

Chagas disease

Trypanosoma cruzi: transmission, tissue injury, and clinicopathologic consequences

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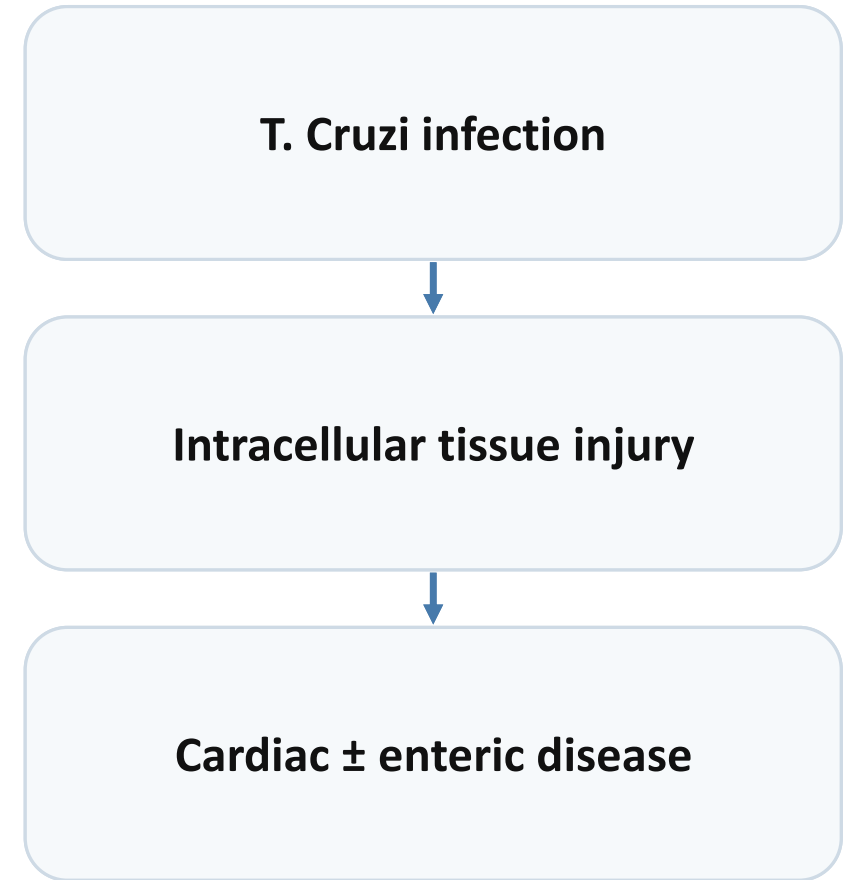
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Learning objectives

- Explain transmission of T. Cruzi and its intracellular replication sequence.
- Relate acute infection and persistent immune injury to cardiac disease.
- Recognize acute and chronic myocardial morphologic patterns.
- Connect myenteric plexus injury to megacolon and esophageal dilation.

American trypanosomiasis: The disease identity

- Chagas disease is caused by *Trypanosoma cruzi*.
- The pathogen is a kinetoplastid protozoan and an intracellular parasite.
- Its most important long-term target is the heart.



Schematic

Distribution and burden

- Endemic distribution includes Mexico, Central America, and South America.
- The source estimates 6–7 million infected individuals globally.
- It reports approximately 28,000 new cases and 12,000 deaths annually, with a decline over the preceding 30 years.
- Vector-associated disease is described as rare in the United States.

Animal hosts sustain transmission

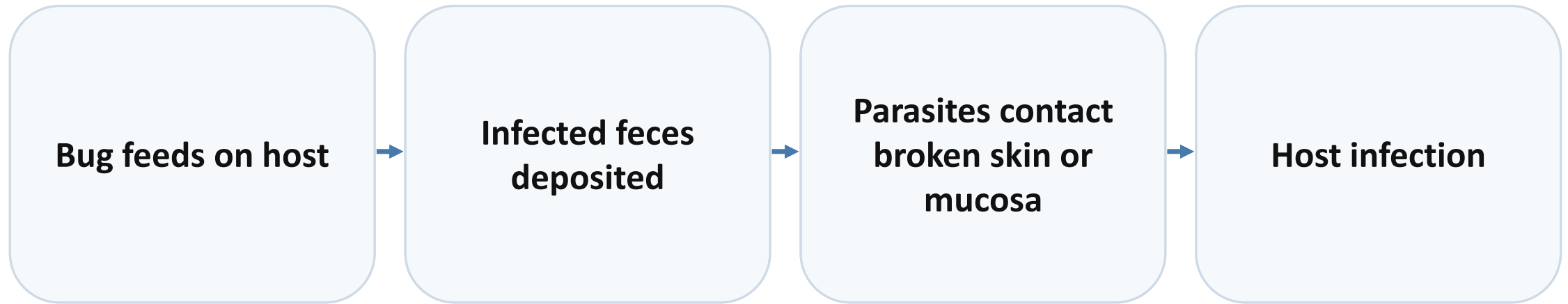


- T. Cruzi infects multiple animals, including cats, dogs, and rodents.
- Animal infection contributes to a reservoir beyond humans.

Triatomine vector ecology

- Triatomine bugs are also termed kissing bugs or reduviids.
- They shelter in cracks of loosely constructed houses.
- Feeding on sleeping occupants creates opportunities for exposure.
- Transmission depends on infected bug feces, not simply its bite.

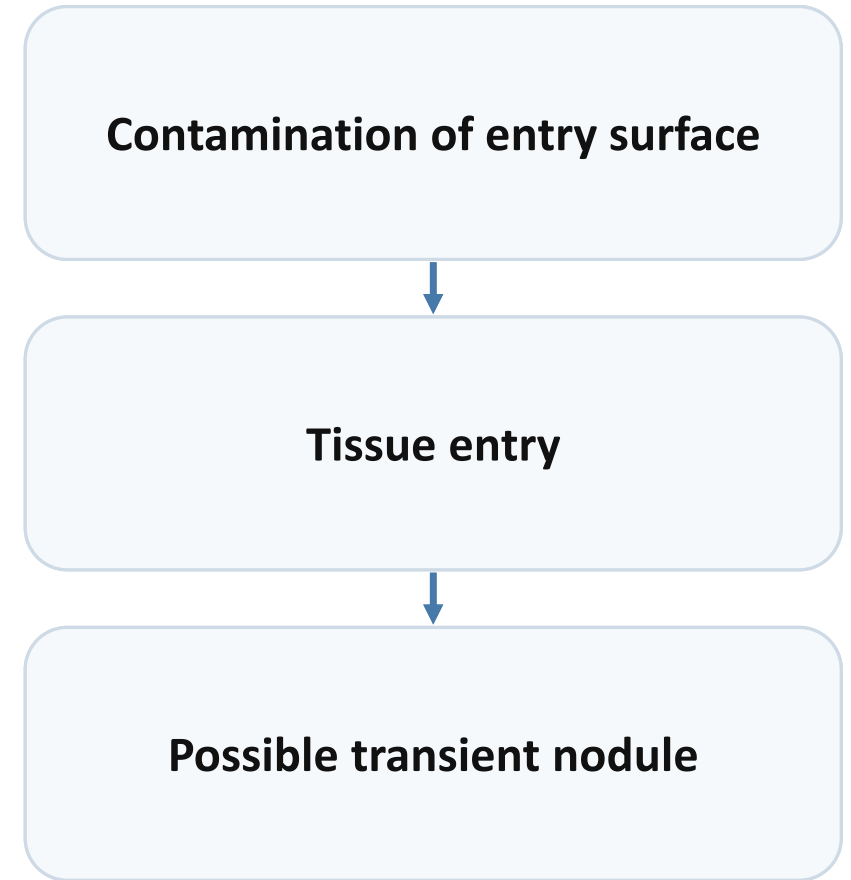
Fecal transmission: Critical causal sequence



- Inoculation occurs after fecal contamination of an entry surface.

Portal of entry and early local response

- Infectious parasites enter through damaged skin or mucous membranes.
- A transient erythematous nodule may occur at the cutaneous entry site.
- The local lesion is not necessary for the subsequent systemic disease.



Schematic

Routes beyond the insect vector

- Congenital transmission remains an important non-vector route.
- Ingestion of contaminated food can transmit the organism.
- Infected blood products and transplanted organs can transmit infection.
- Transmission history therefore extends beyond remembered bug exposure.

