

Neural Tube Defects

Developmental mechanisms · Morphology · Clinicopathologic consequences

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Learning outcomes

- Explain the two distinct developmental pathways to neural tube defects.
- Classify lesions by site and by whether meninges or neural tissue is displaced.
- Connect structural abnormalities to neurologic effects and infection risk.
- Describe the evidence and timing of folate-related prevention.

Neural tube defects are midline malformations

- Neural tissue, meninges, overlying bone and soft tissue may be affected together.
- These abnormalities form the most common group of CNS malformations.
- The physical lesion is often a combination of defects rather than an isolated one.

Overlying soft tissue / skin

Bone / vertebral arch or calvarium

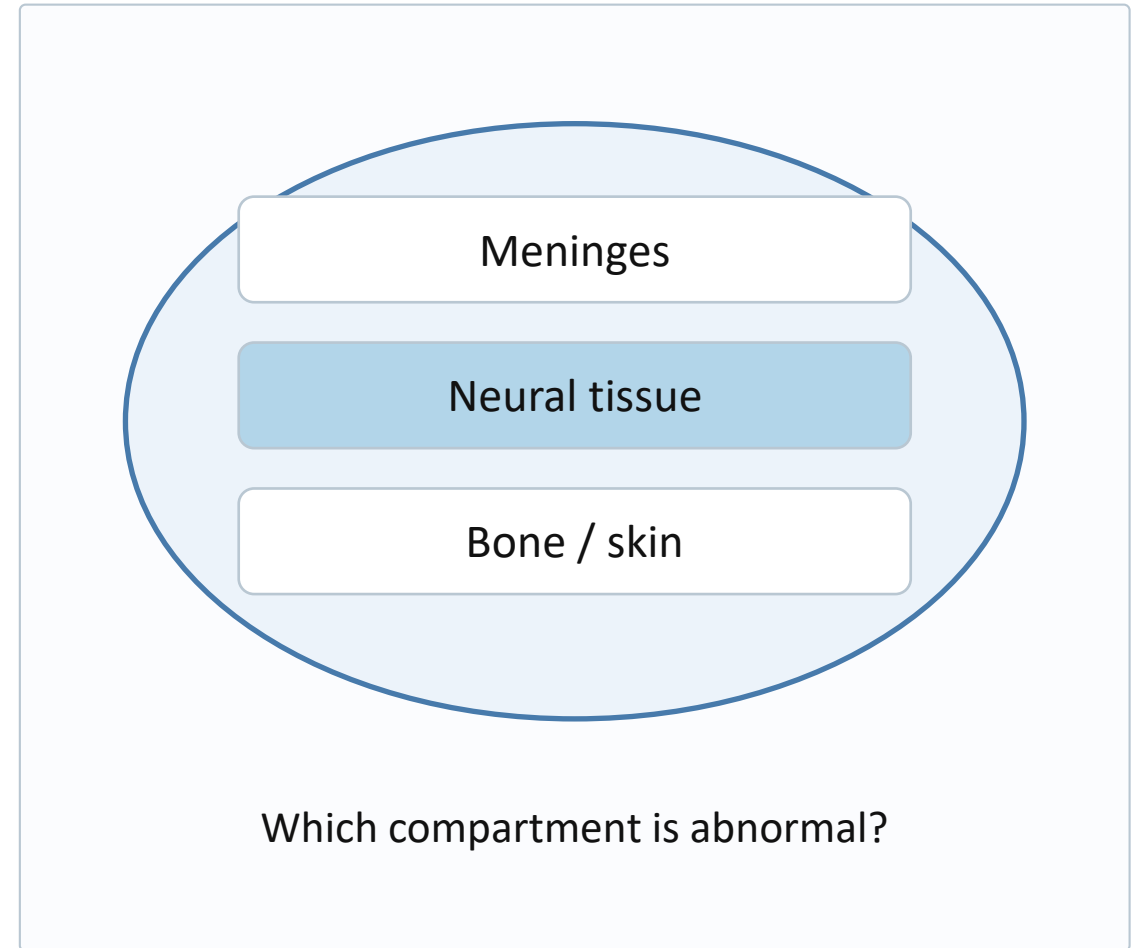
Meninges

Neural tissue

Any combination may be malformed

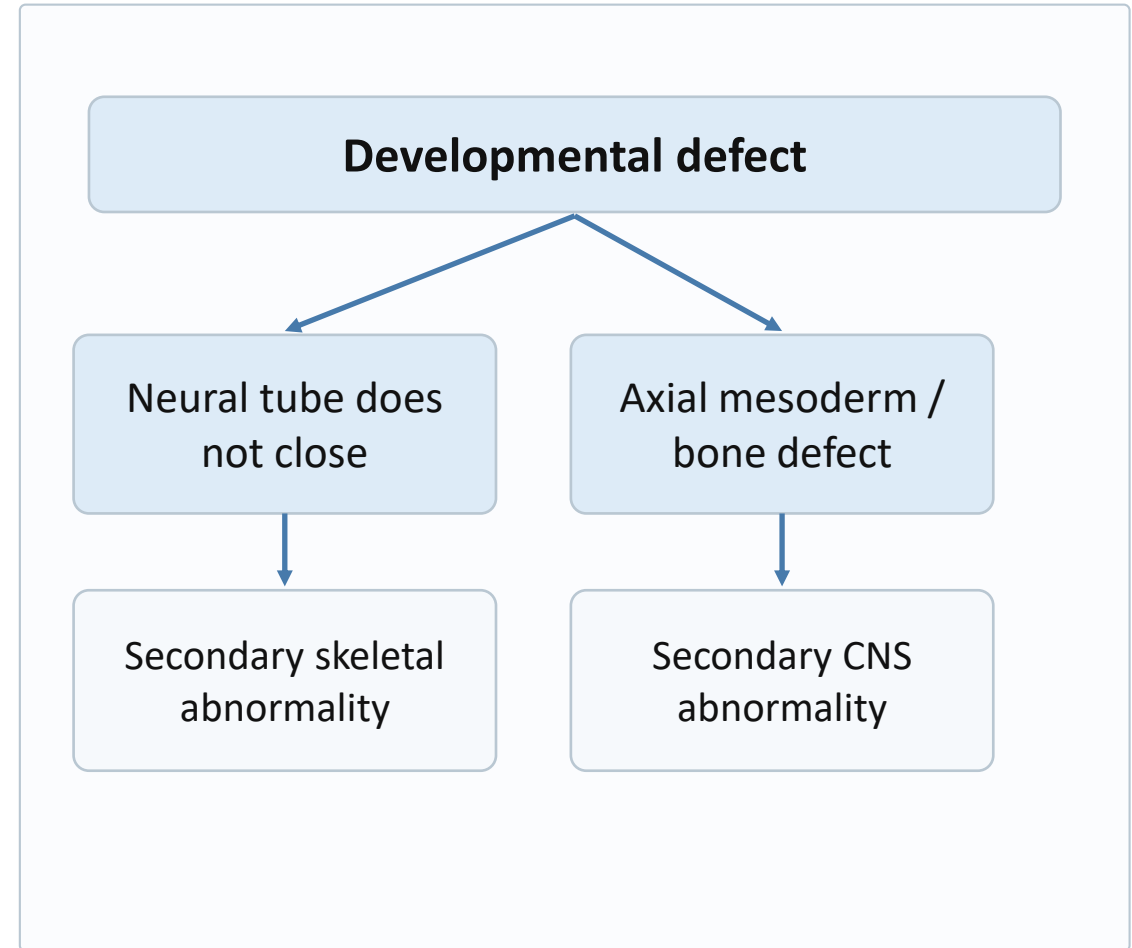
Why the tissue layers must be considered together

- A surface defect may conceal involvement of the meninges or nervous tissue.
- A bony defect does not, by itself, specify what is present in a protruding sac.
- Morphologic naming is based on the affected anatomic compartments.



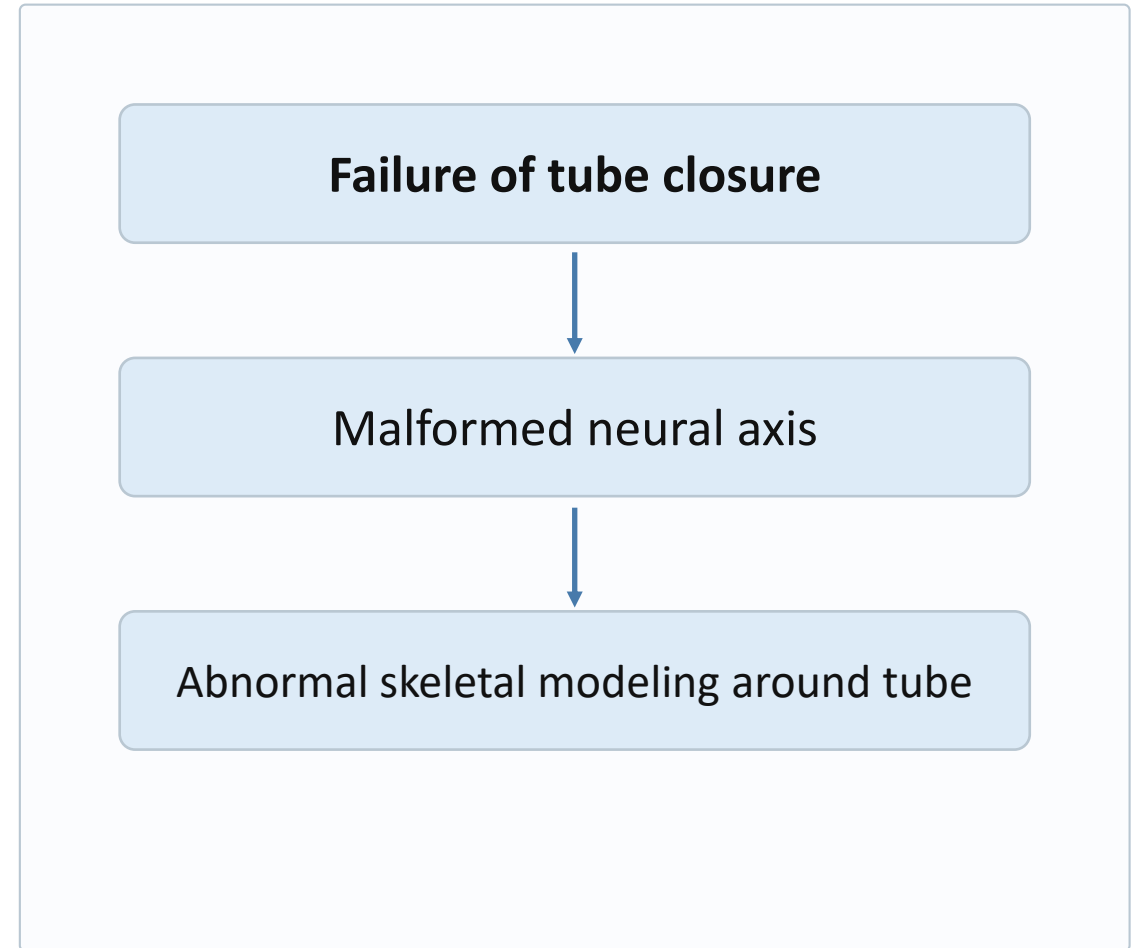
Two developmental routes converge on midline defects

- Route 1: Neural tube closure fails; Skeletal abnormalities develop secondarily.
- Route 2: Abnormal axial mesoderm produces a primary bony defect.
- Both routes can lead to composite CNS and supporting-tissue malformations.



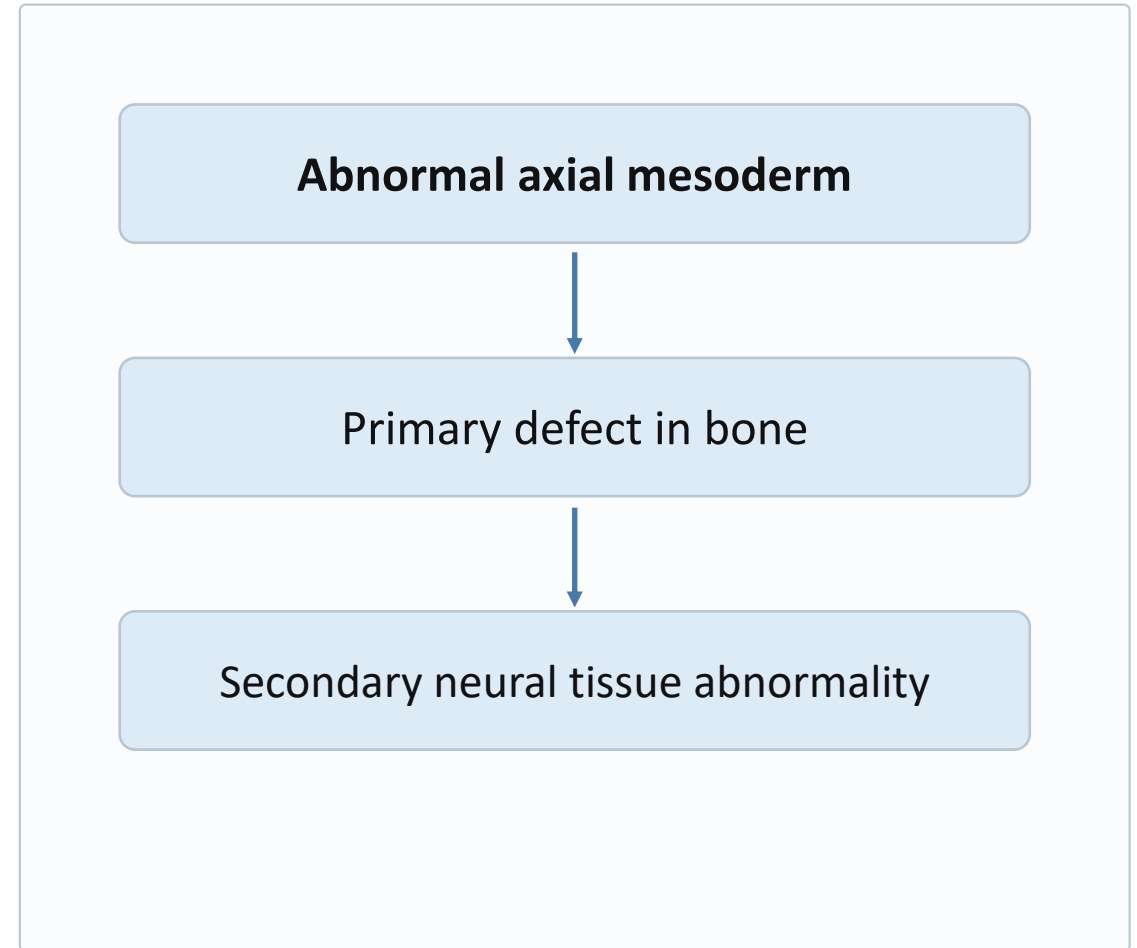
Neural tube closure failure: The primary event

- A malformed neural tube is the initial developmental abnormality.
- Aberrant skeletal modeling develops around the malformed tube.
- Anencephaly and myelomeningocele are the textbook examples.



Primary mesodermal defect: The alternative route

- An abnormal axial mesoderm disrupts formation of the bony midline.
- Neural structures are then affected secondarily by the skeletal defect.
- Encephalocele, meningocele and spina bifida illustrate this pathway.

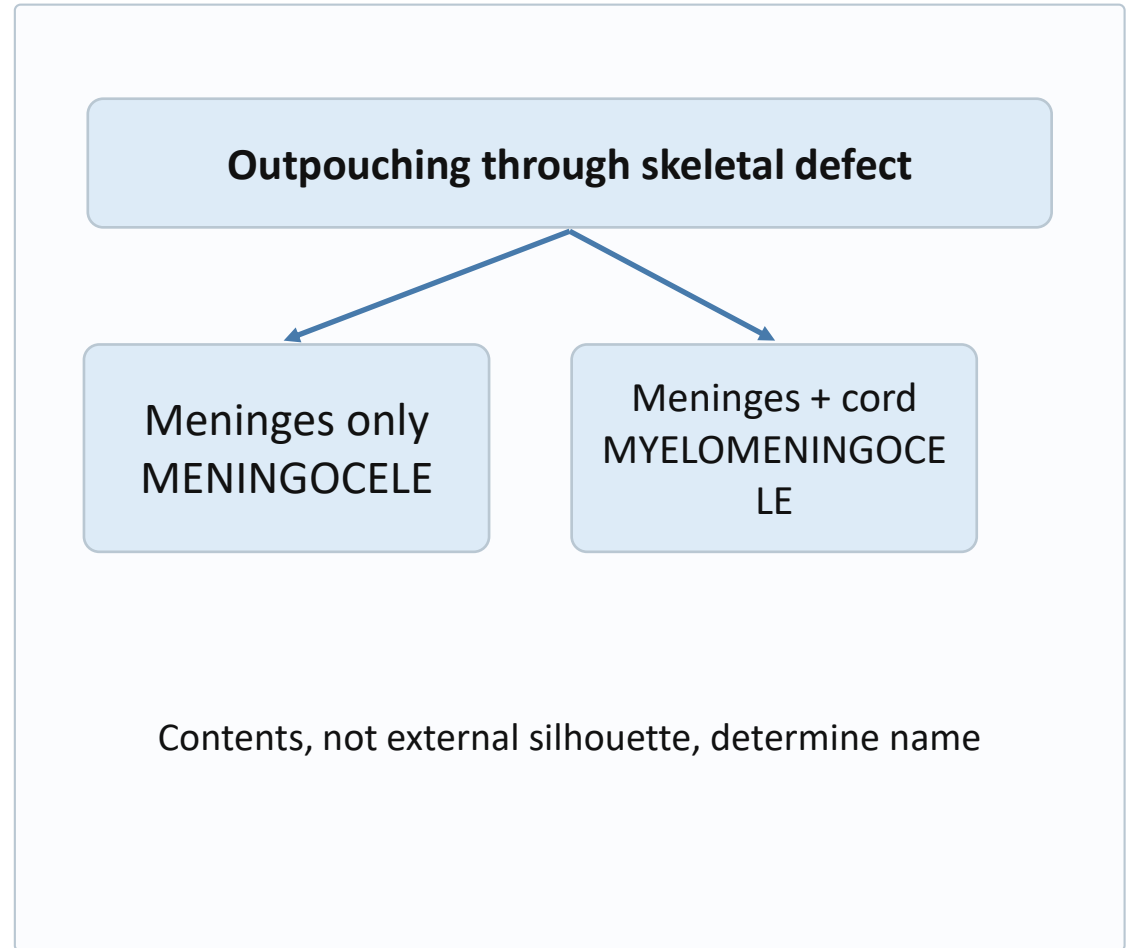


Mechanism comparison: What fails first?

