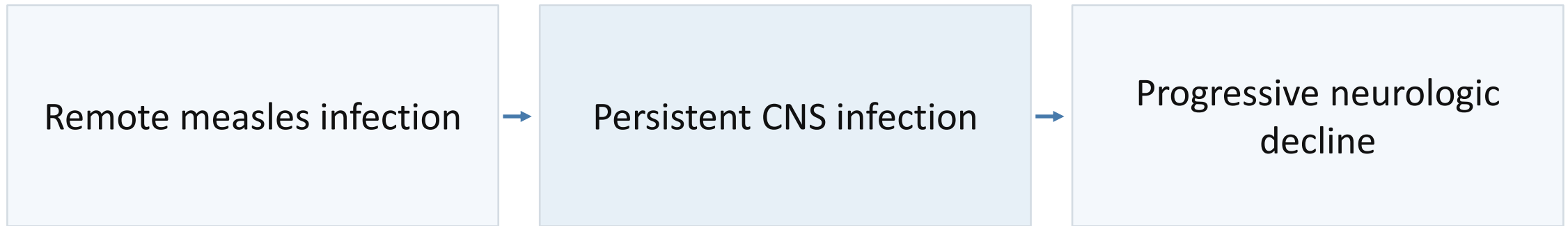


Subacute sclerosing panencephalitis

Delayed measles-associated neurodegenerative encephalitis



An uncommon but largely fatal late complication of measles

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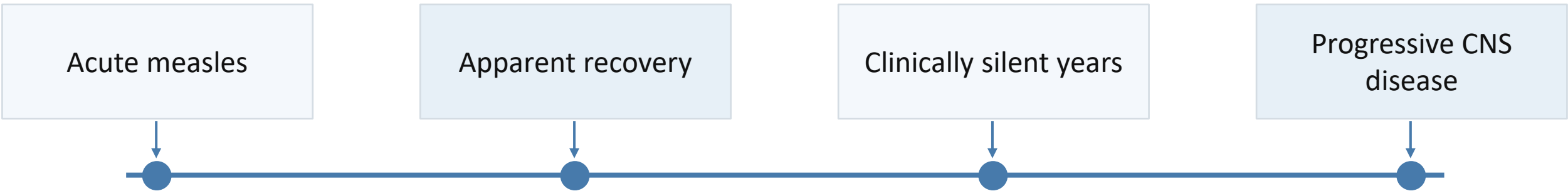
Learning objectives

- Explain why remote measles infection can cause delayed encephalitis.
- Connect viral persistence to neuronal injury, gliosis, and demyelination.
- Interpret clinical evolution, CSF measles antibodies, EEG, and MRI.
- Differentiate SSPE from mimics and explain prevention.

Core definition and diagnostic identity

- SSPE is a progressive inflammatory–degenerative disorder of the CNS after measles infection.
- Disease onset follows an often prolonged clinically silent interval.
- Cognitive deterioration and myoclonus are important clues, not universal entry symptoms.
- Measles-specific intrathecal antibody synthesis is central to diagnosis.

The long interval is the defining temporal clue



- Typical latency is years; CDC describes 7–10 years after measles.
- The interval and clinical presentation are variable; Remote infection may be forgotten.

SSPE is not acute measles encephalitis

- Acute measles encephalitis accompanies or shortly follows primary infection.
- SSPE arises years after the original illness, often without acute systemic symptoms.
- The pathology of SSPE reflects persistent brain infection and progressive tissue injury.
- Timing is a practical first discriminator when reviewing post-measles neurologic disorders.

SSPE in the spectrum of measles neurologic disease

Entity	Approximate timing	Dominant concept
Acute measles encephalitis	During or soon after measles	Acute CNS complication
Postinfectious ADEM	Days to weeks after infection	Inflammatory demyelinating syndrome
Measles inclusion-body encephalitis	Often immunocompromised host	Progressive direct viral encephalitis
SSPE	Years after measles	Persistent-virus panencephalitis

These syndromes differ in timing, host context, and dominant pathogenesis.

Who is at risk?

- SSPE is uncommon relative to the number of measles infections.
- Measles infection at a very young age is associated with greater subsequent SSPE risk.
- Most recognized cases present during childhood or adolescence; Adult presentations occur.
- Population-level risk is context dependent; Avoid applying one estimate universally.

