

1. The molecular defect in Duchenne muscular dystrophy resides in _____.

- A. a large, plasma membrane-associated protein
- B. a key calcium-transport molecule
- C. a mitochondrial electron transport chain protein
- D. a metabolic enzyme involved in glycolysis
- E. contractile protein interactions

Answer A: Duchenne's muscular dystrophy (DMD) is an X-linked disorder involving the Xp21. This region encodes for the protein dystrophin, which serves as a link between the cytoskeleton and transmembrane proteins. Altogether, they are called dystrophin-associated protein complex and function as anchors between the cell and the matrix. It is thought that this system transfers the forces of contraction from the myocyte to the surrounding matrix. In its absence due to the genetic defect, this force transfer does not occur smoothly and damage to the sarcolemma (muscle cell membrane) occurs, eventually self-destructing the entire muscle with each contraction.

2. Wallerian degeneration _____.

- A. is seen in oligodendroglia
- B. is a paraneoplastic syndrome
- C. involves distal axonal degeneration
- D. is the destruction of myelin sheaths

Answer C: When an axon is damaged, the body of that neuron undergoes a process called "central chromatolysis", a regenerative process aimed at increased production of proteins to heal the damaged axon. The part of the axon distal to the damage eventually degenerates and dies, and the debris cleared up by macrophages. If, as in some crush, rather than transaction injuries, the axon sheath (Schwann cells encasing the axon) remains relatively intact, the regenerative process is faster and healing is better, as the regenerating axon has a "template" to grow in.

3. A 62-year-old woman had an acute myocardial infarction. Right after arriving at the emergency room, she had cardiac arrest. Resuscitation efforts for 15 minutes were successful and she was admitted to the intensive care unit (ICU). However, she developed a fatal arrhythmia and died on her third day in ICU. Autopsy was performed. This picture of brain tissue shows:

- A. viral inclusions
- B. reactive astrocytes
- C. normal white matter
- D. normal cortical gray matter
- E. eosinophilic neuronal necrosis

Answer E: When neurons are subjected to hypoxic/ischemic conditions, the earliest light microscopic changes are seen 10-12 hours post-injury and are termed "eosinophilic neuronal injury", "acute neuronal injury" or simply "red neurons, as they lose their crisp basophilic appearance and become opaque red/pink cells with smudgy chromatin. However, the person should live up to 10-12 hours after the event, so that these changes can be identified.

4. While walking home after a party where he consumed five cans of beer, a 28-year-old man fell and hit his head on the curb. He got up and went home. An hour later, he became unconscious and was brought to the emergency room by his roommate. Initial physical exam showed a severe contusion of the left temporal area. The most likely explanation for his condition is rupture of the _____.

- A. left middle meningeal artery
- B. left middle cerebral artery
- C. anterior communicating artery aneurysm
- D. bridging dural veins
- E. posterior cerebral artery

Answer A: The history describes a “lucid interval” that is associated with epidural hemorrhage. Most common reason for an epidural hematoma is the damage to middle meningeal artery by a skull fracture. Cerebral arteries and arteries of the circle of Willis are associated with intracerebral hemorrhage and aneurysms, while damage to bridging dural veins result in subdural hematoma.

5. A 29-year-old man was found dead in the street. Autopsy showed hemorrhage under the occipital scalp, and contusions of both occipital poles. Which of the following is the most likely explanation?

- A. metastatic lung cancer secondary to heavy smoking
- B. intracranial hemorrhage secondary to hypertension
- C. slipped and fell on his back, hitting his head to concrete pavement
- D. he was previously strangled to death and later the body was dumped in a remote street, at which time his head hit the concrete pavement
- E. he was hit on the back of his head by a baseball bat

Answer E: This is a review of coup and contrecoup injury pattern. While a real life forensic scenario can be very complicated, for the purposes of principle injury patterns, if a head trauma occurs while the head is still, there will be damage at the skin, subcutaneous tissues, bone and brain at the trauma site. If the trauma occurs while the head is in motion, then, there will be skin and soft tissue injury at the trauma site, as well as some damage to the bone and brain, but there will also be considerable damage on the brain surface directly opposite to the trauma site. Therefore, one can identify the trauma site, as well as whether the head (i.e., the victim) was in motion by examining the head.

The answer comes down to answers C and E. We are not told of any brain injuries on the opposite side of the trauma site. Therefore, he was hit in the back of his head (creating the skin and occipital lobe injuries), rather than falling and hitting the back of his head on the curb, which would also create frontal brain injury due to bouncing of the brain back and forth in the calvarium.