Feature	Neural closure failure	Primary skeletal defect
Initial problem	Closure of neural tube	Axial mesoderm / bone development
Secondary abnormality	Skeletal modeling	CNS structures
Robbins examples	Anencephaly; Myelomeningocele	Encephalocele; Meningocele; Spina bifida

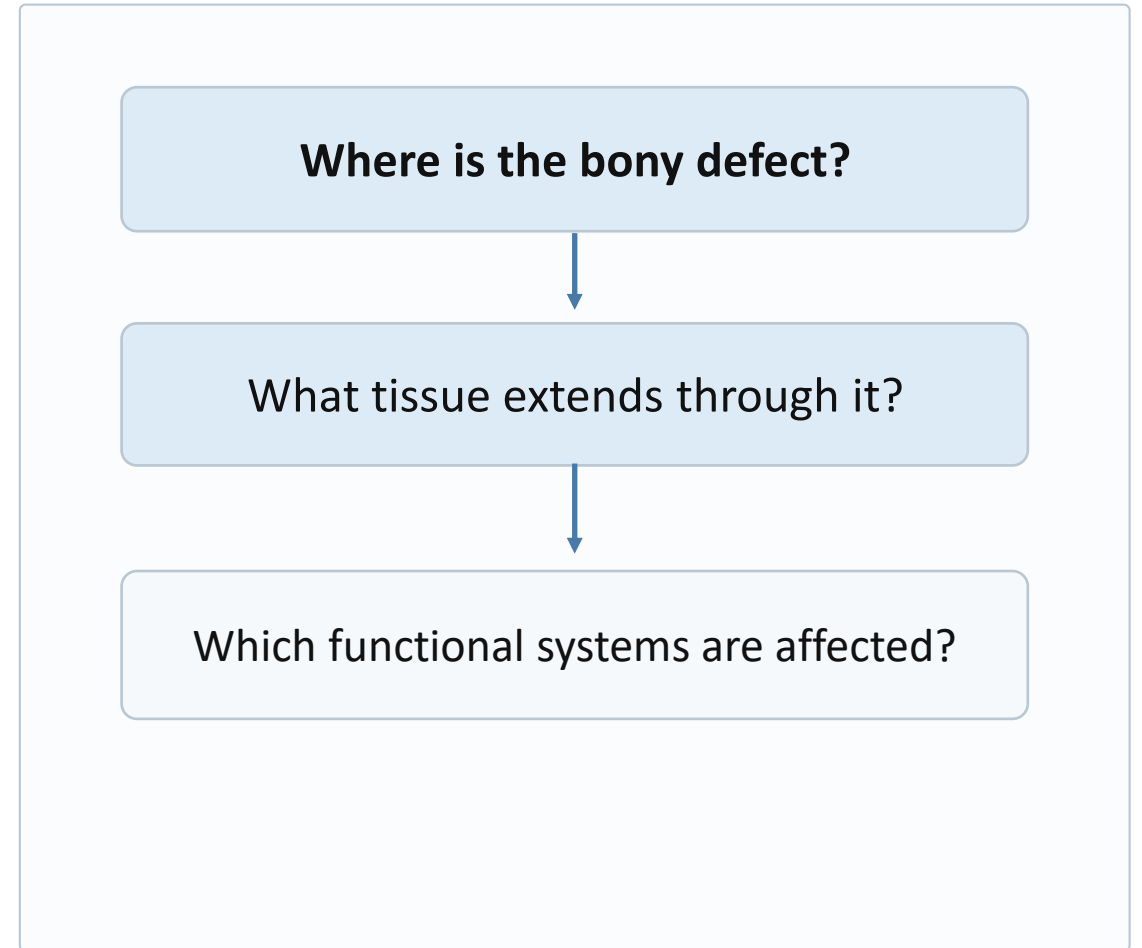
The same surface site may imply different lesion contents

- External location helps orient the defect but does not fully classify it.
- Both may contain meninges;
Myelomeningocele additionally contains spinal cord.
- A sac containing cord parenchyma establishes neural tissue involvement.



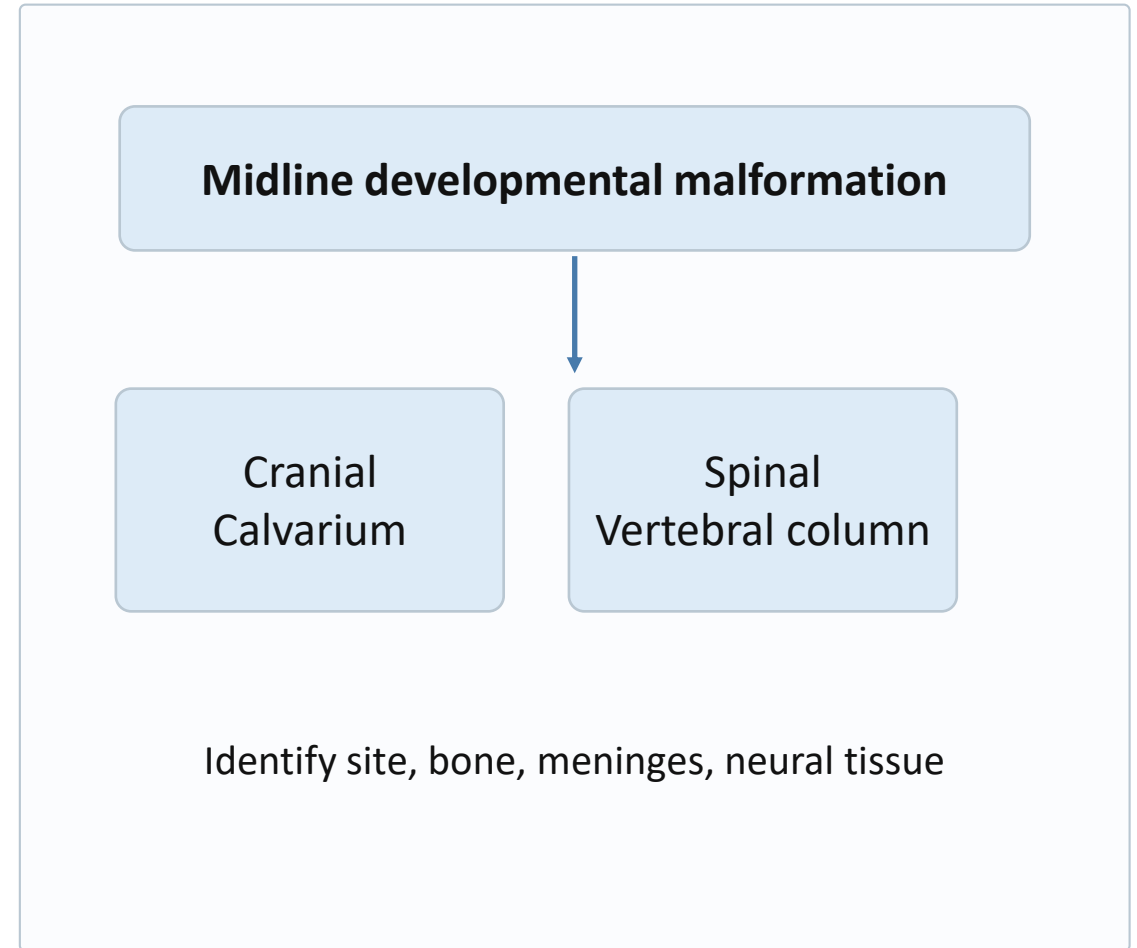
Start classification with anatomy—not a label

- First localize the defect: Cranial or vertebral midline.
- Then identify involved bone, meninges, neural tissue and skin.
- Finally, interpret clinical dysfunction according to the involved neural level.



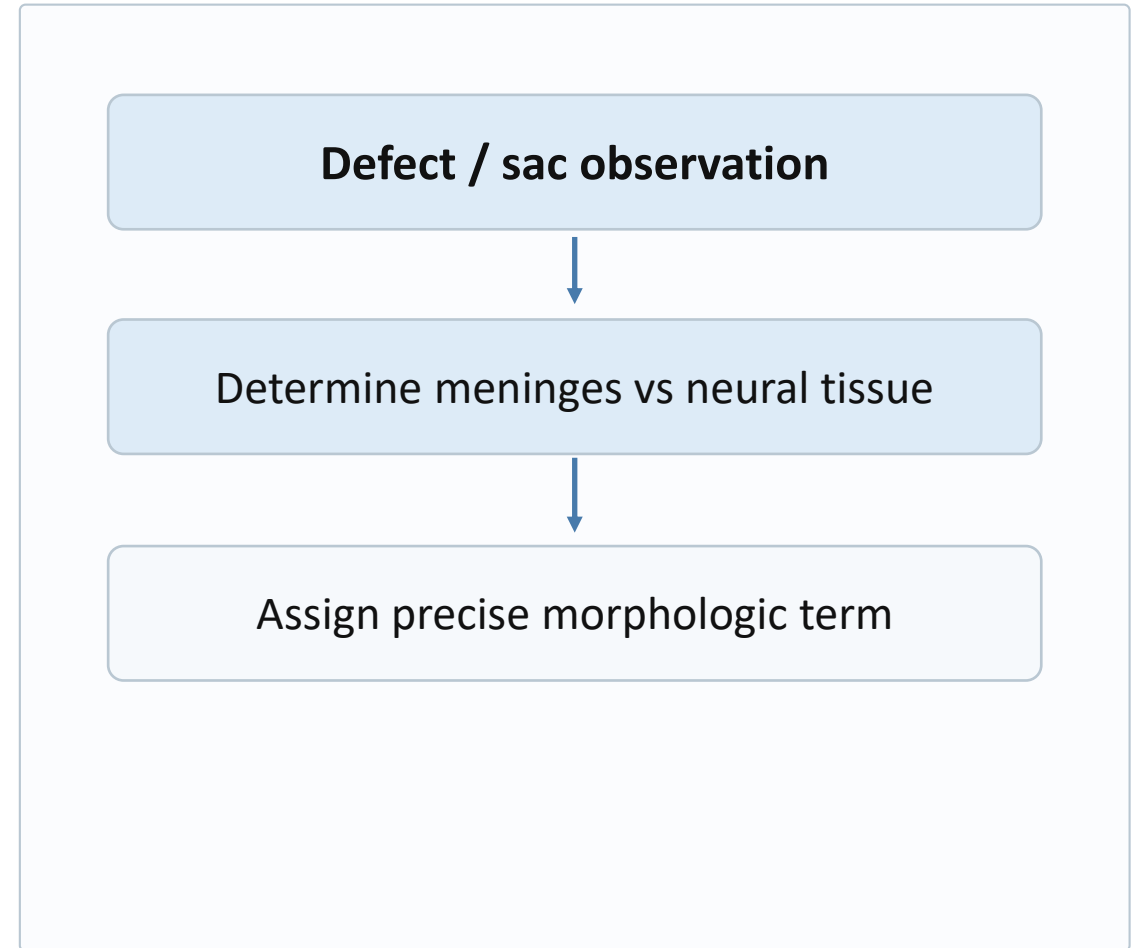
Cranial and spinal defects share a developmental theme

- Cranial forms involve calvarial and brain relationships.
- Spinal forms involve vertebral arches, meninges and spinal cord.
- The common denominator is an abnormal midline developmental interface.



Anatomic vocabulary controls the diagnosis

- -cele denotes an outpouching or protrusion in the named lesions.
- Meninges refer to protective coverings; Myelo- identifies spinal neural tissue.
- Encephalo- identifies brain tissue, allowing meaningful differentiation.

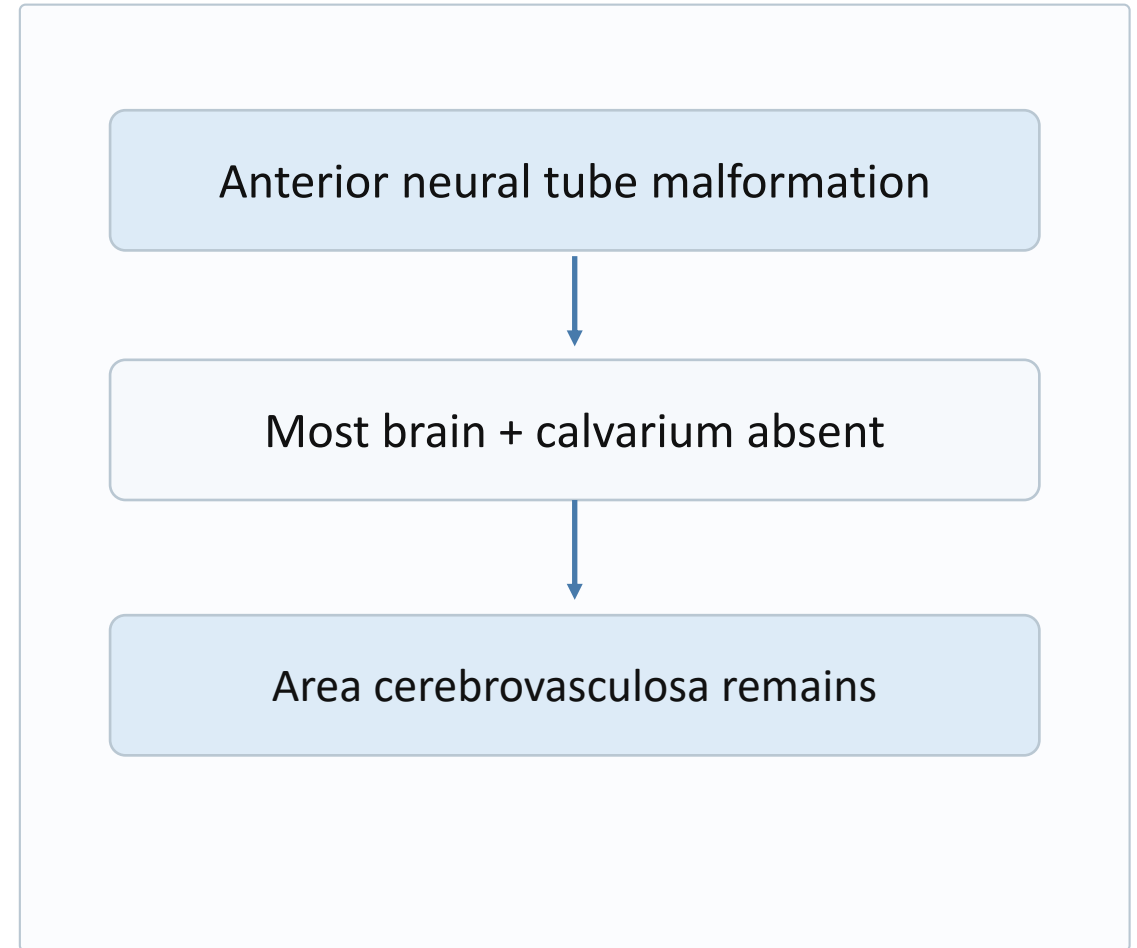


Major neural tube defect phenotypes

- Anencephaly: Major absence of brain and calvarium.
- Myelomeningocele and meningocele: Spinal meningeal / neural extrusion.
- Encephalocele: Brain tissue through a cranial defect.
- Spina bifida: Broad spinal dysraphism spectrum.

Anencephaly begins at the anterior neural tube

- A defect in anterior neural tube development disrupts formation of the forebrain.
- This disruption at approximately day 28 of gestation.
- The resulting pathology involves both neural structures and calvarium.



Anencephaly: The defining gross anatomy

- Most of the brain is absent.
- Most of the cranial vault (calvarium) is absent.
- A flattened remnant of disorganized tissue remains rather than a developed forebrain.