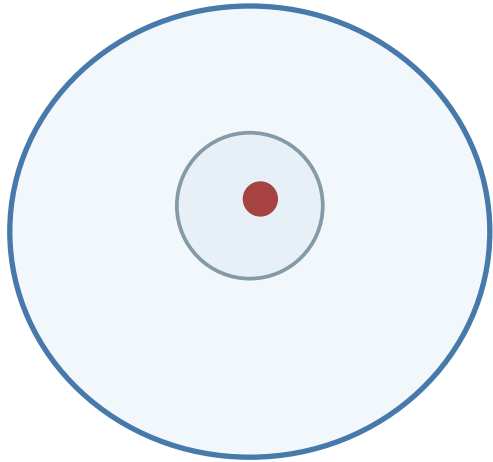
Epidemiologic context changes with vaccination

- Measles incidence and transmission determine the pool at risk for later SSPE.
- The latent interval means SSPE cases can appear long after an outbreak.
- Sustained vaccination reduces measles infections and therefore prevents later SSPE.
- Clinical vigilance remains important in regions with measles transmission.

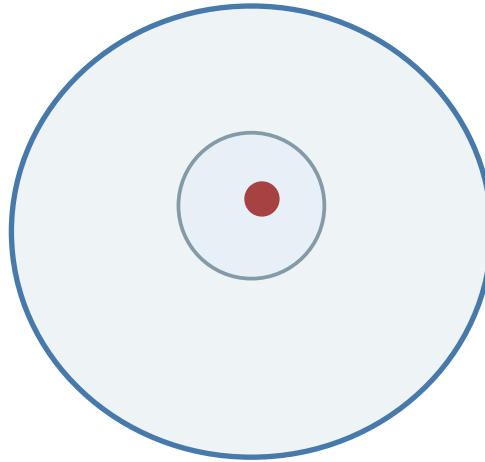
What does “persistent infection” mean here?

- The initiating event is infection with measles virus, an enveloped RNA virus.
- Viral genetic material and proteins can persist within CNS cells.
- Continued intracellular infection differs from an ordinary acute viremic illness.
- The exact initial route into and establishment within brain tissue remain incompletely resolved.

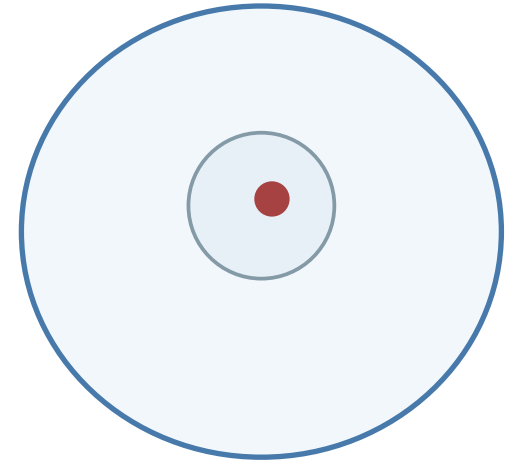
Neurons and glia are the key injured compartments



Neuron



Oligodendrocyte



Astrocyte

Simplified cell schematic — not a histologic image

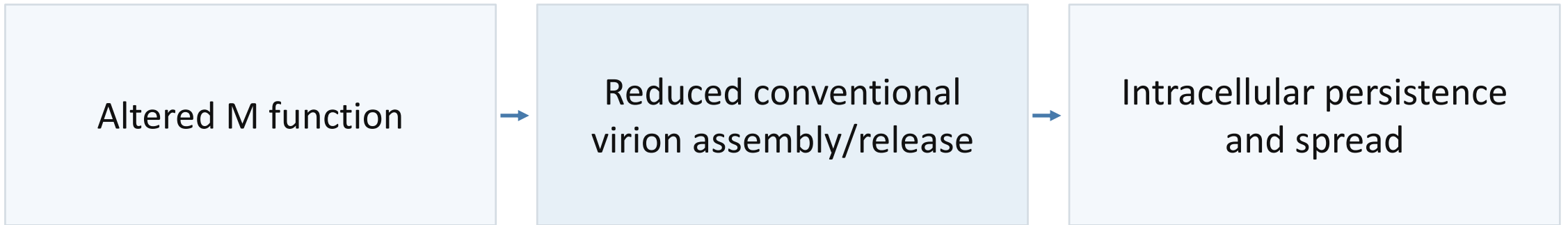
Intracellular viral material occurs in neurons and glial cells.

Measles virus: The structural proteins that matter

- Matrix (M) protein supports virion assembly and release.
- Fusion (F) protein mediates membrane fusion.
- Hemagglutinin (H) attachment protein participates in receptor interactions.
- Nucleocapsid proteins package viral RNA and may accumulate as inclusions.

