

African Trypanosomiasis

Transmission • antigenic variation • tissue pathology • CNS disease

Dr Abu Suraih Sakhri

MBBS, MD (Pathology)

www.abusuraihsakhri.com

Learning outcomes

- Distinguish the transmission ecology of gambiense and rhodesiense disease.
- Trace VSG-mediated antigenic variation and explain recurrent fever.
- Identify the tissue lesions of systemic and CNS disease.
- Explain the diagnostic importance of cerebrospinal fluid examination.

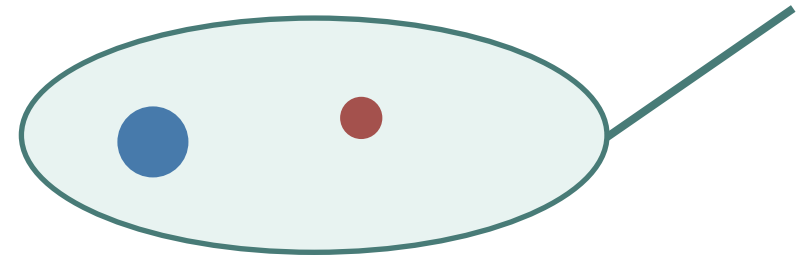
Core definition: Extracellular kinetoplastid disease

A blood- and tissue-associated infection that can evolve into sleeping sickness

- African trypanosomes are kinetoplastid protozoan parasites.
- They proliferate extracellularly in blood and tissue interstitial spaces.
- Disease may progress from systemic inflammation to brain dysfunction.

Kinetoplast: The defining cellular feature

- The kinetoplast is a large DNA-containing structure within the parasite.
- Kinetoplastid is a taxonomic descriptor, not a host-cell location.
- Bloodstream African trypanosomes are described as slender forms figure caption.



Organism body

Kinetoplast = DNA-containing structure

Schematic — no diagnostic scale

Where the organism lives

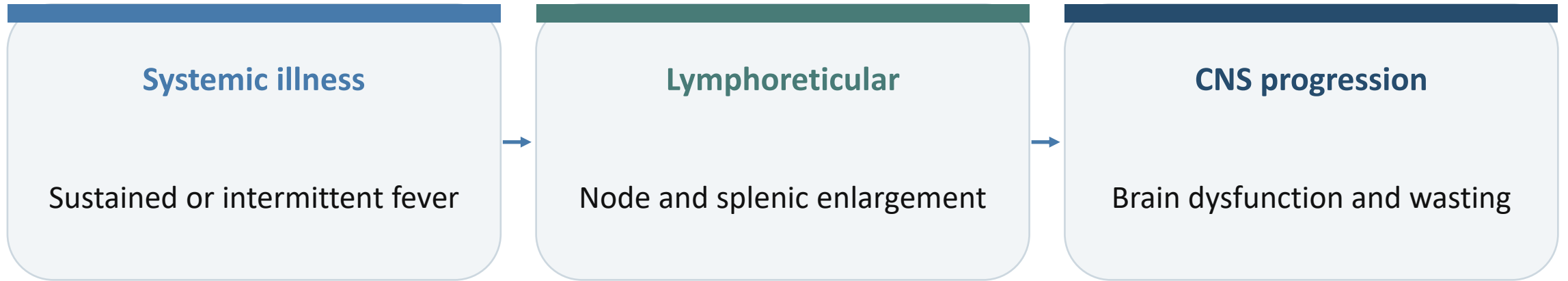
Bloodstream

- Trypanosomes proliferate as extracellular organisms.
- The circulating population encounters host antibodies.
- Blood smears can reveal parasites.

Tissue interstitium

- Parasites also inhabit extracellular tissue spaces.
- A bite-site lesion can contain numerous organisms.
- Tissue involvement produces inflammatory pathology.

Clinical syndrome: The organ-system progression



The combination of fluctuating fever and later neurologic dysfunction is a diagnostic clue.

Two human African trypanosome infections

T. B. Gambiense

- Western and central Africa
- Human-to-human transmission through tsetse bites
- Active detection and treatment emphasized

T. B. Rhodesiense

- Eastern and southern Africa
- Transmission from infected animals through tsetse bites
- Often acute and virulent; Vector reduction emphasized

