Adrenergics Module

Winter 2026

Module Content

Learning Objectives

1. To list the types of receptors that bind norepinephrine and epinephrine (adrenergic receptors), and the relative affinity of each ligand for these receptors.

2. To understand the effects of agonists and antagonists binding to adrenergic receptors.

3. To appreciate how the baroreceptor reflex alters the initial effects of ligands binding to adrenergic receptors.

4. To understand the types of cholinergic receptors, and how ligands binding to them affect the cardiovascular system.

5. To define the following terms related to drug actions on the cardiovascular system:

    - Sympathomimetic
    - Sympatholytic
    - Chronotrope
    - Inotrope

6. To apprehend the actions of the following drugs, and how they affect heart rate, cardiac contractility, and total peripheral resistance:

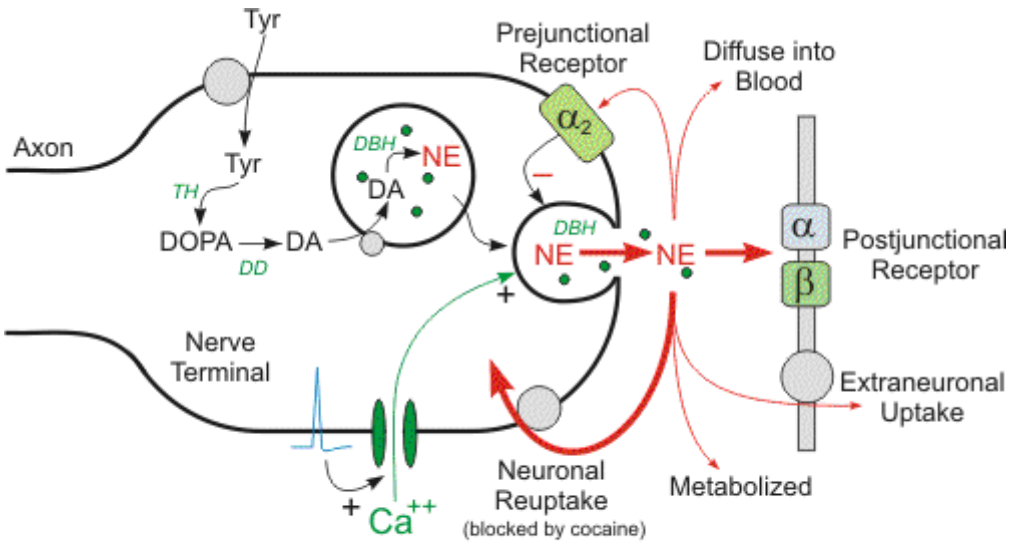
    - Epinephrine
    - Norepinephrine
    - Dopamine
    - Isoproterenol
    - Dobutamine
    - Clonidine
    - Prazosin / Doxazocin / Terazosin / Tamsulosin (α-1 receptor antagonists)
    - Phenoxybenzamine / Phentolamine (nonselective α receptor antagonists)

7. To describe the effects of hypercalcemia and hypocalcemia on the cardiac action potential and electrocardiogram.

Adrenergics Module

Part 1: Adrenergic Transmission

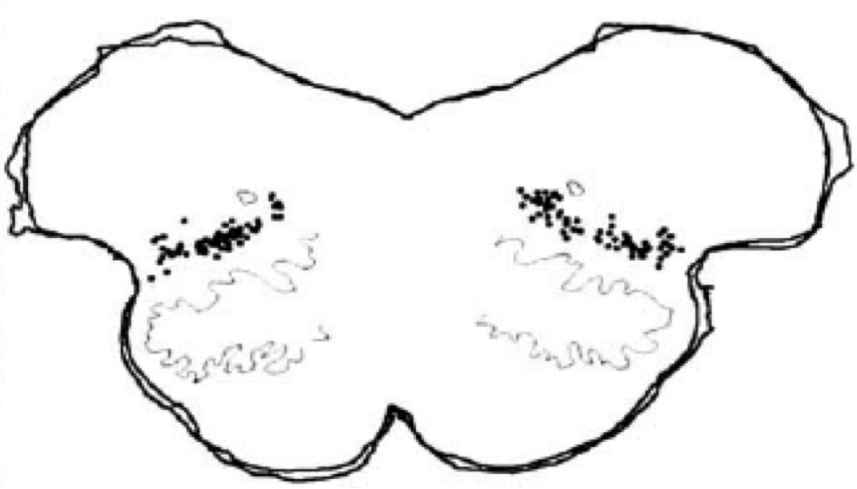
Norepinephrine and Epinephrine



Tyr = tyrosine; TH = tyrosine hydroxylase; DD = DOPA decarboxylase; DA = dopamine; DBH = dopamine β-hydroxylase; NE = norepinephrine

