

Arthropod-Borne Viral Encephalitis

Neuropathology | Transmission, pathogenesis, morphology and diagnosis

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Learning objectives

- Explain why arboviral infections can cause epidemic meningoencephalitis.
- Trace the West Nile virus transmission and neuroinvasion sequence.
- Recognize the characteristic clinical, CSF, and neuropathologic findings.
- Integrate morphology with etiologic testing and differential diagnosis.

Arboviruses: A transmission-defined group

- “Arbovirus” denotes an arthropod-borne virus; It is not a single viral family.
- Animal hosts and arthropod vectors are central to the infectious cycle.
- The encephalitides encompass multiple viruses with overlapping pathology.
- The causative virus therefore cannot be established by morphology alone.

Viral encephalitis is parenchymal infection

- Infection involves the brain parenchyma rather than the meninges alone.
- Meningeal inflammation usually accompanies parenchymal involvement.
- The resulting clinicopathologic pattern is meningoencephalitis.
- Extension to the spinal cord produces encephalomyelitis.

Meninges

Brain parenchyma

Spinal cord

Meningitis, encephalitis and myelitis: Localization

Meninges

Inflammatory CSF

Meningeal irritation

Brain

Parenchymal neuronal injury

Encephalopathy, seizures

Spinal cord

Motor-system involvement

Paralysis

- Meningeal disease explains meningitic manifestations and CSF inflammation.
- Brain parenchymal disease produces impaired cognition or consciousness and seizures.

Neural tropism is not uniform

- Viruses differ in the neural cell types they can infect.
- Other viruses preferentially involve specific brain regions.
- The clinical syndrome reflects anatomic distribution as well as injury severity.
- A shared histologic pattern does not imply identical tissue distribution.

Direct viral encephalitis versus immune injury

Direct infection

Virus reaches CNS

Infectious encephalitis

Postinfectious response

Immune-mediated damage

Not proof of CNS invasion

- Viral invasion of neural tissue directly produces a parenchymal infection.
- Systemic infections can also be followed by immune-mediated CNS disease.

Why arboviruses matter in neuropathology

- Arboviruses are important causes of epidemic encephalitis.
- The burden in tropical regions.
- Infections can produce serious neurologic morbidity and high mortality.
- Outbreak context is useful, but pathology and virology must establish the diagnosis.

Transmission involves hosts, vectors and susceptible people



- Animal hosts maintain viral circulation in nature.
- Arthropods transfer infection between susceptible hosts.
- Humans can acquire infection when an infected vector feeds.

Vector does not mean reservoir

Vector

Arthropod that transmits infection

Mosquito in the West Nile cycle

Reservoir

Host supporting persistence/circulation

Birds in the West Nile cycle

- An arthropod vector transfers infection between hosts.
- A reservoir sustains infection within an ecological cycle.

Mosquito- and tick-borne encephalitis

Mosquito-associated

West Nile; Equine; St. Louis; La Crosse

Several named diseases

Tick-associated

Tick-borne encephalitis

Europe/Russia

- Mosquito-associated arboviruses include the equine encephalitis viruses and West Nile.
- Tick-borne encephalitis is a separate named arboviral syndrome.

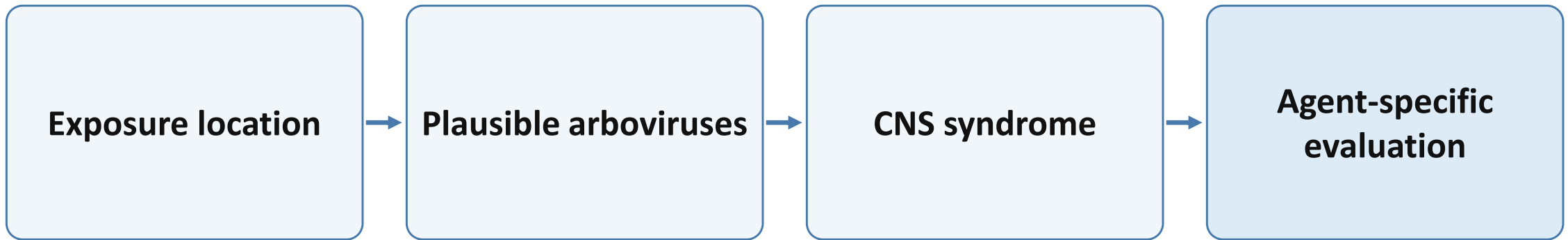
Western Hemisphere: Named encephalitis viruses

- Eastern equine encephalitis virus.
- Western equine and Venezuelan equine encephalitis viruses.
- West Nile and St. Louis encephalitis viruses.
- La Crosse encephalitis virus.