Compare transmission routes

Route	Source-described exposure	Practical interpretation
Vector	Infected feces contacting skin break or mucosa	Bite alone is an incomplete history
Vertical	Congenital transmission	Maternal infection matters
Oral	Contaminated food	No insect contact need be recalled
Iatrogenic	Blood products / transplantation	Exposure may occur in clinical care

Two relevant parasite forms

Trypomastigote

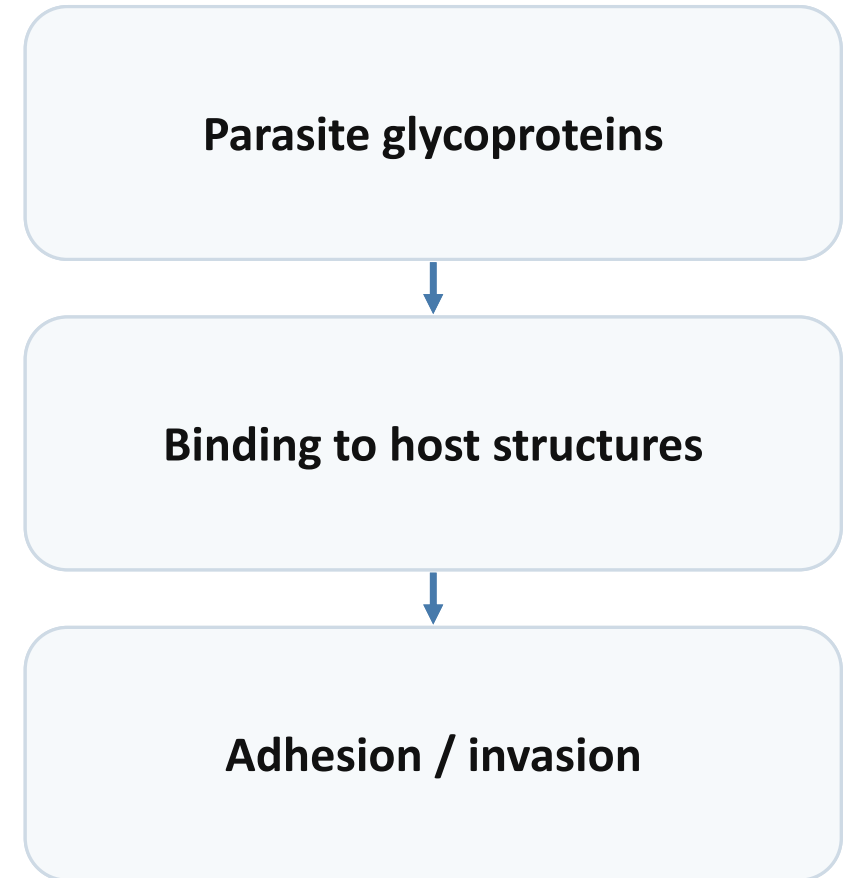
- Flagellated form implicated in cell entry and blood dissemination.
- Induces host-cell processes that facilitate invasion.

Amastigote

- Rounded intracellular replicative form.
- Multiplies within host-cell cytoplasm.

Surface glycoproteins initiate host interaction

- T. Cruzi expresses many GPI-anchored surface glycoproteins.
- These proteins participate in cell adhesion and invasion.
- Parasite attachment precedes intracellular replication.

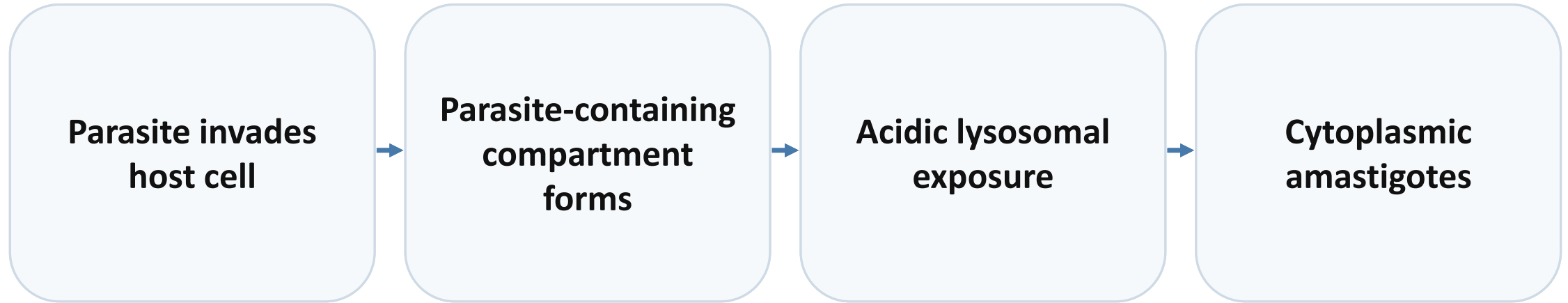


Schematic

Multiple ligands facilitate adhesion

Host-associated ligand	Role described in the textbook
Laminin	Glycoprotein-binding partner
Fibronectin	Glycoprotein-binding partner
Collagen	Glycoprotein-binding partner
Cytokeratin	Glycoprotein-binding partner
Other extracellular proteins	Additional interaction partners

Intracellular entry is not the final step



- Unusually, *T. Cruzi* needs brief acidic phagolysosomal exposure during its intracellular development.

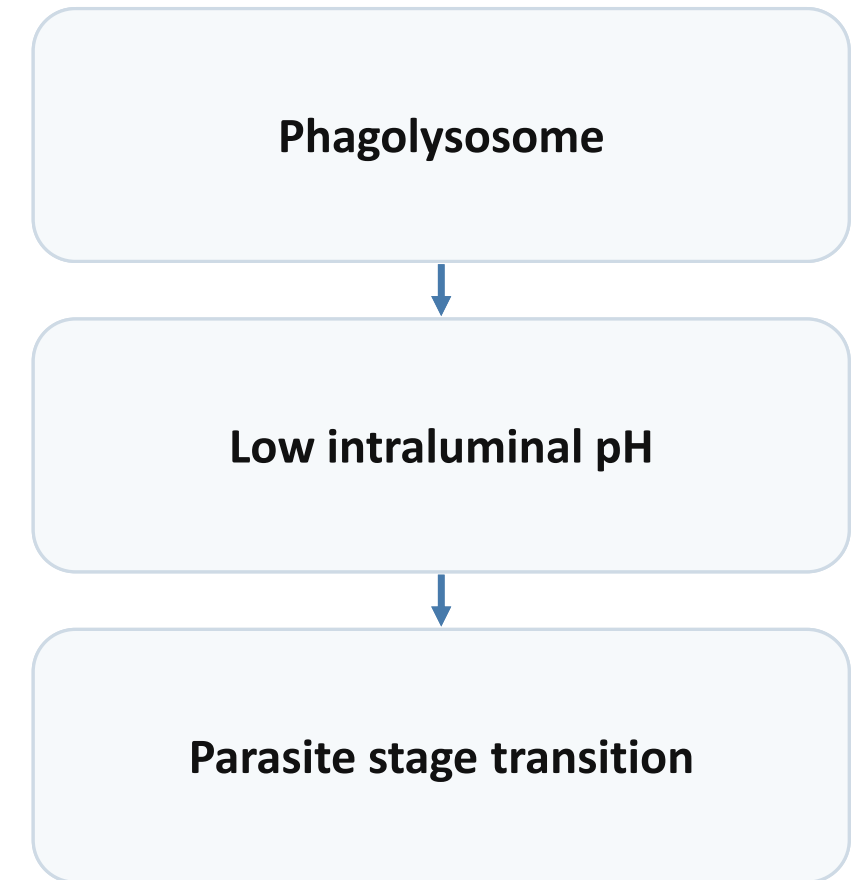
Host cytoplasmic calcium promotes lysosome fusion



- The organism promotes a host-cell signal that brings lysosomal contents into contact with the parasite.
- This step supports progression toward the amastigote stage.

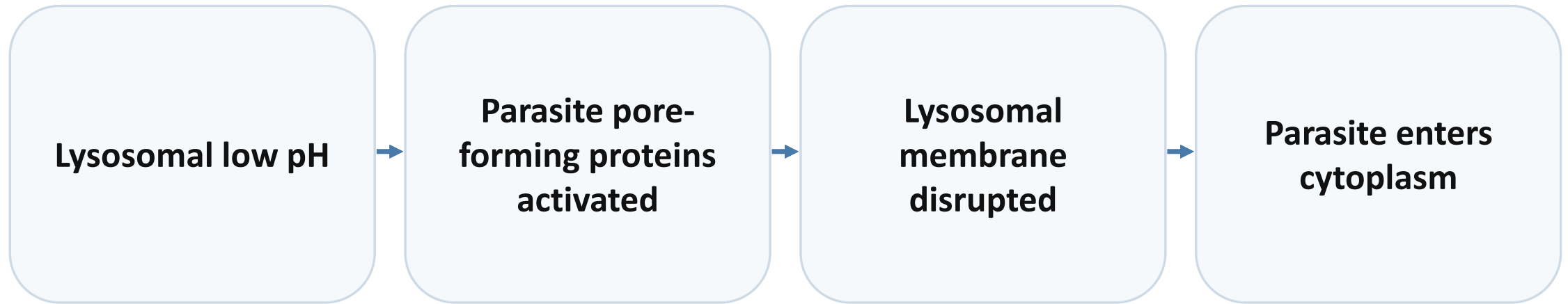
A lysosomal environment that enables development

- Brief exposure to the acidic phagolysosome is required for amastigote development.
- This contrasts with intracellular pathogens that avoid lysosomes.
- Acidity also activates the parasite-mediated escape mechanism.



