UNITED COUNCIL FOR NEUROLOGIC SUBSPECIALTIES

Clinical Neuromuscular Pathology
Written Examination
Content Outline

Rev 12-10-13
The UCNS Clinical Neuromuscular Pathology examination was established to determine the level of competence for Clinical Neuromuscular Pathology Care specialists.

The following content outline is provided to examination candidates interested in the certification examination. The content outline consists of three primary categories followed by subcategories.

	Content Area	Percentage of Questions
I.	**Core Clinical Neuromuscular Pathology**	**20%**
II.	**Muscle Diseases**	**40%**
III.	**Nerve Diseases**	**40%**

I. Core Clinical Neuromuscular Pathology

A. Performance and Processing of Biopsies
   1. Site selection
   2. Specimen type and purpose

B. Complications of Biopsies
   1. Choice of site for muscle biopsies
   2. Artifacts due to muscle biopsy procedure
   3. Choice of site for nerve biopsies
   3. Artifacts due to nerve biopsy procedure

C. Nerve and Muscle Anatomy

D. Nerve and Muscle Electrophysiology

II. **Muscle Diseases**

A. Artifacts
1. Freezing artifacts
2. Sectioning artifacts
3. Staining artifacts
4. Insufficient biopsy size
5. Common mitochondrial artifacts, swelling, size variation, cristae, inclusions

B. What is normal
1. Age-related features: fiber size in development
2. Raged red fibers in aging
3. Lipofuscin
4. Amount and size of lipid droplets

C. Basic reactions of muscle
1. Patterns and histochemical properties of fiber types
2. Analysis of muscle fiber diameters
3. Central migration of nuclei
4. Features of necrotic and regenerating fibers – process of regeneration, with plump basophilic nuclei; failure of complete fusion in regeneration ("split" fibers)
5. Evaluation of connective tissue elements
6. Recognition and significance of different types of muscle fiber inclusions
7. Recognition and causes of type 2 fiber atrophy
8. Recognition and causes of type 1 fiber atrophy
9. Denervation
10. Reinnervation
11. Chronic denervation and reinnervation
12. Target fibers
13. Moth eaten fibers; light microscopic correlates of myofibrillar disruption
14. Myofibrillar myopathies; desmin, etc
15. Inclusion bodies
16. Cytoplasmic bodies
17. Autophagolysosomes, lysosomal accumulation

D. Congenital myopathies
1. Specific morphologic features of currently recognized congenital myopathies
2. Nonspecific morphologic features of currently recognized congenital myopathies
3. Currently recognized disease genes for congenital myopathies

E. Metabolic
1. Specific and nonspecific features of glycogen storage myopathies
2. Available histochemical methods for the diagnosis of glycogen storage myopathies
3. Currently recognized etiologies of glycogen storage myopathies
4. Histologic features and causes of a lipid storage myopathy; normal lipid droplet size and density

5. Histologic features pointing to mitochondrial myopathies
6. Mitochondrial abnormalities secondary to aging
7. Histologic features and causes of recent episode of rhabdomyolysis; time course of regeneration and resolution of necrosis in acute necrotizing myopathies

F. Channelopathies
1. Histologic features associated with Na and K channelopathies of skeletal muscle

G. Inflammatory, Idiopathic, and Infectious
1. Principal histologic features of the major inflammatory myopathies; concept of primary inflammation surrounding and invading non-necrotic myofibers
2. Methods to phenotype of inflammatory cells and their usefulness
3. Methods to display the muscle fiber microvasculature
4. Distinguishing features of necrotizing and other types of vasculitis in muscle
5. Identification of parasites in muscle
6. Pyomyositis

H. Systemic Disorders
1. Systemic sclerosis
2. Sarcoidosis
3. Identification of and knowledge of causes of amyloid deposits in muscle
4. Hypokalemic myopathy
5. Uremic hyperparathyroidism
6. Malnutrition
7. Critical illness myopathy

I. Muscular Dystrophies
1. Knowledge of gene centered classification of muscular dystrophies
2. General histologic features of muscular dystrophies
3. Available monoclonal antibody tests for specific diagnosis
4. Special histologic features suggesting dystrophinopathy, sarcoglycanopathy, dysferlinopathy, and myofibrillar myopathy
5. Knowledge of gene centered classification of muscular dystrophies
6. Available gene tests for specific diagnosis

J. Neurogenic Disorders
1. Patterns of recent denervation
2. Patterns of chronic denervation associated with reinnervation

K. Toxic and mechanical
1. Statin myopathy and other necrotizing myopathies
2. Emetine myopathy
3. Colchicine myopathy
4. Chloroquine myopathy
5. Zidovudine therapy

6. HMG-CoA reductase inhibitors
7. Fibric acid derivatives
8. Organophosphate poisoning
9. Acute alcoholic myopathy; differentiate necrotizing from vacuolar
10. Myopathy caused by intramuscular injections
11. Focal myopathy cause EMG examination