Reported disease burden: Historical textbook context

Gambiense infection

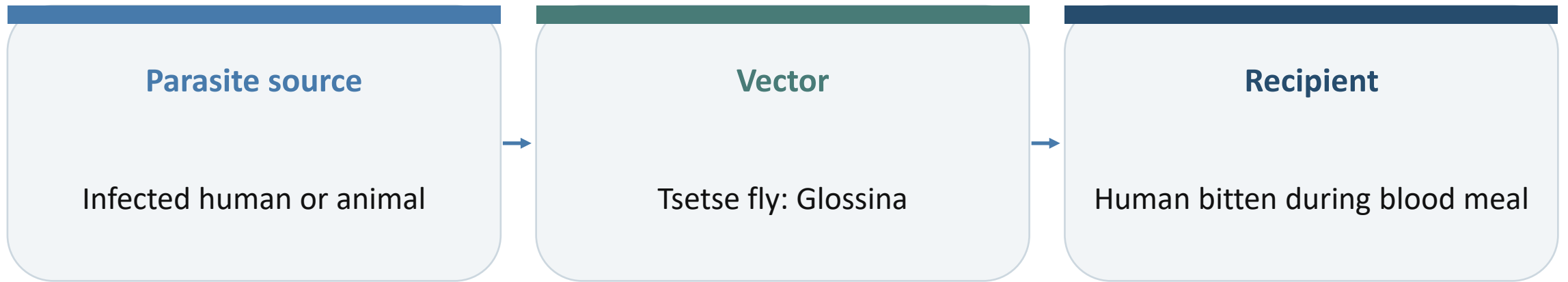
- Approximately 800 cases reported in 2022.
- Many were reported from the Democratic Republic of Congo.
- Source describes a marked reduction over the preceding two decades.

Rhodesiense infection

- Fewer than 50 cases reported in 2022.
- Geographic focus is eastern and southern Africa.
- Source emphasizes zoonotic transmission.

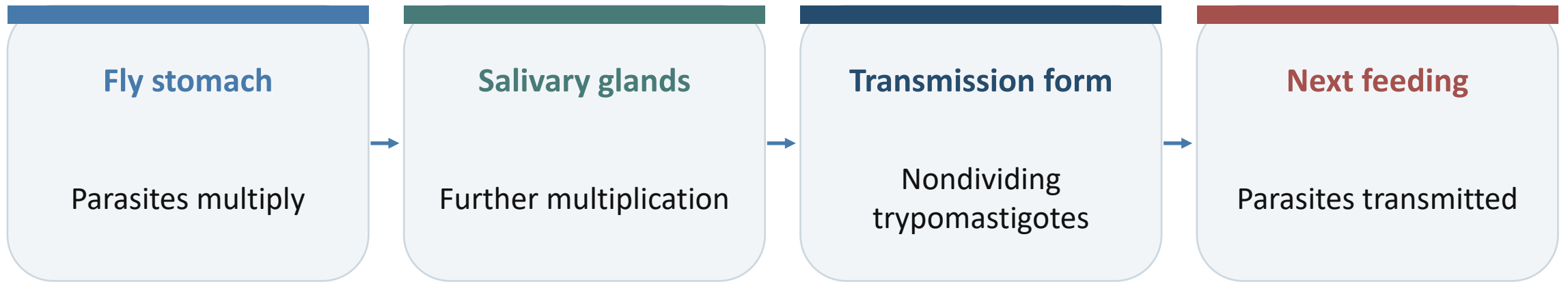
2022 textbook data only — not a present-day incidence comparison

The tsetse fly connects reservoirs and recipients



Reservoir differences change prevention strategy, even though the vector genus is the same.

Development of African trypanosomes inside the fly



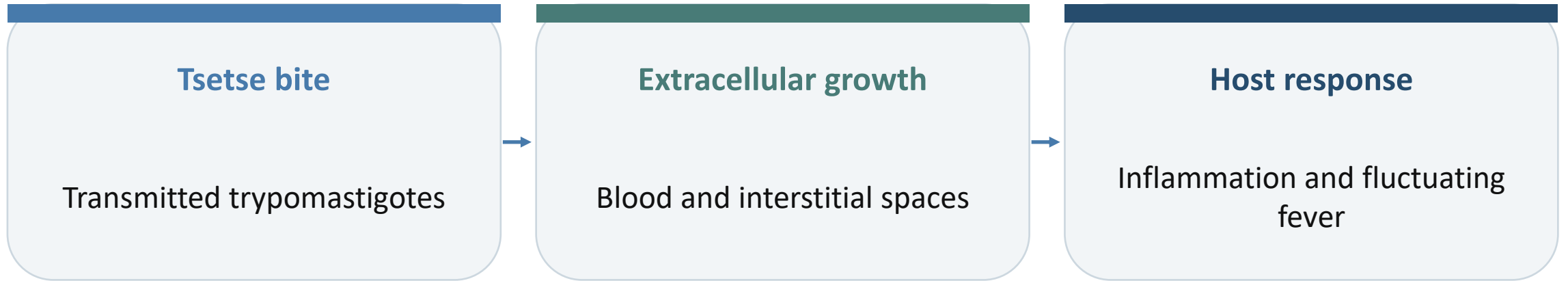
Transmission form: Nondividing trypomastigotes

- The fly produces a nondividing trypomastigote stage before transmission.
- This form enters another human or animal during the fly's next blood meal.
- Nondividing at transmission does not mean the infection remains nonproliferative in blood.