Norepinephrine is synthesized from the amino acid **tyrosine** through by a series of enzymatic steps in particular cells in the central nervous system, as well as by most **postganglionic neurons** of the sympathetic nervous system. Norepinephrine is released like most neurotransmitters: when an action potential invades a nerve terminal, voltage-gated calcium channels (typically **N-type**) open, and the entry of calcium causes fusion of the norepinephrine-containing vesicles with the membrane, thereby releasing norepinephrine into the synaptic cleft.

Norepinephrine is converted to epinephrine by the enzyme **phenylethanolamine N-methyltransferase** (PNMT). This enzyme is abundant in the cytoplasm of most **chromaffin cells** located in the **adrenal medulla**. Chromaffin cells are innervated by preganglionic neurons of the sympathetic nervous system. Acetylcholine released from nerve terminals of sympathetic preganglionic neurons binds to nicotinic receptors on the chromaffin cells, causing the release of epinephrine *(or norepinephrine for cells lacking PNMT)* into the bloodstream. Typically, epinephrine constitutes about 80% of the hormones released into the bloodstream from the adrenal medulla.



A few neurons in the central nervous system also contain **PNMT**. Interestingly, many of these neurons are located in the **rostral ventrolateral medulla** (RVLM), the brainstem area that plays a primary role in controlling blood pressure by regulating the activity of sympathetic preganglionic neurons. The axons of RVLM neurons project to the thoracic and lumbar spinal cord, and make synaptic connections with sympathetic preganglionic neurons. This diagram shows the locations of PNMT-containing neurons in a section through the human brainstem. Presumably the stained neurons are located in the RVLM.

Receptors for Norepinephrine and Epinephrine

Norepinephrine and epinephrine bind to two main subtypes of **metabotropic receptors**: α and β. The α subtype can be divided into the ***α-1*** and ***α-2*** subtypes. The β subtype can be divided into ***β-1***, ***β-2*** and ***β-3*** receptors, although β-3 receptors are less important than the other subclasses.

The effects of norepinephrine/epinephrine binding to these receptors are summarized in the table below:

Receptor	Effects of binding to the receptor
α1	Activates **phospholipase C**, resulting in an increase in intracellular Ca2+
α2	Decreases cAMP by inhibiting adenylate cyclase
β (all subtypes)	Increases cAMP by activating adenylate cyclase

Based on this information, it appears that binding of ligand to α2 and β receptors would have opposite effects. However, there is a complication. α2 receptors are mostly presynaptic ***autoreceptors***, such that ligand binding to the receptor reduces norepinephrine release from the nerve terminal. In contrast, α1 and β receptors are usually postsynaptic.

The adrenergic receptors of most importance in regulating the cardiovascular system are indicated in the following table:

Receptor	**Location** ***(for cardiovascular control)***	**Effect of Agonist**	**Effect of Antagonist**
α1	Vascular smooth muscle *(most tissues)*	Increased blood pressure *(due to vasoconstricton and increased peripheral resistance)*	Decreased blood pressure *(due to vasodilation and decreased peripheral resistance)*
α2	Brainstem *(including terminals of neurons projecting to the RVLM) and terminals of sympathetic efferent fibers*	Decreased blood pressure *(due to decreased RVLM activity)*	Not in common use
β1	Heart *(pacemaker cells, conduction system, cardiac muscle)*	Increased heart rate and contractility	Decreased heart rate and contractility
β2	Vascular smooth muscle *(skeletal muscle arterioles, coronary arterioles, hepatic arterioles)*	Decreased blood pressure *(mainly due to dilation of skeletal muscle arterioles)*	Not in common use

Drugs acting on α and β receptors have a variety effects on targets outside the cardiovascular system. Thus, the use of these drugs elicits many physiological effects in addition to those listed in the table above.