Other regional arboviral encephalitides

Region	Representative viruses
Americas	Eastern / Western / Venezuelan equine; West Nile; St. Louis; La Crosse
East Asia	Japanese encephalitis
Australia / New Guinea	Murray Valley encephalitis
Russia / Eastern Europe	Tick-borne encephalitis

Geographic framing is a diagnostic clue



- Compare residence, travel and arthropod exposure with the known regional viruses.
- Geographic plausibility narrows which agents to test for.

West Nile virus: A flavivirus example

- West Nile virus belongs to the flavivirus group.
- Robbins also places dengue and yellow fever viruses in that group.
- Its clinical presentations range from mild illness to neuroinvasive disease.
- It offers a concrete model for linking transmission to CNS pathology.

West Nile virus has broad geographic distribution

- Africa, the Middle East and Europe.
- Its distribution also includes Southeast Asia and Australia.
- West Nile virus entered the United States in the 1999 New York City outbreak.
- Geography should be interpreted as a changing epidemiologic context.

West Nile: Birds are central to the reservoir cycle



- Infected birds can develop prolonged viremia.
- Birds serve as the major West Nile virus reservoir.
- Mosquitoes transmit the virus among hosts.

Humans are incidental West Nile hosts

Reservoir bird

Prolonged viremia

Maintains enzootic circulation

Human

Incidental infection

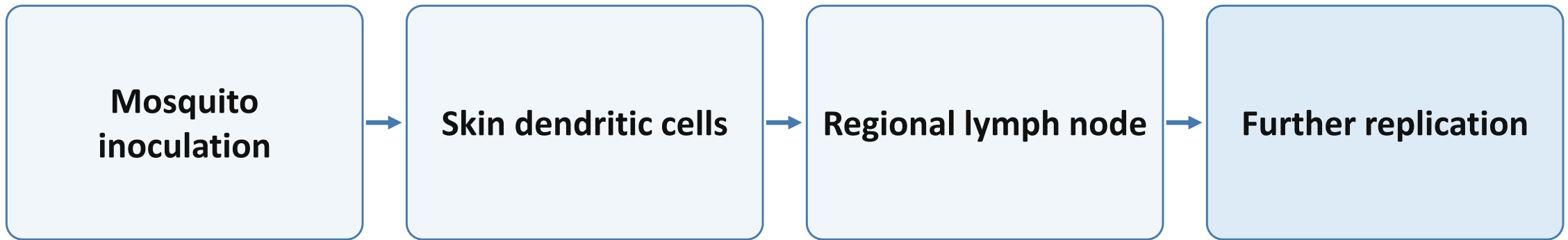
May develop systemic or CNS disease

- West Nile virus is transmitted to both birds and mammals by mosquitoes.
- Humans are incidental hosts, not the principal reservoir.

West Nile: Non-mosquito transmission is possible

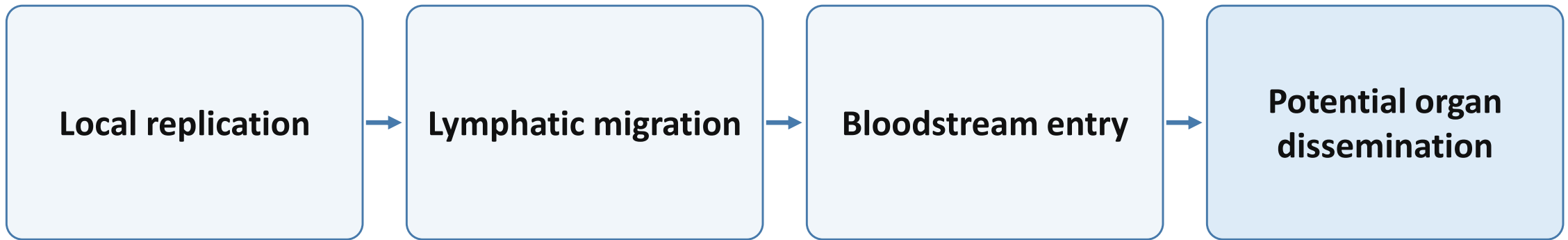
- Transfusion-associated infection is described.
- Organ transplantation is another reported route.
- Vertical transmission and breastfeeding-associated transmission are noted.
- These routes are less common than mosquito-borne acquisition.