Life-cycle contrast

Nondividing transmission form → proliferating bloodstream forms

From bite to systemic disease



The parasite does not need an intracellular tissue phase to produce systemic disease.

Why gambiense control emphasizes case finding

- The described transmission chain includes an infected human source.
- Undetected infections can remain part of that human-associated cycle.
- The source therefore prioritizes active detection and treatment.

Control target

Find and treat human infection

Why rhodesiense control emphasizes the vector

- The infectious source may be a wild or domestic animal.
- Human case treatment alone cannot directly eliminate animal-to-fly exposure.
- The source explicitly prioritizes reducing infected vector populations.

Control target

Reduce infected tsetse flies

Transmission interpretation: Choose the reservoir

Teaching vignette — hypothetical

An outbreak is reported in an area of eastern or southern Africa. Investigators identify tsetse exposure and infected local animals.

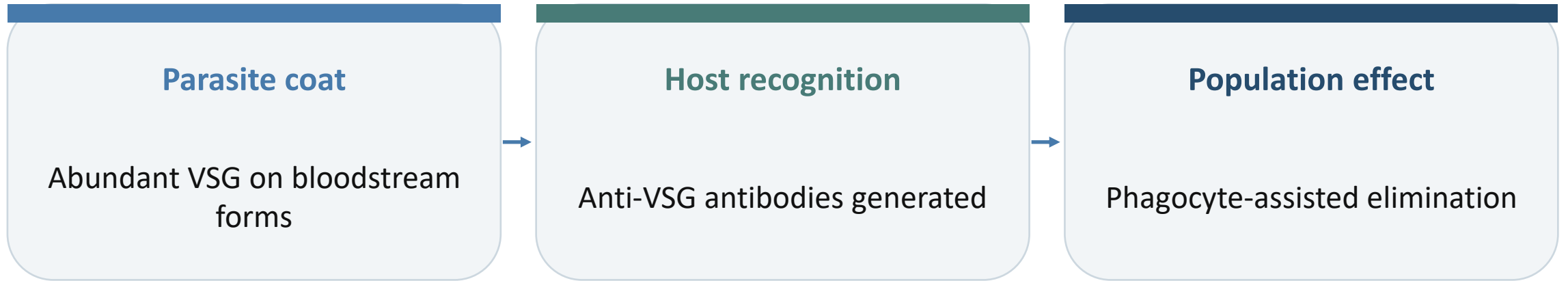
Which African trypanosome transmission pattern best fits?

Transmission interpretation: Explanatory answer

Animal reservoir + eastern/southern Africa → rhodesiense pattern

- The animal-associated pattern is characteristic of T. B. Rhodesiense.
- Its geographic distribution aligns with eastern and southern Africa.
- Vector reduction for this setting.

Variant surface glycoprotein: The surface interface



The same antigenic coat that provokes host immunity becomes the target of immune evasion.

A single abundant VSG dominates the coat

- The surface is covered by variant surface glycoprotein (VSG).
- The expressed surface protein is abundant and glycolipid anchored.
- Antigenic identity of this coat determines antibody recognition.

Key property

A dominant surface antigen can be replaced by a different variant.

How the host initially suppresses parasitemia

VSG recognized

Host makes specific antibodies



Effector collaboration

Antibodies with phagocytes



Majority killed

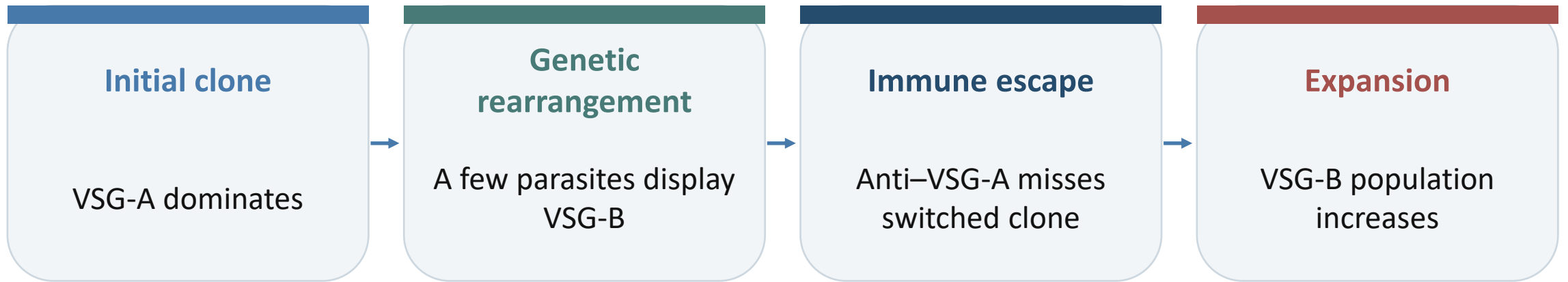
Parasite population contracts

Partial clearance creates a population bottleneck

Immune control is substantial, but not sterilizing.

