Neural pathways involved in controlling function of the lower urinary tract. The sympathetic nervous system inhibits smooth muscle in the bladder, excites smooth muscle of the internal urinary sphincter, and inhibits parasympathetic postganglionic neurons. The sympathetic preganglionic fibers course in the hypogastric nerve until they reach the inferior hypogastric ganglion, where they synapse with postganglionic sympathetic neurons (which project to bladder smooth muscle).

The bladder smooth muscle is excited by the parasympathetic nervous system. Parasympathetic preganglionic neurons project via the pelvic nerve to a ganglion in the wall of the bladder, where the synapse with the postganglionic neurons occurs.

The external urinary sphincter is innervated by skeletal motoneurons in the sacral spinal cord.
In adults, tension receptors in the bladder play a critical role in bladder storage. These afferents produce excitation of external sphincter motoneurons, and in addition excite sympathetic preganglionic neurons that contract the internal urinary sphincter and inhibit bladder smooth muscle. Bladder voiding is dependent on the pontine reticular formation. Reticulospinal neurons in the pons both inhibit sympathetic influences on the lower urinary tract and inhibit external sphincter motoneurons. The reticulospinal neurons also excite sacral parasympathetic neurons that act on the bladder, and inhibit reflex actions of bladder afferents on sympathetic preganglionic neurons and external sphincter motoneurons. Thus, the pontine reticular formation serves as a “switch” between urine storage and urine release.

The central neural pathways involved in control of the lower urinary tract are illustrated in Fig. 2, whereas Figs. 3-4 show inputs and influences of pontine micturition neurons.
Inputs to pontine micturition neurons. The activity of pontine micturition neurons is excited by ascending spinoreticular pathways carrying signals from bladder tension receptors, and inhibited by “higher centers”, including the hypothalamus and frontal cortex.

As you might expect, transection of the spinal cord separates the “pontine switch neurons” from the reflex pathways that regulate urinary function. As a result, it is initially very difficult for a paraplegic to release urine. Over time, however, bladder reflexes undergo reorganization. Switch neurons whose activity is controlled by bladder inputs develop in the spinal cord, causing the reflex voiding of the bladder when it becomes full.

Control of bladder function at the spinal cord level also occurs in young children. Before the age of 2-3, the brainstem does not participate in micturition, and the bladder reflexively releases urine when it is full. Between the ages of 2-5, the pontine reticulospinal micturition system develops, permitting voluntary voiding of the bladder.
2) **The Defense Reaction**

In response to threatening stimuli, animals typically exhibit a combination of observable responses, including piloerection (standing of hairs), vocalization, and arching of the back. These actions are coupled with a serious of simultaneous autonomic responses, including increases in arterial blood pressure and heart-rate, a vasodilatation in the hind-limb skeletal muscle (so that the muscle has a larger blood supply), and a decrease in blood flow to the viscera and kidney (to conserve blood for the systemic circulation). Respiratory effort also increases during these effects, to increase blood oxygenation.

This “defense reaction” can also be elicited by stimulation at several particular sites within the central nervous system, including parts of the amygdala and hypothalamus.

In paralyzed animals (which cannot generate motor responses), stimulation within the hypothalamus or amygdala can produce the same changes in heart rate, blood pressure, and regional blood flow. This observation indicates that the autonomic responses are elicited in parallel with the motor responses, and are not secondary to movement.

Thus, it appears that the hypothalamus, amygdala, and probably several other areas of the nervous system, contain specific neural “pattern generators” that specify simultaneous motor responses and autonomic activity that is appropriate for the movement to take place. The “defense reaction” is an example of such a patterned behavior.

3) **Exercise Cardiovascular Responses**

During exercise, blood flow to contracting muscles increases to provide adequate oxygen and to remove carbon dioxide. In association, heart rate and blood pressure rise to increase blood flow within the body. These responses begin early during exercise, and there is evidence to suggest that the cardiovascular adjustments are triggered even before movement begins. For example, completely paralyzed humans exhibit similar changes in blood pressure and heart rate when they “imagine” performing exercise as when muscle contraction actually takes place (see Fig. 5). Thus, the central nervous system may simultaneously “command” the contraction of muscle and changes in blood pressure, heart rate, and blood flow during exercise.

