TBL Session 1

CPD Patient of the Week – Week 1: Myasthenia gravis
CPD Patient of the Week – Week 3: Athlete in training

CPD Afternoon Case Week 4: Guillan-Barre

Additional cases thus far identified to support Skeletal Muscle LOs:

Muscular Dystrophy
Nutritional supplementation for triathlon training
Steroid use in a high school football player
MELAS
Polio, Amyotrophic lateral sclerosis
Muscle Cramps- could have case of electrolyte abnormality

1. Skeletal Muscle

1.1. Skeletal Muscle Structure

1. List the three types of muscle tissue and compare their structure & functions.

2. Identify the diagnostic features of skeletal muscle and compare these with those of smooth and cardiac muscle.

3. Identify the intracellular locations where contractile filaments are attached to the plasma membranes of muscle cells.

4. Describe the cellular junctions present in smooth and cardiac muscle, but that are lacking in skeletal muscle.

5. Compare and contrast red and white skeletal muscle fibers.

6. Describe the relationship between muscle fibers, stroma and tendons.

1.2. Skeletal Muscle Mechanism of Contraction

7. Draw and label a skeletal muscle at all anatomical levels, from the whole muscle to the molecular components of the sarcomere. At the sarcomere level, include at two different stages of myofilament overlap.

8. Draw a myosin molecule and label the subunits (heavy chains, light chains) and describe the function of the subunits.

9. Diagram the structure of the thick and thin myofilaments and label the constituent proteins.

10. Describe the relationship of the myosin-thick filament bare zone to the shape of the active length:force relationship.
11. Diagram the chemical and mechanical steps in the cross-bridge cycle, and explain how the cross-bridge cycle results in shortening of the muscle.

1.3. Control of Skeletal Muscle Contraction: Excitation-Contraction Coupling and Neuromuscular Transmission

12. List the steps in excitation-contraction coupling in skeletal muscle, and describe the roles of the sarcolemma, transverse tubules, sarcoplasmic reticulum, thin filaments, and calcium ions.

13. Describe the roles of ATP in skeletal muscle contraction and relaxation.


15. List in sequence the steps involved in neuromuscular transmission in skeletal muscle and point out the location of each step on a diagram of the neuromuscular junction.

16. Distinguish between an endplate potential and an action potential in skeletal muscle.

17. List the possible sites for blocking neuromuscular transmission in skeletal muscle and provide an example of an agent that could cause blockage at each site.

1.4. Mechanics and Energetics of Skeletal Muscle Contraction

18. Explain the relationship of preload, afterload and total load in the time course of an isotonic contraction.

19. Distinguish between an isometric and isotonic contraction.

20. Distinguish between a twitch and a tetanus in skeletal muscle and explain why a twitch is smaller in amplitude than a tetanus.

21. Draw the length versus force diagram for muscle and label the three lines that represent passive (resting), active, and total force. Describe the molecular origin of these forces.

22. Explain the interaction of the length:force and the force:velocity relationships.

23. Draw force versus velocity relationships for two skeletal muscles of equal maximum force generating capacity but of different maximum velocities of shortening.

24. Using a diagram, relate the power output of skeletal muscle to its force versus velocity relationship.

25. Describe the influence of skeletal muscle tendons on contractile function.

26. List the energy sources of muscle contraction and rank the sources with respect to their relative speed and capacity to supply ATP for contraction.

27. Define muscular fatigue and muscle cramps. List some intracellular factors that can cause fatigue.

28. Construct a table of structural, enzymatic, and functional features of fast-glycolytic and slow-oxidative fiber types from skeletal muscle.
29. Describe the role of the myosin crossbridges acting in parallel to determine active force and the rate of crossbridge recycling to determine muscle speed of shortening and rate of ATP utilization during contraction.

30. Understand how ATP production is matched to ATP consumption in fast and slow skeletal muscle cells.

31. Discuss the functional consequences of the parallel and series arrangement of myofibrils in a skeletal muscle.

32. Describe how the arrangement of a skeletal muscle to the skeleton can influence mechanical performance of the muscle.