- The anti-VSG response kills most circulating trypanosomes.
- A small minority persists following antigenic change.
- Those survivors can repopulate the bloodstream.

Antigenic switching allows immune escape



Escape depends on surface-antigen replacement, not disappearance of extracellular organisms.

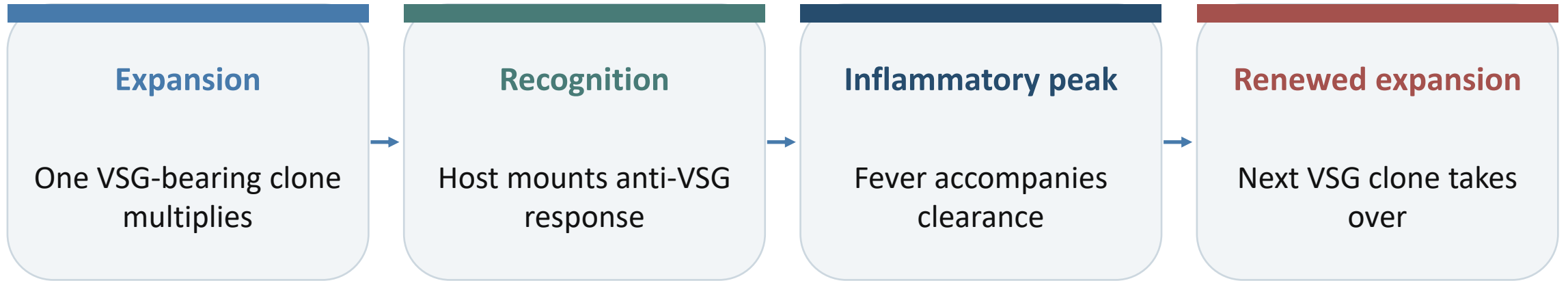
Successor clones explain relapse of parasitemia

- A newly switched population proliferates after escaping the current antibody response.
- The host subsequently develops antibodies against the new VSG.
- Most of that successor clone is killed before another variant expands.

Selection principle

A changing surface antigen defeats a previously effective antibody response.

Why waves of fever recur



The parasite carries a large VSG gene repertoire

- Numerous distinct VSG genes exist in the parasite genome.
- Only one VSG is expressed at a time by bloodstream parasites.
- Sequential use of distinct genes supports recurrent antigenic change.

Genotype vs phenotype

Many VSG genes available; One VSG expressed on the surface.

Gene distribution is not equivalent to gene expression

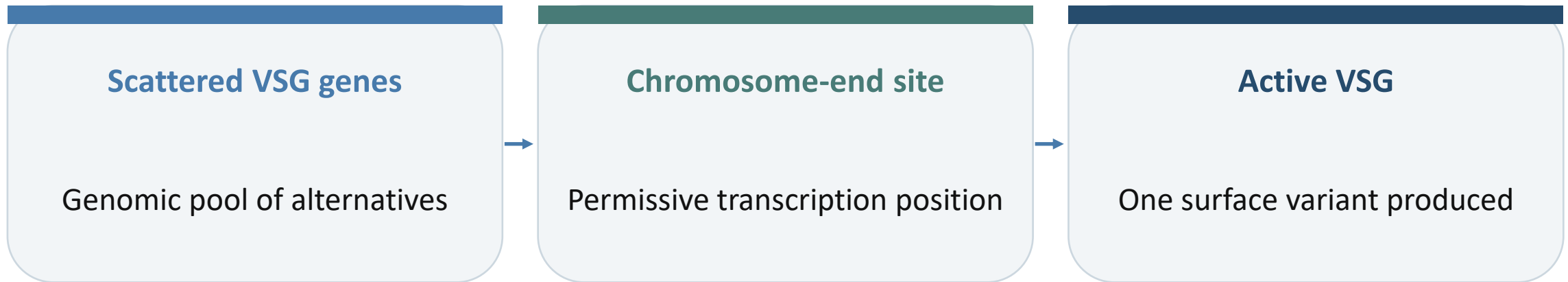
Genomic repertoire

- VSG genes are distributed throughout the genome.
- Different antigenic options exist in reserve.
- Most are not simultaneously expressed.

