

Leishmaniasis

Pathogenesis, morphology and clinicopathologic correlation

Pathology and clinical correlations

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Learning objectives

- Differentiate the promastigote and amastigote stages within the sandfly–mammal cycle.
- Explain Leishmania survival in phagocytes and the opposing Th1/Th2 immune responses.
- Recognize the morphology and clinical consequences of four disease forms.
- Connect disease distribution and pathology to source-supported diagnostic approaches.

Leishmaniasis is an intracellular protozoal disease

- Caused by Leishmania, a kinetoplast-containing protozoan parasite.
- Produces chronic inflammation in skin, mucous membranes or viscera.
- Transmission occurs through bites of infected sandflies.
- Disease phenotype reflects both the infecting parasite and the host.

Three major tissue compartments

Localized infection

- Skin lesions may begin at the site of inoculation.
- Mucosal disease can involve nasopharyngeal structures.
- Tissue inflammation may evolve into granulomas.

Disseminated infection

- Macrophages can transport infection through the mononuclear phagocyte system.
- Spleen, liver and marrow may become heavily involved.
- Systemic inflammatory and hematologic consequences dominate.

The four recognized morphologic forms

Form	Principal distribution	Defining lesion pattern
Visceral	Mononuclear phagocyte system	Systemic organ enlargement and cytopenias
Cutaneous	Exposed skin	Papule evolving into a slow ulcer
Mucocutaneous	Nasopharyngeal mucosa	Destructive mucosal inflammation
Diffuse cutaneous	Extensive skin	Progressive widespread nodules with foamy macrophages

Endemicity spans multiple regions

- The source identifies the Middle East, South Asia, Africa and Latin America as endemic regions.
- “Old World” and “New World” are geographic groupings, not clinical diagnoses.
- Exposure history should be interpreted in relation to local transmission ecology.

Social conditions influence transmission

- Leishmaniasis is associated with poverty in endemic regions.
- The text describes epidemics following forced migration of people with low immunity.
- Movement into an area of intense sandfly transmission changes opportunities for infection.

Disease burden as reported

Measure	Textbook estimate	Interpretive caution
Cutaneous cases per year	0.6–1 million	Reported estimate; Not presented as a 2026 live count
Visceral cases per year	50,000–90,000	Reported global estimate
Deaths per year	More than 20,000	Reported in the source in context of visceral disease

Leishmania is a kinetoplastid parasite

- The organism contains a distinctive kinetoplast: Mitochondrial DNA concentrated into a specialized structure.
- It alternates between an extracellular vector stage and an intracellular mammalian stage.
- Recognition of stage and compartment is central to understanding pathogenesis.

The two developmental forms

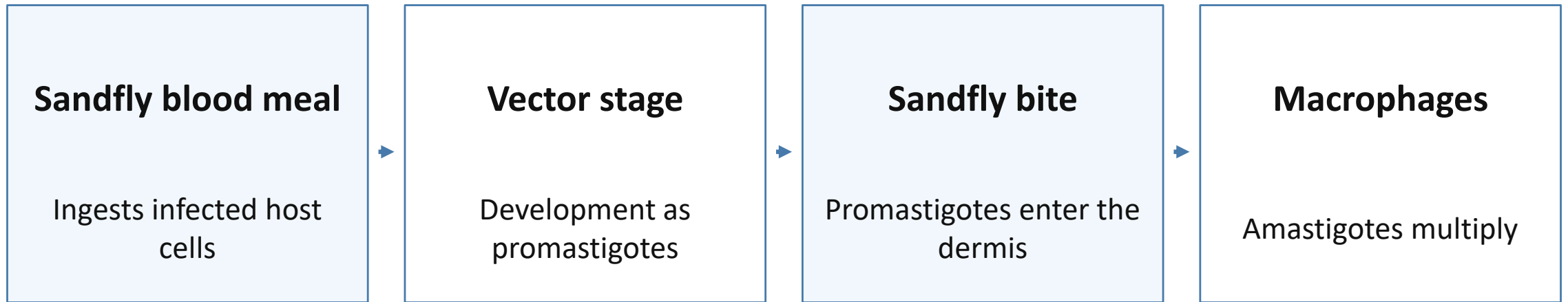
Promastigote

- Extracellular form in the sandfly.
- Slender and flagellated.
- Transmitted during an infectious sandfly bite.

Amastigote

- Round intracellular stage within mammalian macrophages.
- Lacks an external flagellum.
- Proliferates in phagolysosomal compartments.

Transmission cycle at a glance



- The next sandfly blood meal can reacquire infection from an infected host.

Vectors and parasite diversity

- The text identifies more than 90 sandfly species as vectors.
- Approximately 21 *Leishmania* species infect humans, according to the textbook.
- Parasite identity contributes to geographic distribution and tissue phenotype.

The mammalian reservoir interface

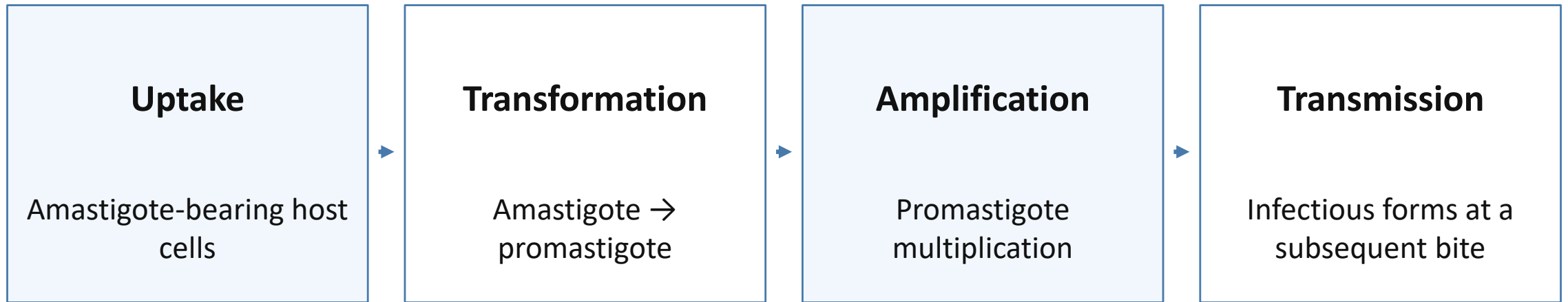
Reservoir mammals

- Rodents are listed as reservoirs.
- Dogs can harbor infection.
- Foxes are another example.

