Visceral Homeostasis - Blood Pressure & Respiration

General Principles

1. The **autonomic, or visceral, nervous system** is the branch of the nervous system innervating our organs
   a. It can monitor the state of the organs and effect changes in their function.
      i. It does so in a largely subconscious manner.
2. The autonomic nervous system has 2 branches: **sympathetic & parasympathetic system** (see below left)
   a. These have “afferent” (sensory) and “efferent” (motor) components just like our “regular” nervous system:
      i. **Sympathetic efferents**
         1. These are motor neurons that mediate the “**fight or flight**” response. Here’s how:
            a. Cholinergic pre-ganglionic neurons live in the IML (which spans T1-L2).
            b. They project to noradrenergic post-ganglionic neurons that live in various bodily ganglia (cervical, celiac, mesenteric, etc).
            c. These post-ganglionic cells exert effects on target organs, such as:
               i. Speed heart rate.
               ii. Dilate bronchioles.
               iii. Slow gut peristalsis.
ii. **Sympathetic afferents**

1. These are sensory neurons that allow us to **sense pain** in our organs. Here’s how:
   a. The neurons have cell bodies in the dorsal root ganglia (see above right).
   b. They send one process out along the sympathetic efferents to the organs.
   c. They send another process into the dorsal horn of the spinal cord to relay any information about organ pain.
      i. These processes synapse on relay neurons which also happen to get sensory info from the skin.
         1. The brain gets confused…it doesn’t attribute the pain as coming from the organ, but rather the skin.
            a. This is called **referred pain**.
            a. For example, because sympathetic afferents innervating the heart come from T1, heart pain is referred to the T1 dermatome (which runs across the upper chest and down the arm).

iii. **Parasympathetic efferents**

1. These are motor neurons mediating the **“rest and digest”** response. Here’s how:
   a. Cholinergic pre-ganglionic neurons live in various places and project to various cholinergic post-ganglionic neurons, which themselves project to various target organs. Here are the pre/post/target triplets:
      i. (FYI) CN III (Edinger-Westphal nucleus) → ciliary ganglion → pupil sphincter.
      ii. (FYI) CN VII → pterygopalatine & submandibular ganglion → lacrimal and salivary glands.
      iii. (FYI) CN IX → otic ganglion → salivary glands
      iv. (Need to know) CN X → post-ganglionic cells in target structures → structures above left colic flexure.
      v. (FYI) S2-S4 → post-ganglionic cells in target structures → structures below left colic flexure.

2. Let’s focus on CN X.
   a. It turns out **there are 2 CN X structures that put out parasympathetics:**
      i. **Dorsal nucleus of the vagus**
         1. For simplicity’s sake, we’ve said up to this point that all organs above left colic flexure get parasympathetics from it
            a. This is an oversimplification … **only non-heart organs (i.e. secretomotor organs) get parasympathetics from it.**
      ii. **Nucleus ambiguus**
         1. For simplicity’s sake, we’ve said up to this point that it is the motor branch of CN X, innervating palate and larynx.
            a. **It turns out that it is also the source of parasympathetics to the heart.**

3. **Summary (AND WHAT YOU NEED TO KNOW FOR THE EXAM):**
   a. Dorsal nucleus of vagus
      i. Parasympathetics to non-heart organs above left colic flexure.
   b. Nucleus ambiguus
      i. Somatic motor to palate & larynx
      ii. Parasympathetics to heart.

iv. **Parasympathetic afferents**

1. These are sensory neurons that allow us to **sense the “state”** of our organs.
   a. For example, they sense O2 tension, CO2 tension, blood pressure, etc.
b. The best example are the afferent fibers of CN IX and CN X, which innervate baroreceptors in the carotid sinus and aortic arch, respectively.
   i. They carry blood pressure info back to nucleus of the solitary tract

Regulation of Blood Pressure
1. Changes in blood pressure are detected by special sensory neurons called baroreceptors.
2. Baroreceptors live primarily in 2 places:
   a. Carotid sinus (i.e. where the common carotid splits into the internal and external branches).
   b. Aortic arch
3. Baroreceptor information is carried back to the nucleus of the solitary tract in two nerves.
   a. Baroreceptor info from the carotid sinus projects to the nucleus of the solitary tract by travelling in the glossopharyngeal nerve (CN IX).
   b. Baroreceptor info from the aortic arch projects to the nucleus of the solitary tract by travelling in the vagus nerve (CN X).
4. To summarize so far: an increase in blood pressure will cause increased baroreceptor activation, which will cause increased nucleus of the solitary tract activation.
   a. How do the activated neurons in the nucleus of the solitary tract lower blood pressure?
      i. They do so in two ways (see diagram below):
         1. They activate the parasympathetic system.
            a. Specifically, they activate parasympathetic preganglionic neurons in the nucleus ambiguus.
               i. Clarification: Dr. Abendschein told us that the preganglionic parasympathetic neurons for the heart come from the dorsal nucleus of the vagus. This is partially true...but since Dr. Price will be writing the exam, learn it his way: they come from the nucleus ambiguus!
               ii. These go to the heart and lower cardiac output (and thus blood pressure, via Ohm’s law) in two ways:
                  1. Decrease heart rate by slowing SA node pacemaker rhythm
                  2. Decrease heart rate by slowing AV node conduction.
         2. They turn off the sympathetic system.
            a. Specifically, they turn off descending neurons from the ventrolateral medulla by activating an inhibitory interneuron (shown in red), that
projects to the descending ventrolateral medulla neurons. These neurons are tonically active, so this will be a decrease from the usual level.

i. These deactivated descending neurons go to the IML, which is itself deactivated. This lowers cardiac output (and thus blood pressure, via Ohm’s law) in four ways:
   1. Decrease heart rate by slowing SA node pacemaker rhythm
   2. Decrease heart rate by slowing AV node conduction.
   3. Decrease contractility
   4. Decrease vasoconstriction (allowing more blood into the periphery, meaning less blood available centrally to pump).