Defective assembly may favor intracellular persistence

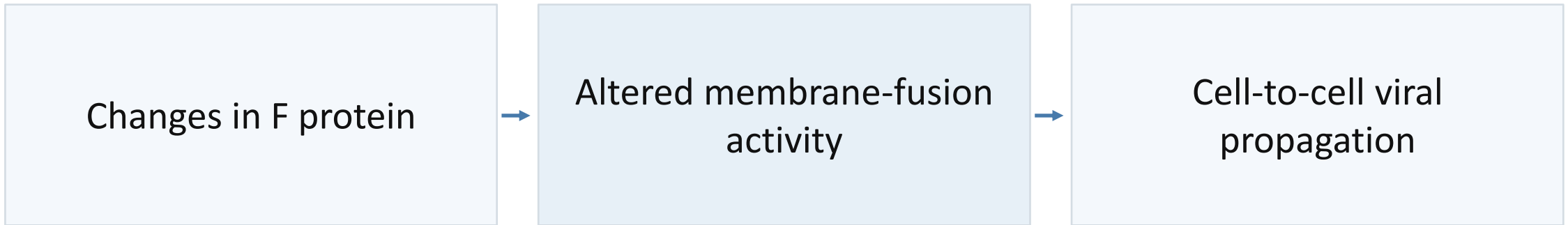
Mechanistic sequence



M-protein defects are implicated in SSPE virus biology, but mechanistic variation exists.

Fusion-protein adaptations facilitate neural spread

Mechanistic sequence



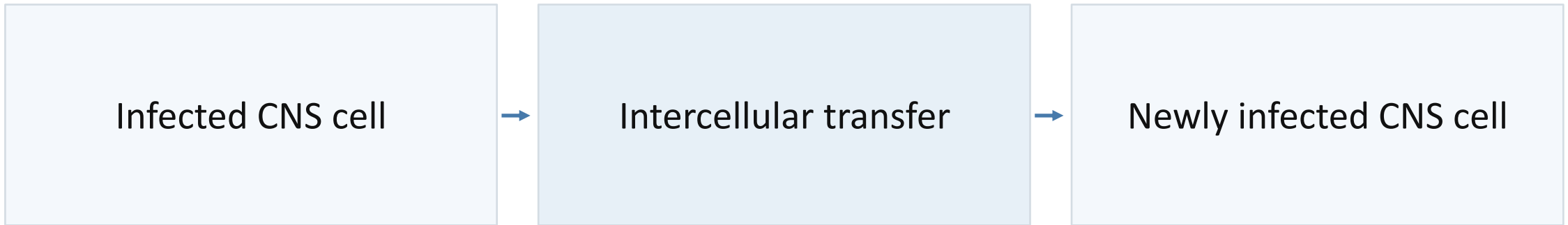
A hyperfusogenic phenotype has been documented in experimental models of SSPE-associated variants.

Measles neurotropism is biologically complex

- Canonical measles receptors do not fully explain spread among mature neurons.
- Laboratory work supports roles for altered viral proteins and neuronal host factors.
- The contribution of individual M, F, and H mutations differs across studied viral genomes.
- Do not reduce a heterogeneous disease to one obligatory mutation.

Cell-to-cell spread helps explain persistence

Mechanistic sequence



The schematic describes a proposed dominant route, not a patient-derived microscopic observation.

Why antibodies do not necessarily clear the virus

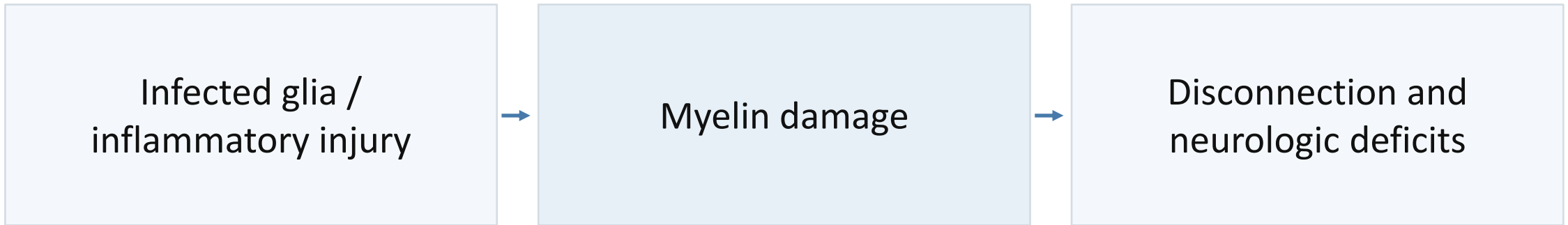
- Measles-specific antibodies can be abundant in serum and CSF.
- Antibody presence is therefore not equivalent to elimination of intracellular infection.
- Cell-associated viral spread may restrict exposure to neutralizing antibodies.
- Both persistent infection and host inflammatory responses contribute to injury.

Inflammation is part of the lesion

- Chronic inflammatory infiltrates may involve meninges and brain parenchyma.
- Perivascular lymphocytes accompany inflammatory tissue injury.
- Astrocytic and microglial responses may amplify local damage.
- Inflammation does not exclude an underlying persistent viral etiology.