Anterior neural tube malformation



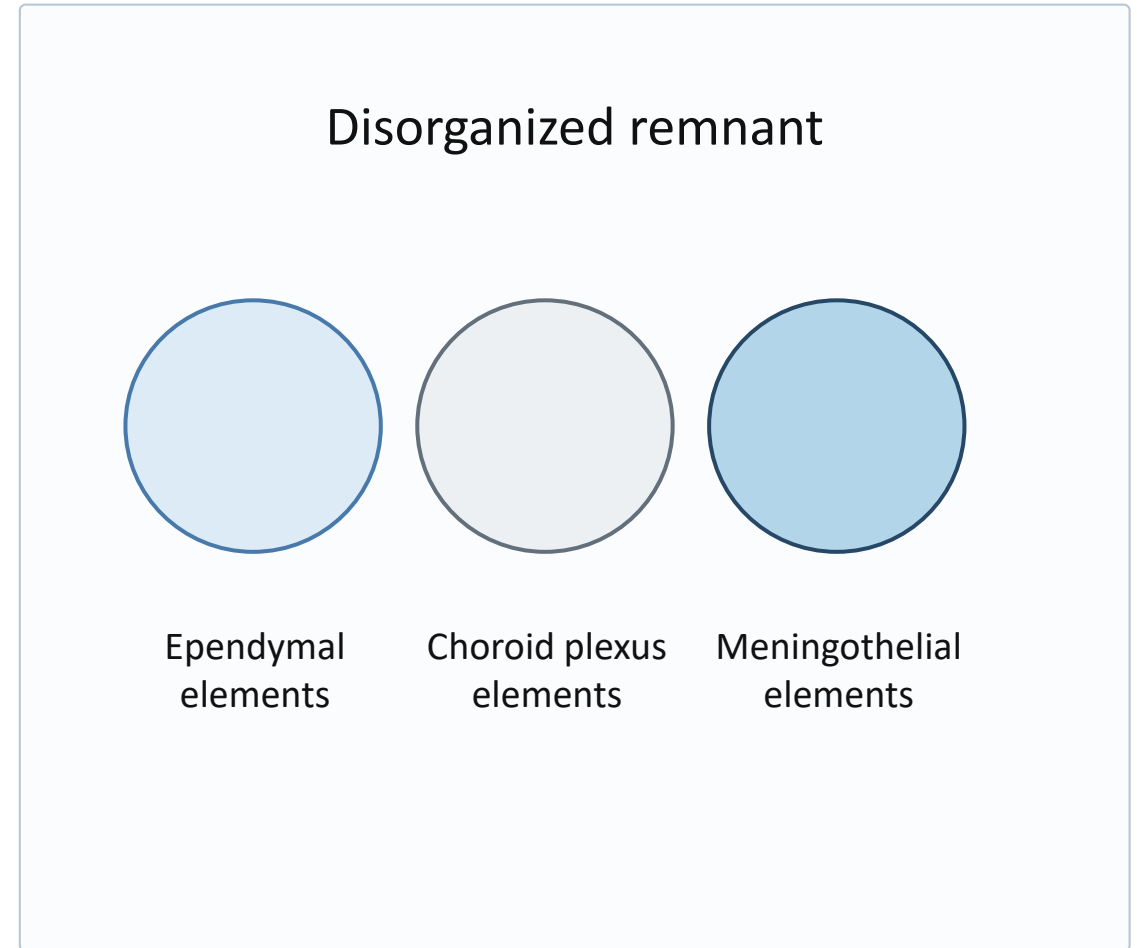
Most brain + calvarium absent



Area cerebrovasculosa remains

Area cerebrovasculosa: The residual tissue

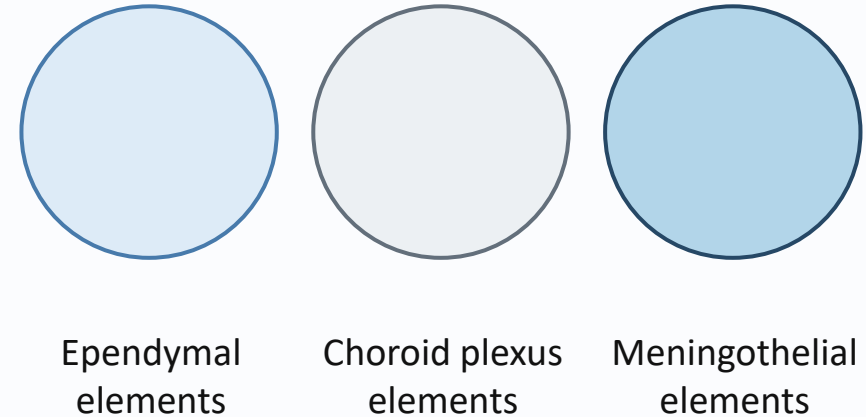
- The residual flattened tissue is termed the area cerebrovasculosa.
- It is disorganized rather than a normally laminated cortical structure.
- Its cellular admixture supports the diagnosis of a disrupted developmental field.



Area cerebrovasculosa is histologically heterogeneous

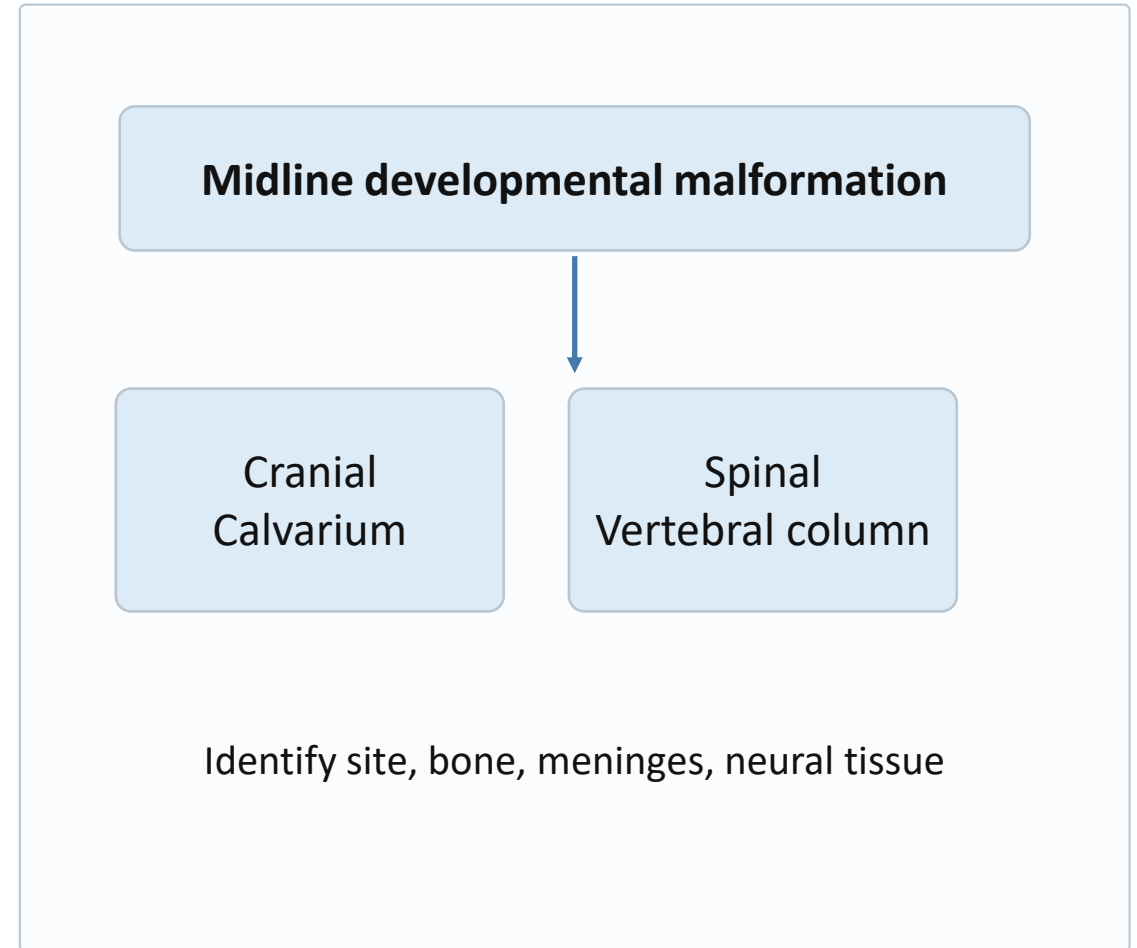
- Ependymal elements may be present in the remnant.
- Choroid plexus components may be admixed.
- Meningothelial cells are also described.
- The combination is not equivalent to a formed cerebral hemisphere.

Disorganized remnant



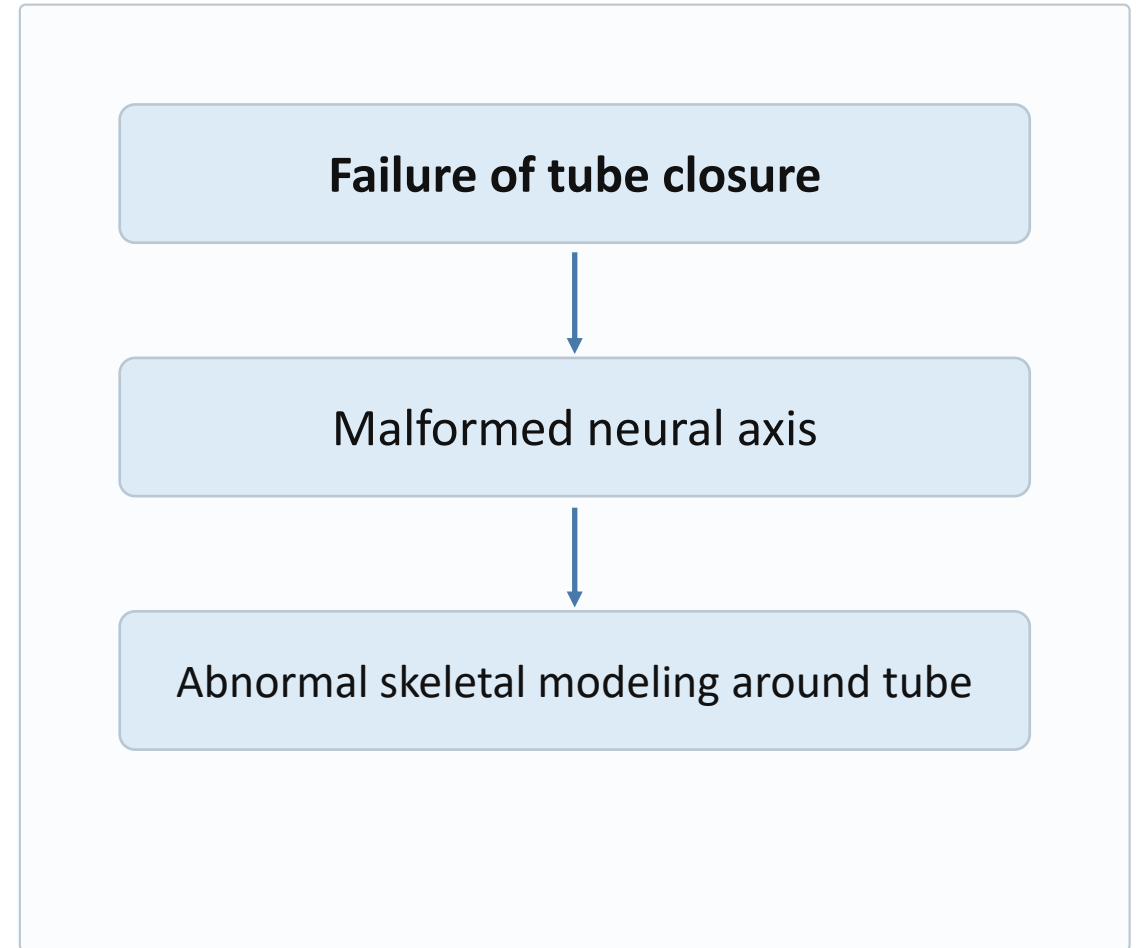
Posterior fossa preservation may vary in anencephaly

- Posterior fossa structures are not uniformly absent.
- Their preservation depends on the extent of the cranial defect.
- Thus, the term anencephaly does not mean all intracranial structures are invariably missing.



The missing forebrain also means missing connections

- Descending tracts arising from disrupted structures are absent.
- Structural loss therefore extends beyond the visible brain remnant.
- Functional expectations must follow the anatomy that did not develop.

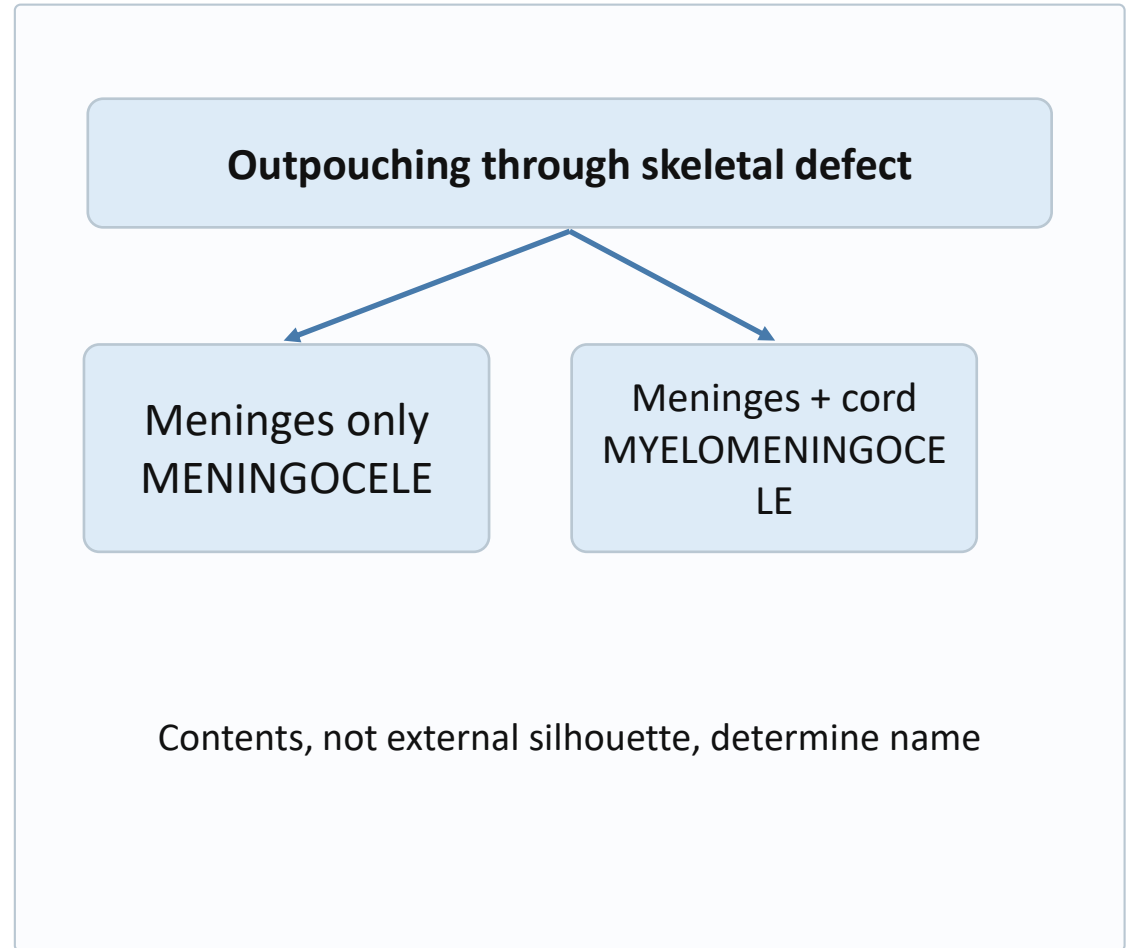


Morphologic checklist for recognizing anencephaly

- Anterior neural tube developmental abnormality.
- Loss of most brain substance and calvarium.
- Residual disorganized area cerebrovasculosa.
- Variable preservation of posterior fossa structures.

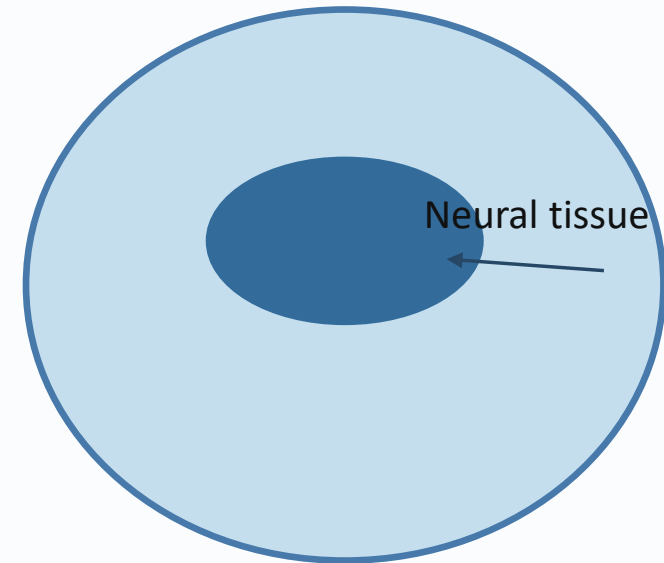
Myelomeningocele: Spinal cord tissue in the sac

- Spinal cord parenchyma protrudes through a defect in the vertebral column.
- The meningeal covering accompanies the neural tissue.
- The neural component distinguishes myelomeningocele from meningocele.



The neural component is diagnostically decisive

- Do not equate every lumbosacral sac with myelomeningocele.
- Identify whether cord tissue is incorporated in the protruding structure.
- A meningeal sac without spinal cord protrusion is termed meningocele.

