

Tuberculosis

of the central nervous system

Tuberculous meningoencephalitis, tuberculomas, and their complications

Neuropathology · morphology linked to mechanisms

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Learning outcomes

- Distinguish diffuse tuberculous meningoencephalitis from parenchymal tuberculomas.
- Explain the origin and pattern of basal meningeal inflammation.
- Link vascular and arachnoid pathology to infarction and hydrocephalus.
- Interpret the characteristic but variable CSF profile and host response.

CNS tuberculosis: Two dominant morphologic patterns

Meningeal / diffuse	Parenchymal / focal
Diffuse meningoencephalitis	One or more circumscribed tuberculomas
Basal gelatinous or fibrinous exudate	Caseating granulomatous mass
Endarteritis and adhesive arachnoiditis	Local mass effect; potential calcification
Hydrocephalus, infarction, cranial nerve injury	Symptoms of an intracranial space-occupying lesion

CNS disease may accompany or outlast pulmonary illness

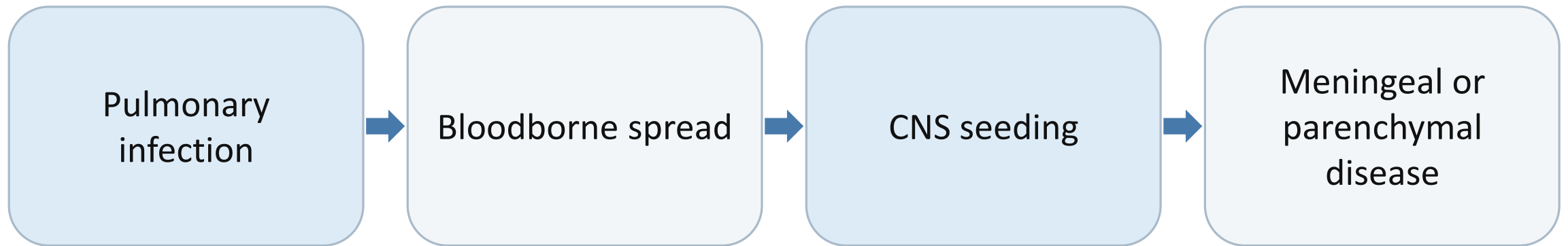
Concurrent active tuberculosis

- CNS involvement can occur with known active disease.
- Pulmonary or systemic lesions provide a plausible source for dissemination.
- The neurologic syndrome is not necessarily the first manifestation.

Apparently isolated CNS tuberculosis

- A patient may have no clinically obvious pulmonary disease.
- Seeding may originate from silent lesions elsewhere, usually lung.
- Absence of known active lung disease does not exclude CNS involvement.

Anatomical route from lung to nervous system

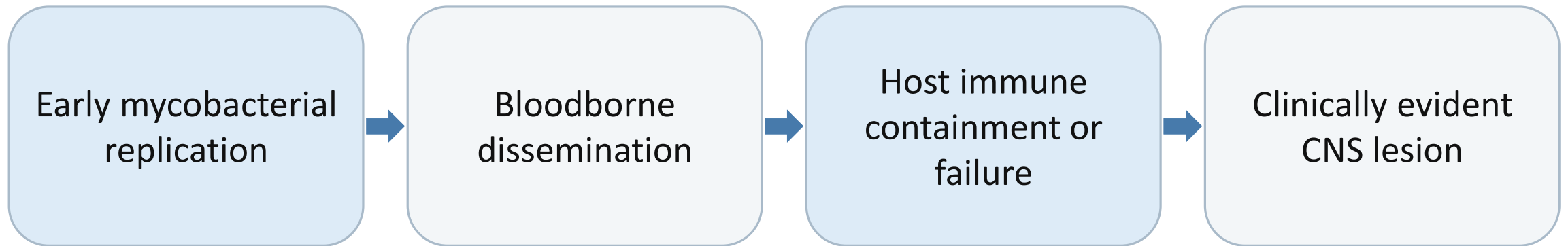


Why hematogenous dissemination matters

Pulmonary and nervous-system disease must be considered together.

- Primary pulmonary infection can disseminate before full cell-mediated control develops.
- Organisms deposited at distant sites may remain clinically silent.
- Later CNS disease can therefore arise without conspicuous concurrent pulmonary symptoms.

Temporal framework of CNS seeding



Simplified explanatory sequence; Not every patient follows the same course.

Host immunity is both protective and injurious

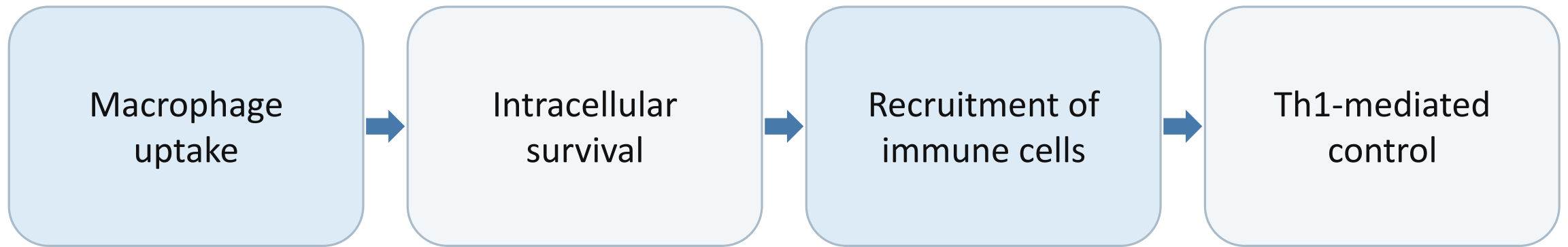
Protection

- Th1 cells activate macrophages to kill or contain mycobacteria.
- Effective immunity limits dissemination and bacterial growth.
- Granulomas help localize infection.