Bloodstream transcription

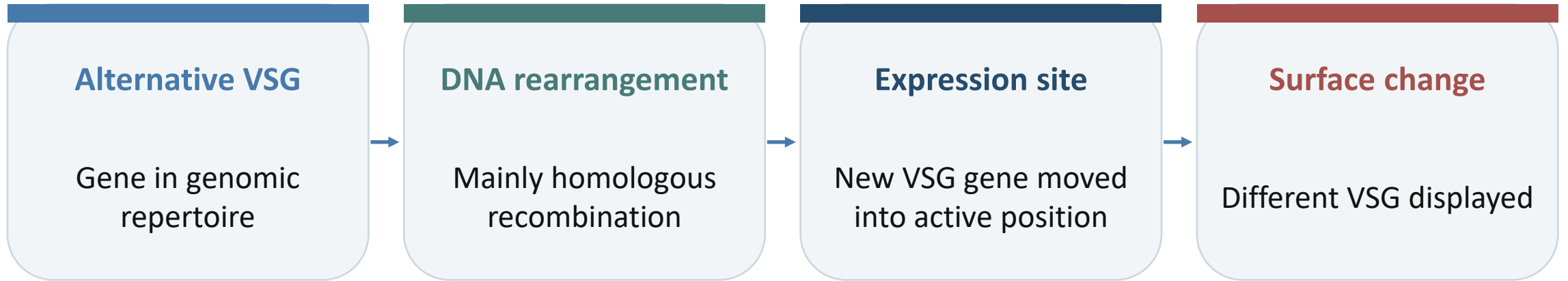
- Only VSG genes near chromosome ends are transcribed.
- Expression is restricted to one bloodstream site.
- One VSG dominates the current coat.

Telomeric localization enables VSG expression



The expression site is a regulatory bottleneck between the gene repertoire and the antigenic coat.

Homologous recombination renews the expressed VSG



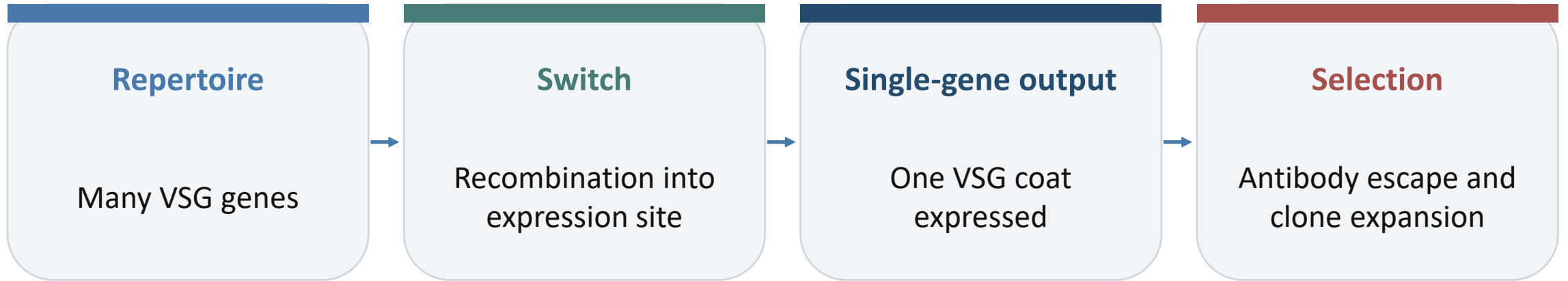
One specialized RNA polymerase expression site

- VSG gene transcription is linked to a specialized RNA polymerase.
- That polymerase associates with only one bloodstream expression site.
- This restriction limits expression to one VSG at a time.

Expression control

One active bloodstream expression site
→ one VSG coat

Integrated mechanism of antigenic variation



What immune evasion does—and does not—require

Supported mechanism

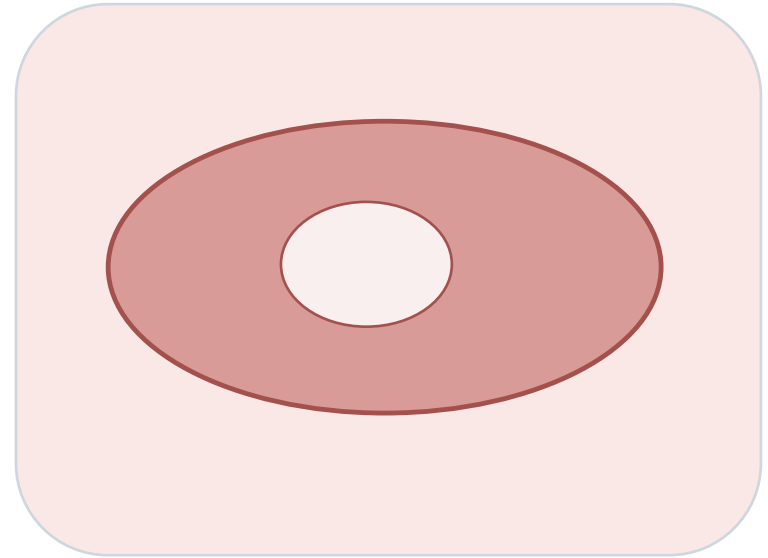
- Extracellular bloodstream growth
- Host anti-VSG antibody responses
- Sequential surface-antigen switching

Not required by this explanation

- Intracellular sanctuary during blood stages
- Simultaneous display of all VSG variants
- Permanent failure to recognize any clone