Schematic

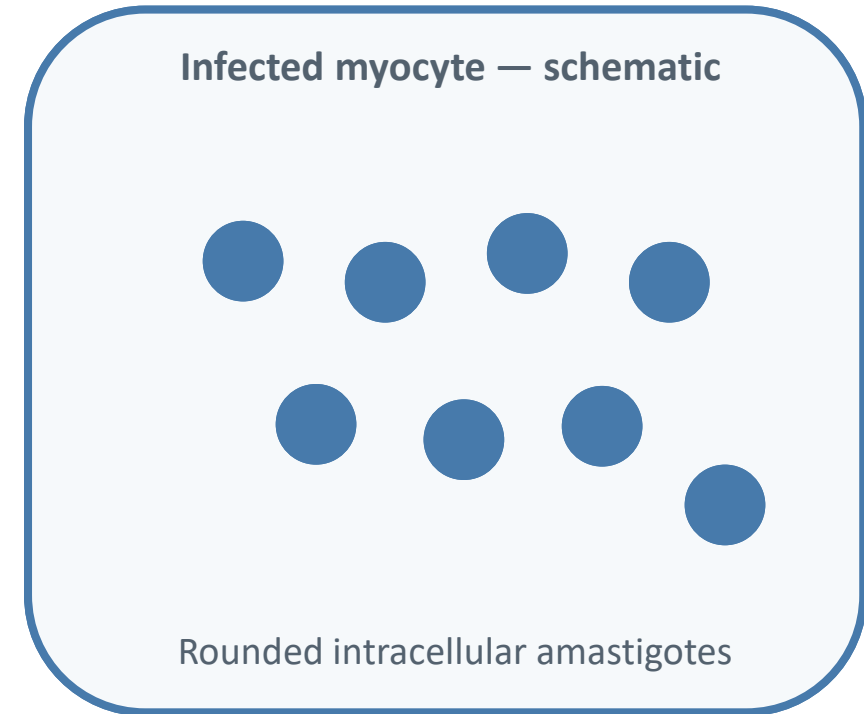
Acid-triggered pore formation permits escape



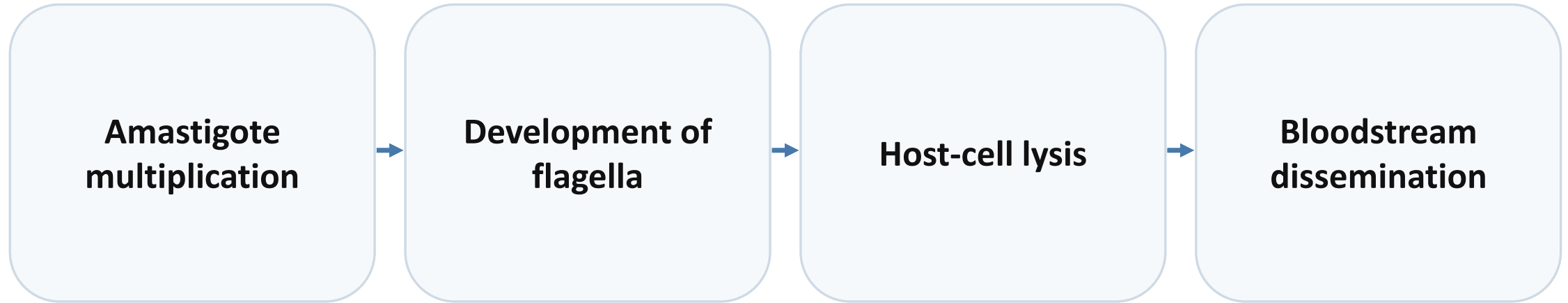
- Membrane disruption precedes extensive cytoplasmic replication.

Amastigotes expand inside host cytoplasm

- The rounded amastigote is the intracellular replicating form.
- An infected host cell can accumulate multiple organisms.
- Intracellular accumulation underlies the pseudocyst morphology seen in acute myocarditis.



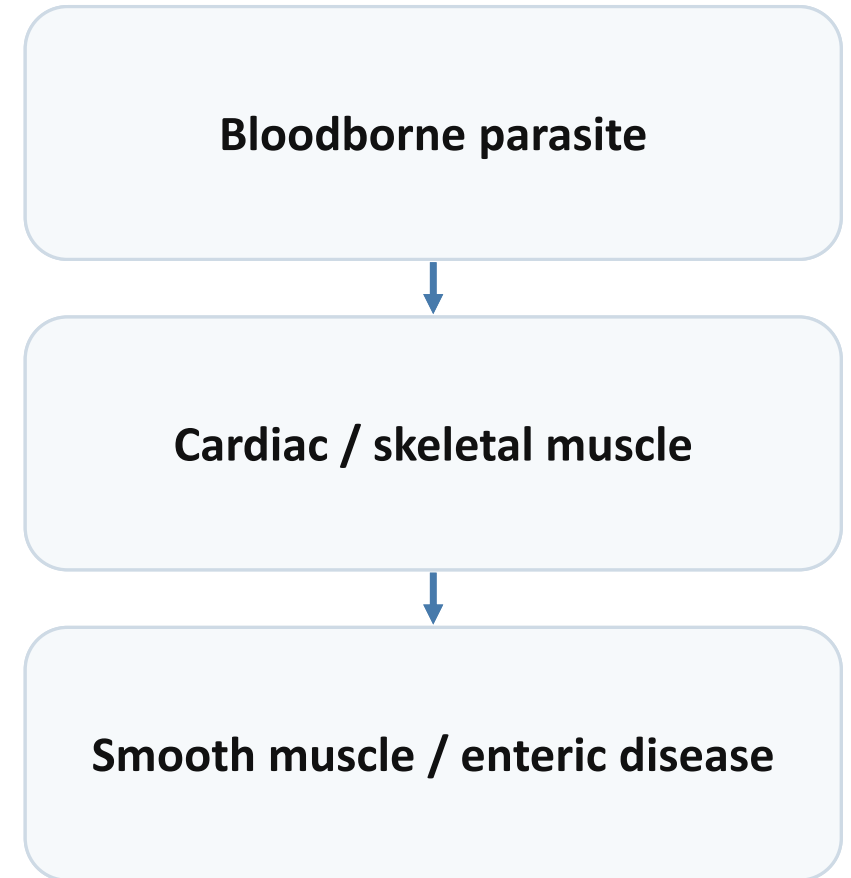
Return to flagellated forms precedes release



- Released parasites can infect further cells and tissues.

Dissemination to muscle tissues

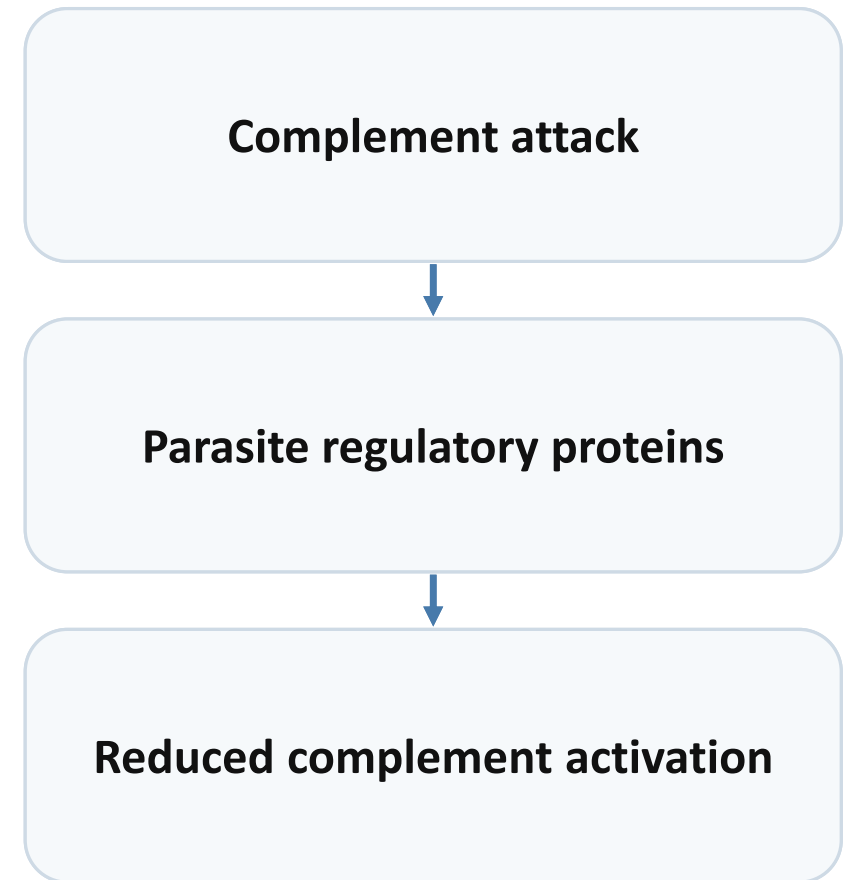
- The source specifies invasion of smooth muscle, skeletal muscle, and heart muscle.
- Myocardial invasion has direct consequences for acute cardiac injury.
- Enteric and cardiac disease reflect injury at different tissue sites.



Schematic

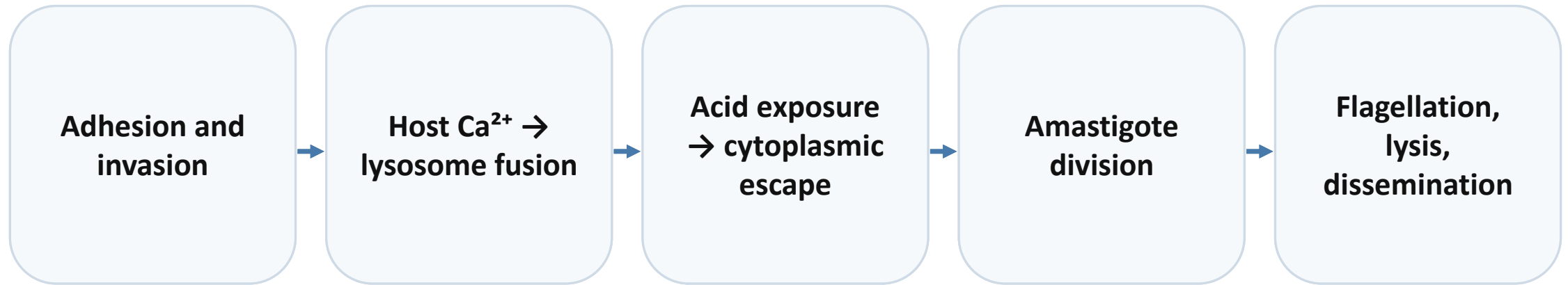
Complement evasion supports survival

- T. Cruzi expresses complement regulatory proteins.
- These proteins counter complement-system activation.
- This mechanism operates alongside intracellular residence and tissue dissemination.