Affinity of Epinephrine and Norepinephrine for α and β Receptors

The table below shows the efficacy of norepinephrine and epinephrine in binding to α and β receptors. Norepinephrine released from sympathetic nerve terminals binds well to α receptors, as well as to β-1 receptors in the heart. However, norepinephrine binds very poorly to β-2 receptors.

In contrast, epinephrine binds well to β-1 and β-2 receptors, and with much less efficacy to α-receptors. However, in very high concentrations (e.g., use of the **EPI-pen**), epinephrine activates α-1 receptors.

Hence, the effects of epinephrine on the cardiovascular system are highly dose-dependent. At normal physiological concentrations, epinephrine activates β-1 and β-2 receptors, resulting in an increase in heart rate and contractility and dilation of muscle arterioles. At high concentrations, epinephrine causes vasoconstricton due to its effects on α-1 receptors.

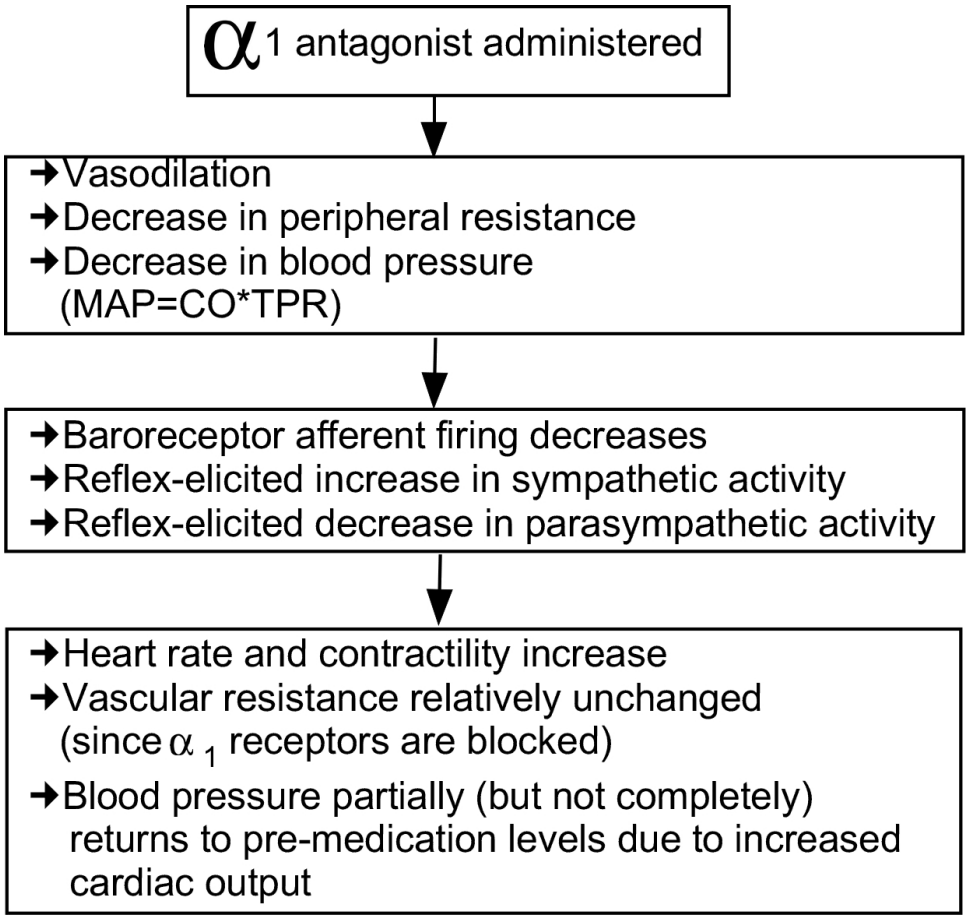
Receptor	Affinity for Norepinephrine and Epinephrine
α	Norepinephrine > Epinephrine *(although Epi binds at high concentrations)*
β1	Norepinephrine = Epinephrine
β2	Epinephrine >>> Norepinephrine *(in effect, norepinephrine does not bind to these receptors)*

The Complication of the Baroreceptor Reflex

Stretch receptors in the large arteries called **baroreceptors** signal changes in blood pressure to the central nervous system. These inputs trigger the **baroreceptor reflex**, which attempts to return blood pressure to the previous level by altering sympathetic and parasympathetic nervous system activity. These actions are summarized in the table below:

Change in Blood Pressure	Change in Baroreceptor Afferent Activity	Change in Activity of Sympathetic Efferents to Heart and Blood Vessels	Change in Activity of Parasympathetic Efferents to Heart
Increase	Increase	Decrease	Increase
Decrease	Decrease	Increase	Decrease

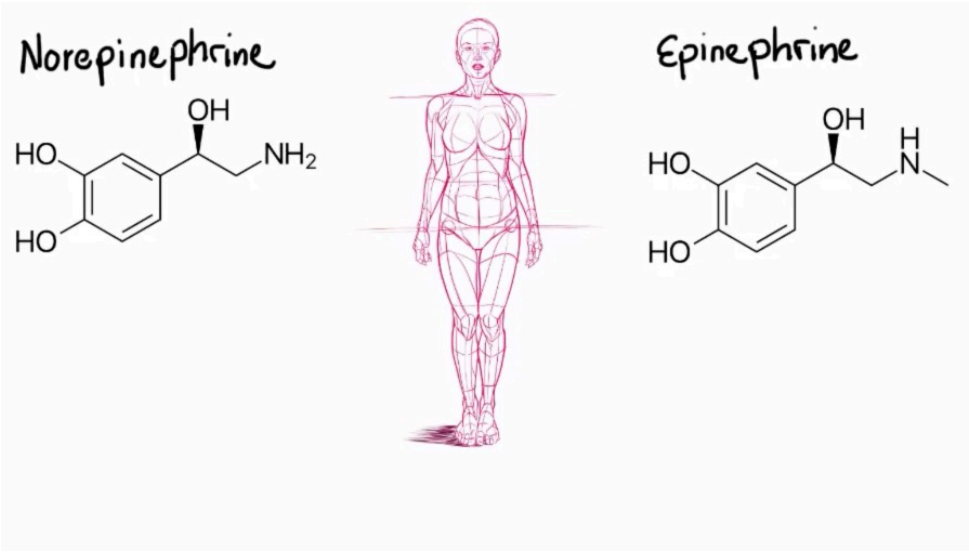
As a consequence of the baroreceptor reflex, a drug that acts on adrenergic receptors can precipitate changes in sympathetic and parasympathetic nervous system activity that tends to offset the effects of the drug. Take, for example, the case of an α1 receptor antagonist. Although such a drug would decrease total peripheral resistance and lower blood pressure, its administration also results in reflex-mediated increases in heart rate and contractility, as shown below.



The baroreceptor reflex-mediated increases in heart rate and contractility precipitated by an α1 receptor antagonist result in increased myocardial oxygen demand, despite the fact that blood pressure (and afterload) have dropped. Hence, such a drug would not be ideal to reduce blood pressure in a patient with coronary vascular disease and impaired ability to supply the myocardium with oxygen.

Review

To review the synthesis, release, and actions of norepinephrine and epinephrine, watch this movie.
If the movie does not play in this window, or you would like to see it in a window of alternate size, download it from this link.



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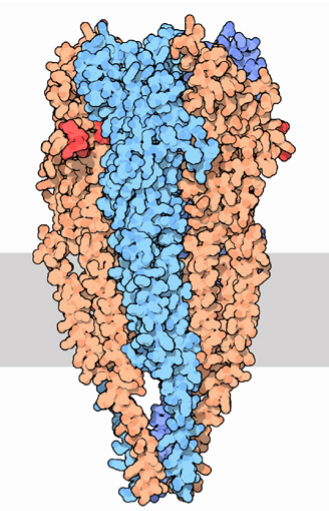
Adrenergics Module

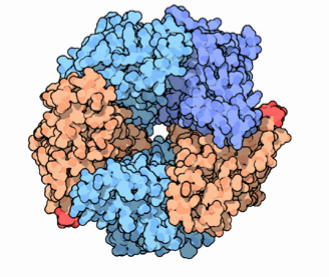
Part 2: Cholinergic Transmission

Introduction

There are two major subtypes of acetylcholine (cholinergic) receptors: **nicotinic** and **muscarinic** receptors. Both nicotinic and muscarinic receptors are present in the central nervous system. In addition, acetylcholine is used as a neurotransmitter by sympathetic and parasympathetic **preganglionic neurons**, as well as parasympathetic **postganglionic neurons**.