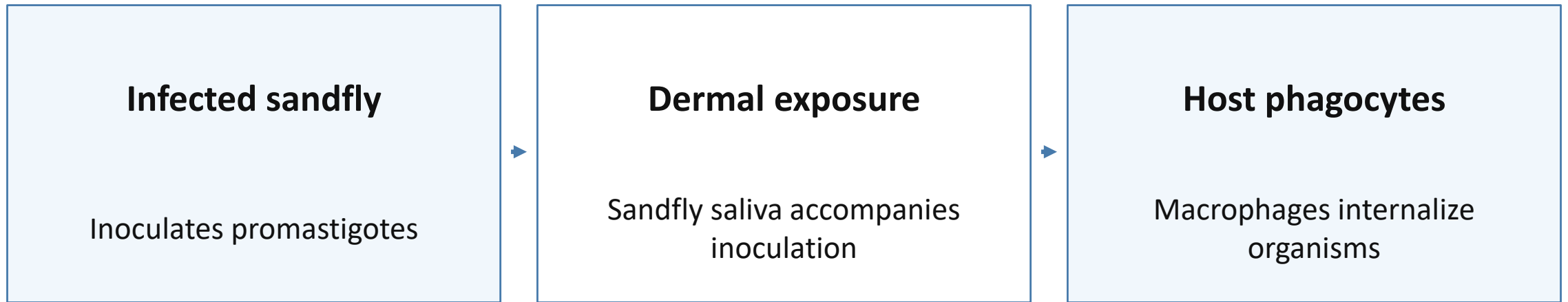
Transmission bridge

- Sandflies feed on infected mammalian hosts.
- Vector acquisition starts a developmental cycle within the insect.
- Infected vectors can subsequently transmit to people.

Events within the sandfly

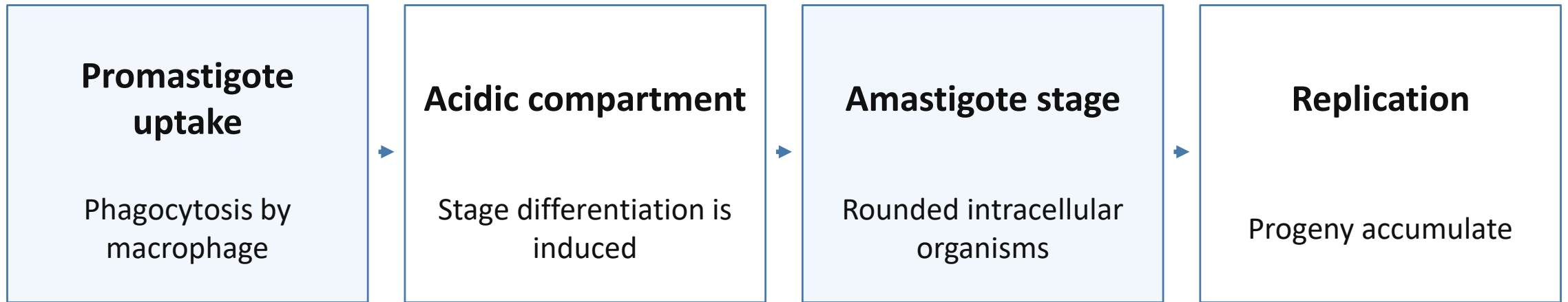


What happens at the bite site?



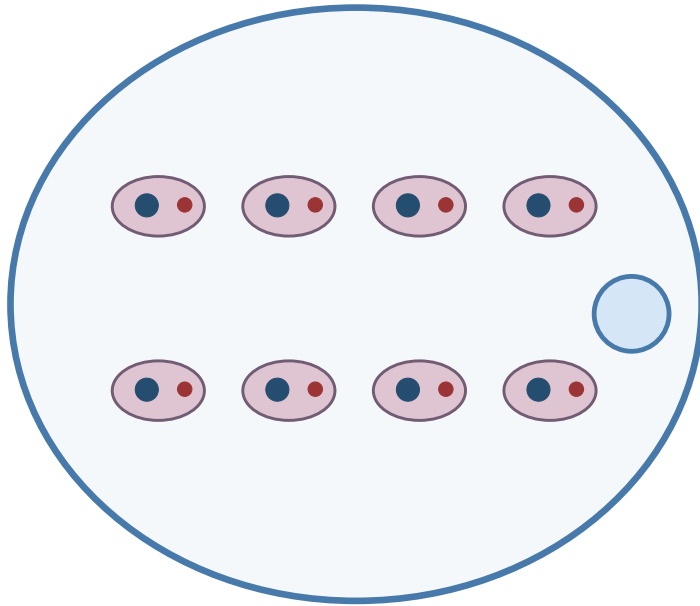
- The source attributes enhanced infectivity to sandfly saliva.