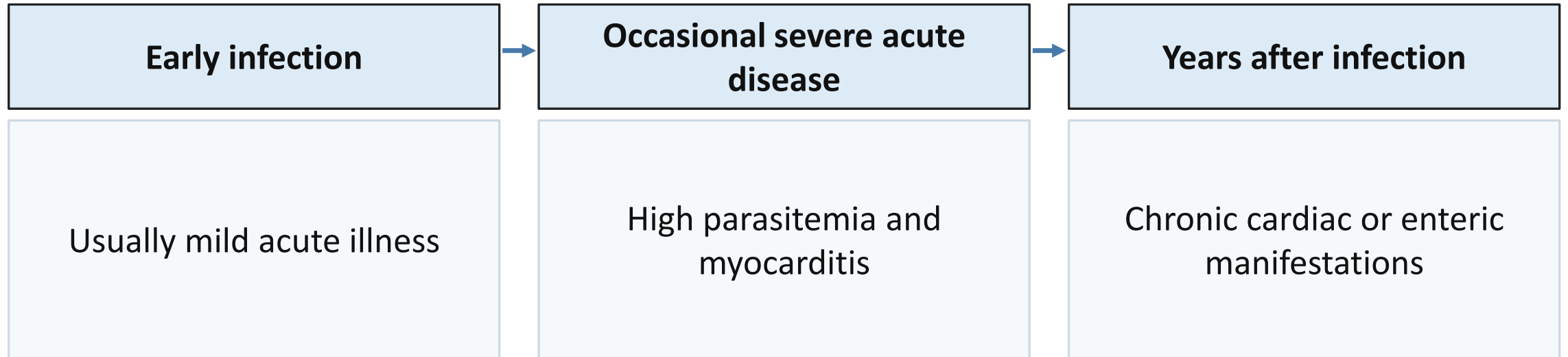
Schematic

Integrating the intracellular replication cycle



- Each stage has a distinct causal role in establishing tissue infection.

Disease is time-dependent



- Chronic disease may become clinically evident long after the initial infection.

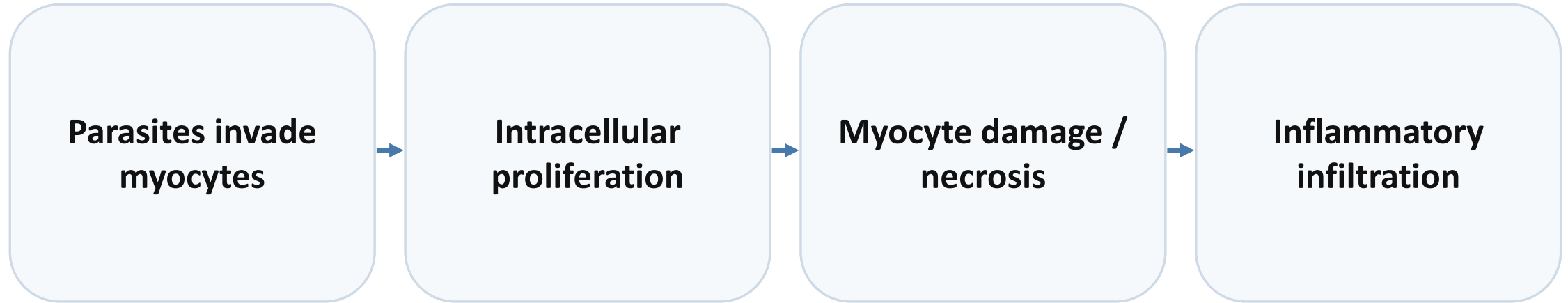
Most acute infections are mild

- Acute Chagas disease is mild in most infected individuals.
- An entry-site nodule may be the transient initial clue.
- Absence of a severe early presentation does not exclude later cardiac disease.

Uncommon severe acute systemic disease

- Severe acute cases may feature high parasitemia and fever.
- Generalized lymphadenopathy or splenomegaly may accompany disease.
- Progressive cardiac dilation and failure are potential severe manifestations.
- The acute severe phenotype is not the usual presentation.

Mechanism of acute myocardial injury

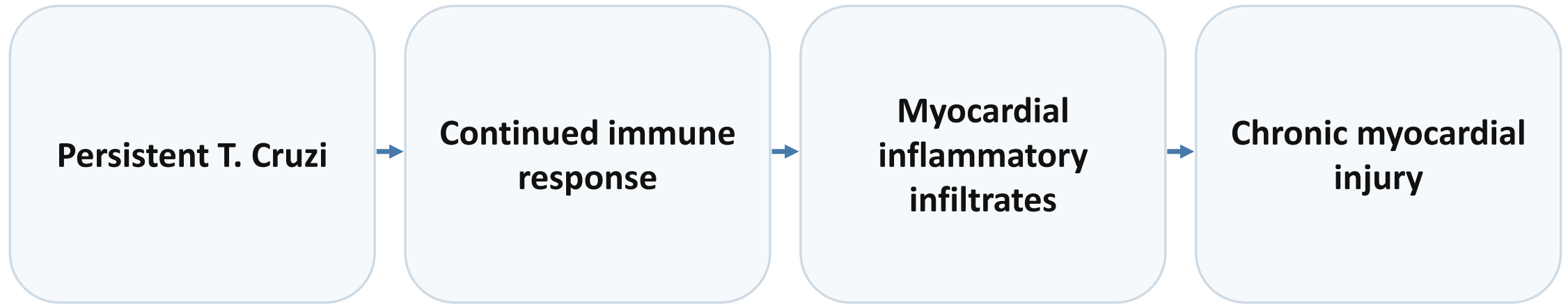


- The acute myocarditis reflects direct infection with a subsequent inflammatory response.

The chronic phase follows a prolonged interval

- Chronic Chagas disease is reported in approximately 20–30% of infected people.
- The textbook places its emergence around 5–15 years after initial infection.
- Late disease may involve the heart and the enteric nervous system.
- These source-specific values should not be assumed to be current surveillance estimates.

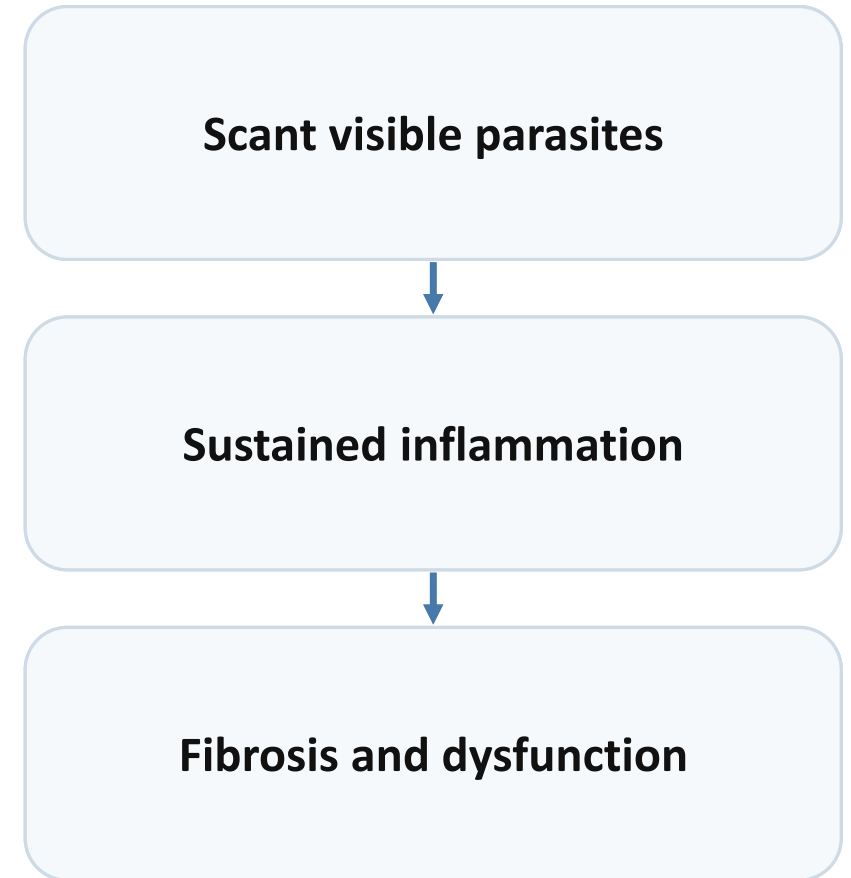
Persistent organisms perpetuate inflammation



- Scant organisms may remain visible despite ongoing inflammation.