The inoculation site: Trypanosomal chancre

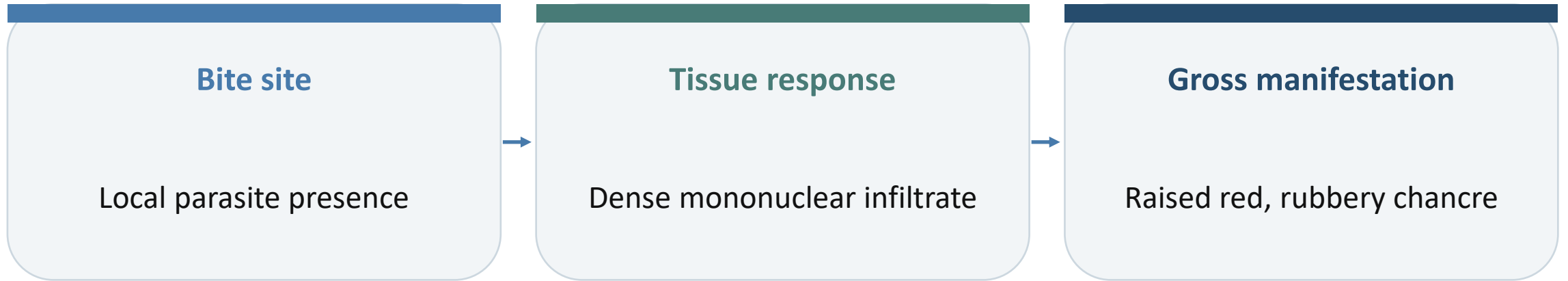
- A large red, rubbery chancre can form at the bite site.
- The lesion contains many parasites.
- The local tissue reaction is predominantly mononuclear.



Skin surface with raised inflammatory lesion

Schematic; Not a clinical photograph

Chancre pathology: Parasite meets inflammation



From local chancre to chronic lymphoid changes

Early bite-site process

- Localized chancre
- Numerous parasites
- Dense mononuclear inflammation

Chronic systemic process

- Enlarged lymph nodes and spleen
- Lymphocytes and plasma cells accumulate
- Macrophages contain dead parasites

Why lymph nodes become enlarged

- Chronic disease produces lymphadenopathy.
- Nodes are infiltrated by lymphocytes, plasma cells, and macrophages.
- These accumulated cells contribute to increased nodal volume.

Histologic correlate

Lymphoplasmacytic–macrophage expansion

Why the spleen becomes enlarged

- Splenomegaly accompanies chronic infection.
- The spleen is infiltrated by lymphocytes, plasma cells, and macrophages.
- The tissue reaction reflects systemic persistence of the extracellular parasite.

Histologic correlate

Mononuclear inflammatory-cell infiltration of splenic tissue

Macrophages may contain dead trypanosomes

Phagocytic debris ≠ intracellular parasite life cycle

- The parasite remains extracellular while viable bloodstream forms circulate.
- The source describes macrophages filled with dead parasites.
- Finding dead parasites inside a phagocyte does not establish an intracellular replicative niche.

Lymphocytes, plasma cells and macrophages

Lymphoid reaction

- Lymphocytes infiltrate enlarged tissues.
- Plasma cells are conspicuous in chronic lesions.
- Plasma-cell immunoglobulin may accumulate as globules.

Phagocytic reaction

- Macrophages accumulate in involved tissues.
- Some contain dead parasites.
- Their presence is consistent with immune clearance.

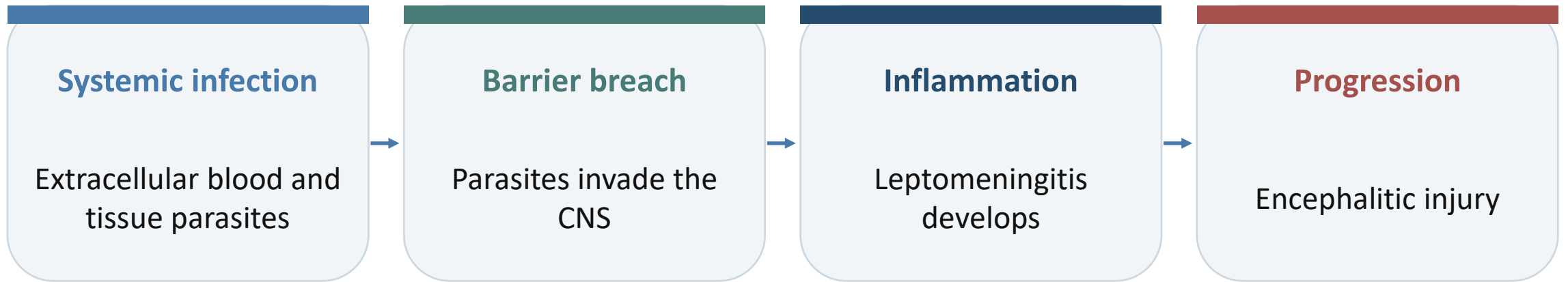
Trypanosomes can concentrate in capillary loops

- The source specifically notes capillary-loop concentrations.
- Two named examples are the choroid plexus and renal glomeruli.
- The observation concerns anatomic localization; No cause of this distribution is provided.