Tissue injury

- The same inflammatory response organizes caseating granulomas.
- Inflammation damages vessels and meninges.
- Fibrosis and necrosis produce neurologic consequences.

Initial cellular events in mycobacterial infection



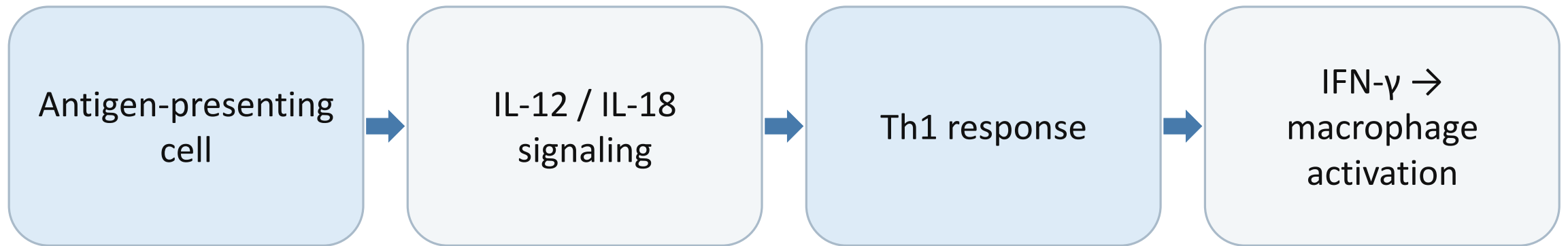
Mechanism is established for tuberculosis generally; Applied here as pathogenesis context.

How mycobacteria persist in macrophages

This helps explain the need for a strong cell-mediated response.

- M. Tuberculosis is phagocytosed through macrophage surface receptors.
- The pathogen interferes with phagosome maturation and phagolysosomal fusion.
- Intracellular persistence permits replication before effective T-cell immunity.

Th1 differentiation and macrophage activation



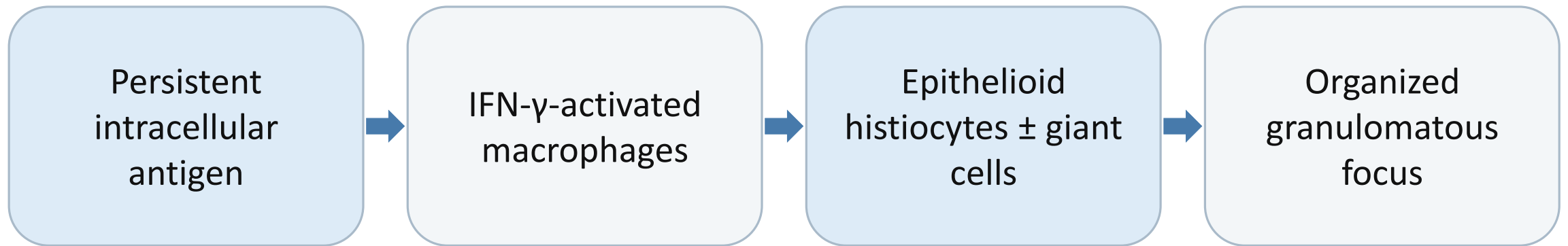
Native vector summary of the textbook pathway.

IFN- γ -dependent antibacterial mechanisms

Failure of these processes increases vulnerability to disseminated disease.

- Activated macrophages generate microbicidal reactive oxygen and nitrogen species.
- Autophagy helps target intracellular organisms.
- Antimicrobial peptides contribute to bacterial containment.

Granuloma assembly



The diagram represents cellular organization, not a photomicrograph.

Why a granuloma is not simply a sign of control

Tuberculosis links cellular immunity to tissue damage.

- Granulomas are a manifestation of effective T-cell recognition of persistent antigen.
- The cellular reaction may wall off organisms without eradicating them.
- Caseating necrosis reflects tissue-destructive consequences of host inflammation.

Immune status changes lesion morphology

More effective cellular response	Marked cellular immune deficiency
Well-developed epithelioid granulomas	Poorly formed or absent granulomas
Organisms may be difficult to find	Macrophages may contain numerous organisms
Necrosis and inflammation can be prominent	Host inflammatory reaction may be blunted
Morphology reflects containment efforts	Morphology may obscure the classic diagnostic pattern

Clinical settings that weaken antimycobacterial control

These are systemic tuberculosis risk contexts, not CNS-specific risk estimates.

- HIV-associated loss of effective Th1 function is a major risk factor.
- Glucocorticoids, TNF antagonism, and transplant immunosuppression increase susceptibility.
- Malnutrition and renal failure can impair host resistance.

CNS compartments relevant to tuberculosis

Tuberculosis affects connected but anatomically distinct CNS compartments.

Leptomeningeal
Subarachnoid space

Exudate and fibrosis

Meningeal
Arteries

Obliterative endarteritis

Ventricular /
Ependymal surfaces

CSF-associated spread

Cerebral
Parenchyma

Tuberculoma mass

Schematic compartment map; Anatomical topology simplified.

Two paths of nervous-system injury

Diffuse meningeal route

- Subarachnoid exudate and chronic inflammation.
- Vessel encasement and endarteritis.
- Arachnoid scarring and CSF-flow disturbance.