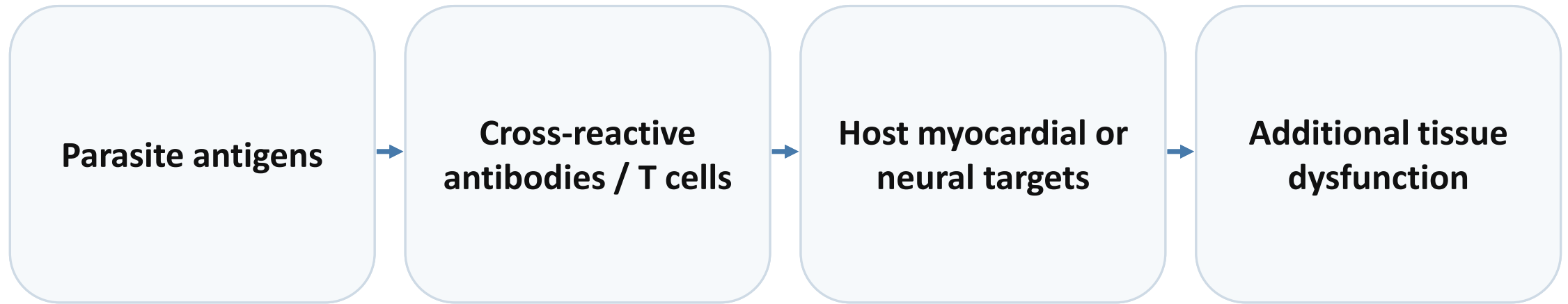
Low organism burden does not imply no injury

- Chronic myocarditis may persist despite sparse demonstrable parasites.
- The host response contributes importantly to continued tissue damage.
- Organism detection and degree of inflammatory injury need not parallel one another.



Schematic

Potential autoimmune contribution



- Autoimmune cross-reactivity as a possible contributor, not the sole proven mechanism.

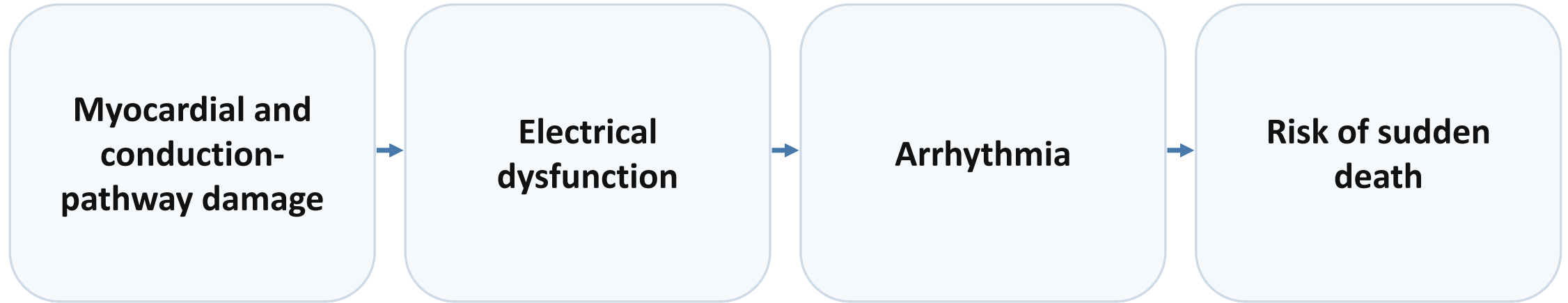
Cross-reactive target structures

- Immune responses against parasite proteins may also recognize myocardial cells.
- Neural cells may be cross-reactive targets.
- Extracellular proteins such as laminin are additionally mentioned.
- Cross-reactive antibodies may disturb cardiac electrophysiology.

Two mechanisms of chronic cardiomyopathy

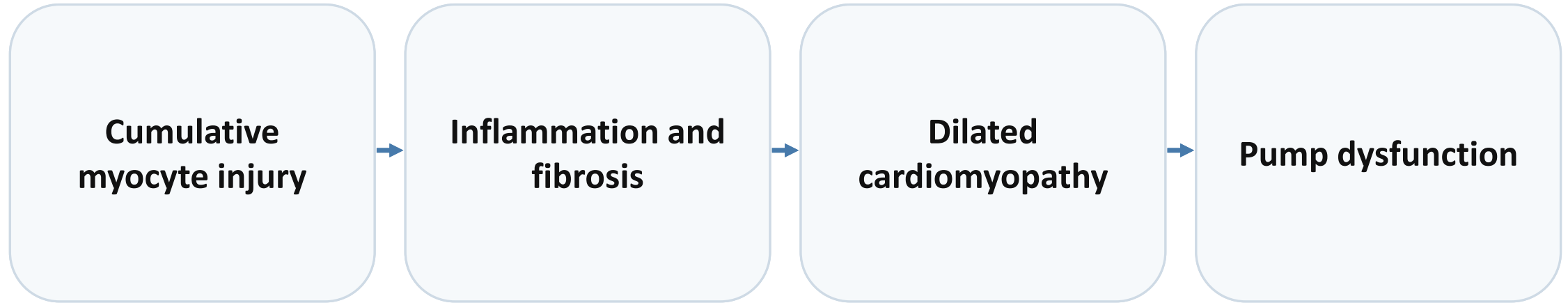
Mechanism	Proposed injury process	Pathologic implication
Parasite persistence	Ongoing antigenic stimulus / inflammation	Continued myocardial cell injury
Potential autoimmunity	Immune cross-recognition of host structures	Possible conduction and tissue dysfunction

Conducting tissue injury produces arrhythmias



- In endemic areas, Chagas disease is a major cause of sudden death from cardiac arrhythmia.

Myocardial damage produces chamber dilation



- Chronic myocarditis produces both structural and electrical consequences.

Sudden death and heart failure are distinct outcomes

Electrical consequence

- Damage to conducting pathways
- Arrhythmia → risk of sudden death

Mechanical consequence

- Progressive myocardial injury and dilation
- Impaired cardiac pumping / failure

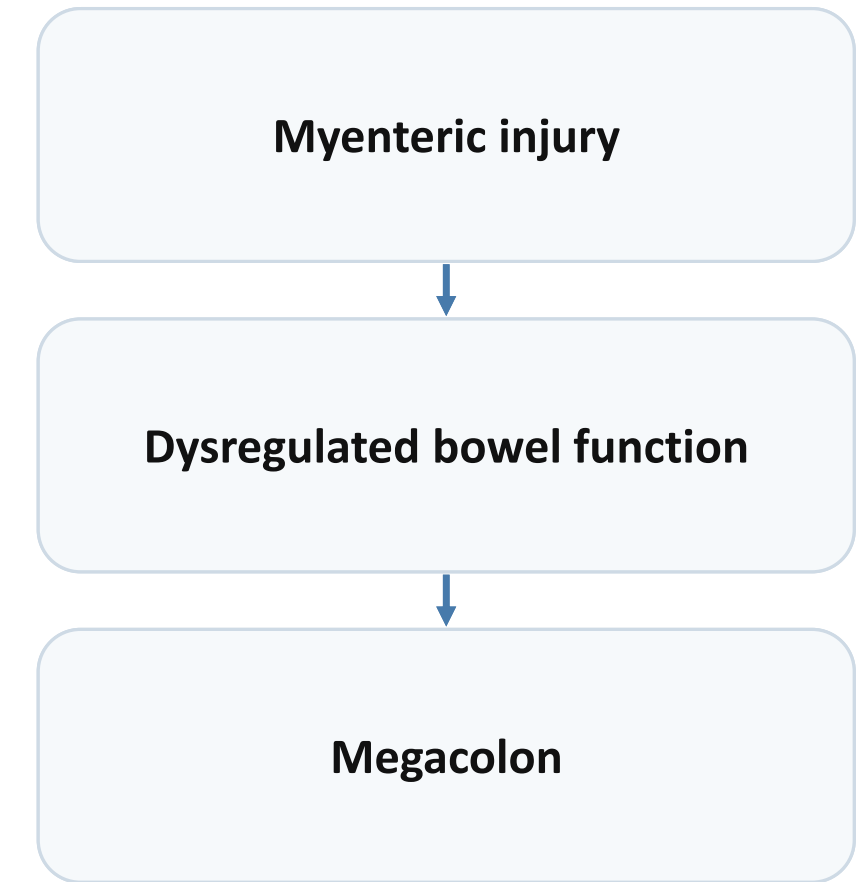
Enteric disease is linked to the myenteric plexus



- The colon and esophagus are the named sites of megavisceral disease.

Megacolon: A neural–structural connection

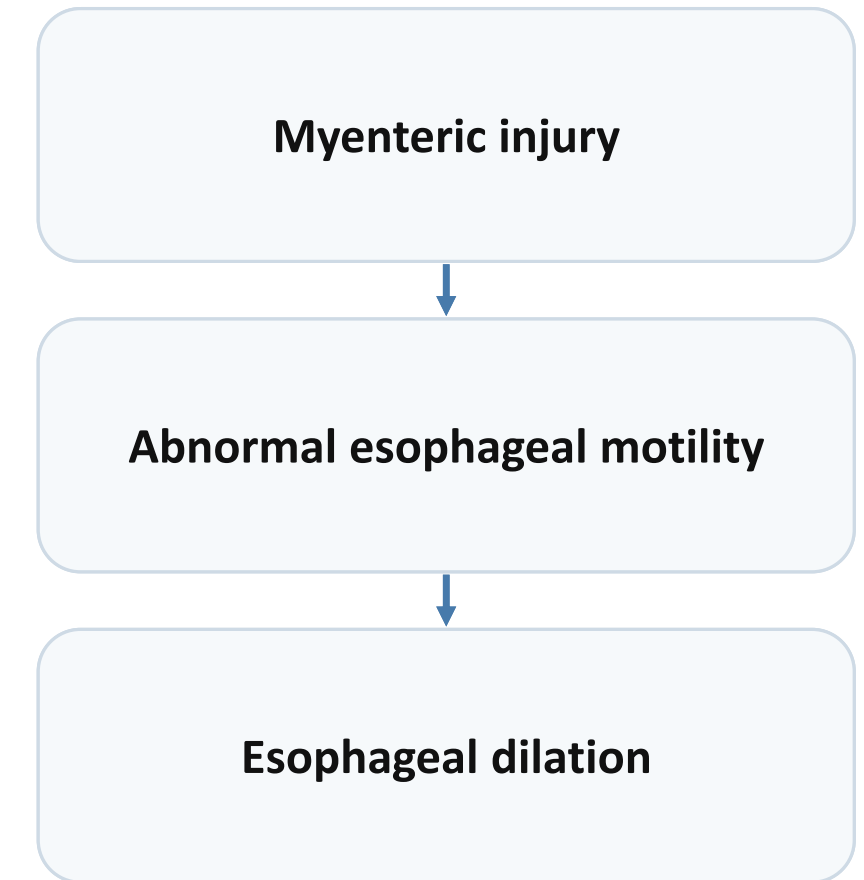
- Damage to enteric ganglion networks is associated with colonic dilation.
- The major clinical pathology is enlargement of the colon (megacolon).
- This is a long-term consequence rather than proof of active organisms within the ganglia.