Mechanistic links to white matter injury

Mechanistic sequence



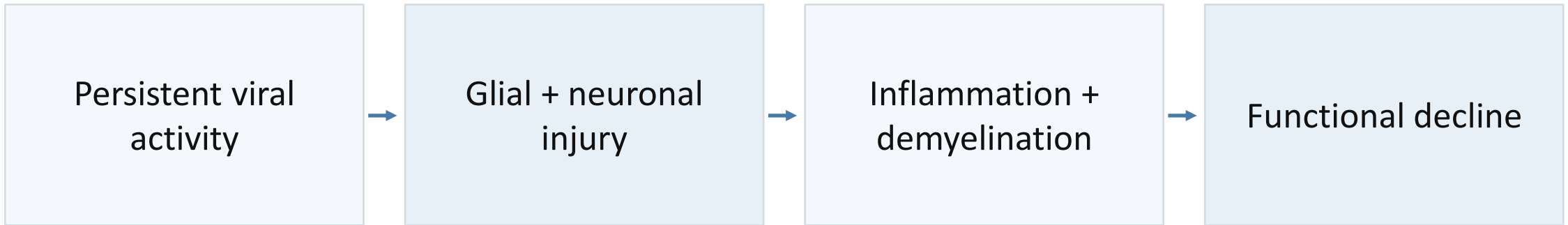
Demyelination is part of SSPE pathology, not its only tissue abnormality.

Neuronal injury produces irreversible deficits

- Neuronal dysfunction can precede frank tissue loss.
- Progressive neuronal loss helps explain advancing cognitive and motor impairment.
- Reactive astrogliosis and tissue sclerosis accompany chronic injury.
- The distribution and timing of injury vary among patients.

From persistent measles to panencephalitis

Mechanistic sequence



This is a teaching synthesis; Mechanisms are not a single proven linear pathway.

Early clinical disease can be deceptively subtle

- Declining school performance or altered work function may be the first sign.
- Personality change, poor concentration, or impaired memory can precede severe movement abnormalities.
- A normal early MRI or atypical EEG does not eliminate SSPE.
- Collateral history helps establish the slope of deterioration.

The cognitive and behavioral phenotype

- Memory, attention, executive function, and learning may deteriorate.
- Behavioral changes may be interpreted initially as psychiatric or educational problems.
- Progression over weeks to months should prompt assessment for organic brain disease.
- Clinical decline often becomes multi-domain rather than isolated.

Myoclonus is a characteristic bedside clue

- Sudden involuntary jerks may be generalized, focal, or segmental.
- Some patients exhibit periodic, stereotyped motor events.
- Myoclonus can produce repeated falls and loss of functional independence.
- The phenomenon may coincide with characteristic periodic EEG complexes.

SSPE has a broad movement-disorder spectrum

- Hyperkinetic features reported include dystonia, chorea, tremor, and tics.
- Hypokinetic manifestations include parkinsonism and rigidity.
- Ataxia and other coordination abnormalities may coexist.
- Atypical motor syndromes should not obscure the underlying progressive encephalopathy.

Seizures and epileptic phenomena

- Epileptic seizures can occur during SSPE and may be an early presentation.
- Not every abnormal jerk is equivalent to a discrete epileptic seizure.
- EEG helps characterize both periodic complexes and superimposed epileptic activity.
- Clinical–electrophysiologic correlation is essential for accurate interpretation.

Visual involvement expands the clinical spectrum

- Visual complaints or impaired visual processing can precede obvious cognitive decline.
- Retinal, optic nerve, and cortical visual manifestations have been described.
- Visual deterioration should trigger consideration of CNS pathology, not just ocular disease.
- An ophthalmic presentation may delay recognition of SSPE.

Progressive motor disability

- Increasing abnormal movements and rigidity impair activities of daily living.
- Spasticity, impaired gait, falls, and swallowing difficulties may develop.
- Late stages can include paralysis and loss of responsiveness.
- Functional decline reflects multifocal cerebral pathology.

The clinical course is progressive, not uniform

Early cognitive
change

Myoclonus / seizures

Rigidity and disability

Unresponsiveness

- 
- This ordered sequence is typical but not obligatory.
 - Relapsing, rapidly progressive, or atypical courses are reported.

Clinical stage I: Subtle higher-function loss

- Behavioral, personality, or intellectual changes predominate.
- School or occupational decline may exceed neurologic examination findings.
- Early-stage disease is easily misclassified as functional or psychiatric.
- Interpret stages as descriptive clinical constructs rather than rigid biologic phases.

Clinical stage II: Myoclonus and motor signs

- Myoclonic jerks become conspicuous in many typical cases.
- Motor coordination, gait, and seizure control may worsen.
- Functional dependence increases.
- Clinical staging systems vary; No single transition time is universal.

