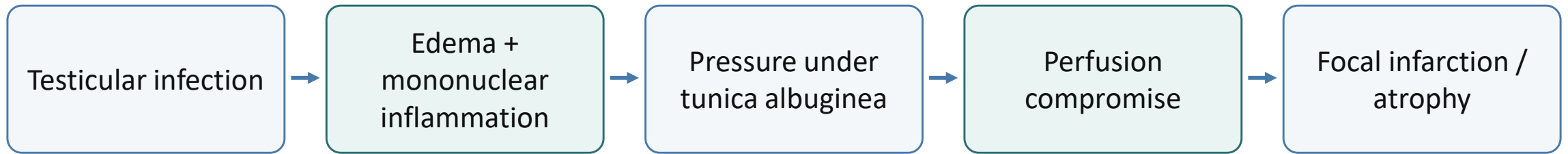
Interstitial compartment

- Edema and lymphocytes, macrophages and plasma cells.
- Inflammatory expansion compresses normal acini and ducts.

Ductal compartment

- Neutrophils and necrotic debris may accumulate within duct lumens.
- Focal epithelial injury and desquamation occur.

Mumps orchitis: Swelling within a rigid capsule



- Hemorrhage may accompany acute testicular inflammation.
- Severe tissue destruction can result in scarring and impaired fertility.

Structural explanation of potential irreversible injury

Pancreatitis and encephalitis in mumps

Pancreas

- Infection of pancreatic acinar cells can liberate digestive enzymes.
- Enzymatic injury may cause parenchymal/fat necrosis and neutrophilic inflammation.

Central nervous system

- Encephalitic pathology can show perivenous demyelination.
- Perivascular mononuclear cuffing is described.

Mumps diagnosis: Clinicopathologic integration

- Parotid pain and swelling are prominent clinical clues.
- Clinical assessment is often sufficient for a presumptive diagnosis.
- Serology or viral RNA detection in saliva can provide confirmation.
- Urine or CSF may be examined in selected clinical settings.

Clinical application: Parotitis and testicular pain

Illustrative case: A patient has painful bilateral parotid swelling followed by testicular enlargement and pain.

Interpretation question

Why can orchitis threaten testicular viability?

Details to integrate

Salivary duct injury

Edema

Encapsulated testis

Case interpretation: Mumps orchitis

Most consistent interpretation

Inflammatory edema compromises perfusion within the tunica albuginea

- Viremia permits spread to extra-salivary organs.
- Interstitial edema and inflammation increase testicular tissue pressure.
- Ischemic injury can produce infarction followed by atrophy or scarring.

Poliovirus: Usually controlled, occasionally neuroinvasive

- Poliovirus is a nonenveloped RNA enterovirus transmitted chiefly by the fecal–oral route.
- Most infections are asymptomatic or mild and self-limited.
- A small minority progress to motor-neuron involvement and paralysis.
- Spinal and bulbar involvement have distinct functional consequences.

Poliovirus enters through the gastrointestinal route



- Infections may also follow exposure to pharyngeal secretions.
- Local lymphoid replication precedes systemic dissemination.