West Nile entry: Inoculation into skin



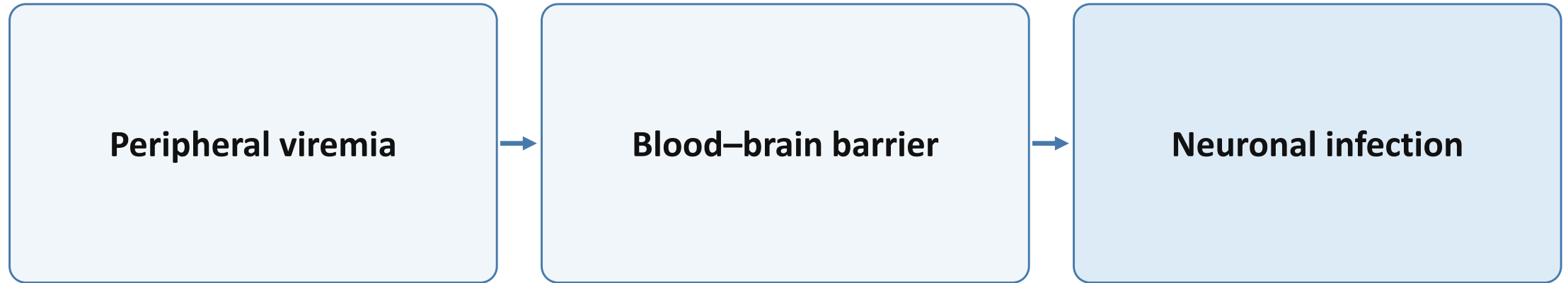
- An infected mosquito inoculates virus during feeding.
- The virus initially replicates in skin dendritic cells.

Lymph-node replication precedes viremia



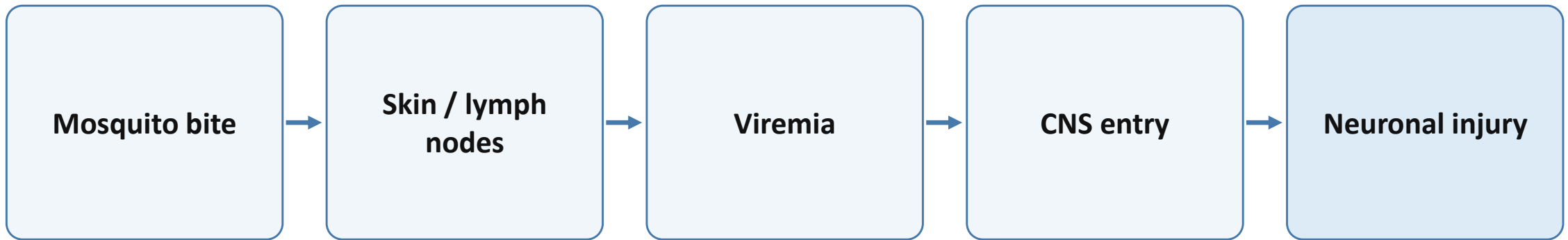
- Virus undergoes additional replication in lymphoid tissue.
- Virus then enters the bloodstream.

Neuroinvasion is a distinct pathogenic step



- In some infected individuals West Nile virus crosses the blood–brain barrier.
- It then infects neurons within the central nervous system.

Integrated West Nile pathogenic sequence



- Skin and regional lymph nodes represent early amplification sites.
- Viremia provides access to distant tissues.

The usual West Nile infection is asymptomatic

20%

**Approximately symptomatic
infections**

- Most infected individuals have no recognized illness.
- Symptomatic infection in approximately 20%.
- Clinical disease is therefore an incomplete measure of transmission.
- Neuroinvasive illness is much less common than all infections.

Systemic West Nile fever: Constitutional symptoms

- Fever and headache are prominent features.
- Myalgia, fatigue and anorexia may accompany illness.
- Vomiting and diarrhea are also described.
- These findings are nonspecific without exposure context or virology.

The skin may contribute a diagnostic clue

$\sim 1/2$

**Symptomatic cases with
maculopapular rash**

- A maculopapular rash may accompany symptomatic West Nile disease.
- Rash in approximately half of symptomatic cases.
- Absence of rash does not exclude infection.
- Rash alone cannot distinguish encephalitis from systemic illness.