33. Define a motor unit and describe the order of recruitment of motor units during skeletal muscle contraction of varying strengths. Relate motor units to the normal checkerboard appearance of muscles in cross section.

34. Describe the relationship between muscle force production and the frequency of action potential generation.

35. Understand developmental changes in skeletal muscle cells and how these are subsequently modified through activity and training.

36. Explain how anaerobic threshold, muscle fatigue, gender and age can alter exercise performance.

2. Bioenergetics, Skeletal Muscle Metabolism & Exercise Physiology

37. Calculate the daily energy expenditure (DEE) based on physical activity and estimated basal metabolic rate (BMR).

38. Review the concepts of cellular energy transformation (bioenergetics).

39. Relate the concept of Gibbs free energy (ΔG) to the potential for ATP to provide energy for mechanical and transport work in muscles cells and the generation of ATP from metabolic processes under anaerobic and oxidative conditions.

40. Review the response of all of the metabolic pathways below to energy demand (ATP, ADP, and AMP levels), oxygen availability (indicated by NADH, NAD⁺), Ca²⁺, feedback regulation, and allosteric regulation. Recall important coenzymes and cofactors in these pathways: glycolysis, glycogenolysis, TCA cycle, oxidative phosphorylation, oxidation of fatty acids and ketones.

41. Relate the fuel utilization and function of the different muscle fiber types to their content of mitochondrial, myoglobin, glycogen, and glycolytic enzymes.

42. Review creatine synthesis in the body and its activation by creatine (phospho)kinase in muscle.

43. Apply the principles of bioenergetics to explain how creatine phosphate is used for energy storage and ATP production.
44. Describe the biological activation of creatine phosphate and indicate why it is a better energy reservoir than ATP.

45. Discuss how creatine (phospho)kinase and creatinine are used in clinical diagnosis.

46. Describe the differences in metabolic regulation between skeletal muscle and liver, including specific tissue responses and hormonal responses.

47. Review the sources of glucose used by muscle during exercise and how this relates to the enzyme defects underlying glycogen storage diseases that affect skeletal muscle function.

48. Review the fuel metabolism of resting muscles in the fed and starved state. Compare this with the fuel metabolism of muscles at different intensities and durations of exercise.

49. Review how fuel utilization changes during exercise with changes in hormone release.

50. Describe the relationship between aerobic exercise and insulin requirements. Identify its underlying basis.

51. Discuss how fuel utilization changes during exercises with changes in blood flow.

52. Review the regulation of glycogenolysis, glycolysis, TCA cycle and fatty acid oxidation, including the regulation of pathway enzymes and carnitine-mediated transport of fatty acids into mitochondria.

53. Review the role of the Cori cycle during anaerobic muscle metabolism.

54. Review branched-chain amino acid metabolism and identify the coenzyme-requiring steps and the anapleoric roles of the metabolites in the TCA cycle.

55. Discuss how skeletal muscle is more “equipped” for branched-chain amino acid metabolism than is the liver.

56. Review the role of the glucose/alanine cycle in providing fuel for muscle and elimination of nitrogen.

57. Discuss the metabolism of aspartate by the purine nucleotide cycle and the importance of this cycle in exercising muscle.

58. Review the production of glutamine from other amino acids and the physiological purpose of glutamine export from muscle to the liver and kidney.

59. Discuss/review the metabolic basis of the muscular symptoms and clinical findings associated with the following conditions or diseases. Where applicable consider how the enzyme, nutrient, or biological factor deficiencies lead to altered muscle function and exercise physiology:
   - glycogen storage diseases
   - myoadenylate deaminase deficiency
   - mitochondrial myopathies (MERRF, MELAS, recurrent myoglobinurias)
   - iron deficiency
   - carnitine deficiency
   - carnitine palmitoyl transferase II deficiency
   - branched-chain aminoacidurias.
3. Introduction to the Musculoskeletal System

3.1. Anatomy, Function & Imaging of Synovial Joints

60. Distinguish the following features of a synovial joint: capsule, synovial membrane, articular cartilage, fibrocartilage.