The macrophage is the replication niche



Amastigote structure: What to recognize

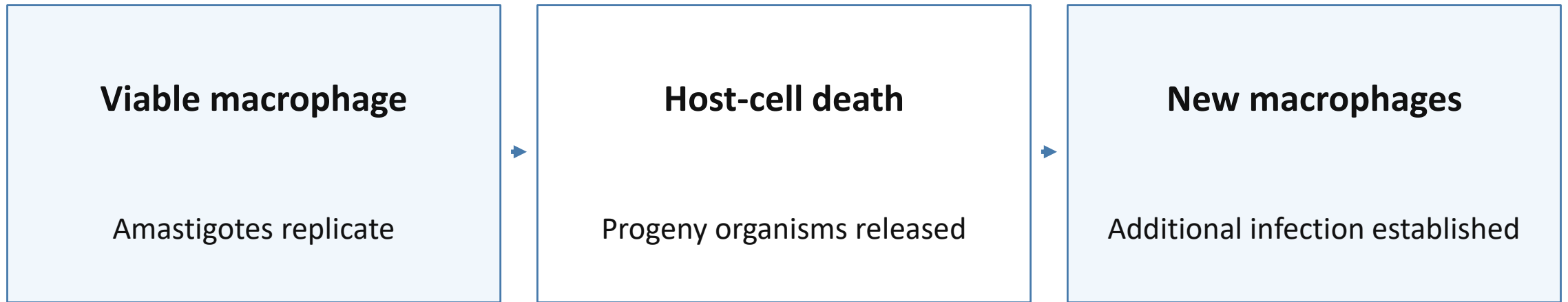
Intracellular organism model



Blue dot: Parasite nucleus Red dot: Kinetoplast

- Amastigotes are rounded organisms within macrophages.
- The kinetoplast is a mitochondrial DNA-containing structure distinct from the nucleus.
- The drawing conveys location and components; It is not a substitute for a stained preparation.

Intracellular amplification and spread



- The cycle increases parasite-containing phagocytes within an infected tissue.

What determines dissemination?

Parasite factors

- Different Leishmania species have different clinical associations.
- Virulence strategies favor survival in innate immune cells.
- The source ties parasite identity to extent of spread.

Host factors

- Host immune response limits or permits intracellular persistence.
- Effective T-cell function is needed to clear infection.
- Immunodeficiency can exacerbate infection.

Species grouping

Grouping	Examples in the source	Regional framing
Old World	L. Major, L. Tropica, L. Donovanii, L. Infantum	Parts of Asia, Middle East, Africa, southern Europe
New World	L. Mexicana, L. Braziliensis, L. Chagasi	Mexico, Central America, South America

Human disease is not confined to classic endemic regions

- The text notes some cases in Texas and Oklahoma.
- Geography informs suspicion but does not independently establish a diagnosis.
- Clinical pattern and tissue or molecular detection remain necessary.

Leishmania actively modifies innate defense

- Survival is not explained solely by passive macrophage uptake.
- The source identifies parasite surface factors and subversion of neutrophil defenses.
- Additional adaptations involve phagolysosomal conditions, iron handling and immune signaling.

Two prominent promastigote virulence factors

Lipophosphoglycan

- Abundant surface glycoconjugate.
- Interferes with the complement pathway.
- Supports early survival at host entry.

Gp63 protease

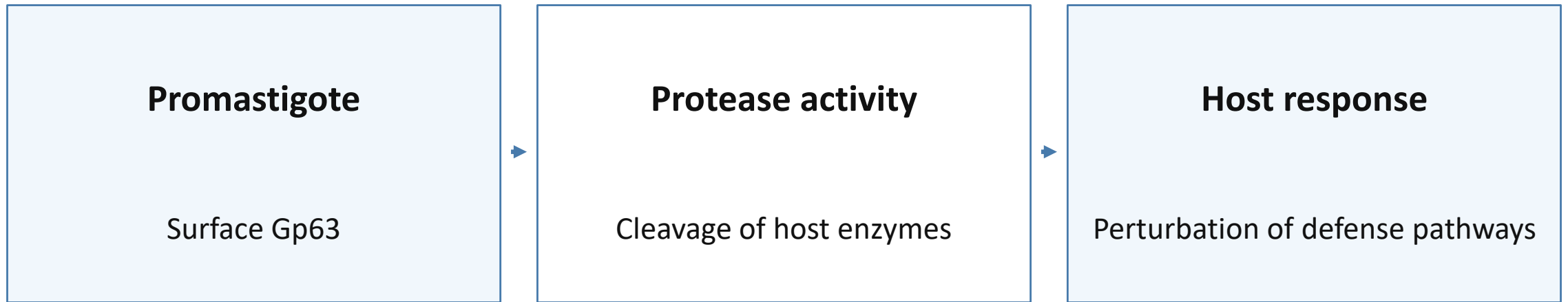
- Zinc-dependent surface proteinase.
- Cleaves host enzymes described as important to defense.
- Illustrates enzymatic subversion of host responses.

Complement interference supports early entry



- This is a mechanistic schematic of the textbook description, not a complete complement cascade.

Gp63: Protease-mediated host interference

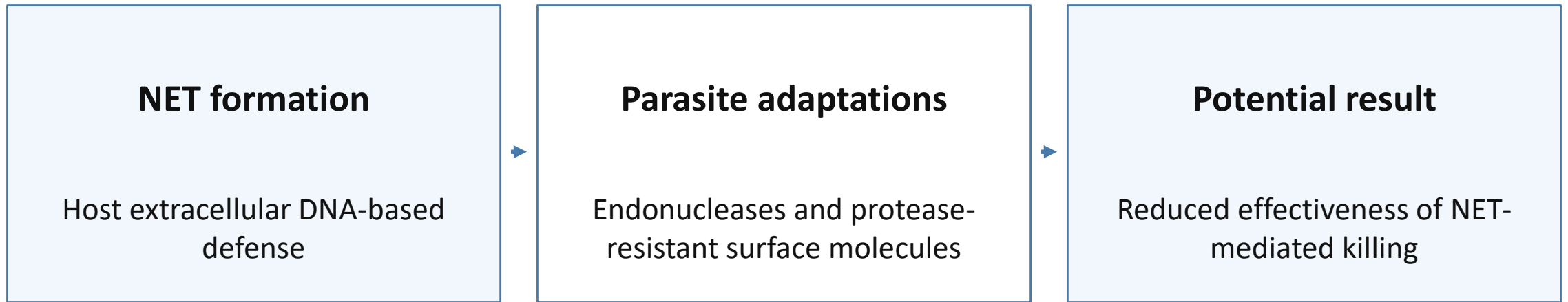


- The source does not enumerate specific enzyme substrates; None are inferred here.