5. It should be obvious that decreases in blood pressure will cause the circuitry to work in the opposite manner to raise blood pressure:
   a. Decreased firing of baroreceptors \( \rightarrow \) decreased activation of nucleus of the solitary tract \( \rightarrow \) decreased parasympathetic/increased sympathetics.

START HERE
High blood pressure info carried back to nucleus of the solitary tract by CN IX and CN X

Pre-ganglionic parasympathetics to the heart are activated to reduce heart rate

Pre-ganglionic sympathetics are deactivated to reduce heart rate and vasoconstriction

6. Regulation of blood pressure over the long-term involves the renin-angiotensin system (see below).
   a. The kidney senses decreased blood pressure and releases renin.
   b. It triggers a cascade such that angiotensinogen is converted to angiotensin II via angiotensin converting enzyme (ACE).
   c. Angiotensin II increases blood pressure in 3 ways:
      i. Causes vasoconstriction (right part of diagram)
         1. Angiotensin II does this directly by constricting vessels.
         2. Angiotensin II does this indirectly by activating the hypothalamus (which itself activates ventrolateral medulla neurons going to the IML sympathetics).
            a. How does angiotensin II get to the hypothalamus?
               i. It crosses the blood brain barrier at locations called circumventricular organs, the most prominent being:
                  1. Area postrema (located in the 4th ventricle).
                  2. Subfornical organ (located in the 3rd ventricle)
                  3. OVLT (located in the 3rd ventricle).
      ii. Causes organism to ingest water/sodium (bottom part of diagram)
1. Angiotensin II gets to the hypothalamus and increases our thirst drive.
   iii. **Causes kidneys to conserve water/sodium** (left part of diagram)
      1. Angiotensin II gets to the hypothalamus and causes release of **vasopressin** through the **posterior pituitary** (which is just an extension of the hypothalamus)
         a. Causes kidney to conserve water.
      2. Angiotensin II gets to the adrenal cortex and causes release of **aldosterone**.
         a. Causes kidney to conserve Na (and thus water, since water follows Na).
7. It should be clear that blocking renin-angiotensin system via ACE inhibitors would lower blood pressure
   a. As you’ll learn next year, ACE inhibitors are indeed used in the treatment of high blood pressure.

**Renin-Angiotensin System**

Respiration
1. The **Pre-Botzinger Complex** in the medulla is the big daddy respiratory center.
   a. It contains cells that set our respiratory rhythm.
   b. To effectively mediate respiration, the pre-Botzinger complex needs to do two things:
      i. **Be attuned to the O2 and CO2 content of the blood:**
         1. This happens via **chemoreceptors** on the **retro-trapezoid nucleus** which sends this info to pre-Botzinger cells.
         2. This happens via chemoreceptors on the **carotid body**, which sends this info to the nucleus of the solitary tract, which itself projects to pre-Botzinger cells.
      ii. **Send outputs to effectors that can physically cause respiration:**
         1. It projects to cells in the **Botzinger Complex**:
            a. This structure **reciprocally inhibits** inspiratory and expiratory motor neurons that are constantly driven by the rostral ventral respiratory group (rVRG) and caudal ventral respiratory group (cVRG), respectively.
            b. Reciprocal inhibition ensures inspiration is inhibited during expiration and vice versa.
2. It turns out that the pre-Botzinger complex can be modulated by the forebrain.
   a. Specifically, forebrain structures (like cortex, hypothalamus, amygdala, etc) project to the **parabrachial nucleus**, which itself projects to pre-Botzinger cells.
      i. This is why our breathing increases when we’re nervous…the emotion centers of our forebrain (like the amygdala) modulate the rhythm put out by the pre-Botzinger complex.
   1. Obviously, this modulation is inactive during sleep, and we rely on the “core” circuitry described earlier to maintain respiration.

**Micturation**

1. **Short loop reflex:**
   a. Operates in babies.
   b. Bladder stretch causes contraction of the bladder.
   c. Individual has no control over when urination will happen.

2. **Long loop reflex:**
   a. Operates in non-babies.
   b. Bladder stretch activates the **parabrachial nucleus**, which projects to sacral spinal cord to cause bladder contraction.
      i. This loop allows for more complete emptying of the bladder.
   c. The long loop reflex can be modulated by the hypothalamus and PAG.
      i. This allows for better control of micturation, so we only urinate when we want to.

3. **Paraplegics:**
   a. Lose functionality of their long-loop reflex.
      i. Prevents bladder emptying, which promotes **urinary tract infection** (UTI).
   b. Need to reestablish the short-loop reflex, which can take months, if it happens at all.