L. Neuromuscular Junction
   1. Identification in biopsies by the nonspecific esterase reaction
   2. Detection of immune deposits (C3-, C5b9-, Protein A-reactivity)

III. Nerve Diseases

A. Basic Histological Alterations and Artifacts
   1. Nerve fiber alterations
      a. Identification of nerve tissue – peripheral nerve, ventral and dorsal root, spinal and autonomic, ganglia and nerve endings in skin
      b. Fiber number – normal; decreased (slight, moderate or severe); increased (slight, moderate or severe); generalized; focal or multifocal
      c. Size distribution of nerve fibers – abnormality of all size classes, selectively of large MF, selectively of small myelinated fibers or selectively of unmyelinated fibers
      d. Pathologic conditions of teased myelinated fibers – normal (A), myelin wrinkling (B), segmental demyelination (C), demyelination and remyelination (D), axonal degeneration (E), remyelination (F), myelin reduplication (G), axonal regeneration after degeneration (H), distal axonal degeneration
      e. Axon alterations – axonal enlargement, axonal atrophy, dark axons with light cores suggestive of ischemic injury, axonal spheroids, polyglucosan bodies, glycogen accumulation, adaxonal sequestration
      f. Myelin and Schwann cell alterations – myelin irregularity; onion bulbs (generalized, focal or multifocal); reduplication; increased spacing of myelin lamellae
      g. Schwann cell inclusion – MLD, Krabbe, Fabry
      h. Artifacts – crush, freezing, poor fixative, poor osmication from inadequate infiltration, inadequate control

   2. Interstitial alterations
      a. Endoneurium – size (normal; increased or decreased; fluid (normal or increased); connective tissue (increased or decreased or abnormality); inflammatory cells (kind and frequency); neoplastic cells (kind and frequency); vessel alteration; (microvessel, arteriole or venule) and histologic change; tissue infiltrates; hemosiderin cellular infiltrates (CD45, CD68 and other); hemosiderin and other
      b. Perineurium – number of lamellae (normal, decreased or increased); increased perineurium (focal or generalized); cellular infiltration (kind and severity); vessel alteration (as in a.)

c. Epineurium – alteration of small arteries, large and small arterioles, venules and microvessels – degenerative alterations, e.g., atherosclerosis, medial arterial calcification, basement membrane reduplication, and infiltration of inflammatory cells or abnormal material (amyloid), inflammatory cell infiltration and histologic reaction, e.g., granuloma (as in a.)

B. Hereditary and Congenital (Non-Metabolic)
1. Aplasia of normal nerve fiber population
2. Maldevelopment of nerve fiber classes, e.g., HSAN 2-5.
3. Schwann cell and other nerve fiber or cellular inclusion in errors of metabolism, e.g., MLD, Krabbe, Tay Sachs, ALD, Fabry, Tangiers disease, etc.
4. Giant axonal polyneuropathy
5. Neuroaxonal dystrophy

C. Metabolic
1. Diabetic neuropathies – cranial, typical DPN (DSPN), atypical DPN, radiculoplexus neuropathies (RPN) – lumbosacral, thoracic or cervical, compression and entrapment neuropathies (median, ulnar and peroneal nerves)
2. Acromegaly neuropathy
3. Hypothyroid neuropathy
4. Hepatic neuropathy and xanthomatous neuropathy
5. MEN, 2b
6. Neuropathies associated with nutritional deficiency
   a. after bariatric surgery
   b. caused by nutritional deficiencies
   c. copper deficiency neuropathy
7. Porphyria

D. Inflammatory and Immune
1. Inflammatory and demyelinating
   a. acute
      i. AIDP
      ii. AMAN
   b. chronic
      i. CIDP
      ii. multifocal CIDP (MADSAM)
      iii. sensory CIDP
      iv. CISP
      v. MGUS associated
2. Multifocal motor neuropathy with conduction block
3. Nerve large vessel vasculitis
4. Nerve microvasculitis
   a. DLRPN
   b. LRPN
   c. inflammatory brachial plexopathy
5. Sarcoid neuropathy

E. Infectious
    1. Syphilis
    2. HIV
    3. Leprosy – lepromatous, tuberculoid and mixed
    4. Lyme borreliosis
    5. Chagas disease
    6. Herpes simplex
    7. Herpes zoster

F. Ischemic neuropathies
    1. Assoc. with DM
    2. Assoc. with nerve large arteriole necrotizing vasculitis
        a. nerve microvessel necrotizing vasculitis
    3. Atherosclerosis

G. Tumor
    1. Sheath tumors – Schwannoma, neurofibroma
    2. Perineurioma
    3. Secondary tumors
    4. lymphoma associated
    5. Paraneoplastic
    6. Amyloid neuropathy
        a. inherited
        b. monoclonal associated
    7. POEMS syndrome

H. Toxic
    1. Toxic neuropathy from industrial agents
    2. Metal neuropathy
        a. arsenic
        b. mercury
        c. thallium
        d. gold
        e. platinum
    3. Drug related neuropathies

I. Miscellaneous
    1. autonomic neuropathies
    2. entrapment neuropathies