Neutrophil escape has several routes

- Parasites interfere with formation of phagolysosomes and fusion with neutrophil granules.
- They may occupy intracellular compartments protected from lytic mechanisms.
- They can resist reactive oxygen species-mediated toxicity.

Neutrophil extracellular trap evasion



- The textbook explicitly describes parasite digestion of NETs.

Amastigotes resist the phagolysosomal environment

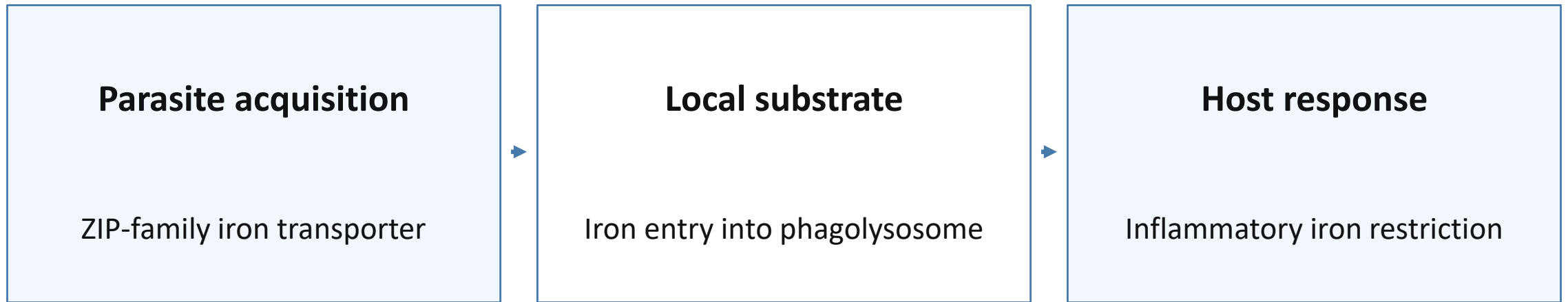
Expected host function

- Macrophage phagolysosomes are antimicrobial compartments.
- Acidity contributes to the hostile environment.
- Killing depends on functional phagocyte defenses.

Source-described adaptation

- Amastigotes alter phagolysosomal conditions.
- Maintenance near pH 6.5 versus typical pH 4.5.
- The stated mechanism supports persistence despite ingestion.

The iron contest occurs inside infected cells



- The same intracellular compartment is a source of nutrients and a site of antimicrobial restriction.

Host defense counteracts parasite iron uptake

- Proinflammatory cytokines inhibit cellular iron absorption.
- The host downregulates transferrin receptors.
- Iron is also removed from the phagosomal compartment.
- These responses oppose parasite nutrient acquisition as.

MicroRNAs contribute to immune disruption

- Posttranscriptional gene regulation through microRNAs.
- It refers to microRNAs in the parasite and host cells.
- Altered cellular signaling is linked to disturbance of protective immunity.
- No individual microRNA species or validated target is specified in the source.

T-helper polarization and infection control

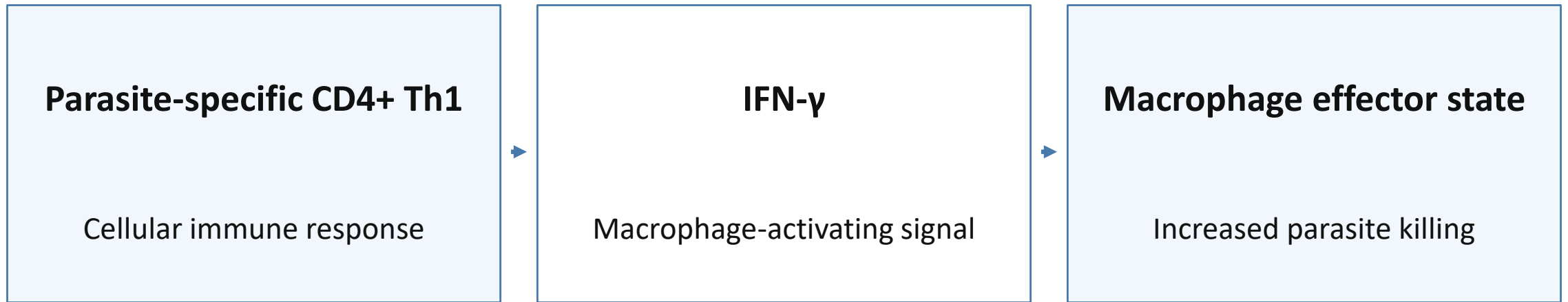
Th1-dominant response

- Parasite-specific CD4+ T cells contribute to control.
- IFN- γ activates macrophages.
- Activated phagocytes become better able to kill parasites.