Focal parenchymal route

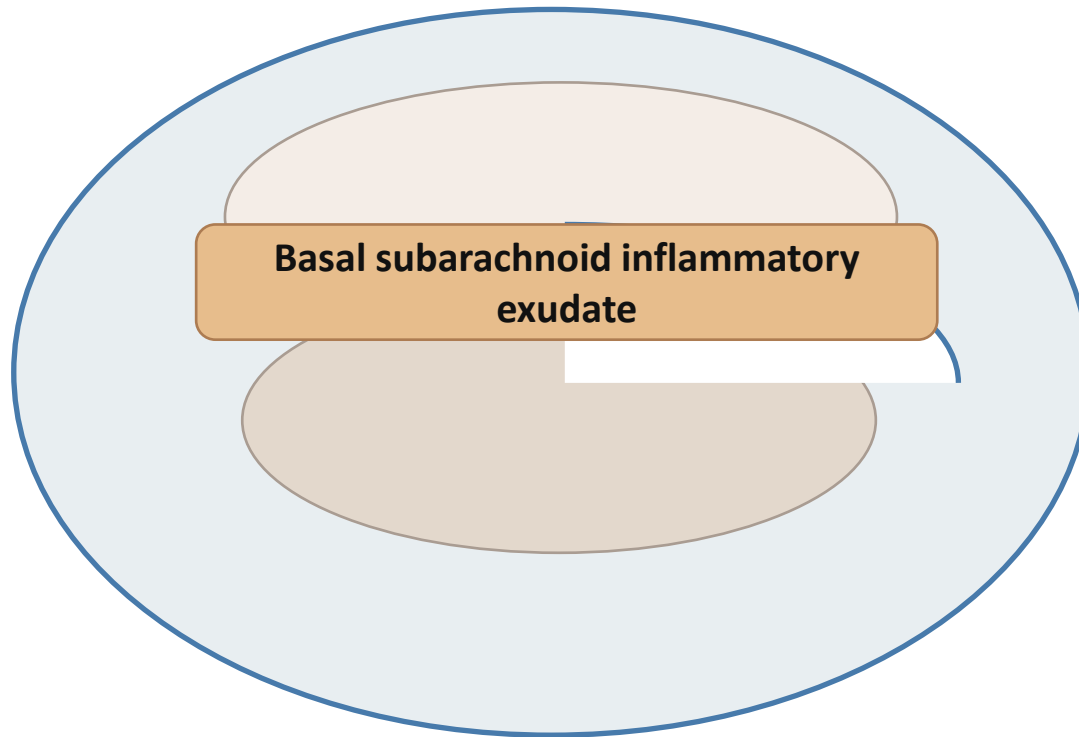
- Localized caseating granulomatous mass.
- Compression/displacement of neighboring structures.
- Signs consistent with an intracranial mass lesion.

Most common pattern: Diffuse meningoencephalitis

Meningeal distribution provides key clinicopathologic clues.

- CNS tuberculosis most commonly produces widespread involvement of the meninges and adjacent brain.
- The dominant macroscopic feature is inflammatory material within the subarachnoid space.
- The distribution shows a characteristic predilection for the base of the brain.

Basal leptomeningeal exudate: Key distribution



Gelatinous or fibrinous material occupies basal subarachnoid spaces.

- Normal cisternal anatomy may be obscured.
- Cranial nerves may be surrounded by inflammatory exudate.
- This gross pattern is more informative than a nonspecific statement of “meningitis.”

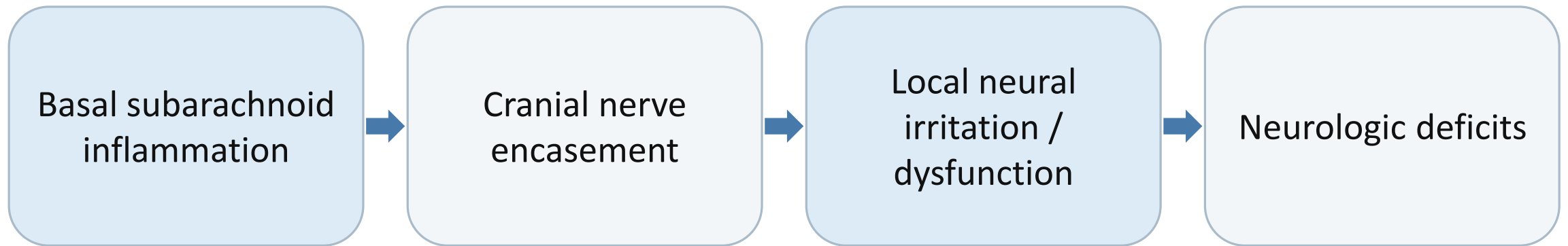
Schematic basal distribution; Not a specimen or scale diagram.

Macroscopic appearance of tuberculous exudate

The visual relationship between exudate and vital structures is central to clinical effects.

- Exudate may be gelatinous or fibrinous.
- The basal cisterns can become effaced.
- Inflammatory material may encase cranial nerves and other structures in the subarachnoid compartment.

From basal inflammation to nerve dysfunction



Causal interpretation based on anatomical distribution; Deficits vary by affected nerve.