6. A 65-year-old woman presents to the hospital with progressive neurological deficits. Several months earlier she had received treatment for a brain tumor. A new brain biopsy shows no tumor, but does show necrosis of cerebral vasculature and of brain tissue. The most likely cause of these findings is previous therapy with:

- A. isoniazid
- B. dehydration
- C. mercury
- D. radiation
- E. vincristine

Answer D: Fibrinoid necrosis of the vessel walls and tissue necrosis are typical changes induced by radiation treatment. There may also be swelling, vascular dilatation and leakage, creating contrast enhancement. If the PET-scan is “hot”, indicating an increased metabolic activity, then a recurrent tumor is suspected. Of the other choices listed, vincristine is important to know, since it also can cause tissue necrosis, especially a very serious condition called “necrotizing myelitis”, but without the described vascular changes.

7. Which of the following is true regarding the pathological process seen in this picture?

- a. Pathological hallmark is the presence of numerous intranuclear inclusions
- b. It is a movement disorder characterized by ataxia
- c. Intracytoplasmic alpha-synuclein-positive neuronal inclusions are diagnostic (correct)
- d. The majority of patients also have dementia
- e. A specific muscle pathology is the cause of the movement disorder

Answer C: This picture shows the cut surface of midbrain, where substantia nigra is seen as symmetrical pigmented structures in the normal picture. The patient's substantia nigra is pale, meaning that the pigmented neurons are lost, indicating a neurodegenerative condition involving substantia nigra. The prototypical disease is Parkinson Disease (PD). The diagnostic neuropathological feature of PD is the Lewy body, a round, eosinophilic, intracytoplasmic, neuronal inclusion found in the still-intact pigmented neurons. This movement disorder clinically presents with shuffling gait, pill-rolling movement of fingers and intentional tremor, not ataxia. These are due to the problems with the cholinergic-dopaminergic system and the skeletal muscles are intact. Lewy bodies are alpha-synuclein positive (synucleinopathy). Only approximately 5-10 % of patients have dementia, especially if there is associated diffuse Lewy body disease and/or Alzheimer disease.

8. A 26-year-old man presents to clinic with weakness in his right arm. Two years previously he had an episode of difficulty speaking that improved considerably after several days. One year before that he had an episode of decreased vision in his left eye that did not resolve. He has no other known medical illnesses or conditions. The most likely cause of these episodes is:

- A. accumulation of amyloid deposits in the brain
- B. an inborn metabolic error of sphingolipid metabolism
- C. chronic arsenic poisoning
- D. episodes of brain myelin destruction by macrophages
- E. viral infection of oligodendrocytes

Answer D: The question describes a young individual with recurrent episodes of various neurological problems, which cannot be described by involvement of a particular neurological structure or system. Therefore, these lesions are randomly distributed. These features are typical of multiple sclerosis, which is the destruction of myelin by macrophages. Accumulation of amyloid deposits in the brain is consistent with Alzheimer disease. A typical viral infection of the oligodendrocytes is progressive multifocal leukoencephalopathy (PML), which also causes demyelinating lesions, but is usually associated with an immunocompromised condition.

9. Perivenous encephalomyelitis is thought to result from _____.

- A. an autoimmune attack on central nervous system myelin
- B. exposure to canine distemper virus
- C. inappropriate astrocytic expression of major histocompatibility antigens
- D. a neurotoxin elaborated by an anaerobic bacillus
- E. a systemic vasculopathy

Answer A: Perivenous encephalitis (acute disseminated encephalomyelitis; ADEM) is a demyelinating process following a viral infection or immunizations by 1-2 weeks and is thought to result from an attack of immunized lymphocytes to myelin sheaths. Even though the demyelination has a perivascular arrangement, it is not a vasculopathy.

10. Examine the gross photograph of a brain from a newborn child, taken from the posterior. The abnormality shown here results from a failure of:

- a. neural tube formation
- b. organogenesis (correct)
- c. neuroblast migration
- d. aqueductal patency
- e. myelination

Answer B: This is a posterior view of a brain with holoprosencephaly, which is the failure of cerebral hemispheres to separate. This is an example of a problem with organogenesis. Heterotopia is an example of neuroblast migration. Spina bifida is a problem with neural tube formation.

Notes for question set:¹

¹ PathMD strives for the highest quality and accuracy. However, the *PathMD: Board Review Letter* is for review purposes and not meant for clinical decision making. It should not be used in place of review of primary reference texts and the current medical literature. If inaccuracies are identified, please notify us so that a correction may be published. (info@PathMD.com)