Th2-dominant response

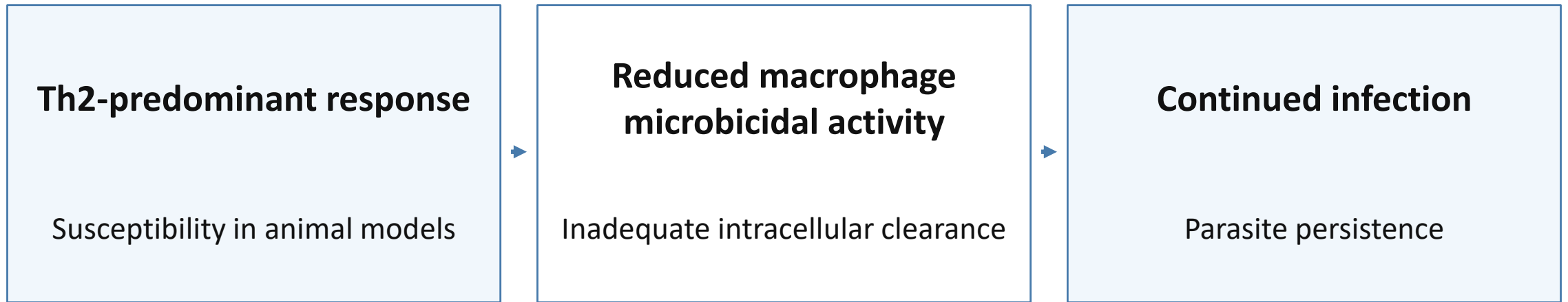
- Susceptible mouse strains show Th2 predominance.
- Th2 cytokines impair effective macrophage killing.
- Infection control is correspondingly weakened.

Protective cellular immunity acts through macrophages



- This protective mechanism in experimental models and humans.

A Th2-biased response may favor persistence



Avoid interpreting Th1 and Th2 as an absolute binary

- The textbook uses Th1–Th2 polarization to explain major determinants of susceptibility.
- The cited direct strain comparisons are from mice.
- Human phenotypes also depend on parasite species and broader immune status.
- Th1 and Th2 are teaching mechanisms here, not stand-alone diagnostic tests.

T-cell dysfunction aggravates leishmaniasis

- Impaired T-cell function increases vulnerability to intracellular organisms.
- The source compares this susceptibility with mycobacterial, Histoplasma and Toxoplasma infections.
- An immune response is necessary for durable parasite clearance even when effective drugs exist.

HIV coinfection is clinically important

- The source notes that many individuals with leishmaniasis are coinfecting with HIV.
- Compromised cellular immunity may worsen intracellular parasite control.
- A systemic leishmanial phenotype should be interpreted in the context of immune competence.

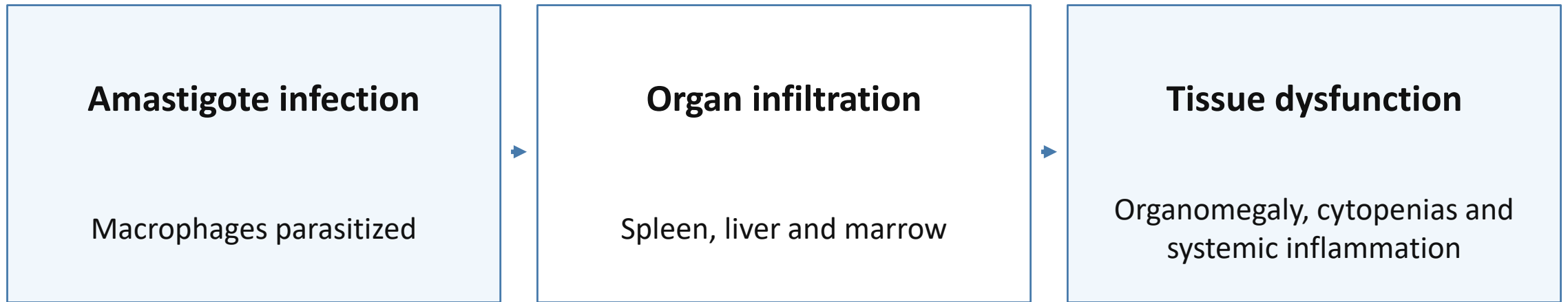
Disease extent shapes the pathologic phenotype

Extent	Dominant host tissue	Characteristic consequence
Localized dermis	Skin macrophages	Cutaneous papule and ulceration
Mucosal disease	Nasopharyngeal tissue	Inflammatory destruction and scarring
Widespread dermis	Skin macrophages	Disseminated nodular lesions
Systemic dissemination	Mononuclear phagocyte system	Organomegaly, marrow dysfunction, inflammation

Visceral leishmaniasis is the most severe form

- The source describes untreated visceral leishmaniasis as almost always fatal.
- Macrophage infection becomes widespread in mononuclear phagocyte organs.
- The clinical syndrome combines systemic inflammation, enlargement of organs and cytopenias.

Systemic macrophage involvement drives visceral disease

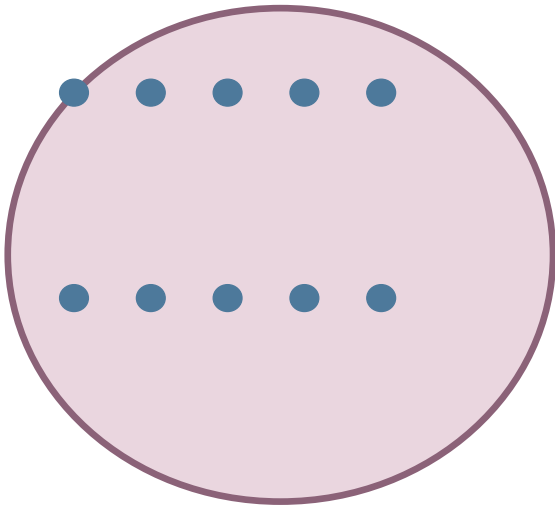


The visceral syndrome has a recognizable cluster

- Fever and weight loss reflect systemic illness.
- Hepatosplenomegaly and lymphadenopathy reflect mononuclear phagocyte organ involvement.
- Pancytopenia signals hematologic consequences.
- No single component is pathognomonic; The source recommends parasite detection.