Disseminated surface lesions may be visible

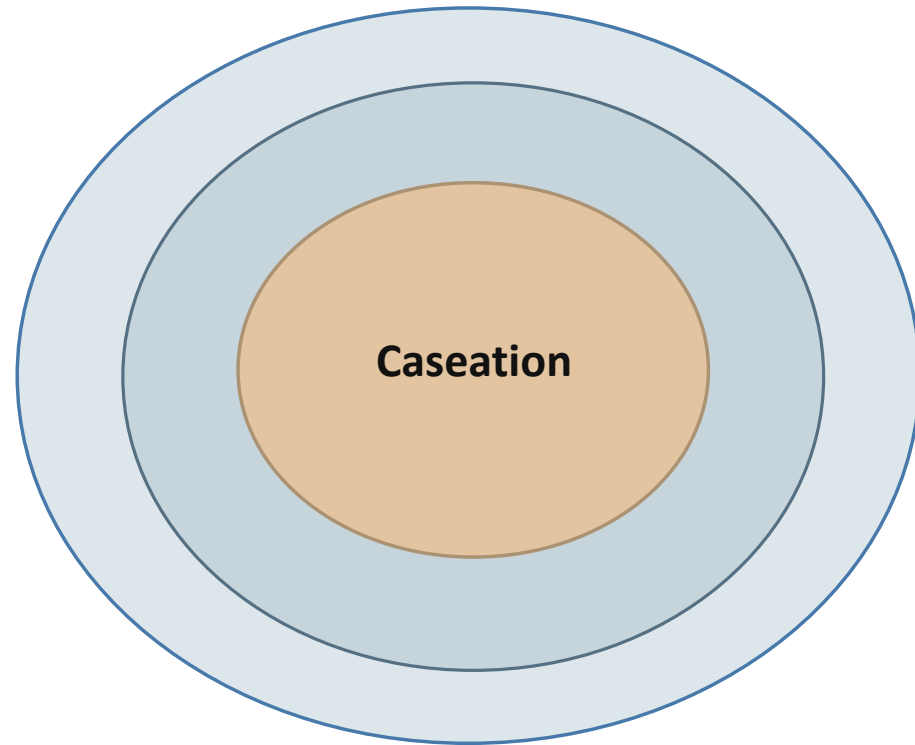
These nodules do not imply a tumor without histologic context.

- Some brains show scattered, discrete white inflammatory foci on the leptomeninges.
- These foci accompany the more diffuse meningeal reaction.
- Macroscopic foci should be correlated with the tissue reaction microscopically.

Microscopic cells in affected meninges

Population	Pathologic implication
Lymphocytes	Cell-mediated chronic inflammatory response
Plasma cells	Component of chronic inflammatory infiltrate
Macrophages	Granulomatous / phagocytic response
Epithelioid histiocytes and giant cells	Organized granulomatous inflammation in florid cases

Recognizing a necrotizing tuberculous granuloma



Central caseous necrosis

Epithelioid histiocytes / giant cells

Surrounding chronic inflammatory cells

Original editable schematic of lesion architecture; Not H&E microscopy.

Epithelioid histiocytes are activated macrophages

In tissue, interpret architecture together with organism testing and clinical context.

- The epithelioid appearance follows cell-mediated macrophage activation.
- These cells aggregate within granulomatous foci.
- The organization is informative but is not microbiologically specific by itself.

Giant cells: Cellular response, not a species label

Giant cells support a granulomatous pattern rather than proving TB.

- Some activated macrophages fuse to form multinucleated giant cells.
- Giant cells may accompany caseating granulomas in florid CNS tuberculosis.
- Their presence alone cannot establish the causative microorganism.

Caseous necrosis and the viable lesion edge

Necrotic center

- Granular, acellular tissue destruction may occupy the granuloma center.
- Necrosis is a response to persistent infection and immune injury.
- The central zone need not contain an easily identifiable bacillus.

Cellular margin

- Activated macrophages and other inflammatory cells surround the necrosis.
- The margin may form a recognizable epithelioid aggregate.
- The extent of organization depends on the host response.

Why acid-fast organisms can be difficult to identify

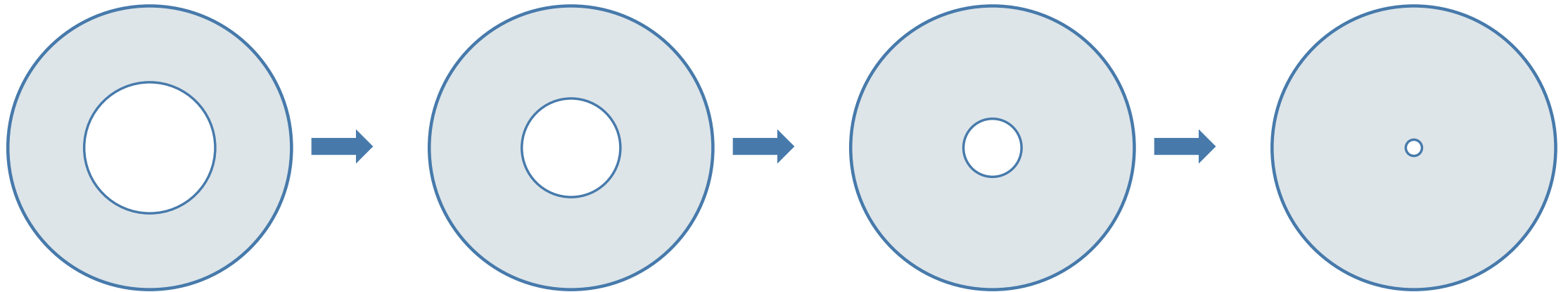
Avoid equating bacillary visibility with disease severity.

- The pathologist may find very few demonstrable bacilli in inflammatory lesions.
- A negative or sparsely positive acid-fast stain does not negate granulomatous morphology.
- Extensive searching may be required in some tissue sections.