Neuroinvasive West Nile disease is uncommon

1 in 150

Infections with CNS complications

- CNS complications include meningitis, encephalitis and meningoencephalitis.
- CNS complications in about 1 of 150 infections.
- Affected patients may sustain major neurologic injury.
- The denominator is all infections, not only symptomatic cases.

Syndromic spectrum of neuroinvasive disease

Meningitis

Meningeal syndrome

Inflammatory CSF

Encephalitis

Brain dysfunction

Seizures / confusion

Myelitis

Spinal cord dysfunction

Weakness / paralysis

- Meningitis describes predominant meningeal inflammation.
- Encephalitis indicates brain parenchymal involvement.

Generalized neurologic dysfunction

- Seizures may result from brain parenchymal involvement.
- Confusion and delirium indicate cerebral dysfunction.
- Stupor or coma occurs with more severe encephalitis.
- These are major manifestations described for arboviral encephalitides.

Altered mental status establishes encephalitic severity

Confusion

Delirium

Stupor

Coma

- Confusion indicates impaired cognition or awareness.
- Delirium reflects more pronounced disturbance of cerebral function.
- Stupor and coma identify profoundly impaired consciousness.

Focal deficits may coexist with generalized disease

- Reflex asymmetry indicates uneven involvement of neural motor pathways.
- Ocular palsies demonstrate focal cranial motor dysfunction.
- Focal signs do not exclude diffuse meningoencephalitis.
- Clinical examination can reveal the distribution of neurologic injury.

West Nile encephalitis may involve spinal cord

- Spinal cord involvement is explicitly.
- The resulting syndrome may resemble poliomyelitis.
- Paralysis can accompany a West Nile neuroinvasive infection.
- This finding shifts localization beyond brain and meninges.

Meninges

Brain parenchyma

Spinal cord

Polio-like paralysis is a localization clue

West Nile neuroinvasion

May include spinal cord

Polio-like paralysis

Poliovirus infection

Anterior horn motor-neuron injury

Spinal poliomyelitis

- A polio-like phenotype suggests injury to lower motor neuronal circuitry.
- West Nile belongs in the differential of acute paralysis with encephalitis.

Who is at greatest risk of severe West Nile disease?

Older age

Greater risk of severe disease

Interpret neurologic symptoms urgently

Immunosuppression

Greater risk of severe disease

Heightened concern for CNS complications

- Older adults are more vulnerable to severe disease.
- Immunosuppressed individuals are another high-risk group.

West Nile meningoencephalitis can leave sequelae

~10%

**Mortality in West Nile
meningoencephalitis**

- Approximately 10% mortality in meningoencephalitis.
- Long-term cognitive or neurologic deficits occur in many survivors.
- Acute survival does not necessarily mean full neurologic recovery.
- Prognosis differs considerably between mild and neuroinvasive infection.

Linking the clinical findings to anatomy

Meninges

CSF inflammation

Meningeal syndrome

Brain

Neuronal injury

Seizures / delirium

Spinal cord

Motor-system injury

Paralysis

- Meningeal inflammation corresponds to inflammatory CSF findings.
- Brain parenchymal injury explains seizures and altered consciousness.

CSF macroscopic appearance and pressure

- The CSF is generally colorless in arboviral encephalitis.
- Opening pressure may be mildly elevated.
- Normal gross appearance does not exclude neuroinvasive viral disease.
- The inflammatory profile is more informative than CSF color alone.