Spleen: Gross enlargement and structural disruption

Schematic of marked splenomegaly

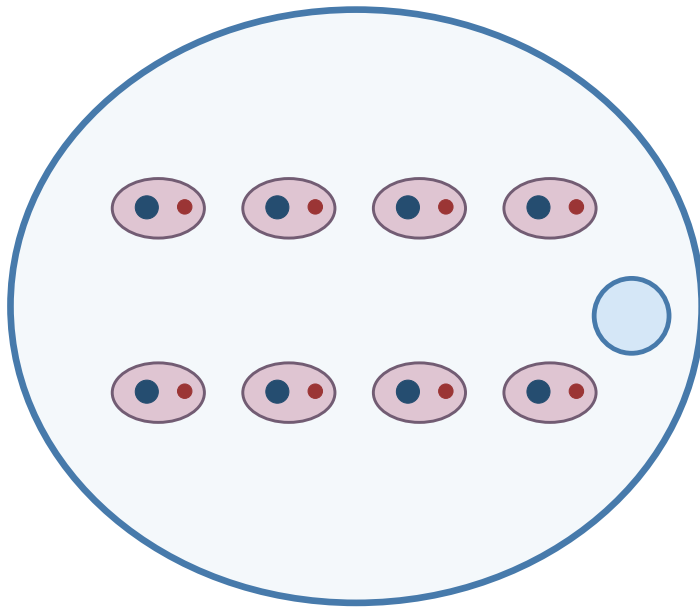


- That the spleen may reach approximately 3 kg.
- Phagocyte expansion and plasma-cell accumulation distort normal splenic architecture.
- Organ enlargement is part of the systemic mononuclear phagocyte response.

Original editable schematic — not a histologic or clinical specimen

Spleen: Parasitized macrophages dominate

Simplified cellular model



Blue dot: Parasite nucleus Red dot: Kinetoplast

- Phagocytic cells are enlarged and filled with organisms.
- Numerous plasma cells are present.
- Normal splenic architecture may be obscured by the infiltrate.

Bone marrow infiltration contributes to blood-count changes

- The source describes marrow crowded by parasite-containing phagocytic cells.
- Visceral disease is clinically marked by pancytopenia.
- Marrow infiltration provides a tissue-level explanation for hematologic compromise, although causation is not exclusive.

Hepatic disease evolves during progression

- Macrophage involvement accompanies visceral dissemination.
- The liver enlarges during systemic disease.
- In late stages, the source describes increasingly fibrotic hepatic tissue.
- Histologic severity should be considered in relation to disease duration.

Dissemination can extend beyond the core organs

- Parasite-containing phagocytes may be present in lung tissue.
- Gastrointestinal tract, kidneys and pancreas may be involved.
- The testes are also listed among potential locations.
- This distribution is described in advanced visceral involvement, not as universal disease.

Kala-azar: The pigmentation association

- Cutaneous hyperpigmentation in some patients of South Asian ancestry.
- The designation “kala-azar” refers to “black fever” in Hindi.
- Pigmentation is a clinical correlate; Diagnosis should not depend on its presence.

Renal pathology may be immune mediated

- The source reports immune complex–mediated mesangioproliferative glomerulonephritis.
- Amyloid deposition may occur in advanced disease.
- These lesions illustrate that organ injury may extend beyond direct parasite-containing macrophage infiltrates.

Serious consequences of visceral infection

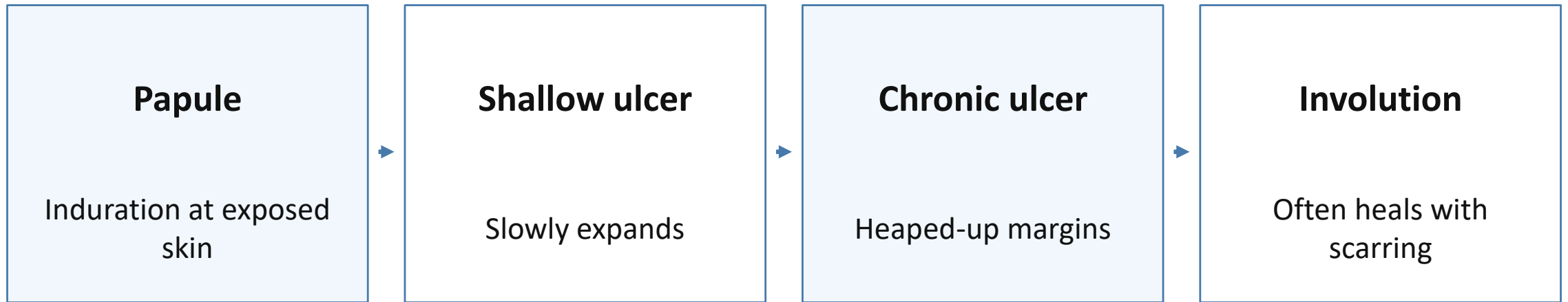
Infectious complications

- Life-threatening secondary bacterial infections occur in advanced disease.
- The text gives pneumonia and sepsis as examples.
- Tuberculosis is also mentioned.

Hematologic complications

- Thrombocytopenia contributes to bleeding risk.
- Hemorrhage can be fatal.
- Cytopenias coexist with extensive organ involvement.