![Effect of intended contraction on heart rate and blood pressure in a totally paralyzed subject. Bars indicate the time when contractions were attempted, and values indicate the relative size of the contraction that was requested.](image)
Take-Home Message:

Skeletal muscle contractions and changes in sympathetic and parasympathetic nervous system activity often occur in parallel, and are coordinated together. These synchronous motor and autonomic responses allow particular behaviors to take place more efficiently, as the autonomic challenges presented by a movement are accounted for rapidly and completely.

A Return to the Cardiovascular System

We now turn to considering how the heart operates to pump blood throughout the body. One “pumping cycle” of the heart is called a cardiac cycle. Amazingly, the initiation of an action potential at one autorhythmic cell results in a wave of electrical activity that spreads throughout the heart, inducing a coordinated contraction of the atria and ventricles. An essential component of regulating contraction is that heart cells are electrically coupled via gap junctions. Thus, electrical activity passes from autorhythmic cells to a myocardial cell, then to another myocardial cell, etc.

Of course, the contraction of myocardial cells in different parts of the heart must be timed appropriately in order for blood pumping to occur efficiently. The chambers of the heart are electrically isolated from each other, so special conduction pathways must pass the electric current between the atria and ventricles.

During a cardiac cycle, the depolarization begins at the SA (sino-atrial) node, located in the right atrium near the superior vena cava. Specialized noncontractile conducting cells carry the depolarization from the SA node to the AV (atrio-ventricular) node, a group of pacemaker cells located near the floor of the right atrium. At the same time, a slow wave of depolarization begins to sweep across the atria, and the atria begin to contract.

The conduction of impulses through the AV nose is quite slow. Eventually, however, the impulses are fed from the AV node to rapidly-conducting conducting cells that form the bundle of His. The bundle of His transmits the depolarization to the bottom of the ventricles, where contraction begins. Many small conducting cells, called Purkinje fibers, carry the impulses from the bottom of the heart up towards the top.
What are the specializations in this conducting system?

First, conduction through the A-V node is slow. The delay introduced insures that the ventricles will contract later than the atria.

Second, the contraction of ventricles begins at the bottom and proceeds to the top. As such, blood is squeezed out of the top of the ventricle. This arrangement makes sense, as blood leaves the ventricles from the top.

Note that all the elements in the conduction pathway are pacemaker cells. However, since they are coupled by gap junctions, the cells that generate action potentials first will induce the others to fire. The SA node pacemaker cells fire faster than any of the others. If the conduction pathway is blocked, then the ventricles will begin contracting at a different rate than the atria.

If damage occurs to the SA node (for example, during a myocardial infarction or “heart attack”), then coordinated contraction of the atria is discontinued. However, as we will see in the next lecture, contraction of the atria is not required for ventricular filling. The most striking effect of damage to the SA node is that the AV node autorhythmic cells become the fastest-firing elements in the network, and begin to time the ventricular contractions. AV node cells have an intrinsic firing rate of about 50/ min, so ventricular contraction will occur slower than before the damage. However, this heart rate is adequate for perfusion of the body, so medical intervention is not required.

A more serious problem occurs following damage to the AV node. The atria continue to contract at their normal rate, driven by the firing of SA node cells, but there is no means for this firing to be relayed to the ventricles. The contraction of the ventricles is now driven by the fastest-firing autorhythmic cells in the ventricular conduction network. These cells are located in the Purkinje fibers, and fire at about 35 times per minute. Thus, after AV block, the ventricles contract much less frequently than normal, and the timing of this contraction is completely desynchronized from the atrial contractions. As a result, perfusion of the body is not adequate. Under such circumstances, an artificial pacemaker must be surgically implanted into the heart to provide electrical stimulation at a predetermined rate.

Another medical problem that can occur is the development of ectopic pacemakers in the conduction pathway. If a single neuron in the conduction network develops unusually rapid firing, then the other cells will begin to “follow” this leader. Obviously, this can induce an unproductive pattern of heart contraction. The location of ectopic pacemaker cells can be identified through careful monitoring of the electrocardiogram at many electrodes, and then these cells are destroyed to restore normal heart contractions.