CSF protein and glucose pattern

CSF protein

Increased

Reflects inflammatory involvement

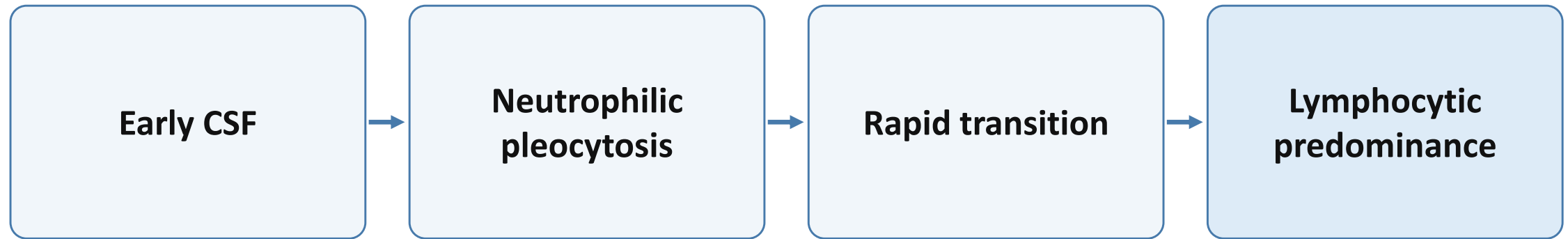
CSF glucose

Usually normal

Not a virus-specific marker

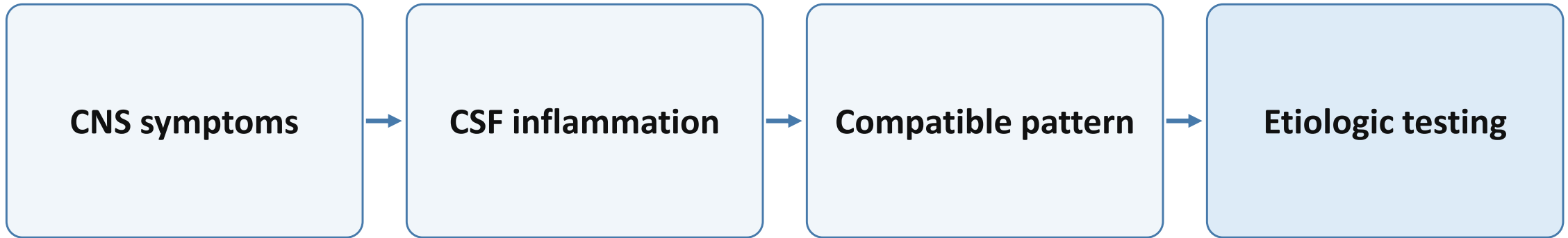
- CSF protein is typically elevated.
- CSF glucose is generally normal.

CSF cells change over the course of illness



- An early neutrophilic pleocytosis may occur.
- The cell differential rapidly shifts toward lymphocytes.
- An early sample can therefore appear neutrophil-predominant.

The CSF profile is supportive, not definitive



- Cell count and protein indicate central nervous system inflammation.
- Normal glucose and evolving lymphocytosis fit the textbook description.

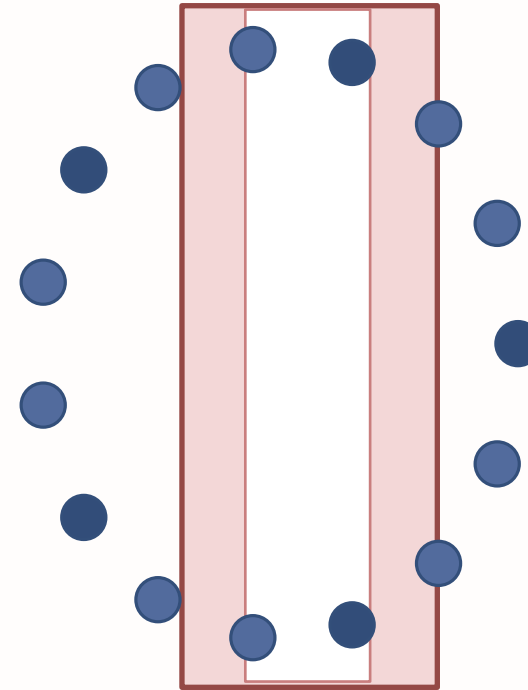
Arboviral encephalitides share a morphology

- A common pattern is meningoencephalitis with mononuclear inflammation.
- Histologic differences often concern severity and extent.
- Parenchymal tissue injury accompanies perivascular inflammation.
- Histology identifies encephalitis better than it identifies the individual arbovirus.

Perivascular lymphocytic cuffing

- Lymphocytes accumulate around CNS blood vessels.
- This produces the characteristic perivascular cuff.
- Cuffs are a morphologic signature of viral meningoencephalitis.
- The finding should be interpreted with neuronal and microglial changes.

Lymphocytes surrounding a vessel

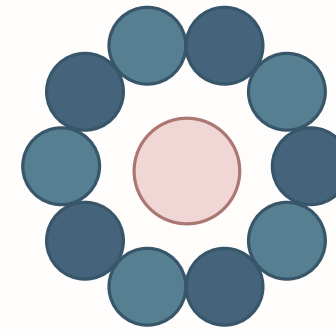


Schematic — not a tissue specimen

Microglial nodules: Focal glial response

- Microglial cells assemble into small aggregates in affected tissue.
- These aggregates are termed microglial nodules.
- They accompany focal tissue injury and inflammation.
- The finding is characteristic but not specific to a single arbovirus.