Schematic

Esophageal dilation has a parallel mechanism

- The esophagus can become dilated in chronic Chagas disease.
- Its association with myenteric injury parallels the mechanism of megacolon.
- The pathology extends beyond the myocardium.



Schematic

Cardiac and enteric manifestations may coexist

- Frequent coexistence in some endemic areas of Brazil.
- It reports esophageal or colonic disease in as many as 50% of patients with lethal carditis in those settings.
- The figure is context-specific and should not be generalized to every infected population.

Acute lethal myocarditis: Global morphology

- Changes may be distributed diffusely throughout the heart.
- Myocardial inflammation accompanies parasitized cells.
- Four-chamber cardiac dilation may be present in lethal acute cases.

Diffuse myocyte infection



Acute inflammatory injury

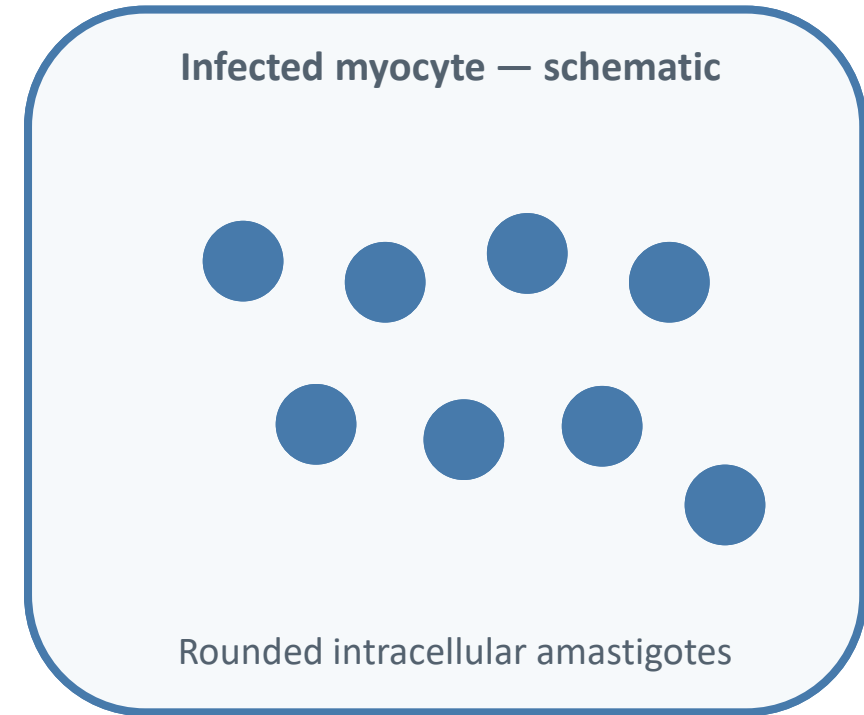


Possible four-chamber dilation

Schematic

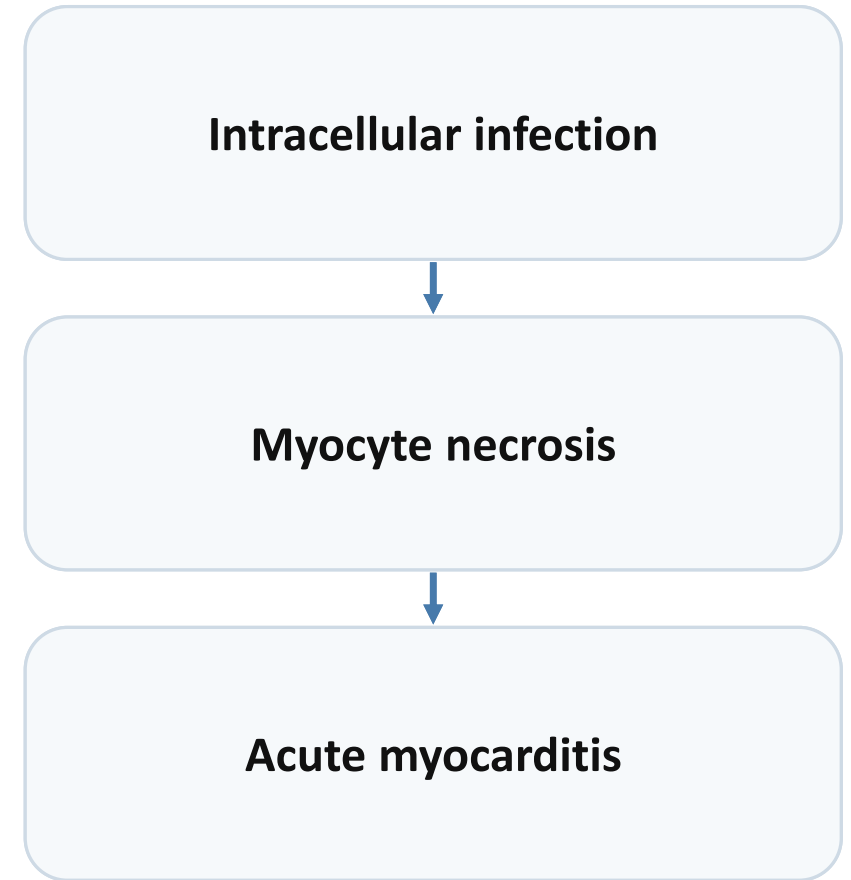
Amastigote clusters form intracellular pseudocysts

- Clusters of amastigotes expand individual myocardial fibers.
- The term pseudocyst describes organisms accumulated inside an infected cell.
- This is a schematic, not a substitute for an authentic H&E photomicrograph.



Myocyte necrosis localizes structural injury

- Foci of myocardial cell necrosis are described in acute lethal disease.
- Necrosis appears with dense inflammatory infiltration.
- Together with parasitized myocytes, these findings support an infectious myocarditis pattern.



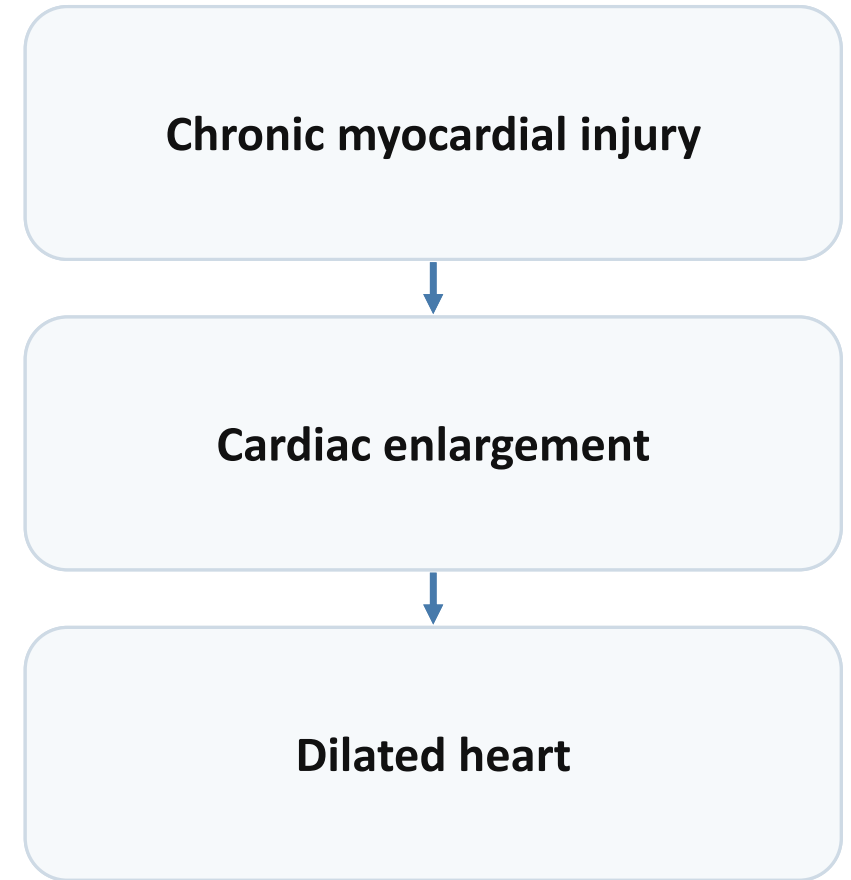
Schematic

Acute interstitial inflammation can be extensive

- Dense, extensive acute interstitial inflammatory infiltration.
- The response extends throughout the myocardium in lethal acute cases.
- Pathologic severity reflects both infected cells and the inflammatory reaction.

Chronic cardiomyopathy: Gross phenotype

- The heart is typically dilated.
- Heart size and weight are increased.
- The gross pattern reflects advanced cardiomyopathic remodeling.