Clearly, coordination of myocardial contraction is essential for normal cardiac function. In extreme cases, the ventricular myocardial cells begin to contract in an unsynchronous fashion. This condition is known as ventricular fibrillation. As a result, ejection of blood from the ventricles diminishes, which can be life-threatening. In order to resolve this problem, it is necessary to re-synchronize the electrical activity of all of the myocardial cells. This can be done by passing a large electrical current through the heart, thereby depolarizing all the myocardial cells at once. This is a common procedure in hospital emergency rooms.
The electrocardiogram (ECG or EKG)

As early as the beginning of the 20th century, physiologists learned that electrical activity generated by the heart could be recorded from leads placed on the body surface. The Dutch physiologist Einthoven defined clinical procedures for recording the ECG which are still used today. He received the Nobel Prize for this work.

To record the ECG, Einthoven placed electrodes on both arms and the left leg. The effects of electrode positions on the components of the ECG are discussed below. Despite where it is recorded, the ECG is composed of 5 waves: **P, Q, R, S and T**. The P wave is associated with the depolarization of the atria. The **Q, R and S waves** are associated with the depolarization of the ventricles. The **T wave** is associated with the repolarization of the ventricles. The repolarization of the atria occurs at the same time as the Q-R-S complex, and is swamped-out by the larger potential. The time between identical waves in two consecutive ECG complexes (e.g., time between R waves) is often measured to accurately determine heart rate.
One standard way of recording the ECG is to place two leads on the body, and to compare the voltage recorded at those two leads. Three configurations of electrodes placed on the limbs are used in standard bipolar ECG recording. In **LEAD I** recordings, the negative terminal of the ECG is assigned to the right arm and the positive terminal is connected to the left arm. Thus, when the potential recorded from the right arm is negative to that in the left arm, the ECG appears as a positivity (as an upward deflection). When the opposite is true, the ECG appears as a downward deflection. In **LEAD II** recordings, the negative terminal is connected to the right arm and the positive terminal is connected to the left leg. Therefore, when the right arm is negative with respect to the left leg, an upward deflection appears on the ECG. In **LEAD III** recordings, the negative terminal is connected to the left arm and the positive terminal is connected to the left leg. This means that the ECG is recorded as an upward potential when the left arm is negative with respect to the left leg.

By comparing the ECG recorded using the three limb lead configurations, the wave of depolarization that sweeps through the heart during the cardiac cycle can be mapped. If the net electrical potential in the heart moves toward the positive electrode, the tracing of the ECG goes up from baseline. If the net current moves towards the negative electrode, the tracing of the ECG goes down from baseline. It is important for a cardiologist to compare the ECG recorded from multiple leads in order to diagnose heart pathology.

In the figure above, note a triangle drawn around the heart. The apices of the triangle indicate the relative locations of the bipolar limb leads (or, more precisely, where the limbs connect with the fluid conducting the electrical potentials from the heart). This triangle is often referred to as “Einthoven’s Triangle.”

Einthoven also noted that because of the geometry of the recording electrodes and the relative assignments of positive and negative leads, it should be possible to “predict” a recording from one lead if you know the other two. **Einthoven’s Law** states that a mathematical summation of the potentials recorded from any two leads equals the potential recorded from the third lead. When performing this calculation, it is essential to consider the sign (positive or negative) of the leads from which potentials were recorded.
Although recording from any of the limb leads reveals the basic ECG pattern and can be used to diagnose such problems as arrhythmias, this technique does not allow the determination of whether damage has occurred in the ventricular or atrial muscle. Thus, cardiologists add more leads to typical ECG recording in order to diagnose such problems. A series of 6 electrodes is placed across the heart during a typical exam in order to monitor more precisely electrical activity in different regions of the heart. Each of the heart leads is connected in turn to the positive terminal of the ECG, and the negative electrode (indifferent electrode) is connected simultaneously to the left arm, right arm, and left leg. The 6 chest leads used in clinical cardiology are usually called $V_1$, $V_2$, $V_3$, $V_4$, $V_5$, $V_6$.

The diagram to the left shows typical recordings using the 6 chest leads. Because the heart surfaces are close to the chest wall, each chest lead records mainly the electric potential of the cardiac muscle immediately beneath the electrode. Thus, relatively small abnormalities in the ventricles can readily be spotted.

In leads $V_1$ and $V_2$, the QRS recordings of the normal chest are mainly negative because the leads are near the base of the ventricles, which is the direction of electronegativity during most of the ventricular depolarization process. In contrast, the QRS complexes of the other leads are mainly positive because they are positioned near the apex of the heart, which is positively charged during most of depolarization.