61. Distinguish intrinsic vs. extrinsic accessory ligaments of synovial joints.

62. Describe the innervation of joints and the muscles that act upon them.

63. Compare the vascularity and healing potential of the different tissues that form synovial joints.

64. Define bursae and describe their function. Define bursitis.

65. Describe what is meant by joint “stability” and relate this concept to a joint’s mobility and susceptibility to injury. Distinguish passive from dynamic stabilization of joint.

66. Be able to distinguish synovial fluid, fat, bone, cartilage, ligaments and muscles in T1- and T2-weighted MR images.

3.2. Joint Mechanics & Kinesiology

67. Understand the coordination of synergists and antagonists on the skeletal framework.

68. Identify the normal range of motion of the shoulders, hips and knees and describe how to test each.

3.3 Tendon & Ligaments

3.3.1. General Concepts

69. Distinguish regular and irregular dense connective tissues.

70. Identify the types of fibers present in tendons and describe their typical arrangement. Identify the function of tendons.

71. Characterize the attachment of tendons to cartilage, bone and muscle.

72. Discuss the turnover, repair, healing potential and graft of tendons.

73. Describe the different healing potential of a paratenon tendon and a mesotenon tendon.

3.3.2. Clinical Concepts

74. Need objectives on the effect of steroids and quinolones on tendons.

75. Quinolones contraindicated in the pediatric patient.

4. Overuse Injuries and Soft-tissue Trauma
4.1. Muscle Healing & Rehabilitation

76. Define overuse injury and repetitive strain injury.

77. Describe the self-repair of muscle fibers following microtrauma.

78. Identify the physiological effects of excessive force on muscle fibers.

79. Identify indications for the use of heat and cold to treat musculoskeletal injuries.

80. Discuss the rationale of RICE (Rest, Ice, Compression and Elevation) in the treatment of acute musculoskeletal injuries.

81. Define ergonomics. Discuss the role of Physical and Occupational Therapy in preventing occupational injury.

4.2. Treatment of Musculoskeletal Over-Use Injuries

4.2.1. Muscle Relaxants: Direct-acting Cholinergic Agents (Curare, Nicotine, Succinylcholine, Tubocurarine, Cisatracurium, Rocuronium, Mivacarium)

82. Describe the physiology and pathophysiology of transmission at the neuromuscular junction as it relates to pharmacology.

83. Differentiate between depolarizing and competitive neuromuscular antagonists.

84. Compare and contrast depolarizing and competitive neuromuscular antagonists with respect to their use, limitations and adverse effects.

85. Explain the rationale for the combination use of antimuscarinic and anticholinesterase agents in reversal of neuromuscular blockade.

86. Discuss the mechanism of action and clinical applications of botulinum toxin. Describe possible side effects associated with the use of this drug.

87. Explain why nicotine is not used clinically (except as a smoking deterrent), and its historical, social and toxicological significance.

4.2.2. Agents Used to Treat Tendonitis and Bursitis

4.2.2.1. Nonsteroidal Anti-Inflammatory Agents (Introduced in MCM)

88. Review the biosynthesis, physiological and pharmacological effects of the eicosanoids, with emphasis on the role of prostaglandins and leukotrienes as mediators of inflammation.

89. Review the mechanism of action common to all nonsteroidal anti-inflammatory drugs (NSAIDs).

90. Review the adverse affects and drug interactions of the following nonsteroidal anti-inflammatory drugs (NSAIDS):
   - Salicylic acid derivatives
   - Indole and indene acetic acids
   - Heteroaryl acetic acids
91. Review the therapeutic uses and adverse effects of the celecoxib.

92. Compare and contrast the pharmacological properties of selective cyclooxygenase-2 inhibitors with non-selective cyclooxygenase inhibitors.