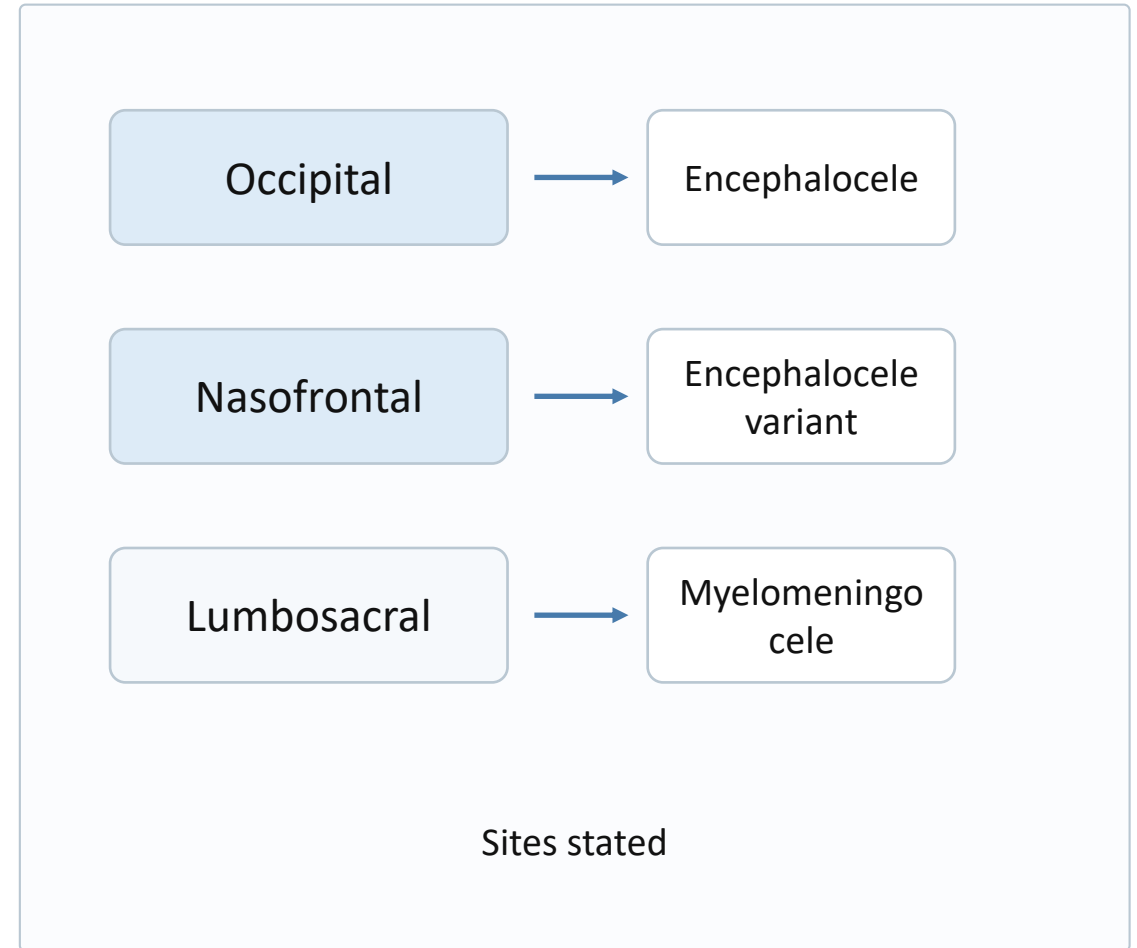


Meningeal covering

Schematic representation of sac contents

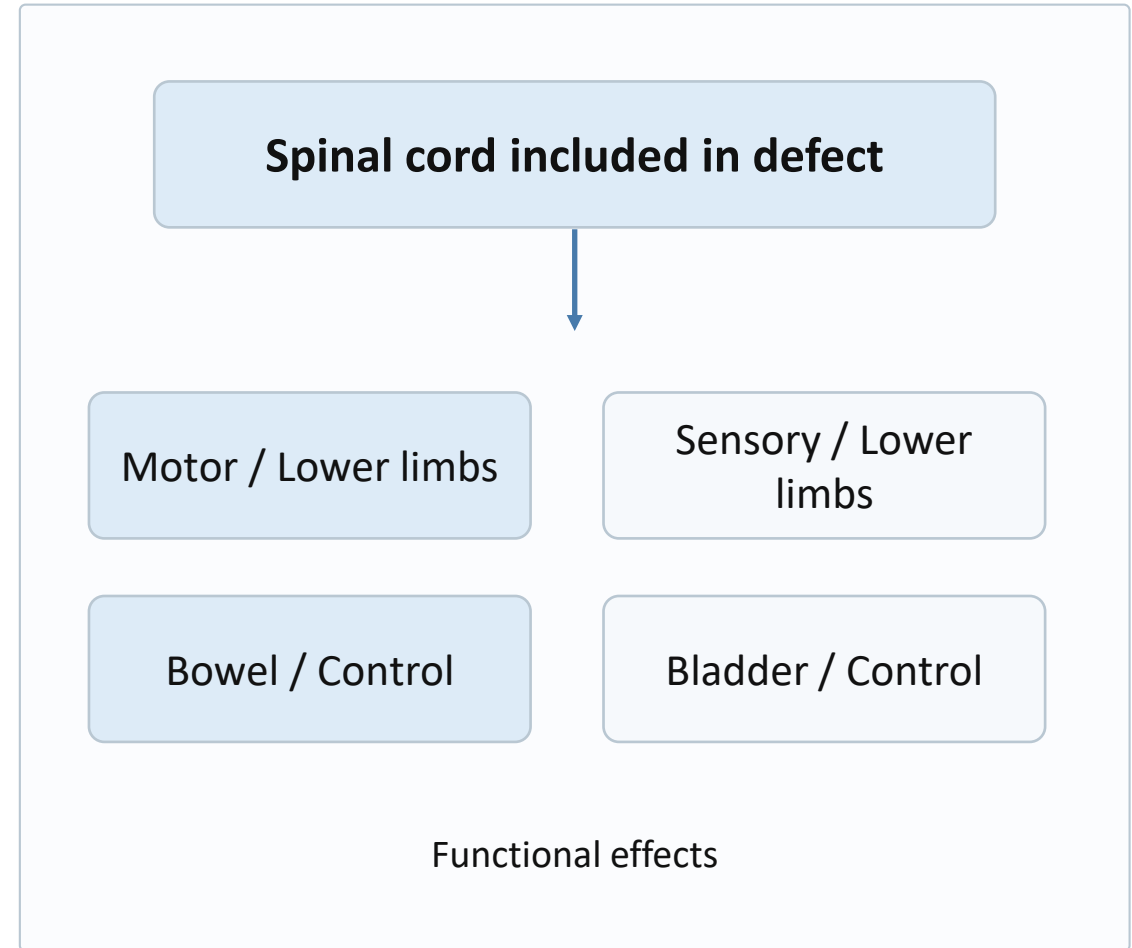
Myelomeningoceles favor the lumbosacral region

- The lumbosacral region as the commonest site.
- The location places developing spinal neural structures at risk.
- Level and tissue involvement help explain downstream neurologic deficits.



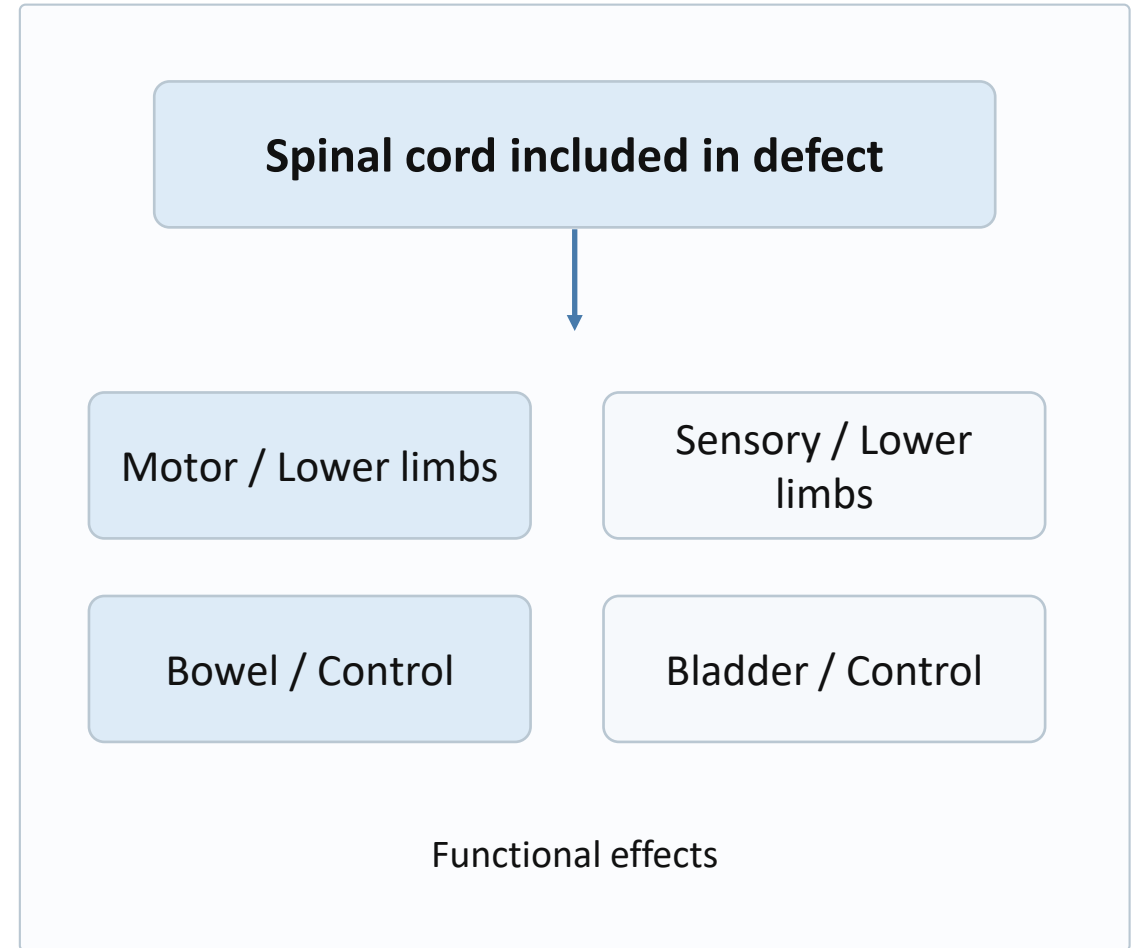
Motor impairment follows spinal cord involvement

- Affected individuals can have lower-extremity motor deficits.
- The deficit is a neural consequence of the malformed spinal cord.
- The external sac is therefore not merely a superficial skin abnormality.



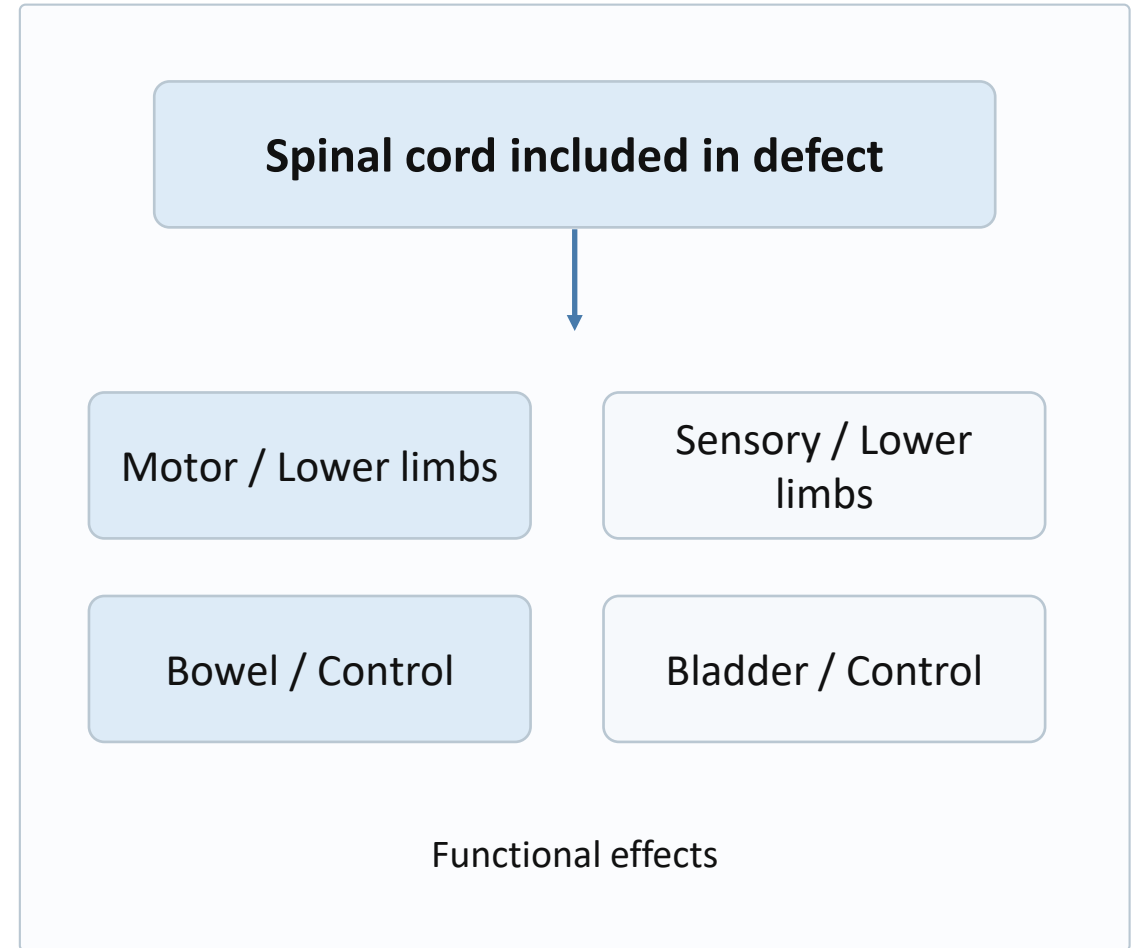
Sensory loss is another consequence of neural injury

- Myelomeningocele may affect lower-extremity sensation.
- Motor and sensory abnormalities may coexist.
- Assessing both domains is necessary to characterize the neurologic burden.



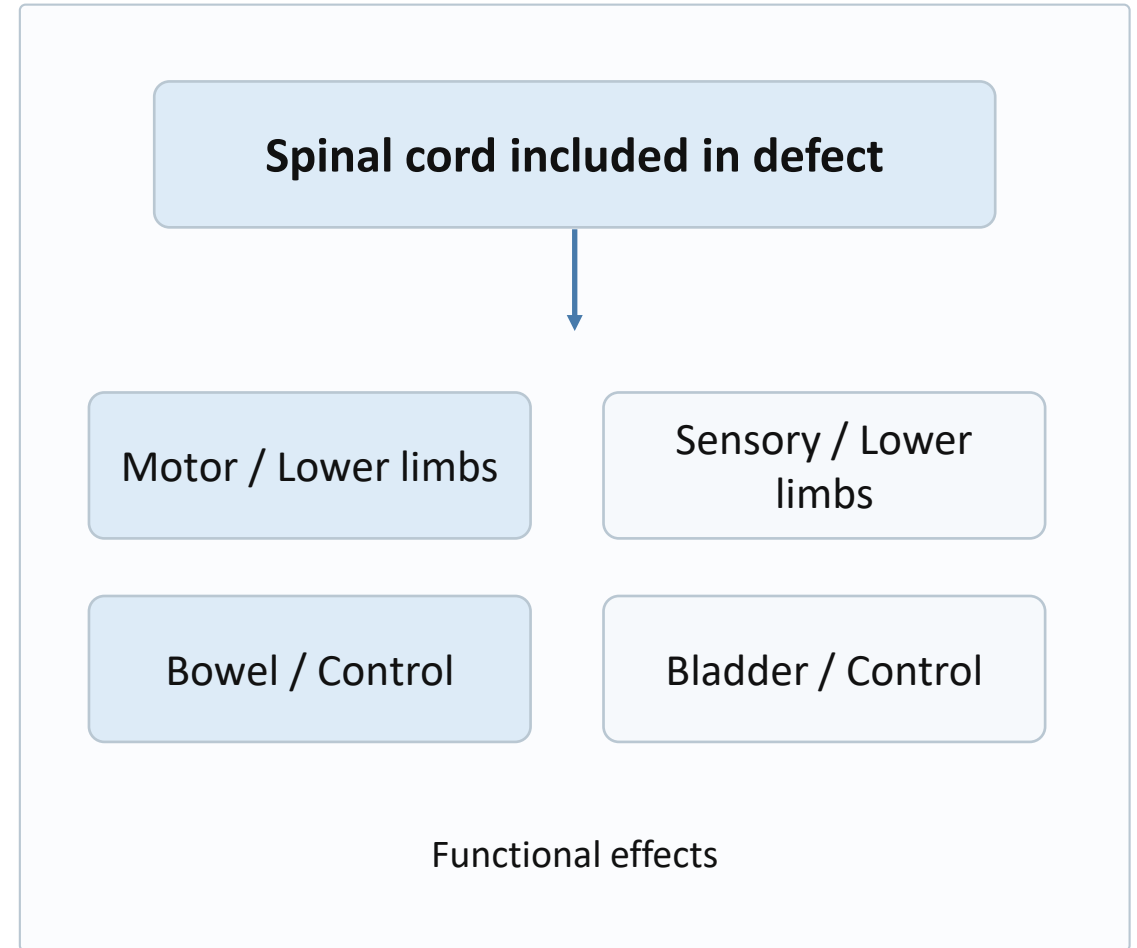
Bowel dysfunction reflects spinal involvement

- Disturbed bowel control is a recognized manifestation.
- This consequence may accompany limb motor or sensory findings.
- The lesion has functional effects beyond the visible anatomic defect.



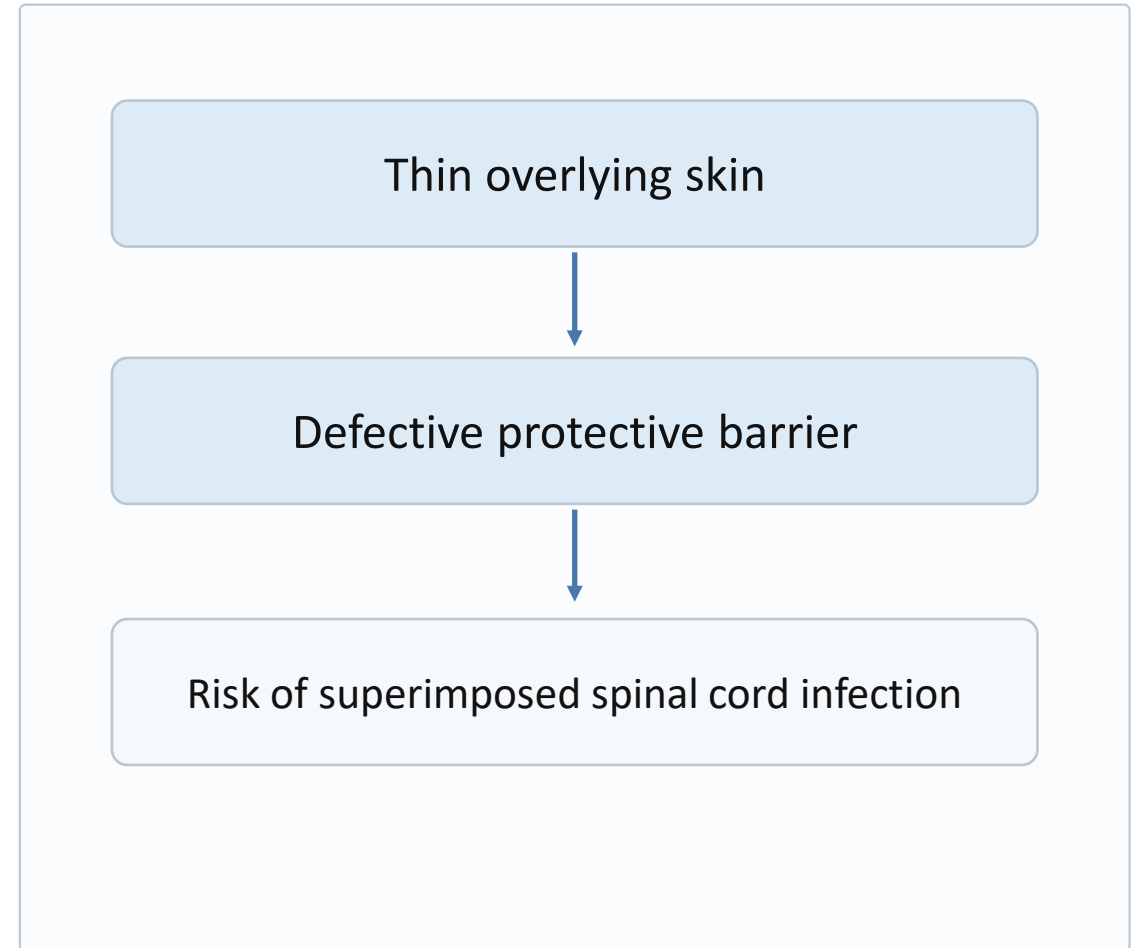
Bladder dysfunction is a core clinical consequence

- Disturbed bladder control accompanies many myelomeningoceles.
- Bowel and bladder dysfunction should be evaluated together.
- Morphologic involvement of spinal cord tissue explains why pelvic organ function is affected.