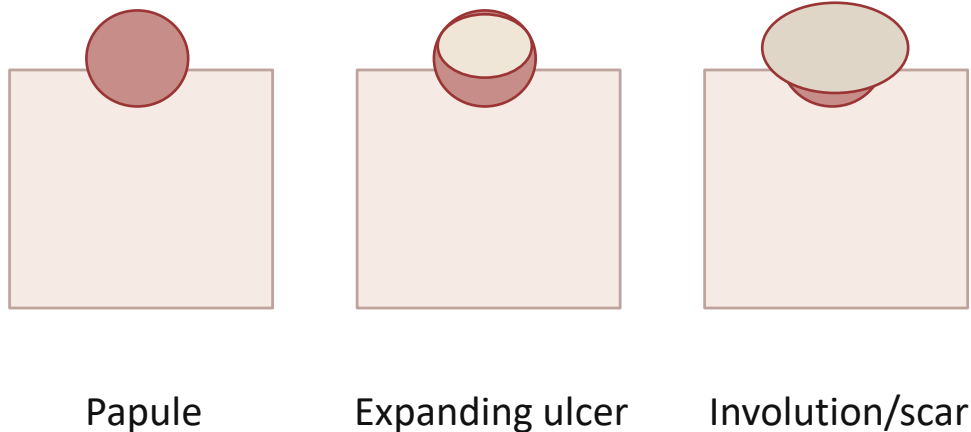
Cutaneous lesions change with time



- The source reports spontaneous healing over approximately 6–18 months in typical disease.

Cutaneous ulcers are slowly progressive

Stylized skin surface (not a lesion photo)



- Exposed skin is a typical site.
- A papule becomes an enlarging superficial ulcer with raised margins.
- The time course can be prolonged before involution.

Original editable schematic — not a histologic or clinical specimen

Cutaneous histology reflects cellular immune response

- Granulomatous inflammation is reported in the lesion.
- Multinucleated giant cells are often prominent.
- Parasites may be few in this inflammatory pattern.
- Low organism conspicuity on a section does not by itself rule out disease.

Localized cutaneous disease may involute

- Many lesions healing without treatment.
- A 6–18-month timeframe is reported for typical involution.
- Healing and the residual scar are distinct from absence of a prior infection.
- Clinical outcomes vary with form, so this course should not be generalized to visceral disease.

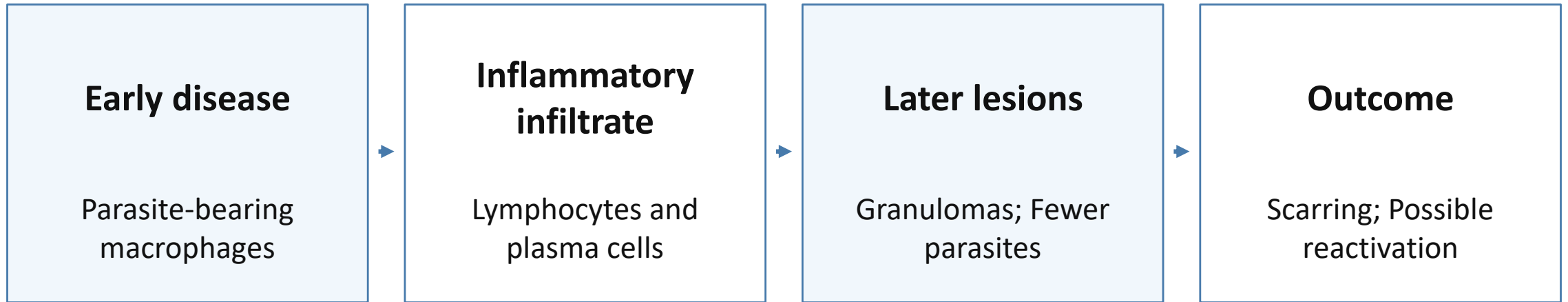
Mucocutaneous disease has a regional distribution

- Robbins particularly highlights Brazil, Ethiopia and Peru.
- The target is nasopharyngeal mucosa rather than skin alone.
- Damage to mucosal structures can produce major disfigurement.

Mucocutaneous lesions can be destructive

- Moist lesions may be ulcerating or nonulcerating.
- Progressive disease may destroy and disfigure nasopharyngeal tissue.
- The clinical risk reflects lesion location and local tissue destruction, not just parasite count.

Mucocutaneous inflammation changes over time



Mucosal reactivation can occur after remission

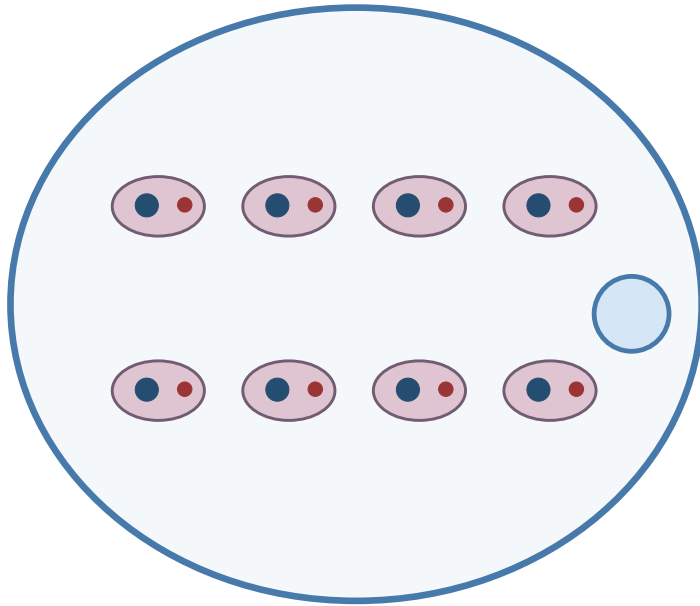
- The text describes lesions that remit and scar.
- Reactivation may occur after long intervals.
- The mechanisms of reactivation are not currently understood.
- Avoid claiming a predictable recurrence interval or molecular trigger.

Diffuse cutaneous disease spreads through the skin

- Diffuse cutaneous leishmaniasis is described as rare.
- It has been reported in Ethiopia, neighboring East Africa and Central and South America.
- The lesion begins as one skin nodule and progresses to widespread nodularity.

Diffuse cutaneous histology has a high parasite burden

Foamy macrophages: Conceptual model



Blue dot: Parasite nucleus Red dot: Kinetoplast

- Foamy macrophages form aggregates within the lesions.
- The cells may be densely packed with Leishmania organisms.
- This contrasts with the pauciparasitic granulomas described for localized cutaneous disease.