Early pathogenesis sequence

CD155 mediates poliovirus attachment

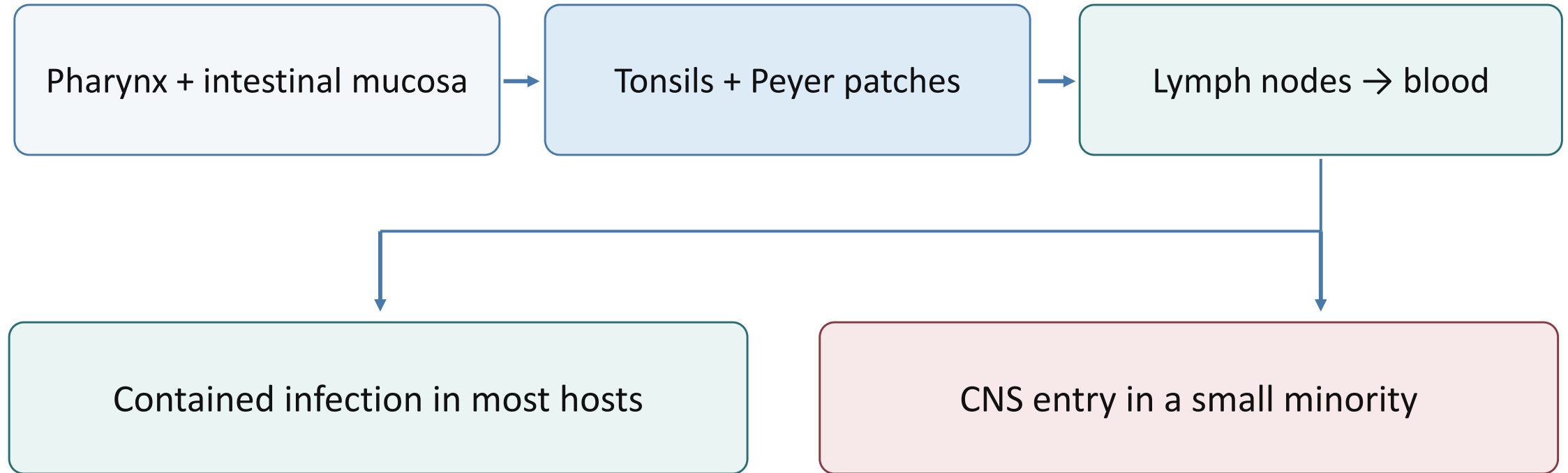
Viral receptor

- Poliovirus binds the cell-surface receptor CD155.
- The source describes CD155 on epithelial cells, lymphocytes and neurons.

Tissue implications

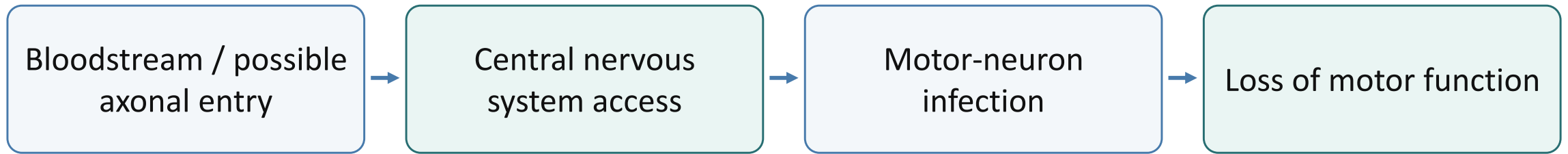
- Receptor expression makes multiple tissue compartments potentially susceptible.
- Neuronal infection is clinically important only when viral spread reaches the CNS.

Antibodies usually contain poliovirus infection



Antibody response usually contains systemic spread.

Neuroinvasion targets motor neurons



- Source proposes hematogenous spread or retrograde axonal transport.
- The basis for failed containment in the small affected minority remains uncertain.

Both neuroinvasion routes are presented as possible, not proved in a given case

Spinal versus bulbar poliomyelitis

Type	Primary region	Functional consequence
Spinal	Motor neurons in spinal cord	Limb-muscle weakness or paralysis
Bulbar	Brainstem motor structures	Potential impairment of respiration and related functions

Polio immunization: Two vaccine approaches

Inactivated poliovirus vaccine

- Injected preparation containing inactivated virus.
- Antibodies protect against poliovirus serotypes.

Oral attenuated poliovirus vaccine

- Live attenuated oral vaccine has been used to support eradication.
- Rare genetic reversion can yield pathogenic vaccine-derived strains.

Why eradication has been achievable

- Humans are the only natural host emphasized by Robbins.
- The virus has comparatively limited genetic variation.
- Antibody responses induced by vaccination neutralize poliovirus.
- Sustained immunization is essential because wild and vaccine-derived circulation can occur.