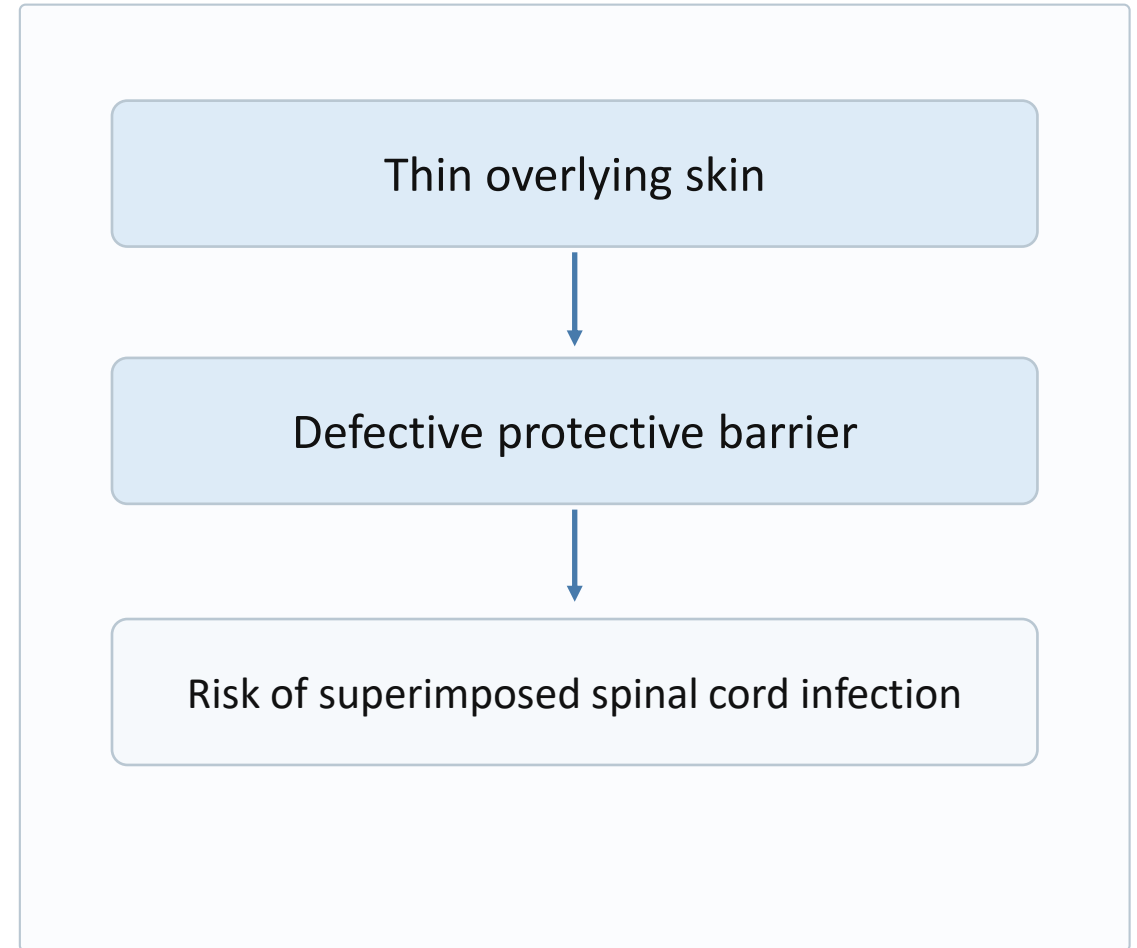
Barrier failure explains susceptibility to infection

- The overlying skin may be thin and insufficient as a barrier.
- Defective barrier function allows vulnerability of exposed spinal tissues.
- Superimposed spinal cord infection.



Neural loss and infection are distinct injury pathways

- Congenital malformation accounts for neurologic abnormalities present with the defect.
- Infection is a potential superimposed complication of poor tissue coverage.
- Distinguishing primary from secondary injury clarifies clinicopathologic interpretation.

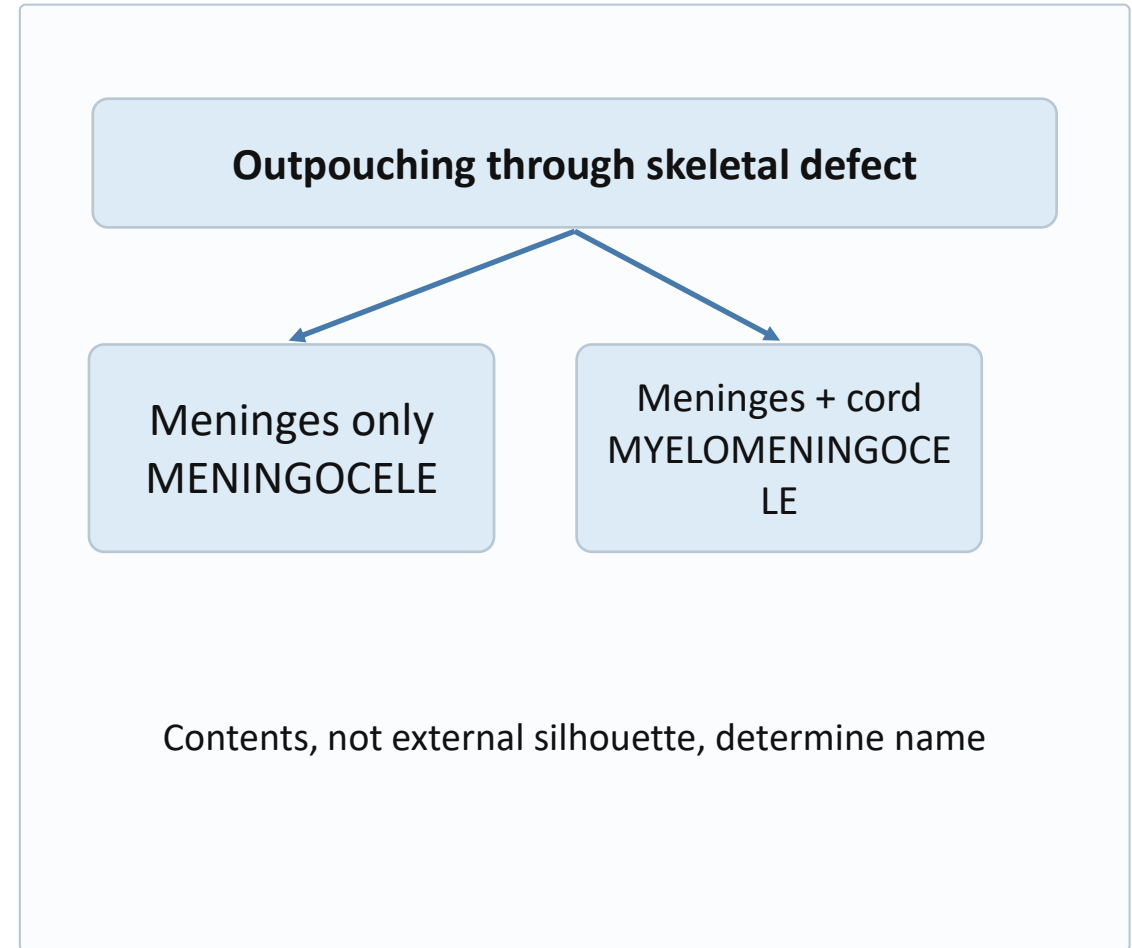


Myelomeningocele: Integrated clinical profile

- Most commonly located in the lumbosacral region.
- Spinal cord parenchyma extends through a vertebral defect.
- Lower-limb motor and sensory abnormalities may occur.
- Bowel, bladder and infectious complications are clinically important.

Meningocele: The meninges protrude without cord tissue

- The defining extrusion consists of meninges.
- A bony defect permits the sac to extend outside its usual compartment.
- The absence of cord tissue from the sac is the key morphologic contrast.

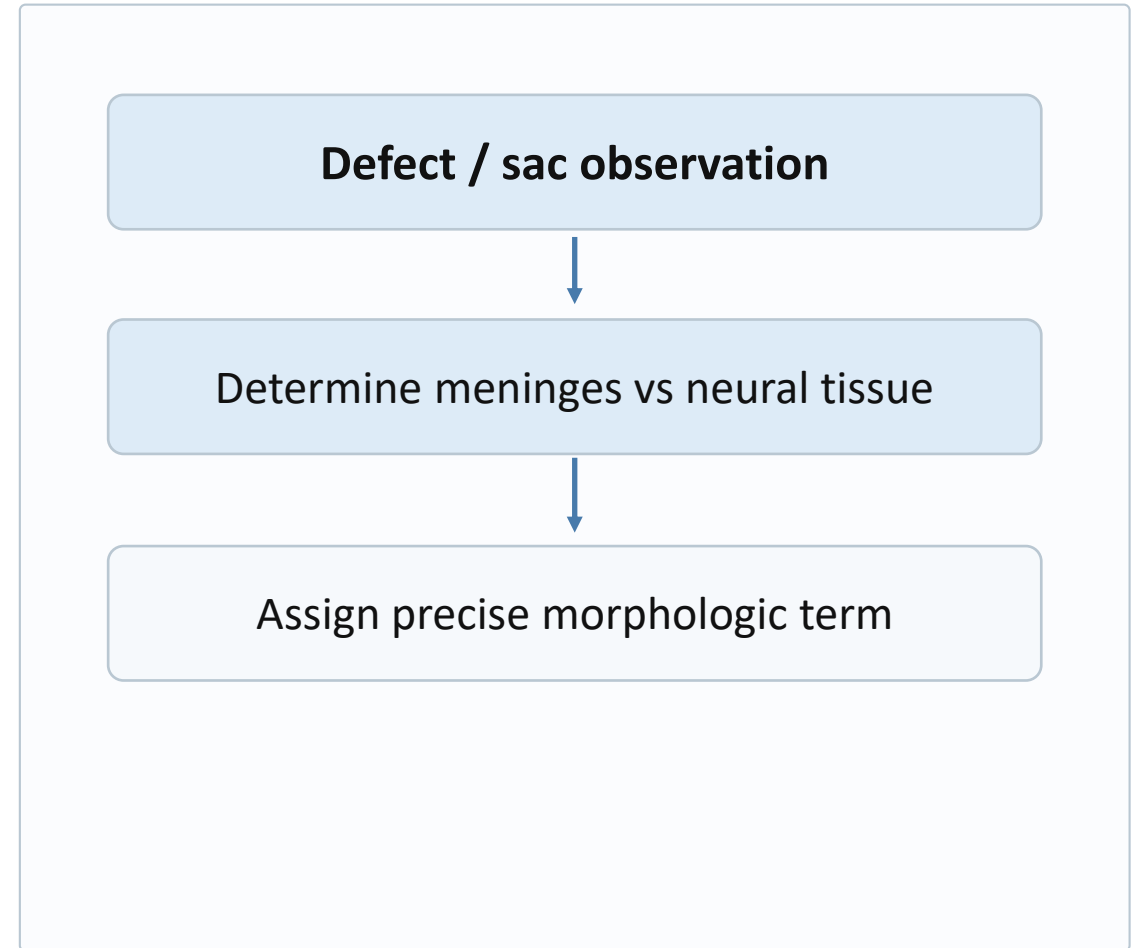


Meningocele versus myelomeningocele

Criterion	Meningocele	Myelomeningocele
Structure protruding	Meninges	Meninges plus spinal cord parenchyma
Underlying bone	Defect present	Vertebral defect present
Definitional contrast	No cord in sac	Cord tissue in sac
Clinical manifestations in excerpt	Not individually specified	Lower-limb and sphincter deficits; Infection risk

What can be inferred from a sac—and what cannot?

- A protruding sac establishes a structural abnormality but not all its contents.
- Neural tissue must be identified to name the lesion precisely.
- The appearance alone does not quantify a patient's neurologic deficits.



Case: A protruding sac at the lower back

A newborn has a midline lumbosacral cyst-like lesion. The clinical description does not say whether the cord enters the sac.

Can the lesion already be classified as myelomeningocele?

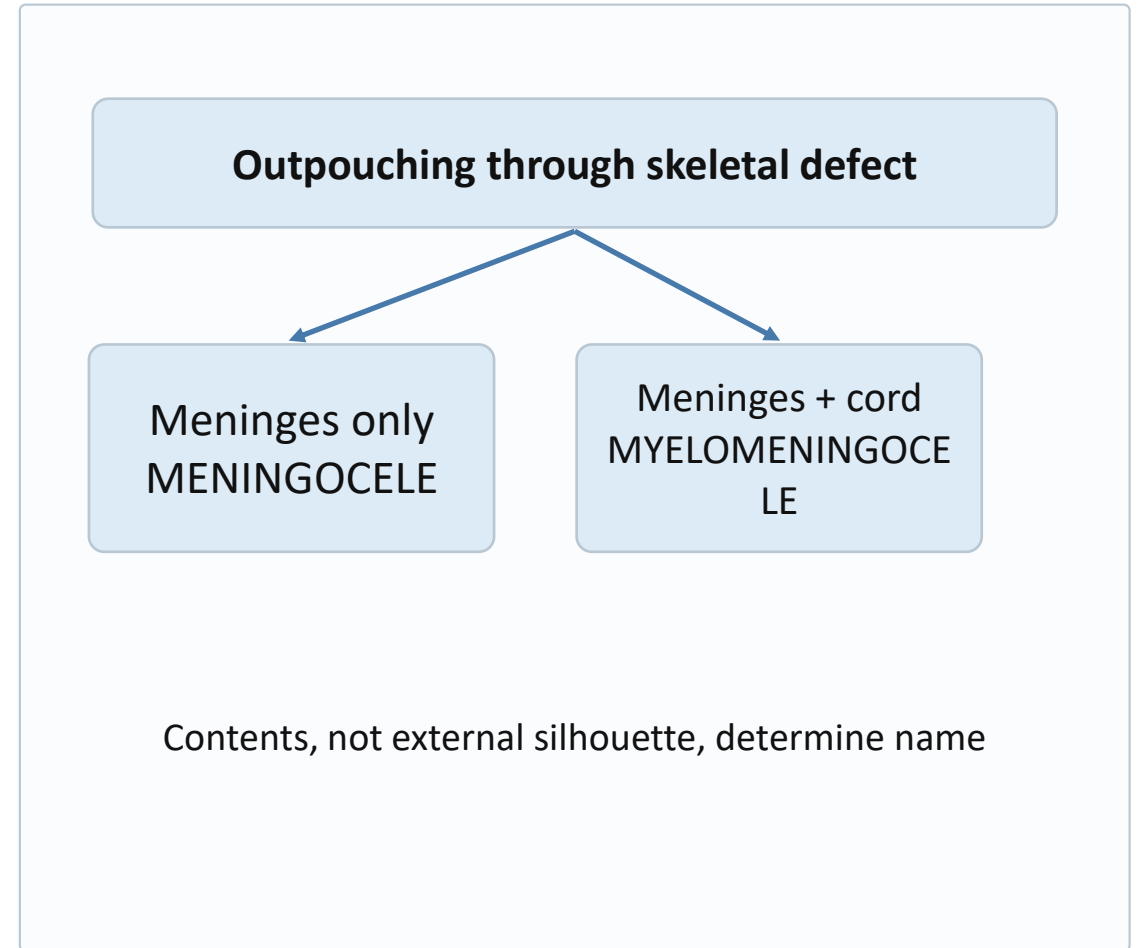
Examine the structure or clinical clue



Name the lesion and justify why

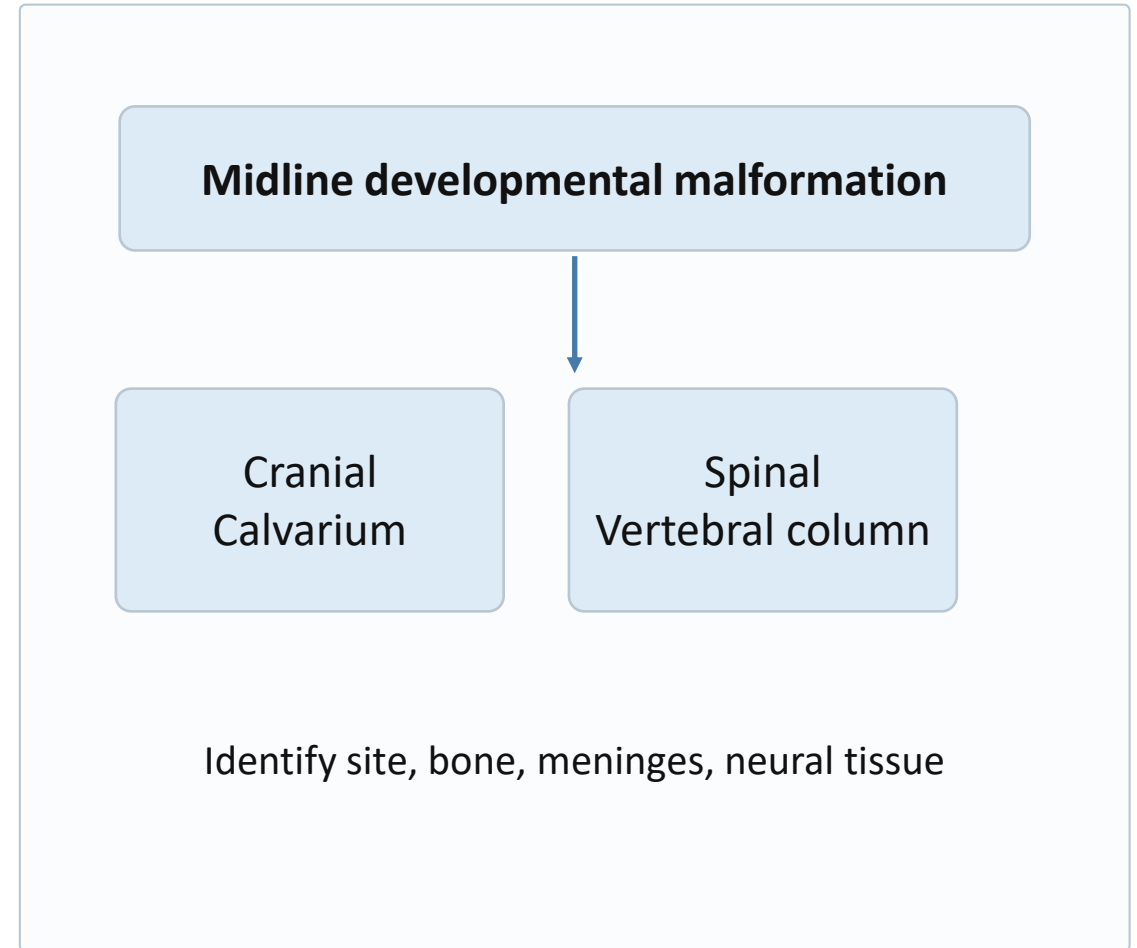
Case interpretation: Tissue content resolves the term

- No: Lumbosacral position alone does not establish myelomeningocele.
- Meninges alone support meningocele.
- Extension of cord parenchyma establishes myelomeningocele.