Original editable schematic — not a histologic or clinical specimen

Localized versus diffuse cutaneous pathology

Feature	Localized cutaneous	Diffuse cutaneous
Clinical extent	Papule → localized ulcer	Progressively widespread nodules
Characteristic cells	Granulomas and giant cells	Aggregates of foamy macrophages
Organism burden	Few parasites in described lesions	Many organisms within macrophages
Natural history in source	Typical involution over months	Continued dissemination across skin

Compare four leishmanial disease patterns

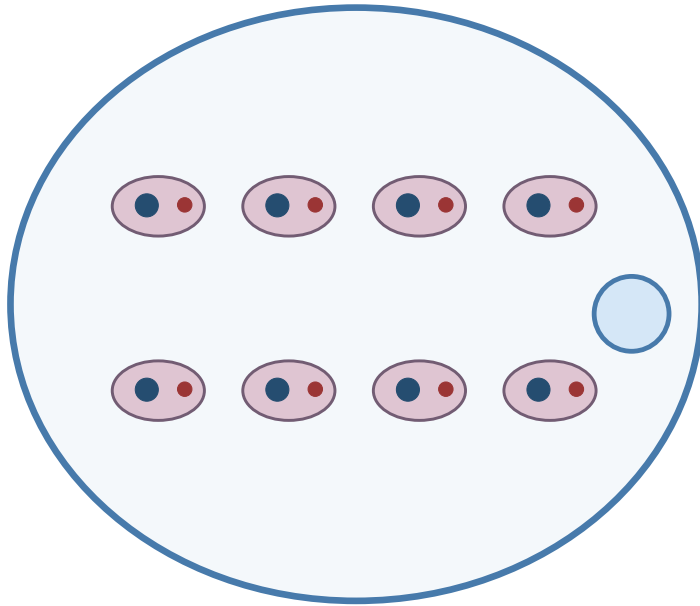
Form	Lesion or organ distribution	Signature microscopic or clinical clue
Visceral	Spleen, liver, marrow	Macrophage infiltration; Organomegaly and pancytopenia
Cutaneous	Localized exposed skin	Granulomas with giant cells; Few parasites
Mucocutaneous	Nasopharyngeal tissue	Inflammation evolves to granulomas and scarring
Diffuse cutaneous	Widespread skin nodules	Foamy macrophages packed with amastigotes

The source recognizes three diagnostic approaches

- Histologic examination can demonstrate tissue involvement and intracellular organisms.
- Culture is listed as a diagnostic method.
- PCR is also listed for detection of infection.
- The text does not provide assay performance, optimal specimen algorithms or validated thresholds.

Recognize parasite-containing macrophages

Schematic macrophage with amastigotes



Blue dot: Parasite nucleus Red dot: Kinetoplast

- Look for intracellular rounded forms within infected macrophages.
- Each kinetoplast-containing protozoan has structures that help identify the stage.
- This model is not a Giemsa stain and cannot establish a morphologic diagnosis.

Original editable schematic — not a histologic or clinical specimen

A tissue pattern alone does not identify Leishmania

- Granulomatous inflammation is a tissue reaction, not a species-specific finding.
- The diagnostic suspicion rests on compatible epidemiology, lesion pattern and direct testing.
- When parasites are sparse, culture and PCR among additional approaches.

Case application: Visceral disease

A patient from an endemic region develops fever, weight loss, marked splenomegaly and pancytopenia. Tissue evaluation identifies macrophages containing intracellular kinetoplastid organisms.

Interpretation

- Most consistent form: Visceral leishmaniasis.
- The mechanism combines systemic macrophage involvement with marrow and splenic pathology.
- The source supports histology, culture and PCR as diagnostic approaches.

Case application: A chronic skin ulcer

An exposed-skin papule slowly becomes a shallow ulcer with raised margins. A biopsy shows granulomas and giant cells, but only rare candidate parasites.

Interpretation

- The pattern is compatible with localized cutaneous leishmaniasis.
- A low parasite burden can accompany a strong granulomatous response.
- Direct diagnostic evaluation is still needed; Morphology alone is not a species determination.

Case application: A destructive mucosal lesion

A patient with relevant geographic exposure has a nasopharyngeal lesion that progresses to local destruction and later scars; The biopsy shows inflammatory cells and evolving granulomas.

Interpretation

- The distribution raises mucocutaneous leishmaniasis as a consideration.
- A later granulomatous phase may contain fewer visible parasites.
- The source acknowledges reactivation after prolonged intervals without a defined mechanism.

Case application: Progressive diffuse nodules

A single skin nodule gradually progresses to widespread nodules. Histologic sections show collections of foamy macrophages containing numerous amastigotes.

Interpretation

- This is the source-described pattern of diffuse cutaneous leishmaniasis.
- Prominent foamy, organism-packed macrophages contrast with localized pauciparasitic granulomas.

Mechanistic synthesis: From vector to clinical syndrome

- Sandfly promastigotes enter dermis and convert to macrophage amastigotes.
- Survival depends on interactions with complement, neutrophils and intracellular phagocyte defenses.
- Th1-dependent macrophage activation opposes persistence; Impaired cellular immunity increases susceptibility.
- Parasite–host interaction and distribution generate distinct tissue patterns.

Reference and interpretive boundaries

- Primary: Robbins, Cotran & Kumar, Pathologic Basis of Disease, 11th ed. (2026), Chapter 8, “Leishmaniasis,” pp. 357–359.
- The supplied Markdown is derived from extracted textbook text and includes column interleaving.
- This deck excludes neighboring babesiosis, malaria and trypanosomiasis material.
- No original chapter PDF or licensed source micrograph was provided; all illustrations are native editable schematics.