Schematic

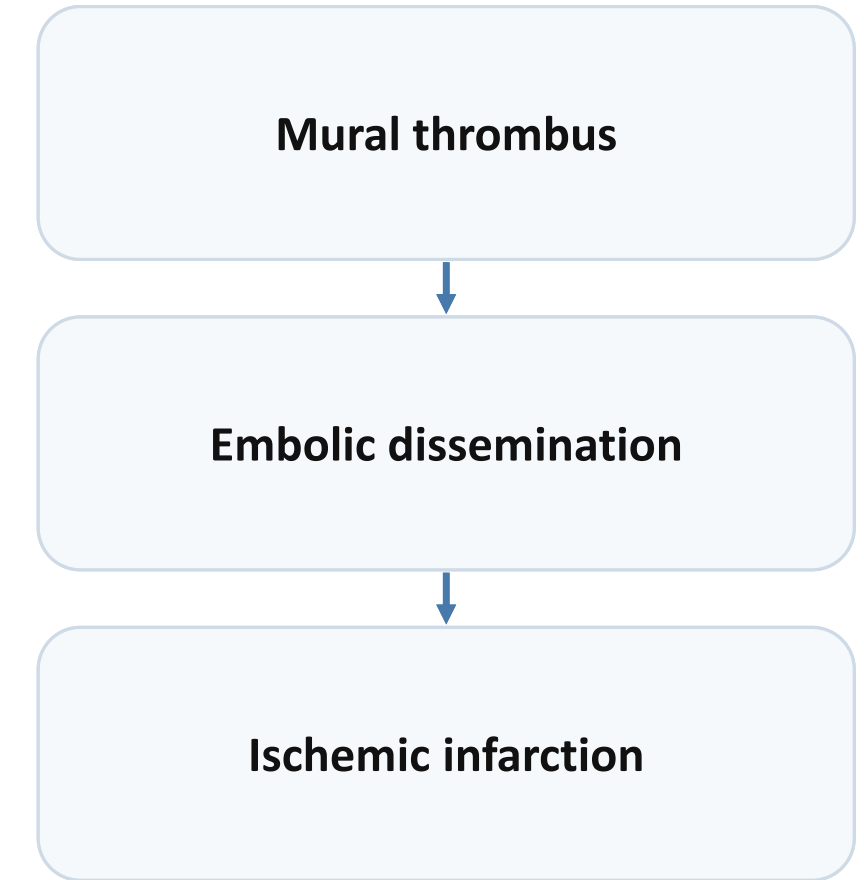
Mural thrombi complicate dilated hearts



- Mural thrombi are often present in chronic Chagas disease.
- The presence of thrombi connects myocardial remodeling to downstream embolic injury.

Emboli and infarcts are major consequences

- Pulmonary and systemic emboli are described in advanced chronic cases.
- Embolization may lead to infarction.
- The source describes emboli or infarctions in about half of autopsy cases with mural thrombi, not half of all patients.

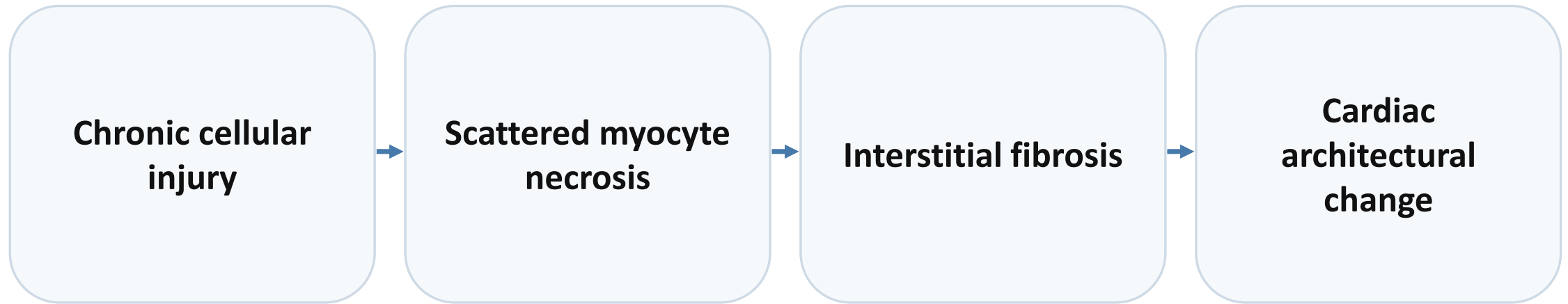


Schematic

Chronic inflammation has a characteristic distribution

- Interstitial inflammatory infiltrates remain in chronic disease.
- Perivascular inflammation is also described.
- The infiltrate comprises lymphocytes, plasma cells, and monocytes.
- Visible organisms can be sparse despite histologic inflammation.

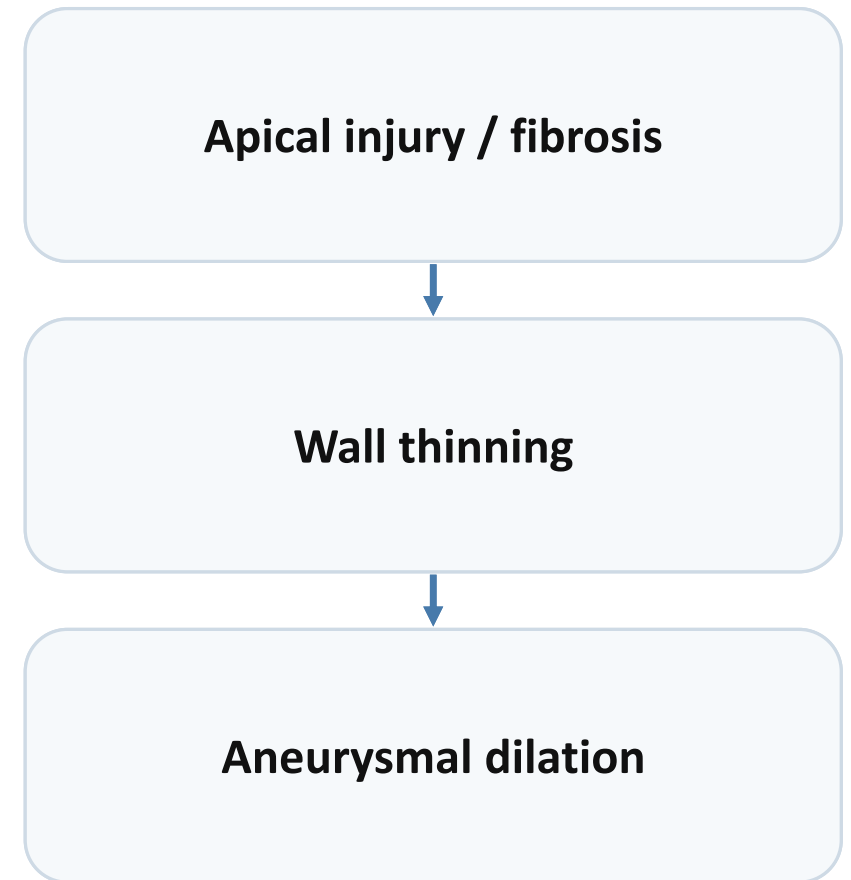
Necrosis and fibrosis mark continuing damage



- Fibrosis is especially emphasized toward the left ventricular apex.

Apical aneurysmal remodeling

- The left ventricular apex may show disproportionate fibrosis.
- Apical wall thinning and aneurysmal dilation can develop.
- This is a localized consequence within an otherwise dilated cardiomyopathy.



Schematic

Megaviscera despite absent detectable ganglionic parasites

- Esophagus and colon may be severely dilated in chronic disease.
- Parasites cannot be found within myenteric plexus ganglia even when dilation is present.
- Consequently, direct microscopic visualization in ganglia is not required to connect the disease with enteric dysfunction.

Acute and chronic myocardial patterns

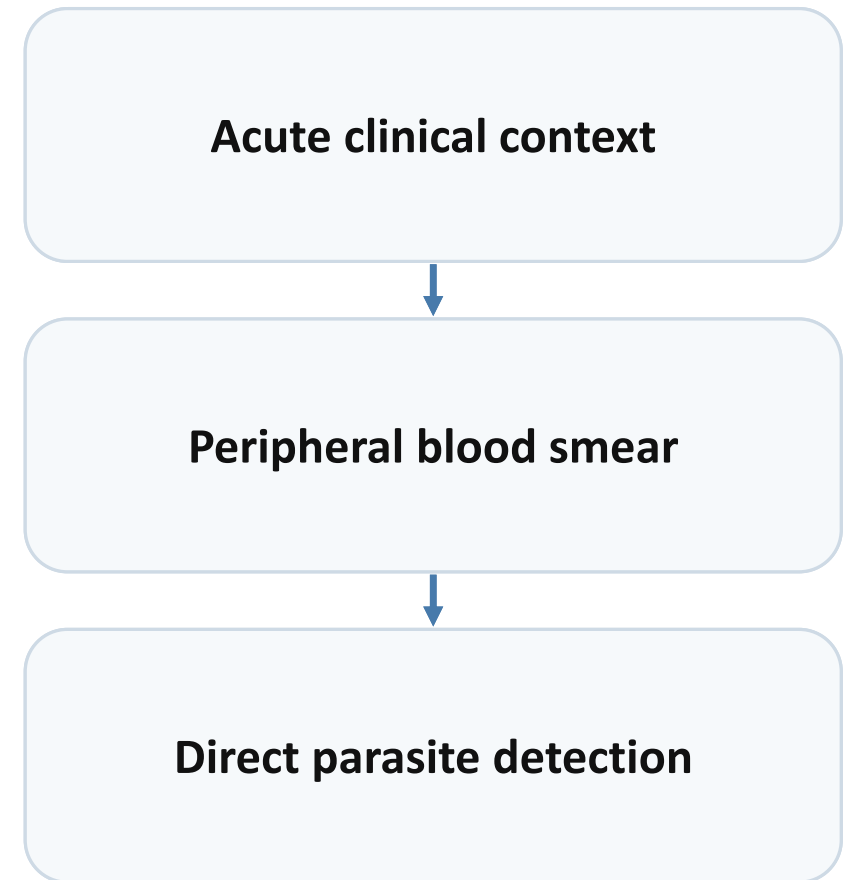
Feature	Acute lethal myocarditis	Chronic cardiomyopathy
Parasite visibility	Amastigote clusters / pseudocysts	Organisms may be scant
Inflammation	Dense acute interstitial infiltrates	Interstitial / perivascular mononuclear cells
Myocyte injury	Focal necrosis, swelling	Scattered necrosis and fibrosis
Gross consequence	May show four-chamber dilation	Dilated, heavier heart; possible apical aneurysm