Focal aggregation of microglial cells

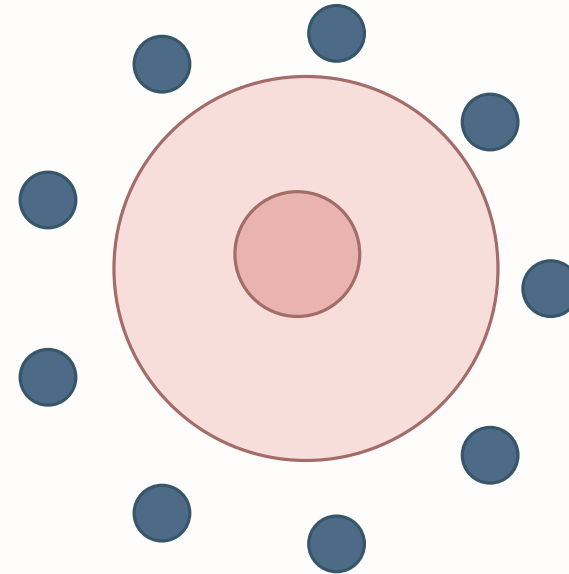


Schematic — not a tissue specimen

Neuronophagia indicates neuronal destruction

- Individual neurons may undergo necrosis.
- Phagocytic cells remove the resulting cellular debris.
- This process is termed neuronophagia.
- It provides microscopic evidence of destructive parenchymal infection.