Clinical stage III: Severe neurologic impairment

- Rigidity, extrapyramidal signs, and progressive motor dysfunction become prominent.
- Communication and self-care may be profoundly impaired.
- Cognitive decline and swallowing or mobility problems increase care requirements.
- Advanced disease may involve profound cortical and subcortical dysfunction.

Clinical stage IV: Terminal dysfunction

- Patients may become unresponsive or enter a vegetative state.
- Severe rigidity, autonomic disturbances, and profound disability may occur.
- Supportive and palliative interventions become central to care.
- Disease is usually fatal despite occasional protracted courses.

Staging is descriptive—not a diagnostic test

- Not all patients traverse stages in textbook order.
- Fulminant presentations can compress the course.
- Unusual age, isolated seizures, or visual symptoms can mask early SSPE.
- Diagnostic reasoning must integrate laboratory and electrophysiologic evidence.

Recognize atypical presentations

- Acute or rapidly progressive clinical deterioration may occur.
- Some cases initially present with seizures, ataxia, visual impairment, or psychiatric features.
- Rare adult presentations complicate the age-based heuristic.
- Persistent suspicion is warranted when the objective findings converge.

Initial assessment: Three questions

- Is this a progressive encephalopathy rather than a stationary deficit?
- Is there remote measles exposure or residence in a setting with measles transmission?
- Are myoclonus, characteristic EEG activity, and intrathecal measles antibodies present?
- Investigate treatable alternatives in parallel.

Diagnostic workup should be convergent

Mechanistic sequence



No isolated positive serum measles IgG result establishes SSPE.

CSF examination: Why the antibody response matters

- CSF may have a normal or only mildly increased cellular count.
- Total protein and glucose can be relatively unremarkable.
- An elevated measles-specific antibody response is a central diagnostic feature.
- Assess paired serum and CSF when an antibody index is available.

Intrathecal synthesis versus passive transfer

- CSF measles IgG must be interpreted in the context of serum antibodies.
- Paired CSF and serum can support evidence of intrathecal measles-specific synthesis.
- A high serum measles IgG titer alone primarily documents previous immunity or infection.
- Laboratory methods and reference limits vary; Do not transpose thresholds across assays.

Serum seropositivity is not diagnostic

- Most vaccinated or previously infected people have measles antibodies.
- A positive serum assay therefore lacks disease specificity for SSPE.
- A compatible clinical syndrome plus a CSF-specific response is more informative.
- Avoid conflating evidence of prior exposure with evidence of current CNS disease.

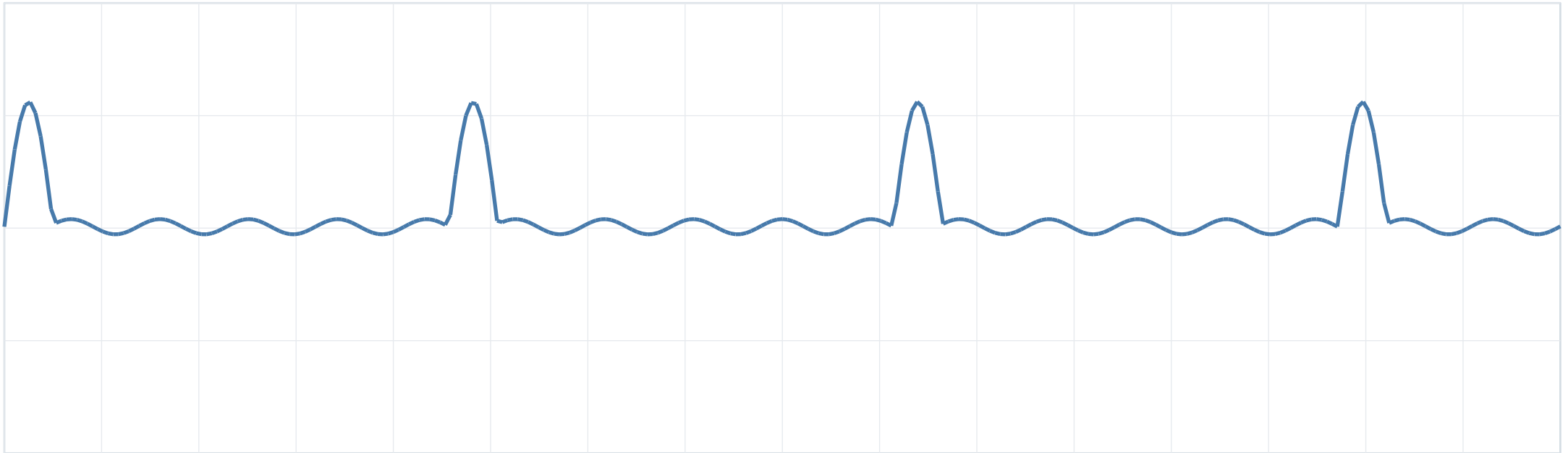
CSF virologic PCR has limitations

- CSF RNA testing may be negative despite proven SSPE.
- Predominantly cell-associated infection limits release of detectable viral material.
- Negative CSF measles PCR must not overrule compelling clinical and antibody evidence.
- Tissue molecular analysis is reserved for selected difficult cases.