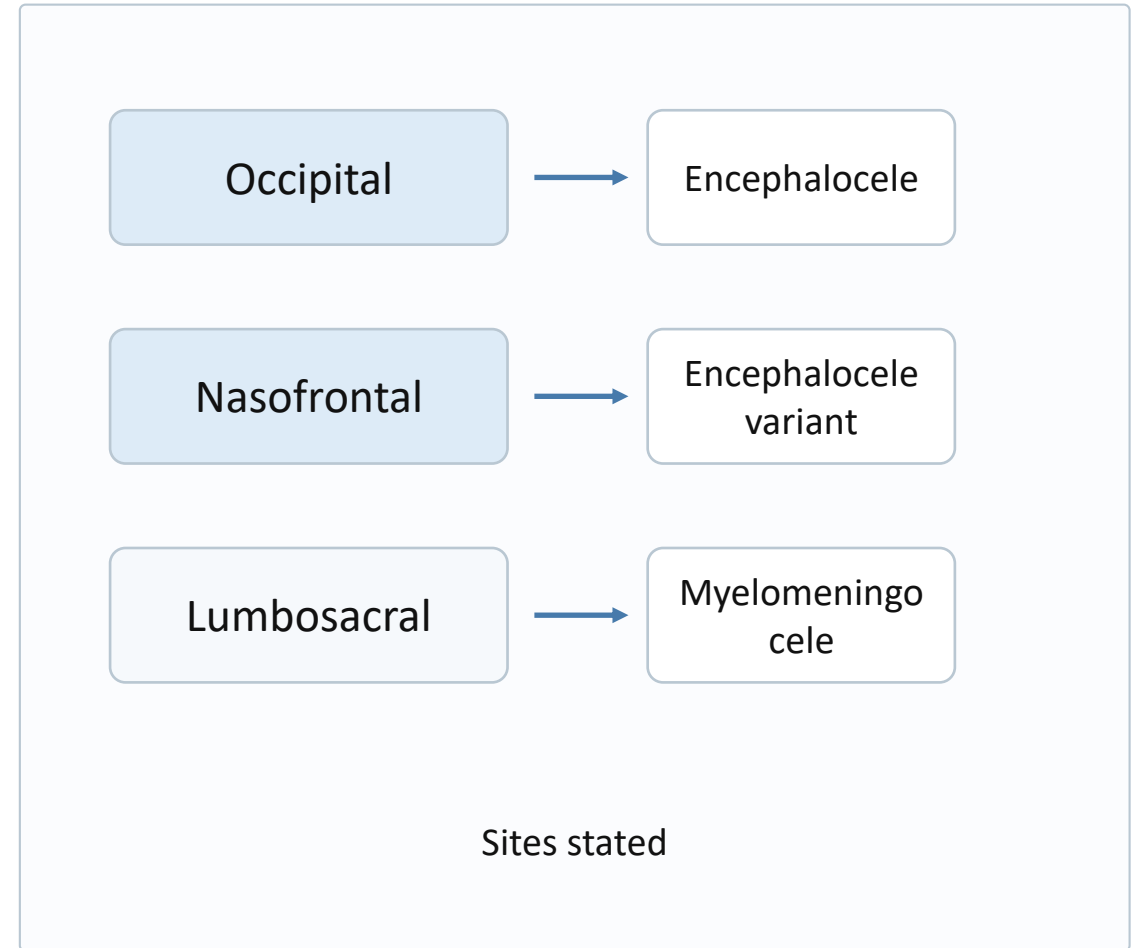
Encephalocele: Brain tissue through a cranial defect

- Malformed brain tissue protrudes through a midline opening of the cranium.
- This is a cranial rather than vertebral extrusion.
- The involved tissue is cerebral, rather than simply meningeal.



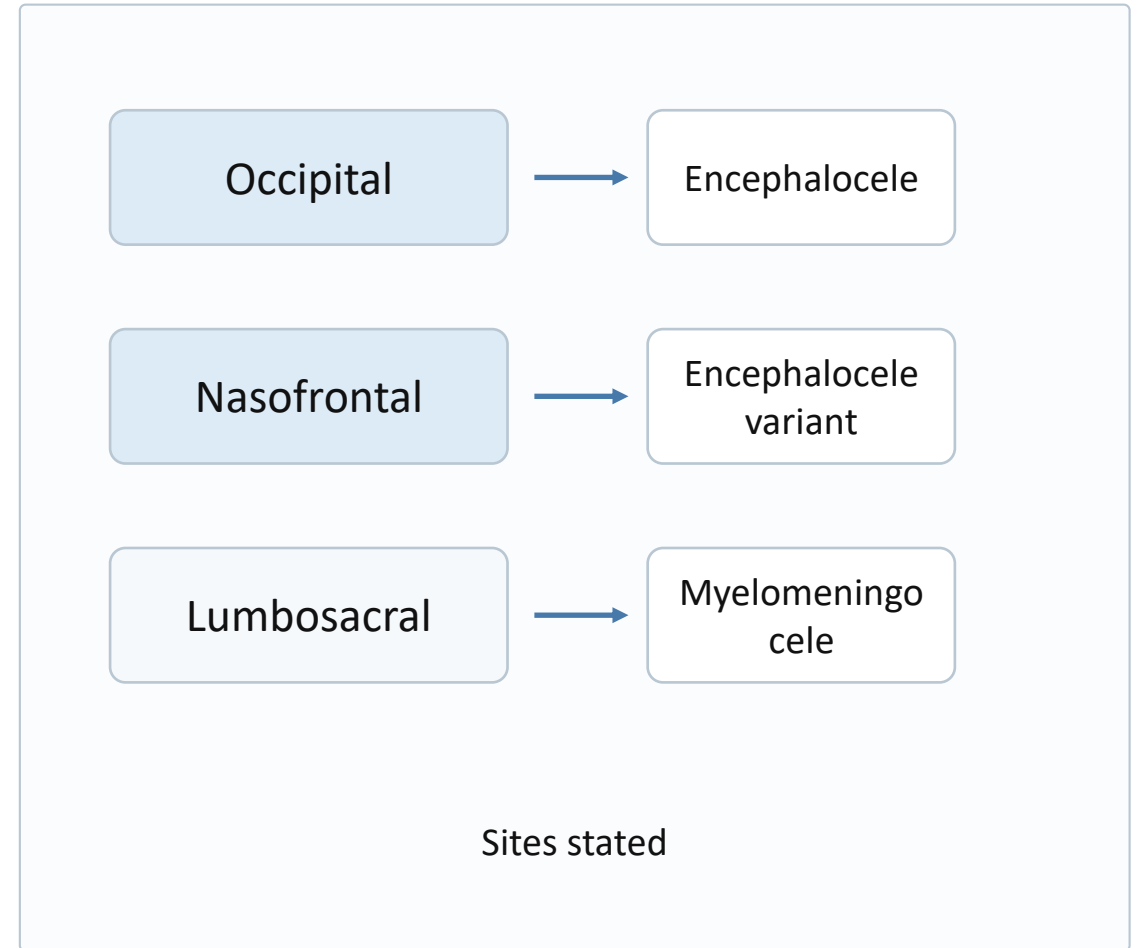
Occipital location is most frequent for encephalocele

- The typical site is the occiput.
- The crucial morphologic feature is the midline skull defect with brain tissue extrusion.
- Site and contents should be stated together in a pathology description.



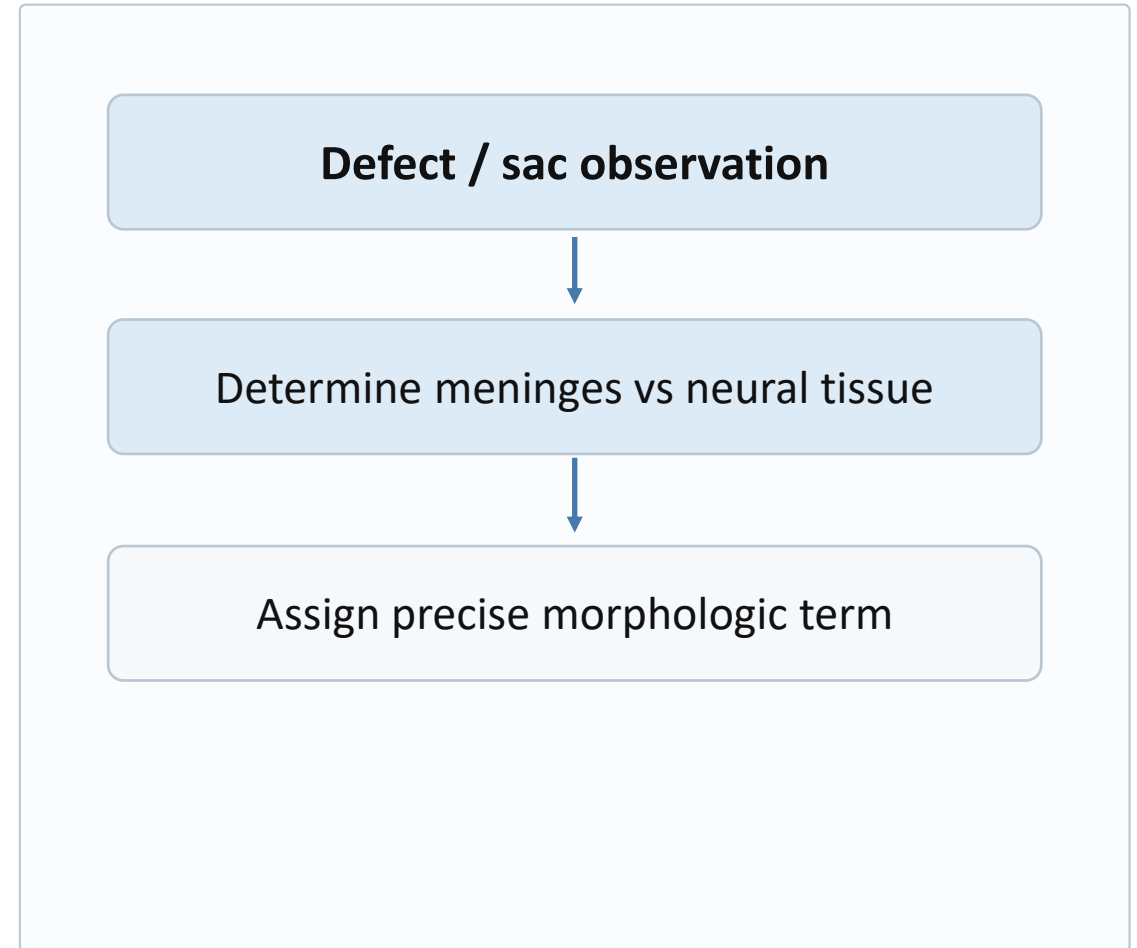
Nasofrontal encephalocele: A less typical location

- Variants may involve the orbit, ethmoid region or cribriform plate.
- These anterior defects belong to the encephalocele spectrum.
- Cranial midline localization prevents confusion with spinal dysraphism.



Nasal glial heterotopia: The naming pitfall

- Robbins mentions nasal glial heterotopia in the nasofrontal variant discussion.
- The colloquial term “nasal glioma” may mislead because it implies a neoplasm.
- Retain the developmental-malformation context when interpreting this name.



Cranial sac lesions versus spinal sac lesions

Feature	Encephalocele	Myelomeningocele
Defect in	Cranium	Vertebral column
Neural component	Malformed brain tissue	Spinal cord tissue
Common location	Occipital	Lumbosacral
General classification	Cranial midline malformation	Spinal dysraphism phenotype

Spinal dysraphism is a spectrum, not one morphology

- Robbins treats spina bifida and spinal dysraphism as a range of defects.
- At one end lies asymptomatic spina bifida occulta.
- At the severe end, a malformed segment of cord accompanies meningeal outpouching.

Spina bifida occulta

Bone defect, no stated symptoms

Meningocele

Meninges extend outward

Myelomeningocele

Cord tissue in lesion

Severe spinal dysraphism

Flattened, disorganized cord

Spina bifida occulta: A bony defect may be silent

- The occulta form may produce no symptoms.
- A bony abnormality alone need not equal severe spinal cord dysplasia.
- Morphologic severity cannot be assigned from the label “spina bifida” alone.

Spina bifida occulta

Bone defect, no stated symptoms

Meningocele

Meninges extend outward

Myelomeningocele

Cord tissue in lesion

Severe spinal dysraphism

Flattened, disorganized cord

Severe dysraphism: Disorganized spinal cord

- A segment of spinal cord can be flattened and disorganized.
- An overlying meningeal outpouching may accompany the cord defect.
- This end of the spectrum differs fundamentally from an isolated silent bony defect.

Spina bifida occulta

Bone defect, no stated symptoms

Meningocele

Meninges extend outward

Myelomeningocele

Cord tissue in lesion

Severe spinal dysraphism

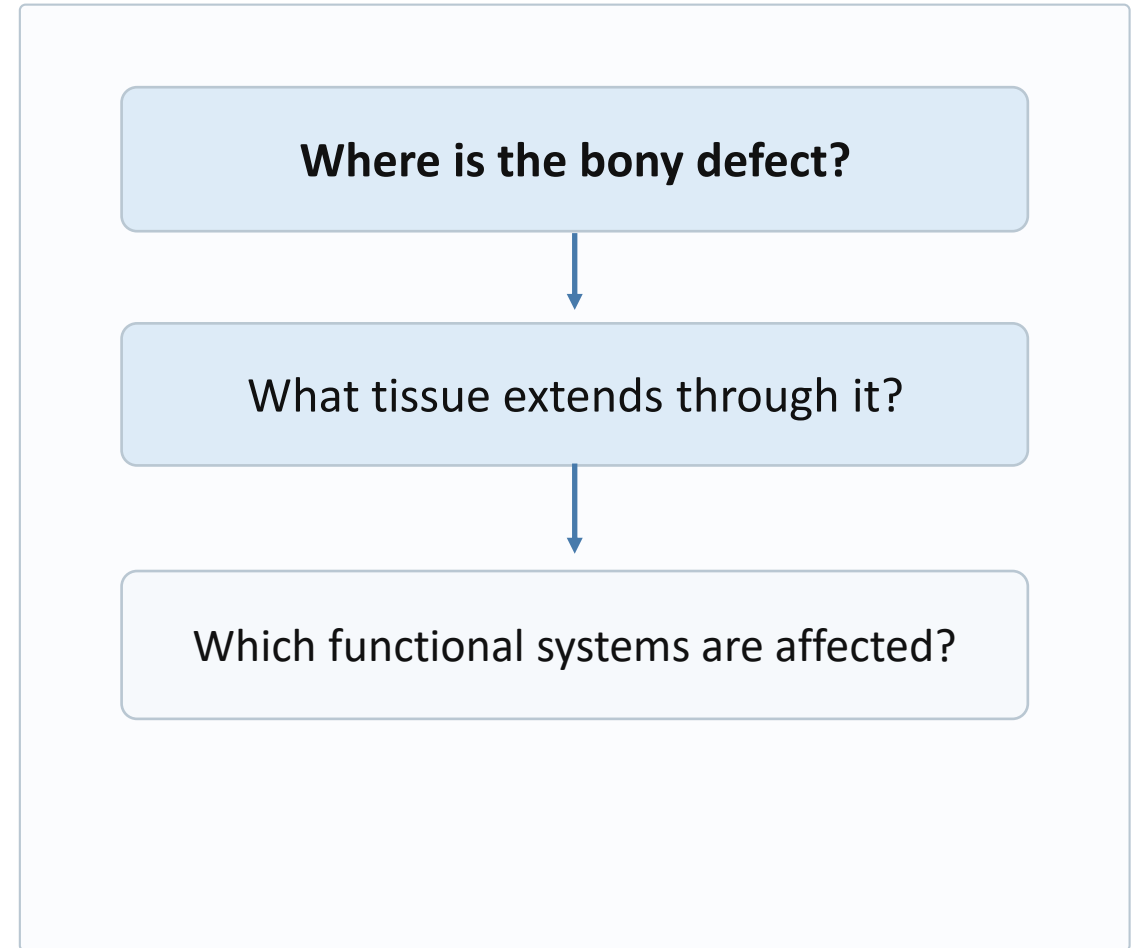
Flattened, disorganized cord

The spinal spectrum links structure and function

Morphology	What it establishes	Source-supported clinical implication
Isolated bony defect (occulta)	Skeletal midline abnormality	May be asymptomatic
Meningeal extrusion	Coverings displaced	Individual deficits not specified in source
Cord within sac	Neural parenchyma involved	Motor, sensory, bowel and bladder deficits
Thin overlying skin	Incomplete protective barrier	Risk of infection