Histology and microbiology answer different questions

Histologic assessment	Organism demonstration
Defines inflammation, necrosis and tissue injury	Seeks the causative bacillus directly
Suggests a granulomatous infectious process	May support a specific mycobacterial etiology
Shows vascular damage and fibrosis	May have low yield in paucibacillary tissue
Does not prove species identity by morphology	Must be interpreted alongside tissue architecture

Tuberculous obliterative endarteritis



Inflammation around a
meningeal artery

Marked intimal
thickening

Progressive luminal
narrowing

Occlusion and ischemic
injury

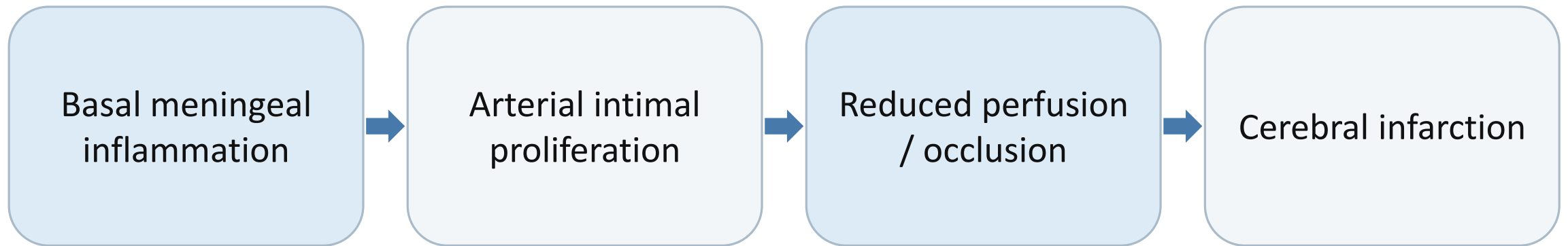
Cross-sections are schematic and not to anatomic scale.

The key vascular lesion is obliterative endarteritis

CNS tuberculosis can cause destructive neurologic deficits without a large tuberculoma.

- Arteries traversing the inflamed subarachnoid space may develop marked intimal thickening.
- Severe narrowing can progress to vascular occlusion.
- The downstream consequence is ischemic injury or cerebral infarction.

Vascular complication sequence



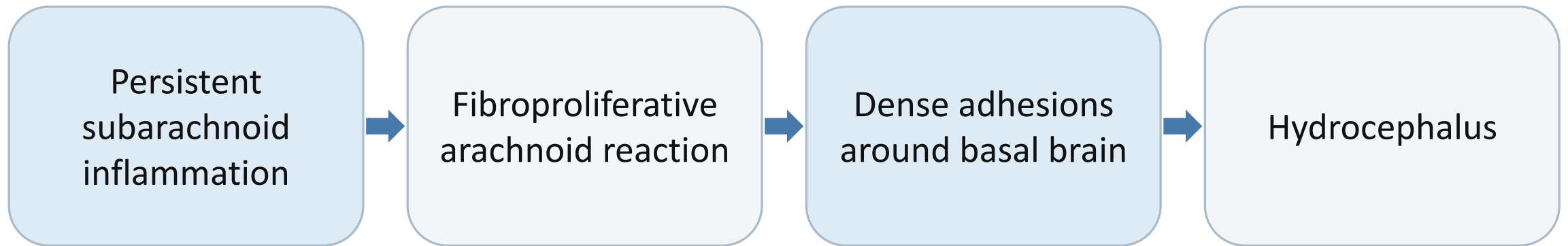
Causal relationship follows the vascular pathology.

Why an infarct may accompany chronic meningitis

Look beyond the meningeal exudate when evaluating a neurologically deteriorating patient.

- The same basal inflammatory process involves nearby vessels.
- Intimal thickening compromises the vessel lumen.
- Tissue loss depends on the territory supplied by the occluded artery.

Adhesive arachnoiditis: A late tissue response



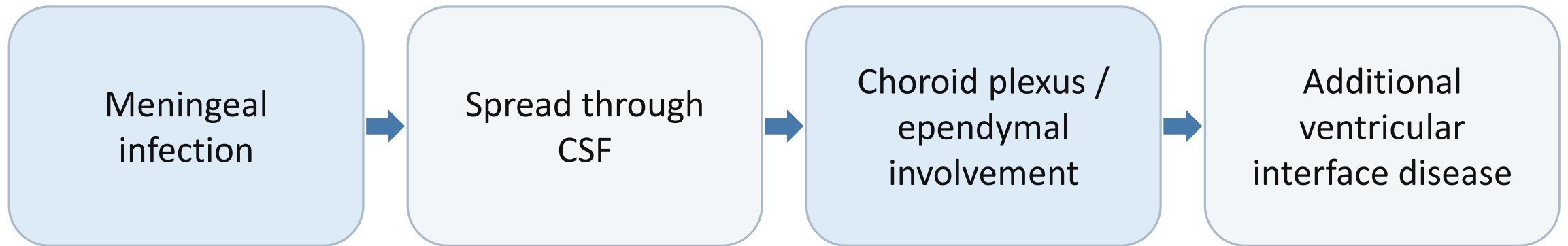
Sequence illustrates the source-described complication without specifying a single universal CSF obstruction site.

Arachnoid fibrosis links inflammation to hydrocephalus

Hydrocephalus is a consequence of chronic tissue organization, not granuloma size alone.

- Longstanding inflammation may evolve into dense, fibrous adhesive arachnoiditis.
- The changes are especially conspicuous near the base of the brain.
- Altered CSF circulation/resorption may then produce hydrocephalus.

CSF pathways can also carry the inflammatory process



Spread to these surfaces; Schematic does not assert its frequency.

Choroid plexus and ependymal spread

The route emphasizes the connected nature of ventricular and subarachnoid spaces.

- Mycobacterial inflammation can involve the choroid plexus.
- The ependymal surface may also be affected through CSF-associated spread.
- Such involvement extends the disease beyond the meningeal surface alone.