Typical EEG: Periodic generalized complexes

- Classical periodic high-amplitude slow-wave complexes are termed Radermecker complexes.
- Events may be bilaterally synchronous and stereotyped.
- They can accompany periodic myoclonic jerks.
- Frequency and morphology vary by disease stage and patient.

What periodicity means on EEG



Stereotyped generalized complexes can recur at regular intervals; Clinical EEG patterns vary.

EEG pitfalls in the early or atypical course

- A normal or nonspecific EEG does not exclude early SSPE.
- Periodic complexes may be absent or atypical at an individual recording.
- Repetition and clinical correlation can be appropriate when suspicion remains.
- Consider seizures and metabolic or toxic encephalopathy as alternative explanations for periodicity.

MRI: Characteristic patterns, not a stand-alone test

- Initial MRI may be normal.
- T2/FLAIR white matter hyperintensities can emerge during disease evolution.
- Posterior subcortical and periventricular involvement is commonly described.
- Progressive cerebral atrophy may dominate later neuroimaging.

How imaging relates to pathology

- White-matter signal abnormalities are compatible with myelin and tissue injury.
- Atrophy is consistent with cumulative loss of brain parenchyma.
- Imaging distribution is variable and neither specific nor perfectly stage correlated.
- MRI should complement, not replace, clinical and CSF assessment.

Modified Dyken criteria: Major elements

Major: Clinical syndrome

- Typical progressive deterioration or recognized atypical clinical evolution.
- Includes unusual age or seizure-led presentations.

Major: Measles antibody evidence

- Elevated anti-measles antibodies, particularly in CSF.
- Assay-specific interpretation is essential.

Published modified criteria generally require both major elements plus supporting evidence.

Modified Dyken criteria: Ancillary elements

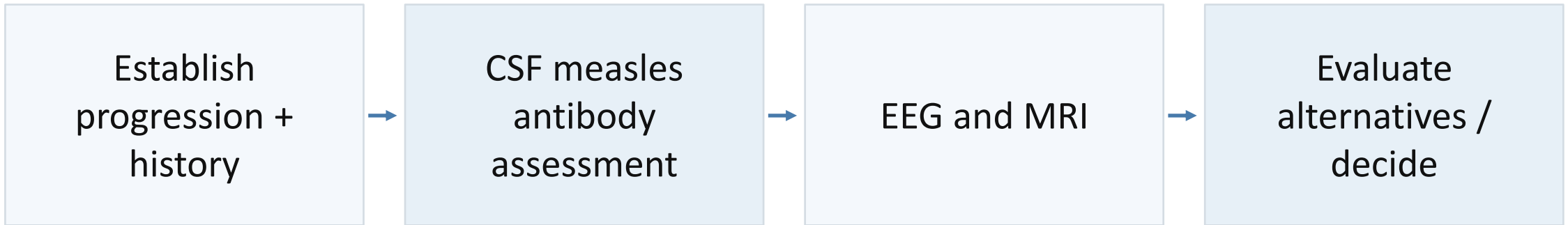
Supporting feature	Diagnostic contribution
EEG periodic complexes	Characteristic but not universally present
Increased CSF immunoglobulin / globulin	Evidence of intrathecal immune response
Compatible brain histopathology	Invasive confirmation in selected cases
Molecular demonstration of altered measles genome	Specialized confirmatory evidence

How to apply diagnostic criteria responsibly

- Use the published version of a criteria set consistently.
- The modified Dyken formulation is a structured framework, not an infallible gold standard.
- Serum titers, CSF assays, and ancillary test performance are context dependent.
- Cases with atypical features may require referral or specialized molecular/pathologic investigation.

Approach to a suspected case

Mechanistic sequence



The pattern of evidence matters more than an isolated test result.

Differential diagnosis: Progressive encephalopathy

Comparator	Shared features	Useful discriminators
Autoimmune encephalitis	Behavior change; Seizures	Time course, antibodies, CSF profile
ADEM	Encephalopathy; White-matter lesions	Postinfectious short latency; Acute inflammatory course
Progressive multifocal leukoencephalopathy	White-matter disease	Immunosuppression; JC polyomavirus context
Other prion / degenerative disorders	Rapid cognitive decline; Myoclonus	Age, course, CSF/EEG and disease-specific testing

ADEM versus SSPE after measles

- ADEM is primarily a monophasic immune-mediated demyelinating disorder.
- ADEM arises much closer to the inciting infection than SSPE.
- SSPE typically has a years-long latency and progressively worsening course.
- Measles-specific intrathecal antibodies and classical periodic EEG support SSPE.

