essential tremor

- **the most common movement disorder**
  prevalence increases with age

- tremor involves the cranial musculature; the head is involved most frequently, followed by voice, jaw, and face
  both upper extremities are typically affected
  mild asymmetry is not uncommon
  muscle tone and reflexes are normal
  Parkinsonian features such as bradykinesia and rigidity are absent

- pathophysiology is not fully known
  perhaps **abnormally functioning central oscillator** (central pattern generator) cerebellar-brainstem-thalamic-cortical circuits are likely involved.
  in some cases (perhaps a majority) - there’s **Purkinje cells** damage and loss
  in other cases - **locus ceruleus cells with Lewy bodies** (abnormal protein accumulation inside cells)

- **familial** in at least 50 – 70% of cases; transmission is autosomal dominant

- **disability is common**

- medical treatments
  **alcohol**
  risks: ET may worsen as alcohol levels decline
  self-medication may lead to alcoholism

  **beta-blockers** - prime treatment
  propranolol and primidone

  other medications (case reports or small open-label studies)
  Clozapine (atypical antipsychotic)
  Topiramate (anti-convulsant)
  Gabapentin (anti-convulsant)
  Mirtazapine (tetracyclic antidepressant)
  Benzodiazepines (antidepressants): clonazepam and alprazolam
  Botulinum toxin (muscle relaxer/muscle paralytic)
  limits release of acetylcholine at neuromuscular junction
  weakness is a side-effect; more applicable for head tremors than for arm tremors

- surgical treatments
  **deep brain stimulation** of thalamus
  **thalamotomy** (ablation of small region in thalamus, ventrointermedius nucleus)
  both tretaments are effective, each has advantages and disadvantages
Motor Systems - Autonomic Motor

**Somatic Motor System**
- Premotor cortex
- Primary motor cortex
- Brain stem
- Interneurons
- Somatic motor neurons
- Skeletal muscle cells

**Autonomic Motor System**
- Cingulate cortex
- Amygdala
- Hypothalamus
- Interneurons
- Preganglionic autonomic motor neurons
- Postganglionic autonomic motor neurons
- Cardiac muscle cells
- Smooth muscle cells
- Gland cells
Autonomic Motor System
Major Divisions

sympathetic
parasympathetic
enteric

Parasympathetic
brain stem and sacral spinal cord

ganglion

ganglion

ganglion

ganglion

ganglia

brain stem

midbrain

pons

medulla

spinal cord
S2-S4

Sympathetic
intermediolateral column
“lateral horn”

spinal cord
levels
paraverterbral chain ganglia

spinal nerve

gray ramus

white ramus

preverterbral ganglia

efferent pathway
Sympathetic
neurotransmitters and receptors

**Parasympathetic**

- PreG: preganglionic neuron
- PostG: postganglionic neuron

**Sympathetic**

**Special Case for Sympathetic Autonomic**
- alpha 1 are found on smooth muscle cells in walls of arterioles in most organs
  - activation of alpha 1 receptors contracts smooth muscle and produces vasoconstriction
- beta 2 receptors are also found on smooth muscle cells in walls of bronchioles
  - activation of beta 2 receptors relaxes smooth muscle cells and produces bronchiole dilation

**Neurotransmitters/Receptors**

**Cholinergic Synapses**
- neuromuscular junctions
  - preganglionic autonomic neurons >>> postganglionic neurons
  - postganglionic autonomic neurons >>> muscle or gland cells

**Adrenergic Synapses**

- Alpha: alpha 1 are found on smooth muscle cells in walls of arterioles in most organs
  - activation of alpha 1 receptors contracts smooth muscle and produces vasoconstriction
- Beta: beta 1 receptors are found on pacemaker and contractile cardiac muscle cells
  - activation of beta 1 receptors increases heart rate and contractility
  - beta 2 receptors are also found on smooth muscle cells in walls of bronchioles
  - activation of beta 2 receptors relaxes smooth muscle cells and produces bronchiole dilation
Autonomic Reflexes and Disorders

Pupillary Light Reflex

from figure 17-38

E-W = Edinger-Westphal nucleus

Argyll Robertson pupil

damage to optic tract or pretectum on side of “X”

Holmes-Adie pupil

damage to oculomotor nerve on side of “X”
Autonomic Reflexes and Disorders

Horner’s Syndrome

**signs/symptoms**

- **miosis**
- **anhidrosis**
- **partial ptosis**
- **apparent enophthalmos**

---

**do the postganglionic neurons survive?**

- place a few drops of peredrine in affected eye
- peredrine - an amphetamine derivative
- enhances release of norepinephrine from axon terminals

---

**before peredrine**

- **small pupil**

---

**after peredrine**

- **large pupil**
- **small pupil**
**Autonomic Reflexes and Disorders**

**Case A**

T.F is 30-years-old and is currently being treated for hypertension. For no apparent reason, T.F. sometimes experiences feelings of anxiety. He also complains of headaches, nausea, abdominal pains and feeling hot. He notes that he’s lost some weight since the onset of his problems. During certain “episodes,” T.F.’s heart races, he sweats profusely and exhibits nervous tremors. His physician schedules a MRI and a urinalysis to check for higher-than-normal levels of catecholamines. Although a final diagnosis await the results of the imaging and lab tests, T.F.’s physician suspects an autonomic problem is at the root of his disorder and that surgery will ultimately be an important part of the treatment.

**Case B**

A developmental abnormality involving the neural crest has lead to serious difficulties in the lower gastrointestinal tract for newborns like J.G. This disorder involves the autonomic/enteric nervous systems and is one of the most common congenital anorectal malformations (1/5,500 births, four times more frequent in males). Neural crest may have failed to migrate toward the developing colon and rectum. Alternatively, neural crest cells reached the colon but failed to survive and differentiate. As a result, enteric neurons in one or more of the plexuses are missing along a variable section of the distal GI tract. Extrinsic (sympathetic and parasympathetic) inputs to the colon and rectum proliferate. The absence of the enteric neurons and the over-abundance of extrinsic inputs disrupt peristalsis and affect smooth muscle tone. Continuous spasm in the aganglionic segment causes a stenosis and diminished motility; massive distention of the normal proximal colon develops secondarily. There is retention of fecal matter in the distended colon. The untreated disease has a mortality rate as high as 80%. Surgical removal of the aganglionic portion of the GI tract is an important part of the treatment regimen.

**Case C**

Several serious and debilitating problems affect R.K., age 67 years. The primary sign of the disorder is orthostatic hypotension. In fact, blood pressure regulation overall is faulty. Sometimes while reclining, R.K.’s blood pressure rises dramatically. R.K. also experience irregular heartbeat, constipation, incontinence and diminished ability to control body temperature. In addition, there are signs such as bradykinesia, rigidity, impaired balance and unsteady gait. R.K. complains of double vision and occasional breathing difficulty. His wife notes that he is becoming more confused. The disease is clearly progressing. Images of the brain suggest atrophy at several points - the basal ganglia, cerebellum and portions of the brain stem. There is no cure for this disorder; management of the symptoms is possible to some degree.