Spinal subarachnoid extension and nerve roots

The expected deficits depend on which roots are involved.

- The infectious process can extend to the spinal cord subarachnoid compartment.
- Adjacent spinal nerve roots may be affected.
- This extension broadens the neurologic manifestations beyond intracranial disease.

Major chronic meningeal complications

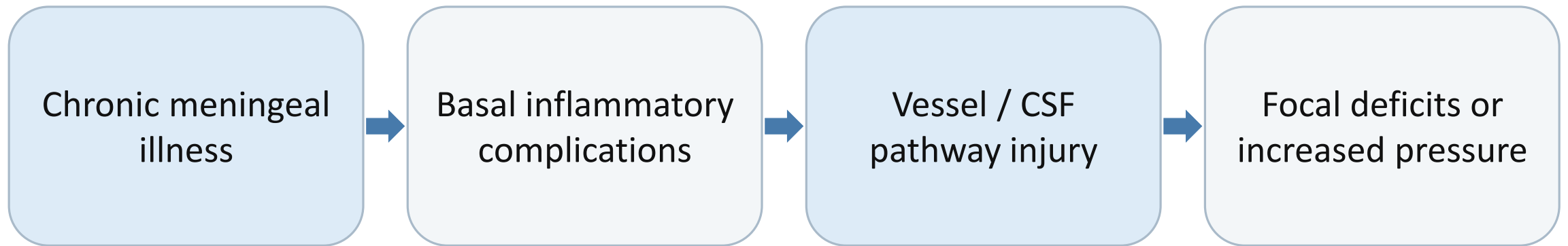
Pathologic lesion	Mechanistic consequence	Potential clinical effect
Obliterative endarteritis	Arterial narrowing / occlusion	Brain infarction
Adhesive arachnoiditis	Impaired CSF dynamics	Hydrocephalus
Basal cranial nerve encasement	Nerve-associated inflammation	Cranial neuropathy
Spinal subarachnoid involvement	Affected nerve roots	Root-related neurologic symptoms

Typical clinical presentation of tuberculous meningitis

Clinical features need to be integrated with CSF and pathology.

- Headache and generalized malaise are common presenting symptoms.
- Mental confusion points to neurologic involvement.
- Vomiting may occur in the clinical syndrome.

Clinical deterioration: Anatomical reasoning



An explanatory framework; Individual cases vary.

CSF pleocytosis can have a mixed differential count

Cell differential alone is insufficient to exclude tuberculosis.

- CSF usually contains increased inflammatory cells.
- Mononuclear cells may predominate.
- A mixture of neutrophils and mononuclear cells is also described.

Marked CSF protein elevation is a useful clue

Interpret alongside cell profile, glucose, and clinical course.

- CSF protein concentration rises in tuberculous meningitis.
- The elevation may be striking.
- This finding is compatible with substantial meningeal inflammation, but is not disease-specific.

CSF glucose may be low—or not

Avoid replacing variable findings with rigid diagnostic cutoffs.

- Glucose as moderately reduced or even normal.
- Normal CSF glucose therefore does not rule out tuberculous meningitis.
- A single chemical variable should not override the total clinical picture.

Tuberculous meningitis: The source-described CSF pattern

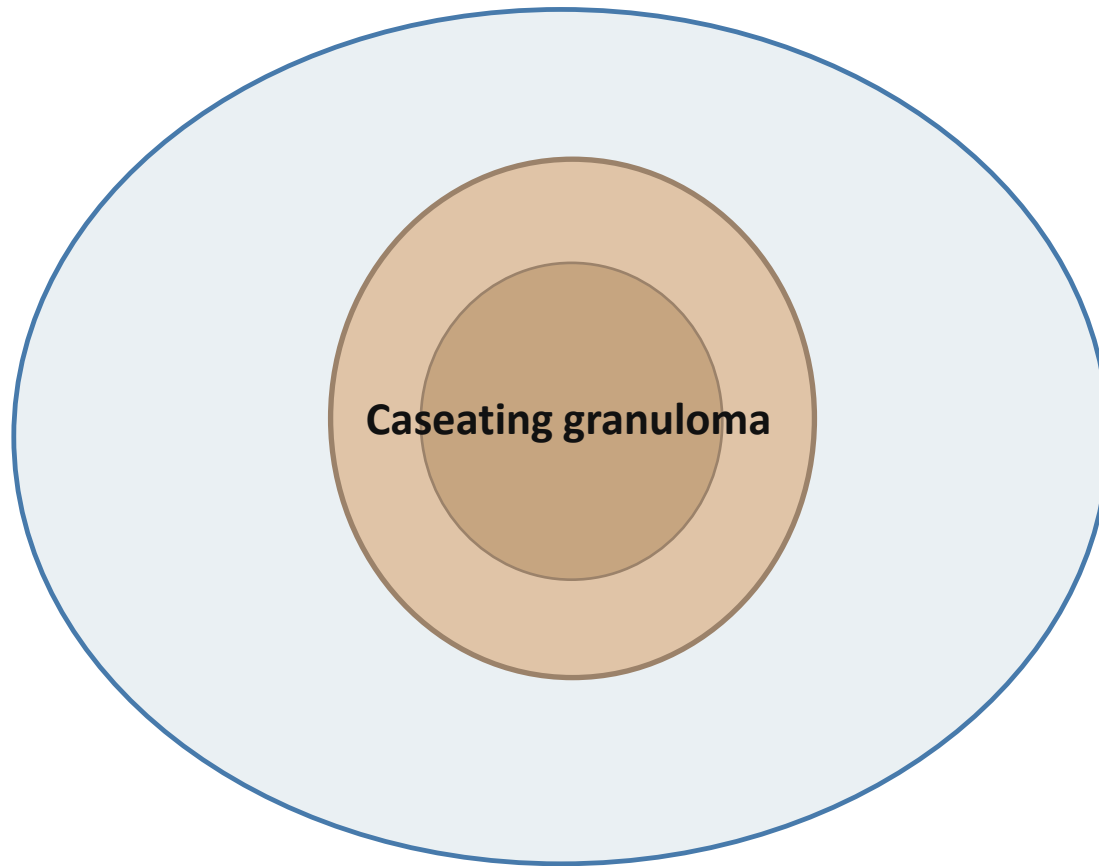
CSF feature	Typical finding	Interpretive caution
White blood cells	Mononuclear or mixed pleocytosis	Neutrophils can coexist with mononuclear cells
Protein	Elevated, sometimes markedly	Not specific to tuberculosis
Glucose	Moderately reduced or normal	Normal level does not exclude disease