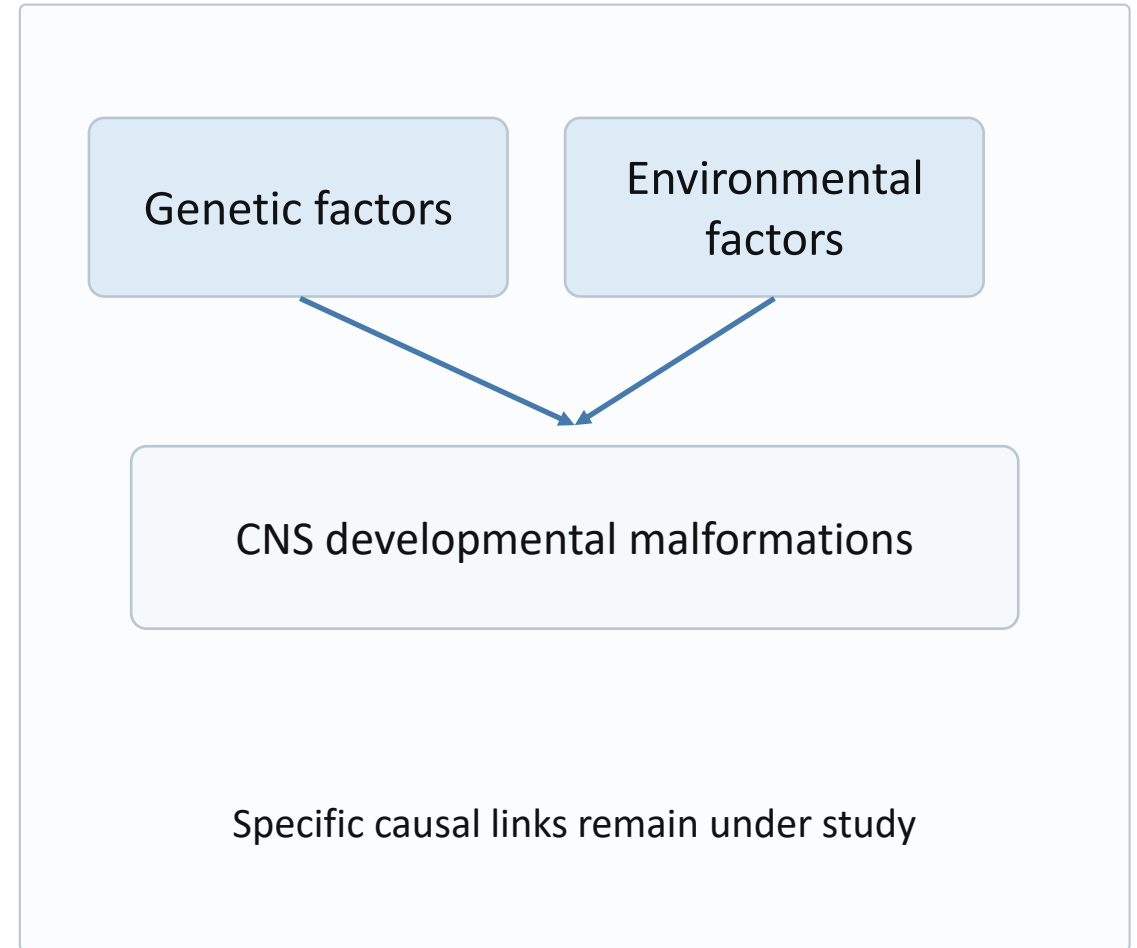
A structured description improves classification

- Identify the anatomic level and whether it is cranial or spinal.
- State whether bone, meninges and neural parenchyma are affected.
- Record any skin barrier abnormality and neurologic manifestations.



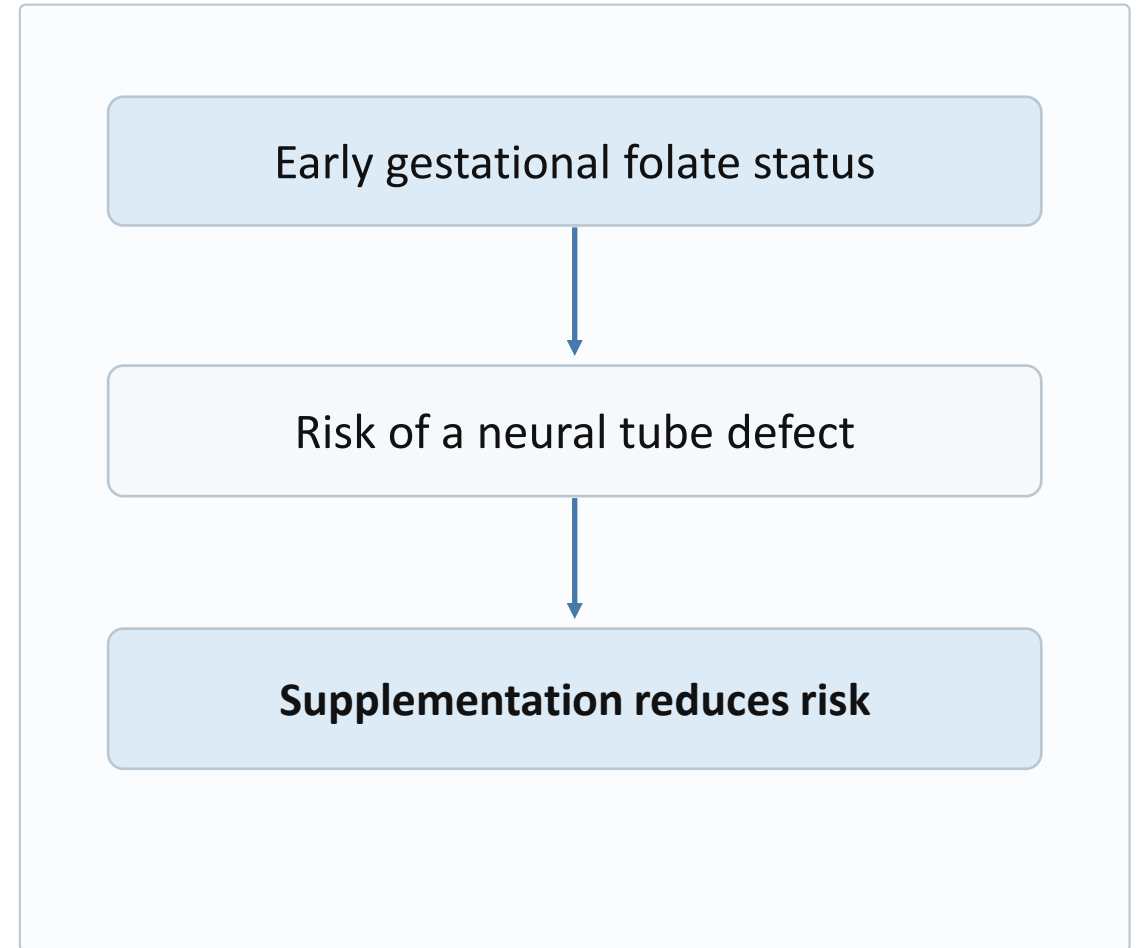
Developmental malformations have mixed influences

- Robbins' parent section identifies both genetic and environmental influences.
- Genomic variants are being uncovered for multiple CNS malformations.
- Causation for many observed gene–malformation associations remains under investigation.



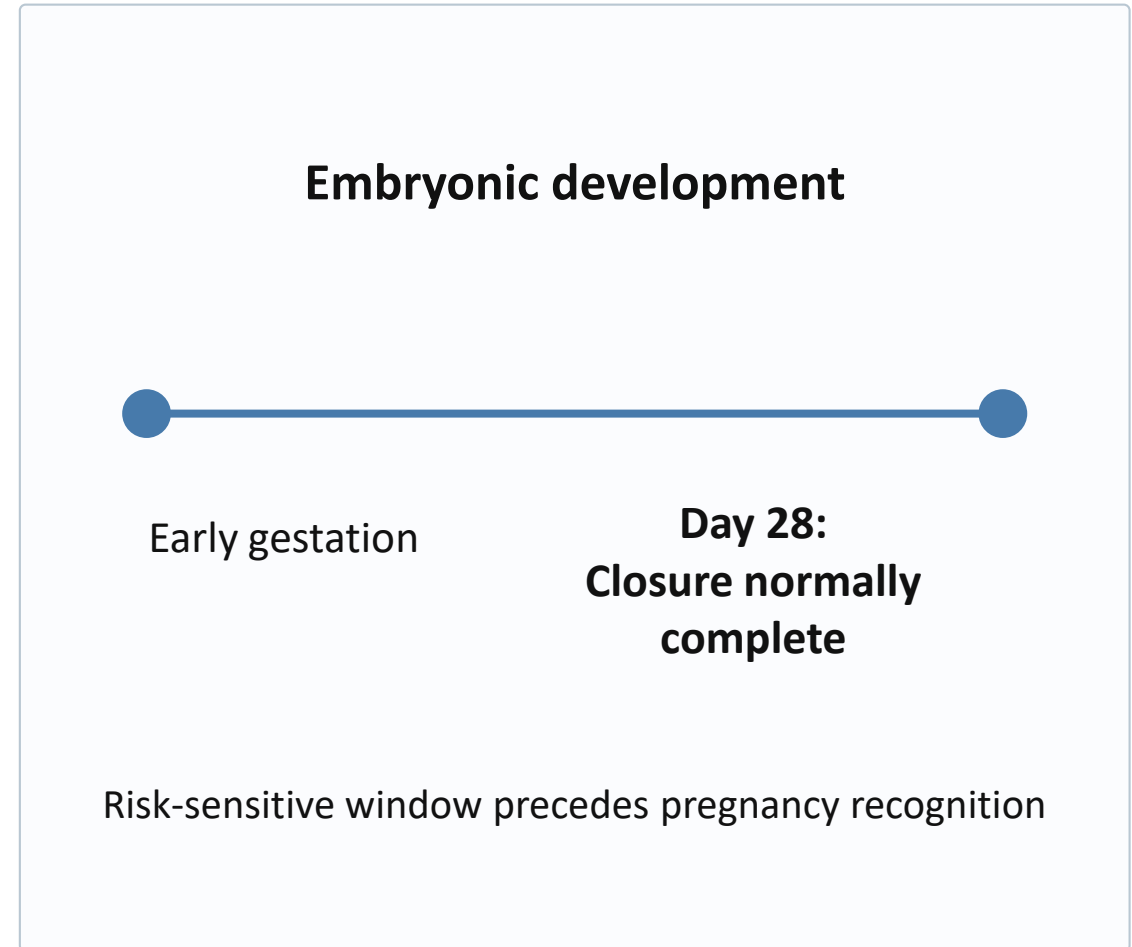
Folate deficiency is a well-established risk factor

- Insufficient folate during the earliest weeks of gestation increases neural tube defect risk.
- Folate supplementation reduces—but does not abolish—the risk.
- This supports prevention before or very early in pregnancy.



The closure timetable explains prevention timing

- Normal neural tube closure is complete by about embryonic day 28.
- Many pregnancies have not yet been recognized at that stage.
- Starting preventive supplementation only after recognition may miss the critical period.



Folate prevention is a preconception issue

- Supplementation throughout reproductive years.
- The rationale is to ensure availability before neural tube closure.
- The recommendation follows from embryologic timing rather than from an identified lesion at birth.

Embryonic development



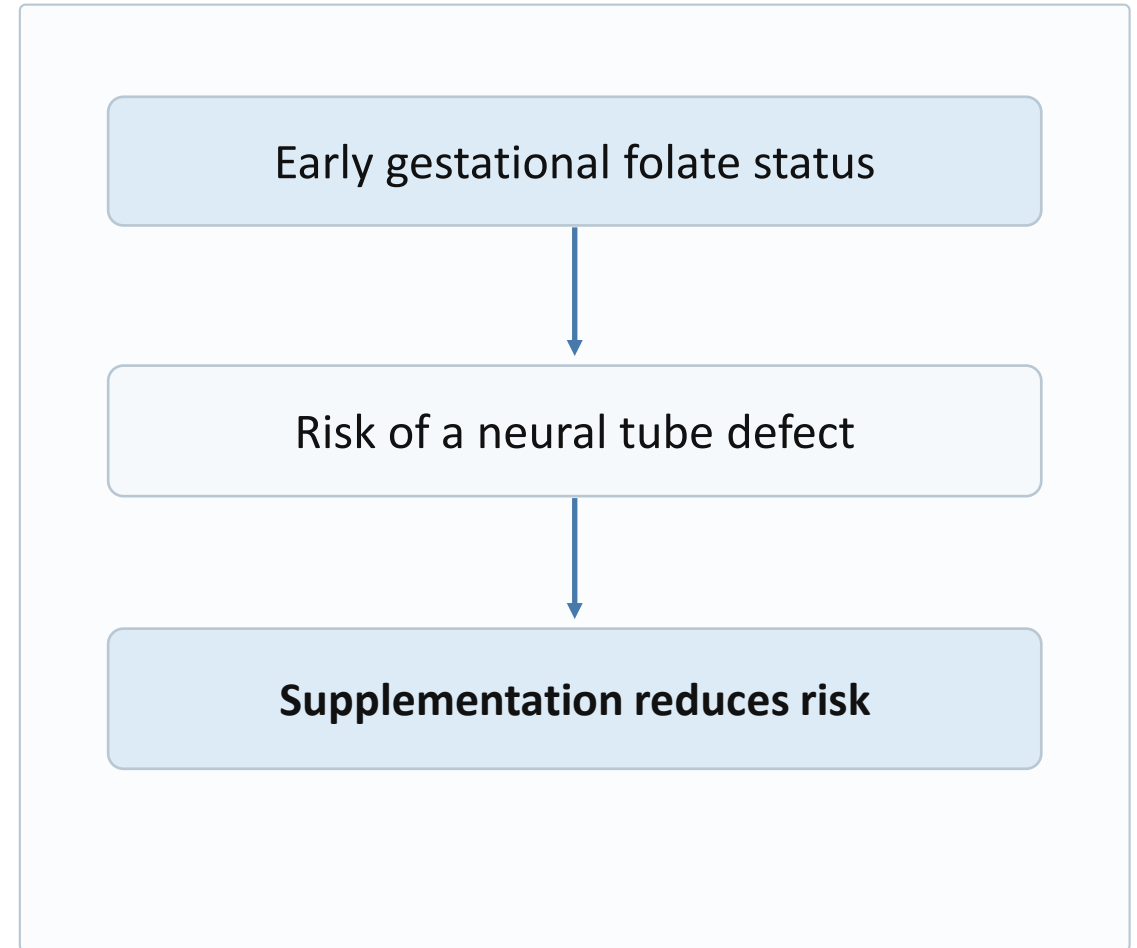
Early gestation

Day 28:
Closure normally
complete

Risk-sensitive window precedes pregnancy recognition

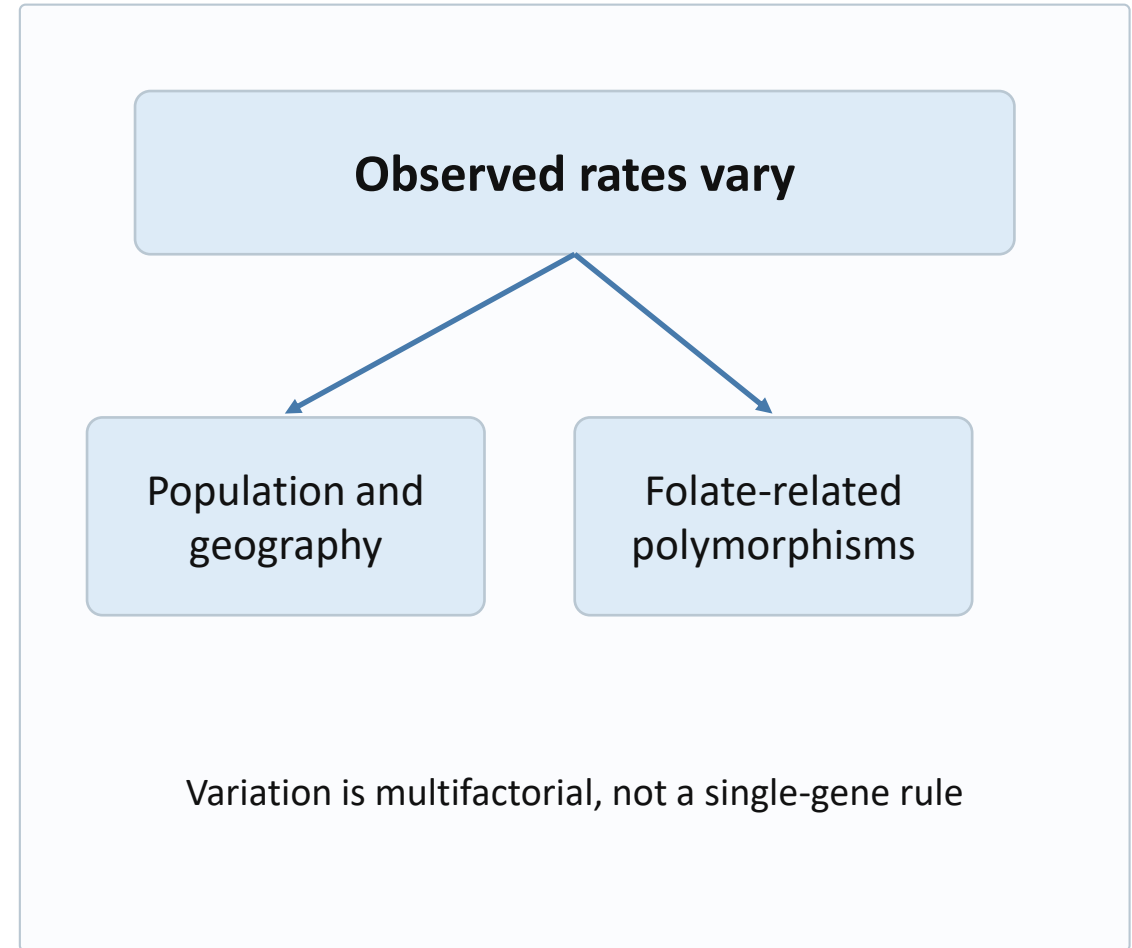
Risk reduction is not the same as complete prevention

- Folate status is important, but not the only contributory factor.
- Population differences and genetic variation also matter.
- A folate-prevention message should avoid implying that every NTD is preventable.