Poliovirus diagnosis depends on virologic detection

- Viral culture is a described diagnostic method.
- Viral RNA can be detected in throat secretions or stool.
- Serology may support diagnosis, depending on context.
- Anatomic and neurologic localization is needed to interpret suspected paralytic disease.

Clinical application: Febrile illness with paralysis

Illustrative case: Following an initial nonspecific febrile illness, a patient develops acute limb weakness involving motor function.

Interpretation question

What anatomic target explains paralytic poliomyelitis?

Details to integrate

Enteric replication

Systemic spread

Motor weakness

Case interpretation: Motor-neuron involvement

Most consistent interpretation

Poliovirus replication in spinal or brainstem motor neurons

- Early mucosal and lymphoid replication can be clinically inconspicuous.
- Neuroinvasion occurs in a small minority despite usual antibody control.
- Neuron injury links CNS infection directly to weakness and paralysis.

Comparison: Entry routes and initial sites

Virus	Predominant acquisition	Early replication / receptor
SARS-CoV-2	Respiratory particles	ACE2-bearing respiratory epithelium
Measles	Airborne aerosols	Respiratory tract; SLAMF1-positive immune cells
Mumps	Respiratory droplets	Respiratory tract and draining lymphocytes
Poliovirus	Fecal–oral	Pharyngeal / gut mucosa; CD155

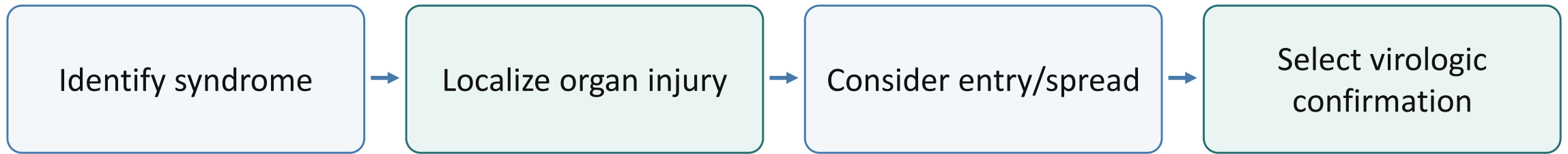
Comparison: Dominant tissue injury

Virus	Morphologic signature	Clinical consequence
SARS-CoV-2	Diffuse alveolar damage; Microthrombi	ARDS / hypoxia
Measles	Perivascular rash; Multinucleated giant cells	Exanthem; Secondary infection risk
Mumps	Salivary interstitial edema, duct injury	Parotitis; Orchitis / pancreatitis
Poliovirus	Motor-neuron infection	Spinal or bulbar paralysis

Common theme: Pathology depends on host response

Syndrome	Direct viral effects	Host-mediated component
COVID-19	Infection of respiratory epithelial cells	Cytokine injury, coagulation disturbance
Measles	Dissemination across organs	T-cell-mediated rash; Altered immunity
Mumps	Duct/acinar infection	Edema, inflammation, ischemia
Poliomyelitis	Motor-neuron infection	Antibody containment protects most hosts

Clinical reasoning: Localize before identifying the virus



- The same virus can cause distinct organ syndromes.
- Histologic patterns are interpreted together with exposure history and molecular tests.

Conceptual diagnostic reasoning, not a treatment guideline

High-yield distinctions among four infections

- SARS-CoV-2: ACE2 / spike-mediated entry; Severe alveolar and thromboinflammatory injury.
- Measles: Airborne dissemination, cell-mediated rash and transient immune suppression.
- Mumps: Salivary duct injury with possible orchitis, pancreatic and CNS involvement.
- Poliovirus: Enteric replication with rare motor-neuron neuroinvasion.

Final integration: four diagnostic questions

- What route allowed infection, and which cell type first supported replication?
- How did the virus disseminate from its primary site to injured organs?
- Which findings reflect direct cytopathic injury, host inflammation or both?
- Which clinical specimen and laboratory method can establish the responsible virus?