Tuberculomas are intraparenchymal mass lesions

The focal pattern contrasts with diffuse meningoencephalitis.

- One or several well-circumscribed granulomatous masses may occur.
- They may appear with or without concurrent meningeal disease.
- Lesions can become several centimeters across and produce substantial mass effect.

Tuberculoma: Cellular pathology of a focal mass



Surrounding inflammatory tissue

Well-circumscribed intraparenchymal lesion

Mass effect on nearby parenchyma

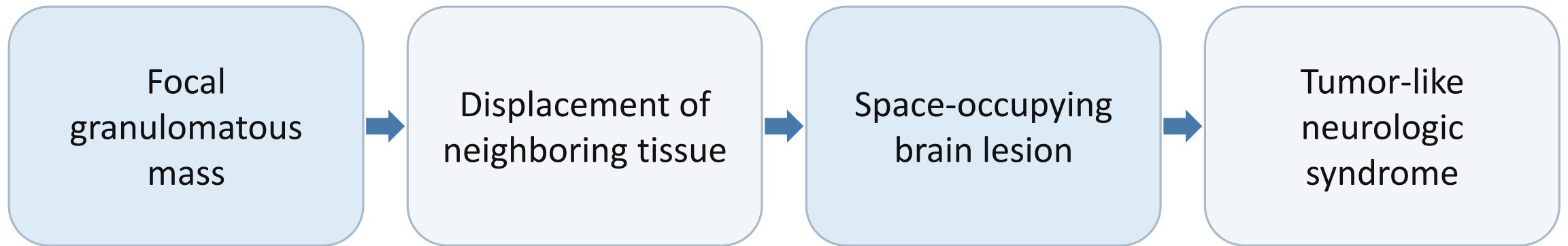
Editable, not-to-scale schematic; Not diagnostic radiology or gross specimen.

Inactive tuberculomas may calcify

The source does not establish a universal time course for calcification.

- Tuberculomas typically have central caseous necrosis.
- Inactive lesions may develop calcification.
- Calcification should be interpreted within the full clinical and morphologic setting.

Why tuberculomas mimic tumors clinically



The source requires distinction from CNS neoplasms; This diagram does not imply identical imaging.

Meningoencephalitis versus tuberculoma

Diffuse meningoencephalitis	Tuberculoma
Basal leptomeningeal exudate	Focal intraparenchymal mass
Diffuse meningeal inflammatory changes	Circumscribed caseating granuloma
Endarteritis / arachnoid fibrosis	Mass effect / possible calcification
Hydrocephalus or infarction	Space-occupying lesion symptoms
Often meningeal CSF abnormalities	May coexist with meningitis

HIV-associated CNS tuberculosis: Pathology changes

Preserved cellular immune response

- More conspicuous immune-mediated tissue reaction.
- Well-organized granulomatous inflammation may be evident.
- Organisms may be sparse on acid-fast staining.

Advanced immune deficiency / AIDS

- The overall pathology may be similar in distribution.
- The host inflammatory reaction is usually less developed.
- Classical granulomatous morphology may be attenuated.

Do not equate scant granulomas with absence of infection

A weaker inflammatory response can occur despite significant infection.

- The ability to form a granuloma depends on cellular immunity.
- Advanced immunosuppression can blunt the expected histologic pattern.
- Atypical tissue responses should prompt careful integration of microbiologic and clinical evidence.

Chronic infectious meningoencephalitis: Key etiologic context

Organism group	Illustrative agent	Scope in this lecture
Mycobacteria	M. tuberculosis	Primary focus: basal meningitis and tuberculoma
Spirochetes	Treponema pallidum	Separate neurosyphilis morphology and presentation
Spirochetes	Borrelia species	Separate neuroborreliosis manifestations

Acute pyogenic versus tuberculous meningitis

Acute pyogenic meningitis	Tuberculous meningitis
Usually acute symptomatic illness	Frequently subacute or chronic course
Cloudy/purulent CSF with numerous neutrophils	Mononuclear or mixed pleocytosis
CSF glucose markedly reduced	CSF glucose moderately reduced or normal
Predominantly suppurative reaction	Granulomatous / chronic meningeal reaction

Case study 1 · meningitis pattern

A patient has a progressive headache, malaise, vomiting, and confusion. CSF shows elevated protein with mixed inflammatory cells; Glucose is not markedly depressed.

Discussion prompts

- Which CNS infection pattern from this lecture is compatible?
- Which macroscopic distribution should be sought?
- Why does the glucose value not settle the diagnosis?

Case study 1 · morphologic interpretation

Interpret the case from anatomical pathology and source-consistent clinical findings.

The syndrome is compatible with tuberculous meningitis, but the findings are not independently diagnostic.