Phagocytes around an injured neuron



Schematic — not a tissue specimen

Necrosis can affect both gray and white matter

Gray matter

Foci of necrosis

Parenchymal damage

White matter

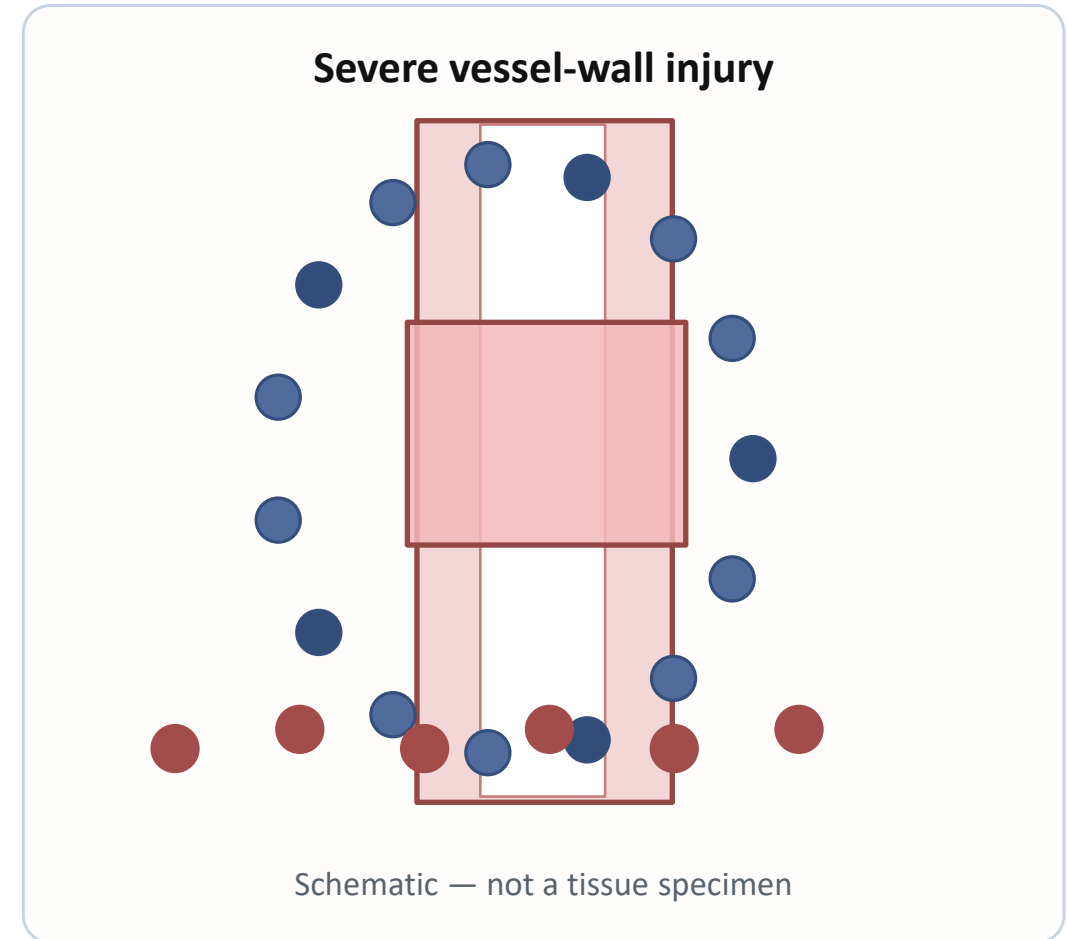
Foci of necrosis

Parenchymal damage

- Multiple foci of necrosis are described across the CNS parenchyma.
- Gray matter may be involved.

Severe cases may develop necrotizing vasculitis

- Vessel-wall injury becomes prominent in severe encephalitis.
- Necrotizing vasculitis in severe cases.
- Associated focal hemorrhages may occur.
- This is not presented as an obligatory feature of every arbovirus infection.



Histologic findings vary with severity

Perivascular cuffs

Microglial reaction

**Neuronal loss /
necrosis**

Severe vascular injury

- Perivascular lymphocytes signal a characteristic inflammatory response.
- Microglial nodules and neuronophagia identify parenchymal cellular injury.
- Focal necrosis documents tissue destruction.

West Nile: Documented tissue distribution

- Perivascular and leptomeningeal inflammation.
- Microglial nodules and neuronophagia are reported.
- Temporal lobes and brainstem are noted among affected regions in fatal cases.
- This distribution is an observation, not a pathognomonic tissue map.

What histology can and cannot establish

Can establish

Pattern of viral encephalitis

Severity and tissue injury

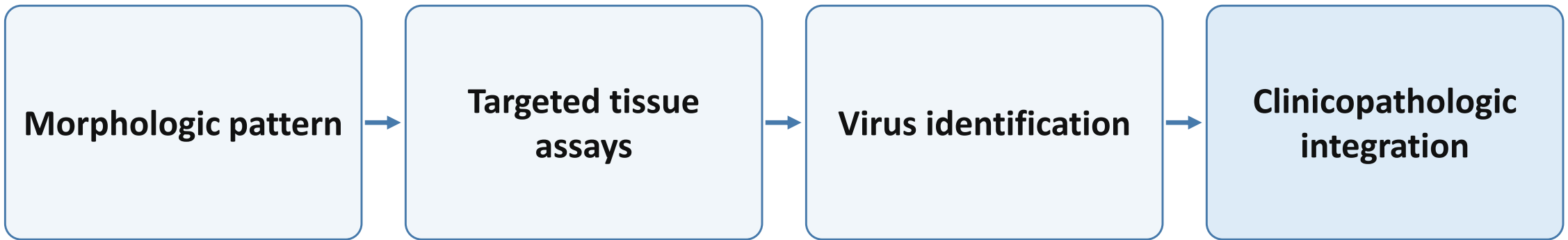
Cannot establish alone

Exact arbovirus

Transmission route or reservoir

- Histology can confirm an inflammatory and destructive encephalitic pattern.
- Cuffs, microglial nodules and neuronophagia are not unique to one virus.

Tissue-based etiologic identification



- Ultrastructural methods among approaches used in tissue.
- Immunohistochemistry can detect relevant viral material.

West Nile diagnosis: Virus-specific IgM

- West Nile virus–specific IgM can be sought in serum.
- Virus-specific IgM can also be detected in cerebrospinal fluid.
- This as the usual diagnostic method.
- Interpret the result alongside the clinical and epidemiologic setting.