PML versus SSPE

- Both can produce progressive neurologic deficits and abnormal white matter.
- PML is associated with JC polyomavirus, especially in immunosuppressed hosts.
- SSPE links to remote measles infection and progressive cognitive–myoclonic syndrome.
- Etiologic testing and host history distinguish the disorders.

The brain lesion is a panencephalitis

- Grey matter and white matter can both be affected.
- Microscopic inflammation involves the neuropil and perivascular compartments.
- Demyelination and neuronal pathology coexist.
- The name captures widespread inflammatory–degenerative involvement.

Gross pathology may be nonspecific

- Gross abnormalities are not required for an early diagnosis.
- Advanced cases may show reduced brain volume and cortical atrophy.
- Distribution and severity reflect duration and affected CNS regions.
- Microscopy, immunostaining, and clinical–laboratory data are more discriminating.

Histologic compartments of injury

Grey-matter pathology

- Neuronal loss and reactive gliosis.
- Perivascular lymphocytes and viral inclusions may occur.

White-matter pathology

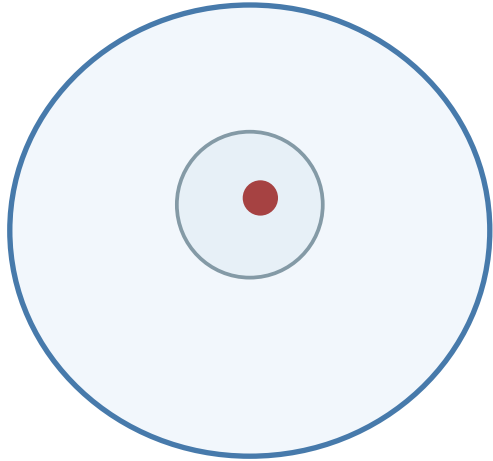
- Variable demyelination and astroglial sclerosis.
- Oligodendroglial infection and inflammation may be detected.

True pathologic confirmation requires patient tissue—not a schematic.

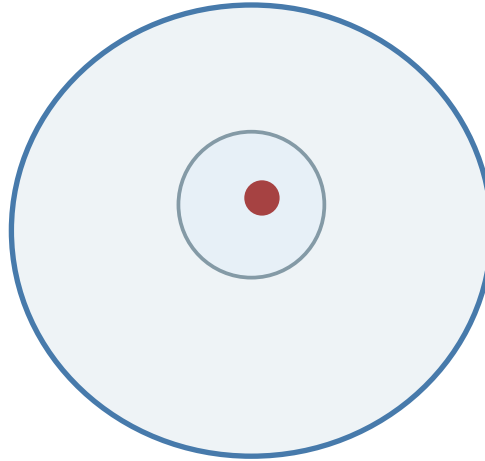
Inclusion bodies: What pathologists recognize

- Viral inclusions may be identified in neuronal and glial nuclei or cytoplasm.
- They reflect accumulated viral material, including nucleocapsid components.
- Inclusions are supportive but can be focal and stage dependent.
- An inclusion alone is not pathognomonic without pathogen-specific evidence.

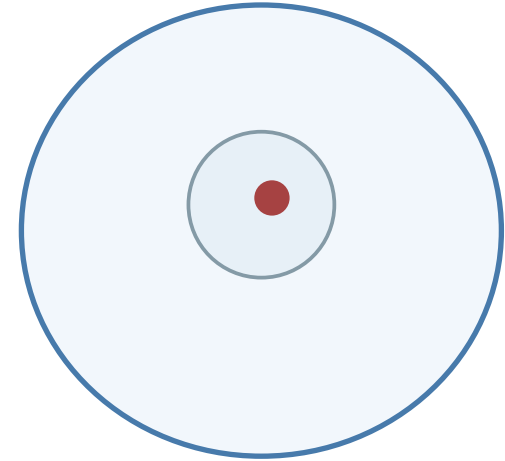
Viral inclusion concept (schematic cells)



Neuron



Oligodendrocyte



Astrocyte

Simplified cell schematic — not a histologic image

Immunohistochemistry and molecular pathology

- Measles antigen can be localized within infected brain cells.
- In situ hybridization or tissue RNA assays may document measles viral genome.
- Distribution of viral antigen and RNA can differ with stage and sampling.
- Use validated laboratory methods and adequate controls; Tissue testing is not routine first line.

Why brain biopsy is usually avoided

- A compatible clinical course with supportive CSF and EEG evidence may suffice.
- Brain biopsy is invasive and can be affected by sampling error.
- Neuropathologic confirmation is considered in unusual or diagnostically unresolved cases.
- Biopsy decisions require individualized risk–benefit assessment.