The expected gross pattern is gelatinous / fibrinous exudate concentrated at the brain base.

CSF glucose can be normal or moderately reduced.

Case study 2 · focal intracranial lesion

A patient has a well-defined intracerebral lesion with mass effect. Tissue examination reveals a circumscribed granulomatous focus with central caseation.

Discussion prompts

- Which CNS tuberculosis manifestation best fits the lesion?
- What alternative disease class must be considered clinically?
- What late change may appear in an inactive lesion?

Case study 2 · pathology and differential

Interpret the case from anatomical pathology and source-consistent clinical findings.

The lesion is consistent with a tuberculoma.

Because it acts as a space-occupying lesion, a CNS neoplasm must be considered in the differential.

Inactive tuberculomas may undergo calcification; Organism evidence is still required for etiologic certainty.

Case study 3 · two complications

A patient with chronic basal meningitis develops hydrocephalus and a new focal neurologic deficit.

Discussion prompts

- Which chronic meningeal lesion explains hydrocephalus?
- Which vascular lesion can account for focal ischemic injury?
- Why can both complications coexist?

Case study 3 · linking anatomy to injury

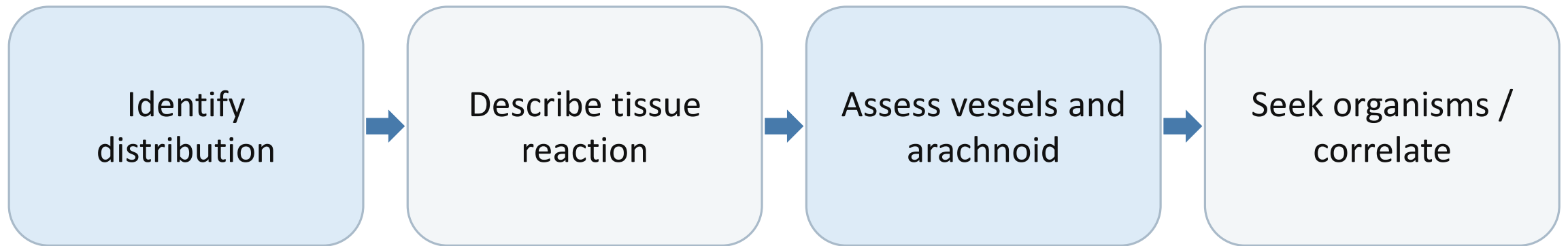
Interpret the case from anatomical pathology and source-consistent clinical findings.

Adhesive arachnoid fibrosis can impair CSF dynamics and lead to hydrocephalus.

Obliterative endarteritis with intimal thickening can occlude arteries and produce infarction.

Both lesions may result from a common persistent basal meningeal inflammatory process.

Specimen-oriented interpretation of suspected CNS TB



This is a pathology reading strategy, not an independent clinical diagnostic guideline.

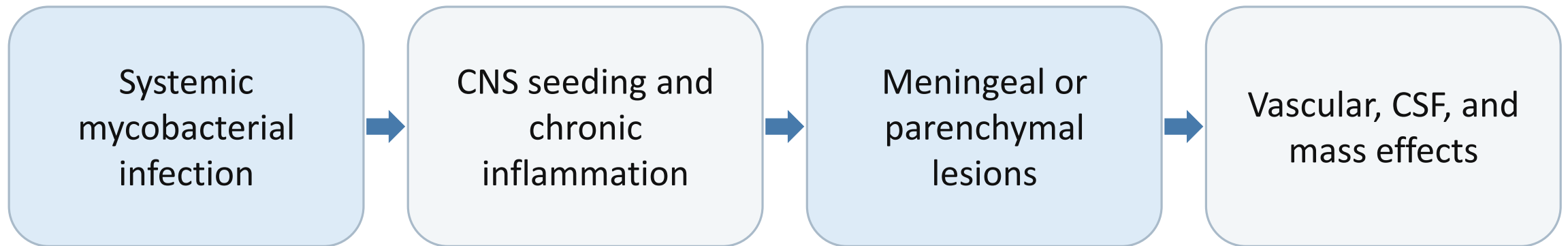
Morphology-to-syndrome integration

Anatomic pathology	Dominant mechanism	Clinical expression
Basal inflammatory exudate	Meningeal inflammatory disease	Headache, malaise, confusion, vomiting
Endarteritis	Luminal narrowing / infarction	Focal neurologic deficits
Adhesive arachnoiditis	Impaired CSF circulation	Hydrocephalus
Caseating tuberculoma	Local mass effect	Tumor-like space-occupying symptoms

Common interpretive pitfalls

- Tuberculosis of the CNS can occur without recognized active pulmonary disease.
- A normal CSF glucose or a mixed neutrophilic response does not exclude tuberculous meningitis.
- Few visible acid-fast organisms do not invalidate convincing granulomatous pathology.
- Reduced granuloma formation in advanced immune deficiency should not be mistaken for low infection burden.

Summary · a unified pathobiologic model



Mechanistic synthesis of Robbins Chapters 8 and 28.

Source and image provenance

Robbins, Cotran & Kumar. Pathologic Basis of Disease. 11th ed. (2026). Chapter 28, pp. 1149–1150: CNS tuberculosis, morphology and clinical features.

Robbins, Cotran & Kumar. Pathologic Basis of Disease. 11th ed. (2026). Chapter 8, pp. 334–338: tuberculosis pathogenesis, host immune response and dissemination.

Adjacent CNS sections: acute pyogenic meningitis and chronic bacterial meningoencephalitis, Chapter 28, pp. 1147–1150.

Figures in this presentation are original native PowerPoint schematics; no external specimen images have been embedded.