Mechanism–morphology–effect linkage

Mechanism	Tissue manifestation	Potential effect
Intracellular proliferation	Myocyte pseudocysts and necrosis	Acute myocarditis
Persistent immune response	Chronic infiltrates and fibrosis	Dilated cardiomyopathy
Conduction-pathway injury	Electrical dysfunction	Arrhythmia / sudden death
Myenteric plexus injury	Megacolon / esophageal dilation	Enteric disease

Blood smear is useful in acute infection

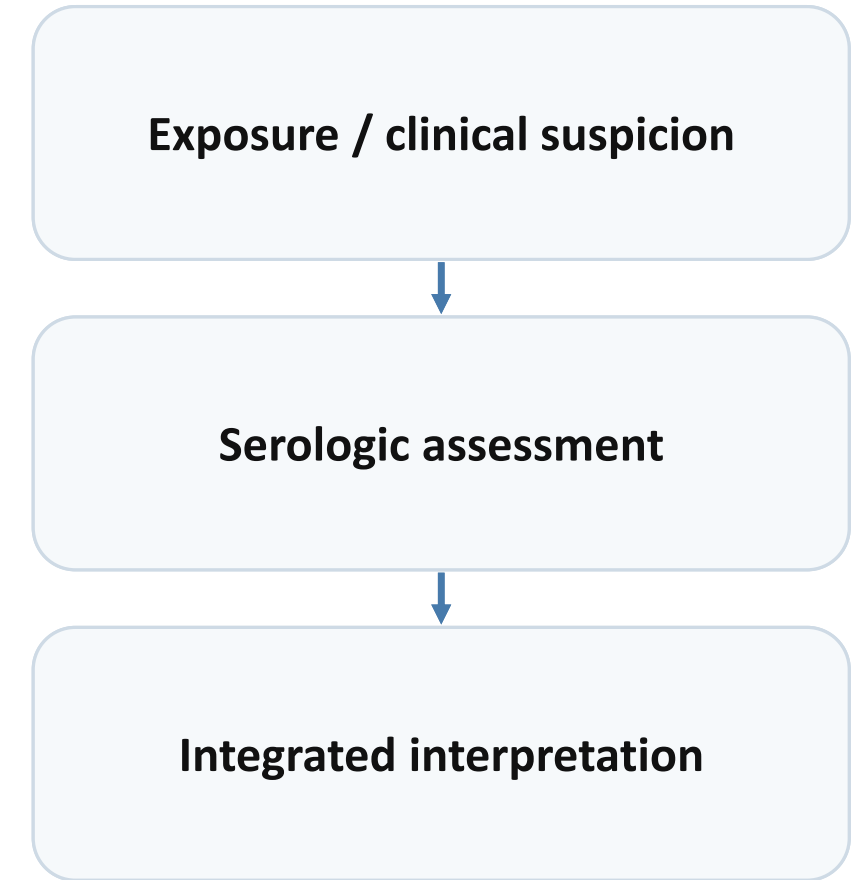
- Blood-smear diagnosis in acute cases.
- High parasitemia in severe acute illness makes bloodstream organisms a meaningful target.
- Test choice must be interpreted in relation to disease phase.



Schematic

Serology is the more common diagnostic approach

- Diagnosis is made more commonly by serology.
- Serology addresses a different diagnostic signal from directly visualizing organisms.
- Clinical timing and exposure history remain essential interpretive context.



Schematic

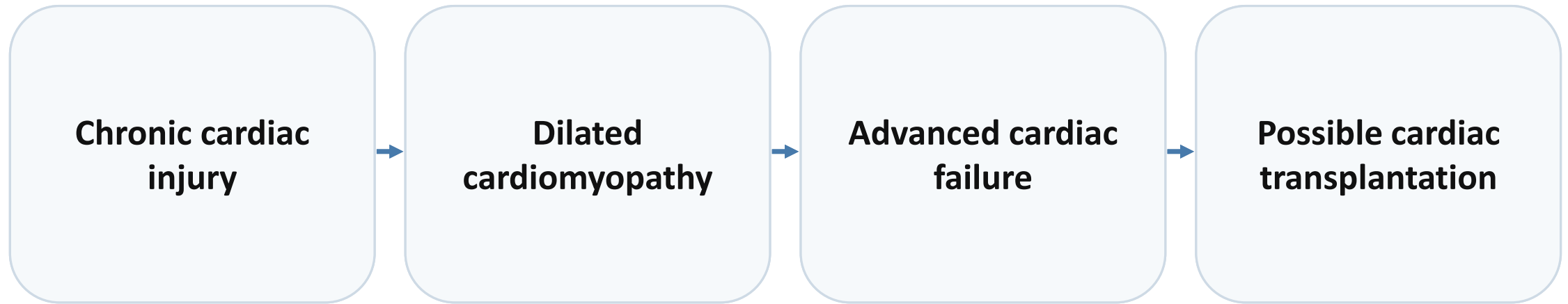
Testing strategy depends on disease phase

Setting	Source-described test	Interpretive constraint
Acute infection	Peripheral blood smear	Visualize parasites when circulating
Many other presentations	Serologic testing	Interpret with exposure and syndrome
Chronic myocardial disease	Morphology + clinical / serologic context	Few organisms may be demonstrable in tissues

Antiparasitic treatment is effective early

- Antiparasitic drugs are effective when given soon after infection.
- The timing statement refers to the early infection period.
- The extracted section does not provide drug selection, doses, or comparative efficacy for late cardiomyopathy.

Advanced cardiomyopathy may require transplantation



- Transplantation as often required in severe chronic Chagas cardiomyopathy.

Case 1 · acute infection

A resident of an endemic area recalls contact with a nocturnal household bug. Afterward, fever and an erythematous entry-site lesion are documented.

Interpret the vignette:

- Which exposure event can transmit the parasite?
- Which direct method does Robbins describe for acute diagnosis?

Case 1 · mechanism and diagnostic interpretation

- Infected bug feces must contact a skin break or mucosal surface.
- A skin entry nodule is compatible with early local infection.
- An acute blood smear may demonstrate bloodstream parasites.
- The bite itself is not the complete transmission mechanism.

Case 2 · a delayed cardiac presentation

An individual previously resident in an endemic region presents years later with cardiac chamber dilation and rhythm disturbance.

Interpret the vignette:

- Which two injury pathways may contribute to chronic disease?
- What morphology is expected in the myocardium?

Case 2 · why the chronic heart fails

- Persistent parasites sustain inflammatory myocarditis even when sparse.
- Potential immune cross-reactivity may add myocardial / electrical dysfunction.
- Chronic infiltrates, focal necrosis, and interstitial fibrosis accompany dilation.
- Conduction damage explains the risk of arrhythmia and sudden death.

Case 3 · gastrointestinal enlargement

A patient with a history of Chagas disease develops major dilation of the colon;
Myocardial involvement is also suspected.

Interpret the vignette:

- Which neural structure is implicated?
- Why is absence of detectable parasites in its ganglia not decisive?

Case 3 · enteric pathology interpretation

- Damage to the myenteric plexus is associated with megacolon.
- Esophageal dilation can occur by an analogous mechanism.
- Absent detectable ganglionic parasites despite megaviscera.
- Cardiac and gastrointestinal disease can coexist in chronic infection.

Chagas disease versus African trypanosomiasis

Property	Chagas disease	African trypanosomiasis
Main agent	T. cruzi	T. brucei subspecies
Host location	Intracellular amastigotes	Extracellular parasites in blood / tissues
Vector route	Triatomine bug feces	Tsetse fly bite
Dominant pathology	Cardiomyopathy; enteric dilation	Fever, lymphoid response, CNS disease

Single causal map: From entry to late disease



- Clinical stage and pathology reflect changing relationships among parasite burden, inflammation, and tissue damage.

Essential clinicopathologic conclusions

- T. Cruzi is an intracellular kinetoplastid transmitted mainly through contaminated triatomine feces.
- Intracellular amastigote multiplication causes acute parasitized-myocyte injury.
- Chronic inflammation and possible immune cross-reactivity damage myocardium and conduction pathways.
- Chronic disease can produce dilated cardiomyopathy, apical aneurysm, thromboembolism, and megaviscera.

Primary source and source limitations

- Robbins, Cotran & Kumar: Pathologic Basis of Disease, 11th edition — “Chagas Disease,” Infectious Diseases.
- Teaching content derived from the supplied chapter extraction and topic Markdown.
- All cellular and process figures in this lecture are original editable schematics; no genuine microscopy is reproduced.