Prognosis: Progressive and frequently fatal

- SSPE causes cumulative neurologic disability in the usual course.
- Most affected patients eventually become severely dependent and unresponsive.
- Rapid, prolonged, and occasionally fluctuating courses are documented.
- Prognostic counseling should acknowledge individual variability without minimizing severity.

No established curative therapy

- SSPE as lacking effective treatment.
- No regimen has convincingly demonstrated a reliable cure.
- Investigated approaches include inosine pranobex, interferon- α , and antivirals.
- Evidence is heterogeneous; Experimental use requires specialist evaluation.

How to read the treatment literature

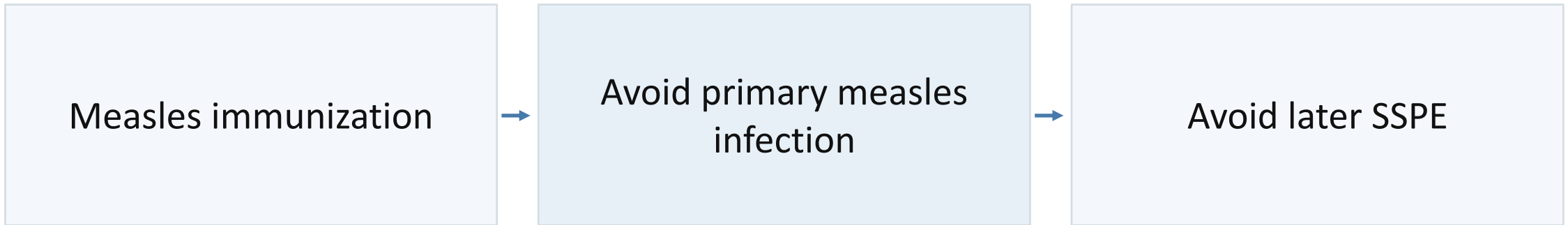
- Small cohorts and nonrandomized series limit causal conclusions.
- Survival differences can reflect stage, referral, and selection bias.
- Some reports describe temporary stabilization rather than eradication of disease.
- Treat investigational claims separately from established standard of care.

Supportive and palliative treatment

- Manage seizures, myoclonus, spasticity, and pain according to clinical needs.
- Address nutrition, swallowing safety, mobility, and pressure injury prevention.
- Provide rehabilitation support and anticipatory guidance where appropriate.
- Early family-centered goals-of-care discussion is essential in advanced illness.

Prevention acts before the silent interval begins

Mechanistic sequence



Vaccination is the effective population-level prevention strategy.

Case A: The diagnostic pattern

A school-age child has declining performance, personality change, recurrent sudden jerks, and a history of measles in early childhood. Routine MRI is initially unremarkable.

Discussion

- Which two investigations would most directly support SSPE?
- Why does a normal early MRI not rule it out?

Case A: Integrated interpretation

- Order CSF measles-specific antibodies, ideally with paired serum assessment.
- Obtain an EEG for periodic generalized complexes and seizure characterization.
- The clinical history and years-long latency substantially increase suspicion.
- Normal early MRI is compatible with SSPE; Continue differential workup.

Case B: An atypical presentation

An adolescent presents with progressive visual decline and episodic seizures. MRI demonstrates nonspecific posterior white-matter changes. Serum measles IgG is positive.

Discussion

- Why is positive serum IgG insufficient?
- What additional evidence would distinguish SSPE from its mimics?

Case B: Avoid premature closure

- Serum measles IgG is common after vaccination or previous infection.
- Assess clinical trajectory and measles-specific intrathecal antibody evidence.
- EEG may be typical, atypical, or nondiagnostic; Interpret dynamically.
- Evaluate inflammatory, infectious, and autoimmune alternatives concurrently.

Application: Five high-value discriminators

- Delay of years after measles, not days.
- Progressive cognitive or behavioral impairment, often with myoclonus.
- Measles-specific CSF antibody response, not serum immunity alone.
- Often periodic EEG complexes, but variable early findings.
- Panencephalitis with neuronal inclusions, gliosis, and demyelination when tissue is examined.

Clinicopathologic synthesis

- A persistent measles-related process injures both neurons and glia.
- Inflammation, demyelination, gliosis, and neuronal loss underlie progressive dysfunction.
- Diagnosis combines clinical context, CSF immune evidence, and ancillary tests.
- No established cure exists; Vaccination prevents the antecedent infection.

Selected primary and authoritative references

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Further reading and evidence notes

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Textbook scope is narrower than the supplementary review literature; edition-dependent diagnostic details are explicitly sourced in presenter notes.

Original chapter PDF and licensed histology images were not available for source-image verification in this build.