93. Review the pharmacodynamics, pharmacokinetics, therapeutic uses, and adverse effects of acetaminophen.

94. Compare and contrast the pharmacological properties of acetaminophen with those of NSAIDs.

95. **Need additional objectives specific to uses in the treatment of tendonitis and bursitis.**

4.2.2.2. **Glucocorticoids (betamethasone, hydrocortisone, cortisone, dexamethasone – introduced in MCM)**

96. Review the chemistry and structure, pharmacokinetics and pharmacodynamic actions of glucocorticoids in relation to their use as anti-inflammatory agents.

97. Review the toxicities associated with the use of glucocorticoids.

98. **Need additional objectives specific to uses in the treatment of tendonitis and bursitis.**

5. **Spinal Reflexes**

5.1. **Alpha motor neurons & Motor Neuron Pools**

99. Identify the location of alpha motor neurons in the spinal cord and describe the distribution (somatotopic organization) of alpha motor neurons supplying axial and limb skeletal muscles.

100. Compare the motor neuron pools supplying axial and limb muscles with respect to the following characteristics: interconnectivity across spinal cord segments; contralateral spinal cord projections.

101. Compare the functions of excitatory and inhibitory interneurons in the spinal cord.

102. Describe the primary function of Renshaw cells and identify their neurotransmitter. Explain the involvement of Renshaw cells in the convulsions seen in strychnine poisoning and tetanus.

5.2. **Muscle Receptors and Spinal Reflexes**

103. Define proprioception and list the mechanoreceptors involved in this sensation. Distinguish the types of information conveyed by these mechanoreceptors. Distinguish intrafusal and extrafusal muscle fibers and identify the type of motor neuron that innervates each.

104. Draw and label the components and signals (inhibitory/excitatory) involved in the stretch reflex (include agonist and antagonist muscles).
105. Identify the spinal cord segments tested by the following muscle reflexes: biceps, triceps, brachioradialis, patellar tendon, Achilles (calcaneal) tendon.

106. Relate the stretch reflex to muscle tone and the maintenance of posture.

107. Define each of the clinical terms: hyperreflexia, hyporeflexia, aflexia, atonia.

108. Draw and label the components and signals (inhibitory/excitatory) involved in the golgi tendon reflex.

109. Draw and label the elements of the gamma loop. Describe the role of the gamma efferent system in the stretch reflex and explain the significance of alpha-gamma co-activation.

110. Draw and label the components and signals (inhibitory/excitatory) involved in the flexor withdrawal/crossed-extensor reflex.

6. Myopathies

6.1. Primary Myopathies

111. Discuss spinal muscular atrophy in terms of etiology, pathogenesis, morphology and clinical features.

112. Describe the structure and function of dystrophin and the role of its multiple genetic promoters.

113. Compare Duchenne, Becker, limb girdle and myotonic muscular dystrophies in terms of the following variables:
   - mode of inheritance
   - age and sex of incidence
   - muscles primary involved
   - pathogenesis
   - morphologic features
   - clinical manifestations
   - prognosis

114. Define floppy infant syndrome.

115. Discuss the following metabolic myopathies in terms of etiology, pathogenesis, morphology and clinical features: phosphorylase deficiency, acid maltase deficiency, and lipid storage myopathies.

116. Describe the genetic basis and clinical presentations of Myoclonic Epilepsy with Ragged Red Fibers (MERRF) and Mitochondrial Myopathy, Encephalopathy, Lactic Acidosis and Stroke (MELAS). Describe the etiology and clinical significance of “ragged red fibers”.

117. Distinguish chronic progressive external ophthalmoplegia (CPEO) from Kearns-Sayre syndrome (KSS).

6.2. Secondary Myopathies
118. Discuss the following inflammatory myopathies in terms of etiology, pathogenesis, clinical presentation, histopathologic findings and prognosis: dermatomyositis, polymyositis and inclusion body myositis.

119. Identify the clinical and pathological features of toxic myopathies.

120. Define diabetic amyotrophy and identify its etiology.

6.3. Clinical Presentation & Evaluation of Myopathic & Neuropathic Disorders

121. Discuss the utility of clinical evaluation, EMG, serum creatine kinase (CK) levels, nerve biopsy and muscle biopsy in the diagnosis of neurogenic and myopathic disorders.

122. Distinguish fibrillations from fasciculations.