West Nile diagnosis: Additional virologic tests

Serologic route

Virus-specific IgM

Serum or CSF

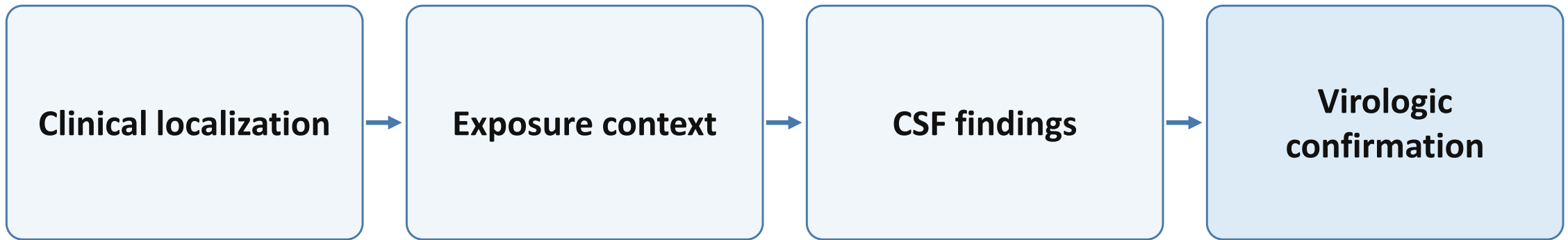
Direct detection route

Culture or PCR

Use in selected settings

- Viral culture is mentioned as a diagnostic method.
- PCR-based tests are also used.

Reasoning from exposure to diagnosis



- Identify a compatible CNS syndrome and its anatomic localization.
- Consider geographic and arthropod exposure information.

Differential pathology: Herpes simplex encephalitis

Arboviral encephalitis

Shared perivascular cuffs and nodules

Confirm with agent-directed methods

HSV-1 encephalitis

Hemorrhagic necrosis; Temporal predilection

Possible Cowdry A inclusions

- HSV-1 classically affects inferior frontal and anterior temporal regions.
- A hemorrhagic necrotizing inflammatory process.

An early neutrophilic CSF is not automatically bacterial

- Robbins explicitly describes early CSF neutrophilia in arboviral infection.
- The differential may evolve rapidly toward lymphocytosis.
- CSF glucose generally remains normal in the described arboviral pattern.
- Diagnostic reasoning must integrate course and microbiology, not one differential count.

Interpret histology without overcalling an agent

- Perivascular cuffing is an inflammatory pattern, not a species marker.
- Neuronophagia and microglial nodules indicate neuronal and glial responses.
- Focal hemorrhage or severe vasculitis may indicate greater injury.
- Only appropriately validated etiologic methods can establish the responsible virus.

Case 1: Acute encephalitis after mosquito exposure

An older adult develops fever, confusion and seizures.

CSF is colorless, with elevated protein and normal glucose.

Early neutrophils become lymphocyte-predominant in a subsequent sample.

Question: What diagnostic category and next line of testing are indicated?

Case 1: Interpret the evidence

- The brain dysfunction and CSF findings support meningoencephalitis.
- The evolving cell differential is compatible with arboviral infection.
- Exposure and host risk justify West Nile evaluation where epidemiologically plausible.
- Use virus-specific IgM in serum or CSF rather than histology alone.

Case 2: Acute paralysis with encephalitis

A patient develops febrile encephalopathy and new limb paralysis.

The motor syndrome suggests concurrent spinal cord involvement.

West Nile virus may produce a polio-like syndrome.

Question: Which additional anatomic compartment requires attention?

Case 2: Localize before naming the virus

- The spinal cord joins brain and meninges in the suspected disease distribution.
- Paralysis does not by itself prove poliovirus infection.
- Consider West Nile neuroinvasion within the relevant exposure context.
- Confirm with appropriate virologic methods.

Case 3: Tissue shows lymphocytic cuffs and nodules

Microscopy demonstrates perivascular lymphocytes and microglial nodules.

Additional sections show neuronophagia.

The findings support destructive viral meningoencephalitis.

Question: Can these findings alone distinguish La Crosse from West Nile?

Case 3: Morphology has an etiologic limit

- No: The shared injury pattern does not identify the exact arbovirus.
- Assess regional exposure and clinical syndrome.
- Use agent-directed tests in serum, CSF or tissue where applicable.
- Report the histopathologic pattern separately from etiologic confirmation.

Clinical and pathologic synthesis

- Arboviral meningoencephalitis links animal–arthropod ecology to CNS infection.
- West Nile illustrates the route from skin replication to viremia and neuronal injury.
- CSF shows elevated protein, normal glucose and an evolving cell differential.
- Perivascular cuffs, microglial nodules and neuronophagia form a shared tissue pattern.

References

- Robbins, Cotran & Kumar. Pathologic Basis of Disease. 11th edition (2026).
- Central nervous system: infections, viral meningoencephalitis and arthropod-borne encephalitis.
- Infectious diseases: West Nile virus clinical features, pathogenesis and morphology.
- Microscopic teaching diagrams in this presentation are original native PowerPoint schematics, not human tissue images.