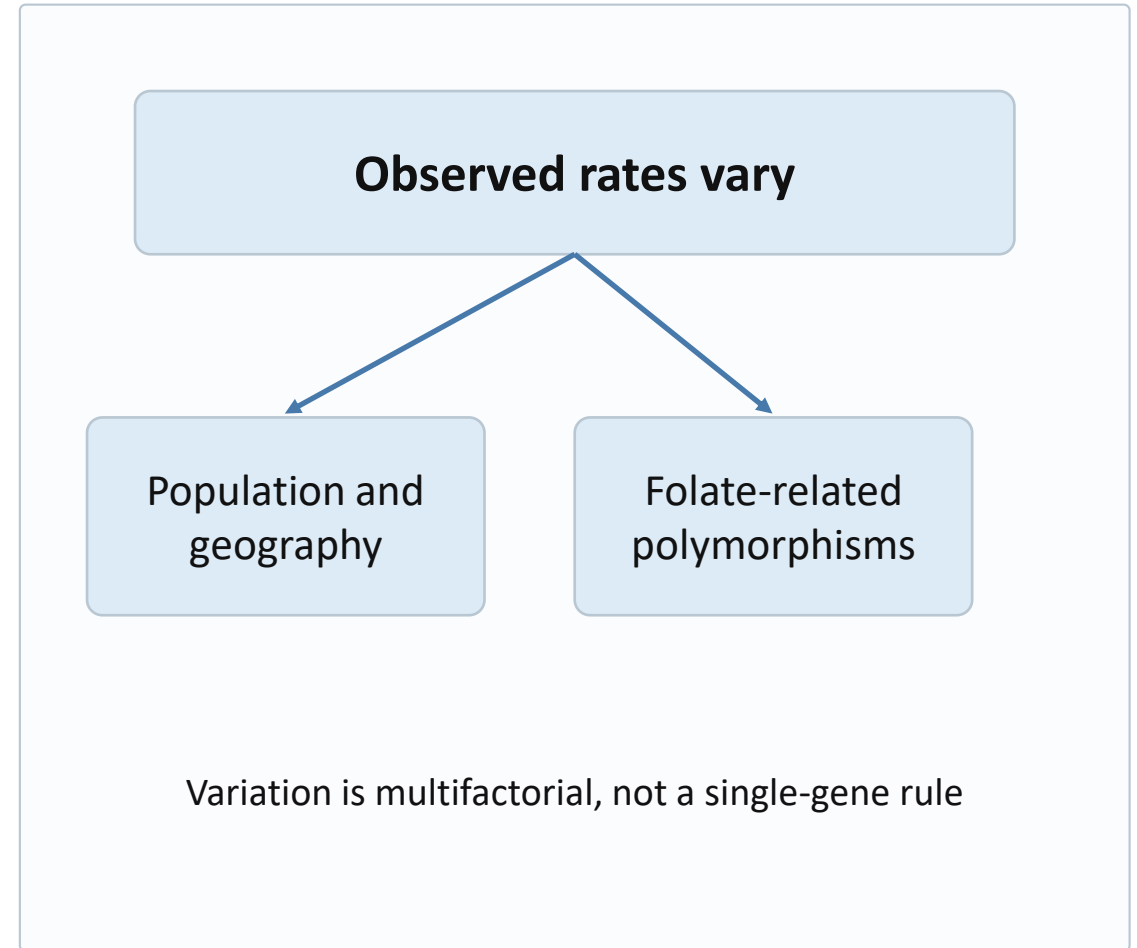
Population rates differ across geographic settings

- Substantial geographic and population variation.
- Folate metabolism polymorphisms contribute to some of this variability.
- A single unqualified incidence figure would obscure this heterogeneity.



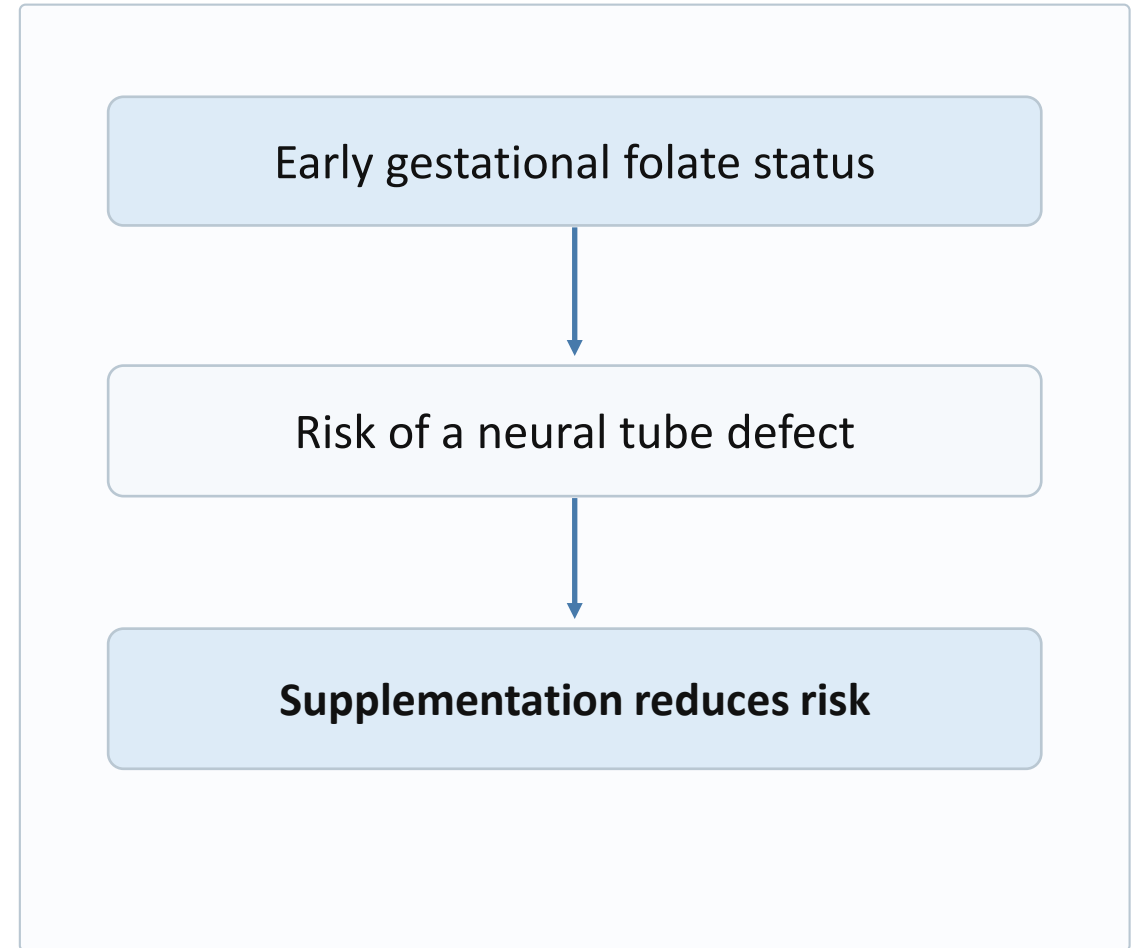
Folate metabolism genetics modify susceptibility

- Polymorphisms in enzymes of folate metabolism are implicated.
- Their distribution can help explain population-level differences.
- This is not equivalent to one universal Mendelian cause for all neural tube defects.



DNA methylation is a proposed mechanistic link

- The exact mechanism of folate-related risk is not established.
- A possible effect on DNA methylation is suggested.
- DNA methylation is an epigenetic mechanism involved in gene regulation.



Avoid overstating the folate mechanism

- Well established: Folate deficiency is a risk factor.
- Observed: Supplementation lowers risk.
- Hypothesis: Effects on DNA methylation may be involved.
- Unresolved: Precisely how deficiency causes the malformation.

Recurrence risk in subsequent pregnancies

- An overall recurrence rate of 4%–5%.
- This is an aggregate estimate across subsequent pregnancies.
- Individual circumstances are not resolved by the single textbook percentage.

4–5%

Estimated recurrence in a later pregnancy

Population-level estimate; Not an individual prediction

Separate recurrence risk from population incidence

- A recurrence estimate concerns a later pregnancy after an affected pregnancy.
- Geographic or population incidence describes a different denominator.
- Combining these measures as if interchangeable leads to false interpretation.

4–5%

Estimated recurrence in a later pregnancy

Population-level estimate; Not an individual prediction

Case: When should folate risk reduction begin?

A patient plans pregnancy but intends to start supplementation only after a pregnancy test becomes positive.

What feature of neural development makes this timing unreliable?

Examine the structure or clinical clue



Name the lesion and justify why

Case interpretation: Closure precedes recognition

- Neural tube closure is normally complete by approximately day 28.
- Many pregnancies are not yet recognized at this stage.
- Robbins therefore emphasizes folate availability before conception / throughout reproductive years.

Embryonic development



Early gestation

**Day 28:
Closure normally
complete**

Risk-sensitive window precedes pregnancy recognition

Case: A child with leg and sphincter deficits

A lumbosacral lesion contains spinal cord tissue. The child has lower-extremity weakness, diminished sensation, and disturbances of bowel and bladder control.

Which named defect best links morphology and clinical features?

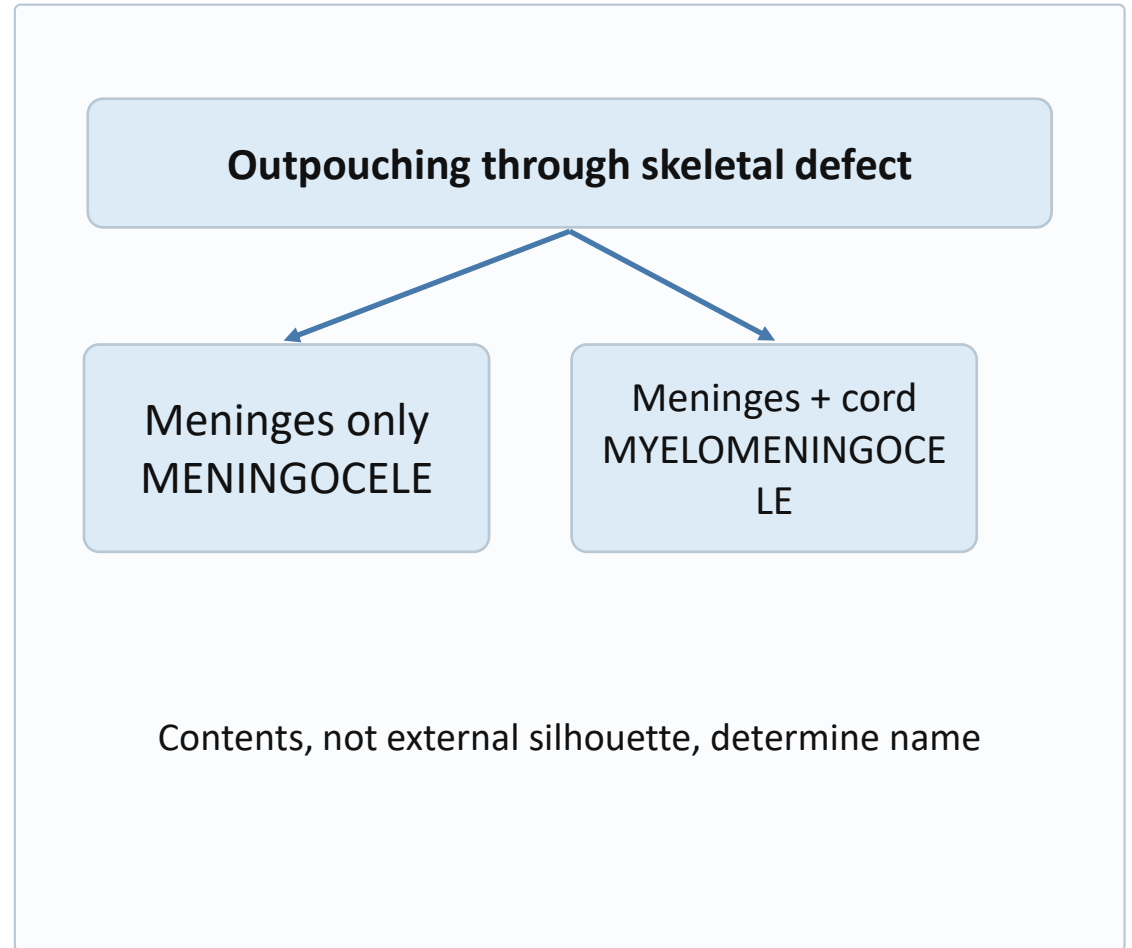
Examine the structure or clinical clue



Name the lesion and justify why

Case interpretation: Myelomeningocele

- Cord tissue extends through the vertebral defect: Myelomeningocele.
- Lumbosacral location matches the common site.
- Lower-limb and pelvic-organ dysfunction are coherent consequences of neural involvement.



Case: A clinically silent vertebral anomaly

A structural examination identifies a spinal bony midline defect in an otherwise asymptomatic individual.

Which end of the spinal dysraphism spectrum does this resemble?

Examine the structure or clinical clue



Name the lesion and justify why

Case interpretation: Spina bifida occulta

- A silent bony defect corresponds to the occulta end of the spectrum.
- The label does not automatically imply cord extrusion.
- Contrast with the severely malformed, disorganized cord in advanced dysraphism.

Spina bifida occulta

Bone defect, no stated symptoms

Meningocele

Meninges extend outward

Myelomeningocele

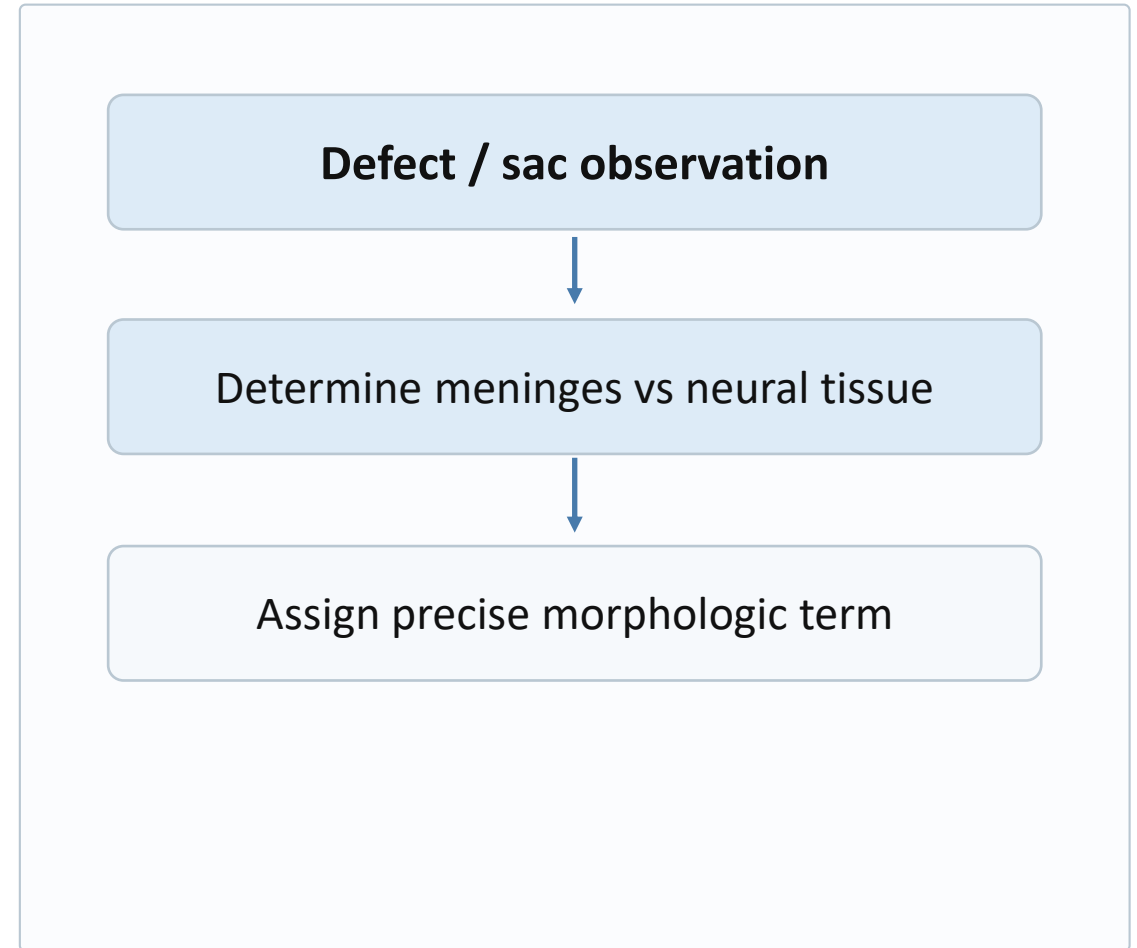
Cord tissue in lesion

Severe spinal dysraphism

Flattened, disorganized cord

Final morphologic sorting exercise

- Cranial defect + malformed brain: Encephalocele.
- Spinal defect + meninges alone: Meningocele.
- Spinal defect + cord tissue: Myelomeningocele.
- Anterior tube disruption with loss of brain and vault: Anencephaly.



Three principles for pathology interpretation

Specify primary tissue or developmental mechanism when known.

Use precise lesion contents to name an extrusion.

Translate morphology into plausible functional effects without guessing an individual outcome.

Three principles for risk interpretation

Folate deficiency: Established early-gestational risk factor.

Folate supplementation: Preventive benefit depends on timing.

DNA methylation: Plausible mechanism, explicitly uncertain.

References and source limitations

- Robbins, Cotran & Kumar: Pathologic Basis of Disease. 11th ed. (2026). Chapter 28: The Central Nervous System, pp. 1133–1134.
- Primary working input: supplied robbins.md and indexed topic extract; extract repaired editorially where adjacent text was interleaved.
- The original chapter PDF and its clinical Fig. 28.6 were not available in the supplied materials; conceptual diagrams are native PowerPoint schematics.