Lecture 15 - Pain and Analgesia -- MacDermott

1. Different kinds of pain:
    Acute
    Inflammatory
    Neuropathic

2. To understand the pharmacology of pain, you must know the anatomy and physiology of the system.

    Peripheral nociceptors
    Dorsal horn – major center for integration of afferent and efferent signaling
    Ascending pathway
    Descending pathway

3. Multiple types of nociceptors may be classified by sensory modality, conduction velocity, sensitivity to growth factors, peptide expression, and site of termination in the dorsal horn.

    Signal transduction in nociceptors
    Nociceptor-specific Na^+ channels
    Afferent fiber conduction and pain
    Nociceptive inputs go to laminae I, II and V in the dorsal horn

4. The spinal cord dorsal horn has a heterogeneous cell population including:
    -projection neurons
    -excitatory interneurons
    -inhibitory interneurons

5. Synaptic transmission in the dorsal horn
    Nociceptors synapse with dorsal horn neurons in lamina I, II, and V.
    Nociceptors and local excitatory interneurons release glutamate as the fast transmitter, some also release co-transmitters such as peptides with slower excitatory action.
    Local inhibitory interneurons release GABA and glycine as fast transmitters, some also release co-transmitters.
    Descending inputs synapse with projection neurons, interneurons, and terminals of nociceptors.

6. Sensitization in the pain pathway results in hyperalgesia (hypersensitivity to a noxious stimulus) and allodynia (pain that results from a non-noxious stimulus).

    Peripheral sensitization
        skin and viscera
    Central sensitization

dorsal horn
higher centers

7. Ascending nociceptive pathway

8. Descending Pathway – regulation of nociception
   Multiple levels of control
   Reciprocal connections
   Include excitatory and inhibitory projections to the dorsal horn

9. Opioids are important regulators of nociceptive signaling and they act at many levels of the nervous system:
   primary afferents
   dorsal horn neurons
   higher centers

Relevant reading: chapter 24 in "Principles"