Three other “leads” also are typically incorporated into clinical cardiology: the augmented unipolar limb leads. In this type of recording, two of the limbs are connected together to the negative terminal, and the third is connected to the positive terminal.

Thus, typical diagnostic ECG recordings usually involve recording from 12 leads: the 3 bipolar limb leads, the 6 unipolar chest leads, and the 3 augmented unipolar limb leads.

**Examples of diagnostic value of ECG recordings.**

As noted above, damage to the AV node is a very serious medical condition. The first sign of damage to this node is the development of a prolonged lapse between the P-Q or P-R wave. Diseases such as Rheumatic fever often affect the AV node, and measuring the delay between the P and R waves is an effective means to track the progress of the disease. An increased conduction time through the AV node is typically referred to as “first degree heart block.”

As damage to the AV node progresses, conduction does not always occur from the atria to the ventricles. As a result, the QRS complex appears to be missing in some cardiac cycles. Such “second degree heart block” is an indication that a life-threatening situation is developing.
If damage to the AV node progresses, the QRS complex disappears completely from the ECG, and there is a complete desynchronization between atrial and ventricular contractions. The ventricles only contract at long intervals (about 35/min) as dictated by the fast-firing autorhythmic cells in the ventricles (located in the Purkinje fibers). Implantation of a pacemaker is normally done in such patients.

Conduction problems can also develop in the Purkinje system. At some times, some of the Purkinje fibers are blocked, so that electrical impulses are not transmitted to all parts of the ventricles during some cardiac cycles. As a result, the amplitude of the QRS complex can vary between cardiac cycles. This condition is called “electrical alternans”.

Sometimes a “premature atrial contraction,” or an unexpectedly early beat will occur in the ECG. Such an early beat developing in the atria is not usually harmful, and actually is common in healthy people.

Premature ventricular contractions, in which a QRS complex occurs without a previous P wave, can be more serious. The development of ectopic pacemakers in the ventricular conduction system signals an increased risk for ventricular fibrillation, which can be lethal!!

Recall that the time when the heart contracts is called **systole**, and the time when it relaxes is called **diastole**. The atria and ventricles do not contract simultaneously, and thus we can think about both atrial and ventricular diastole and systole as separate events. However, in general systole is considered the time when the ventricles contract, as this is the action that ejects blood from the heart.

The left and right heart act as independent pumps, although they are in series and contract at almost the same time. For the sake of discussion, we will consider the two pumps to be identical in terms of time of action.
Let us begin by considering the time in the cardiac cycle after which the ventricles have just ejected blood, and are relaxed (see diagram on the next page). Both the atria and ventricles are in diastole. The opening and closing of the heart valves is dictated by the pressure differences on the two sides. Since the ventricles are relaxed at this stage, the tricuspid and mitral valves are open, because atrial pressure is slightly higher than ventricular pressure (as a consequence of the atria filling with blood returning to the heart). However, the aortic and pulmonary valves are closed because the pressure in the arteries is higher than in the ventricles (the higher pressure in the arteries is a consequence of the properties of the walls of the vessels, as discussed before).

During this phase, blood flows passively from the vena cavae and pulmonary veins into the atria, and passive ventricular filling also occurs. At rest, approximately 80% of ventricular filling occurs during this phase of the cardiac cycle, when both the atria and ventricles are relaxed.

The next event in the cardiac cycle is the contraction of the atria, which forces about another 20% of blood into the ventricles. At this point, near the end of ventricular diastole, the ventricles are fullest. They contain about 135 ml of blood at rest. This volume is referred to as end diastolic volume (EDV).

Ventricular systole then begins. The ventricles begin to contract, which first forces shut the mitral and tricuspid valves. This is the isovolumetric part of systole, as blood volume in the ventricle is not changing. The point of this phase is to build up pressure in the chamber, so blood will forcefully be ejected when the aortic and pulmonary semilunar valves open.

Pressure eventually rises enough to force open the semilunar valves, and blood flows into the great arteries. At the end of systole, blood is still left in the ventricle. This volume is referred to as end systolic volume (ESV), and is typically about 65 ml.

The amount of blood ejected from each ventricle during each cardiac cycle is referred to as stroke volume. As you probably surmised, \( SV = EDV - ESV \). In normal humans, it is close to 135-65=70 ml at rest.