Anatomic sites

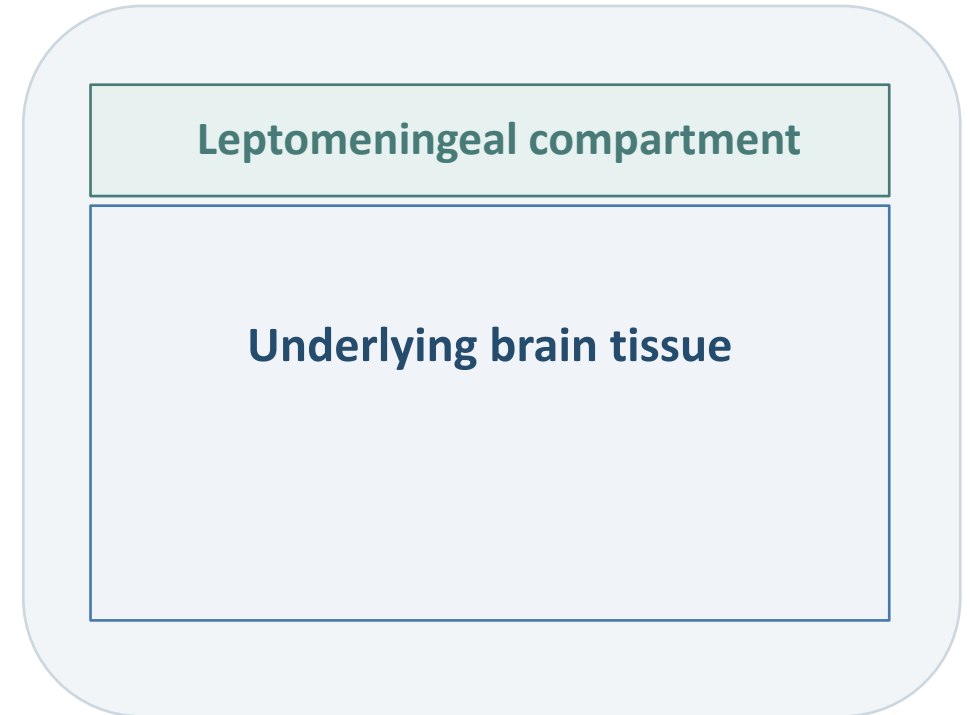
Choroid plexus • glomerular loops

Entry into the CNS marks a major transition



Leptomeningitis follows CNS invasion

- CNS invasion is followed by inflammatory involvement of the leptomeninges.
- Leptomeningitis is an anatomic-pathologic finding—not synonymous with a sleep symptom.
- The disease can extend beyond the meningeal surface.



Schematic anatomy — not histology

Inflammation extends along Virchow–Robin spaces

Leptomeningitis

Inflammation at meningeal surfaces



Perivascular route

Virchow–Robin spaces involved



Parenchymal disease

Wider CNS inflammatory injury

Demyelinating panencephalitis is a late tissue lesion

- The source identifies demyelinating panencephalitis after meningeal and perivascular involvement.
- “Demyelinating” indicates injury to myelin; “panencephalitis” indicates diffuse encephalitic disease.
- These pathologic findings help explain progressive neurologic dysfunction.

CNS pathology sequence

Leptomeningitis → perivascular extension → demyelinating panencephalitis

Mott cells: Plasma cells with cytoplasmic globules

- Mott cells are frequently identified in the source description.
- They are plasma cells containing cytoplasmic globules.
- The globules contain immunoglobulins.

Diagnostic vocabulary

Mott cell = immunoglobulin-globule-containing plasma cell

Mott cells are host cells, not the parasites

Mott cell

- A differentiated host plasma cell
- Cytoplasmic immunoglobulin globules
- Part of a chronic inflammatory reaction

Trypanosome

- Extracellular kinetoplastid parasite
- Variable VSG-bearing surface
- Detected by visualization of organisms

Progressive cachexia: The terminal systemic effect



Clinicopathologic map of organ findings

Site	Pathologic change	Clinical correlate
Bite site	Parasite-rich mononuclear chancre	Red, rubbery lesion
Nodes / spleen	Lymphoplasmacytic–macrophage infiltrates	Lymphadenopathy; splenomegaly
CNS	Leptomeningitis; demyelinating panencephalitis	Progressive brain dysfunction
Systemic	Persistent infection with progressive wasting	Cachexia; decreased energy

Microscopy answers a different question from CSF staging

Diagnostic specimens

- Blood smears
- Lymph node material
- Chancre material
- Microscopy seeks visible organisms

CNS assessment

- Cerebrospinal fluid examination
- Determines whether CNS is involved
- Findings direct the course of treatment

Blood smears demonstrate circulating parasites

- The organism is extracellular in blood.
- Microscopic examination of a blood smear is a diagnostic method.
- The textbook labels a figure of slender bloodstream trypanosomes, but the image was not supplied.

