

Neural Tube Closure and Associated Defects

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Case-Based Questions (please see page 3 for answers)

1.	Closure of the caudal neural tube involves the bending of the neural folds at specific hinge points including the dorsolateral hinge point (DLHP) that are developmentally regulated by Noggin, Shh and BMP. The correct roles for these secreted proteins are?
a.	Noggin, Shh and BMP induce the DLHP to form and bend
b.	Shh induces and BMP represses the DLHP, Noggin represses Shh
c.	Shh represses Noggin which represses BMP, permitting formation of the DLHP
d.	Noggin represses Shh and BMP allowing DLHP to form

2.	In the evaluation of a 16 week fetus after spontaneous (non-medical) abortion the pathologist notes a midline tissue mass in the lumbar regions. The mass is soft, has prominent hair around the border. The lower extremities appear normal. Dissection of the mass demonstrates an open defect of the posterior vertebrae with extrusion of meninges but no elements of the spinal cord. The appropriate diagnosis is?
a.	Encephalocele
b.	Meningocele
c.	Myelomeningocele
d.	Myelocele

3.	Folic acid supplementation has reduced the incidence of neural tube defects accordingly:
a.	Predominately males and cranial defects (anencephaly)
b.	Predominately males and caudal defects (myelomeningocele)
c.	Predominately females and cranial defects (anencephaly)
d.	Predominately females and caudal defects (myelomeningocele)
e.	All neural tube defects, equally in males and females

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Question 1 Correct answer and rationale: **C) Shh represses Noggin which represses BMP, permitting formation of the DLHP**

Correct answer is C. In the caudal neural tube Shh signaling is reduced and thus it does not inhibit Noggin (a normal function) in the dorsal neural tube. Noggin normally inhibits BMP, thus when it is not repressed by Shh it can repress BMP allowing other mechanisms like cell shape change and programmed cell death to shape the formation of the DLHP and enable neural tube closure.

Question 2 Correct answer and rationale: **B) Meningocele**

Encephaloceles involve the cranium, not the spinal cord. Both Myelomeningocele and myelocele involve the elements of neural axis (the spinal cord). Meningocele does not involve the spinal cord, only the meninges and bony defect of the vertebrae. They carry a better prognosis

Question 3 Correct answer and rationale: **C) Predominately females and cranial defects (anencephaly)**

For unclear reasons epidemiologic data indicate there is a greater benefit derived from maternal folic acid supplementation for female children and primarily related to cranial neural tube defects. This is an area of active investigation.