Evidence boundary

No authentic original smear image available in the supplied project files.

Lymph node and chancre samples offer alternatives

- Microscopic examination can be made on a lymph node or chancre specimen.
- These sites align with tissue manifestations described in the morphology section.
- The source does not provide sample-specific sensitivity or an exact diagnostic hierarchy.

Specimen principle

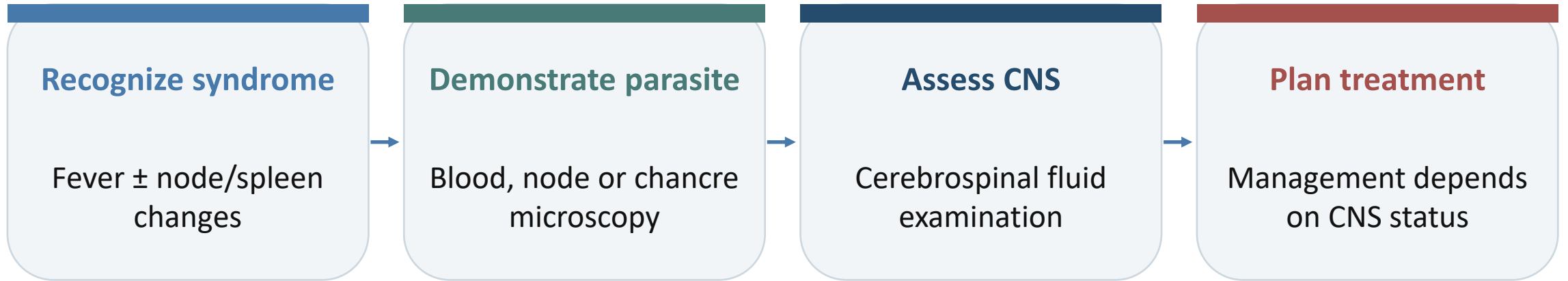
Sample an involved parasite-containing compartment.

Why CSF examination changes management

Detecting trypanosomes ≠ determining CNS involvement

- The bloodstream and peripheral tissues are not the whole clinical picture.
- Central nervous system involvement determines treatment selection.
- The source explicitly requires cerebrospinal fluid examination for this distinction.

Source-based diagnostic reasoning pathway



Case application: Febrile systemic illness

Teaching vignette — hypothetical

A patient with tsetse exposure has fluctuating fever, enlarged lymph nodes and an erythematous bite-site lesion. No CNS evaluation has yet been done.

What can peripheral microscopy establish, and what remains unknown?

Case resolution: Organism detection is not staging

Confirm infection; Then assess CNS involvement.

- Blood, lymph node or chancre microscopy can establish the presence of parasites.
- Peripheral detection does not alone determine whether the CNS is involved.
- The source requires examination of cerebrospinal fluid to guide treatment.

Case application: Progressive brain dysfunction

Teaching vignette — hypothetical

A patient with established African trypanosomiasis develops deteriorating mentation after episodes of systemic illness. The clinician must determine whether the infection has entered the CNS.

Which pathology sequence is relevant, and what specimen is pivotal?

Case resolution: Neuroinvasion changes the question

Neurologic dysfunction demands assessment of CNS disease.

- CNS invasion produces leptomeningitis with perivascular extension.
- Later disease may include demyelinating panencephalitis.
- Cerebrospinal fluid examination is needed to determine CNS infection.

High-yield distinction: Organism, host and lesion

Observation	Parasite-associated component	Host-associated response
Recurrent fever	Sequential VSG-expressing clones	Repeated anti-VSG responses
Chancre	Numerous extracellular parasites	Dense mononuclear infiltrate
Lymphoid enlargement	Dead organisms within macrophages	Lymphocytes, plasma cells, macrophages
CNS disease	Parasites cross BBB	Meningeal/perivascular inflammation; demyelination

Five indispensable pathology associations

- Glossina transmission; Gambiense human-associated and rhodesiense zoonotic patterns.
- Extracellular bloodstream parasites with a single VSG coat.
- Gene rearrangement enables sequential VSG variants and fever waves.
- Chancre, lymphoid enlargement, Mott cells and progressive CNS injury.
- Microscopic parasite detection must be complemented by CSF assessment.

Recommended textbook reading

Robbins, Cotran & Kumar

Pathologic Basis of Disease, 11th edition (2026)

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