Acetylcholine differs from most neurotransmitters, in that it is **NOT** reuptaken into the neuron that released it. Instead, acetylcholine is broken down by an enzyme, **acetylcholinesterase**, which is present in abundance at cholinergic synapses. The physiology of cholinergic synapses can be altered by administering nicotinic or muscarinic agonists or antagonists, **acetylcholinesterase inhibitors** that delay the breakdown of acetylcholine, or **Botulinum toxins** that prevent the release of acetylcholine from presynaptic nerve terminals.





Nicotinic Receptors

All nicotinic receptors are **ionotropic**: binding of acetylcholine to the receptor results in the opening of an ion channel. Nicotinic receptors are comprised of 5 subunits, arranged symmetrically around a central pore. At least 12 building blocks and 17 subtypes of nicotinic receptors have been discovered. One of these subtypes is located in autonomic ganglia, where sympathetic or parasympathetic preganglionic neurons synapse with postganglionic neurons.

The nicotinic receptor subtype in autonomic ganglia can be affected by specific drugs, as indicated in the table below. Such drugs would globally activate or inactivate both sympathetic and parasympathetic postganglionic neurons.

Nicotinic Receptor	Selective Agonist	Selective Antagonist
Ganglion Type	**Dimethylphenylpiperazinium**	**Trimetaphan**

Muscarinic Receptors

Unlike nicotinic receptors, muscarinic receptors are **metabotropic**: they are linked with G proteins. As such, binding of acetylcholine to a muscarinic receptor can elicit a host of effects in the postsynaptic cell.

Muscarinic receptors are located on the peripheral targets of the parasympathetic nervous system (like pacemaker cells of the heart) and in the central nervous system.

There are 5 major subtypes of muscarinic receptors: M1-M5. The most important muscarinic receptor subtype for cardiovascular control is the **M2 subtype**. This subtype is located in the heart, and is involved in the regulation of heart rate and atrial contractility *(note that ventricular contractility is not affected by the parasympathetic nervous system)*. Binding of agonists to the M2 muscarinic receptor subtype result in an increased K+ conductance and a decreased Ca2+ conductance in the postsynaptic cell.

Are Cholinergic Drugs Used in Cardiology?

Cholinergic neurotransmission plays a major role in regulating the activity of the sympathetic and parasympathetic nervous systems, and thus is profoundly involved in cardiovascular control. Nonetheless, cholinergic drugs are not extensively used in cardiology.

The reason is that drugs that affect cholinergic receptors are not very selective, and have widespread effects.

For example, although there are pharmacological agents that selectively activate or inhibit nicotinic receptors in autonomic ganglia, it would be problematic to globally increase or decrease the activity of all sympathetic and parasympathetic postganglionic neurons in unison. In addition, most muscarinic agonists and antagonists have effects on multiple receptor subtypes. It is possible to elicit more specific effects on the cardiovascular system with drugs that act on adrenergic receptors than on cholinergic receptors.

This is not to say, however, that common drugs affecting cholinergic receptors don't have pronounced effects on the cardiovascular system. A good example is **atropine**, a muscarinic receptor antagonist that produces a high heart rate along with many other physiological responses (e.g., dry mouth, large pupils, urinary retention, constipation). Atropine might be used as a rescue drug to treat a patient with bradycardia, but has few general uses in cardiology.

Adrenergics Module

Part 3: Adrenergic Drugs Used in Cardiology

Terminology

To get started, let's review the terminology used for drugs that affect adrenergic transmission.

Sympathomimetics: drugs that act like the neurotransmitters released by the sympathetic nervous system (like norepinephrine and epinephrine).

This drug class includes:

- Direct-acting sympathomimetics --> Drugs that directly stimulate α and β receptors.
- Indirect-acting sympathomimetics --> Drugs that cause the release of norepinephrine from nerve terminals, or block the uptake of the neurotransmitter.
- Mixed-acting sympathomimetics --> Drugs that cause the release of norepinephrine from nerve terminals **AND** stimulate adrenergic receptors.

Sympatholytics: drugs that oppose sympathetic nervous system actions, such as antagonists of α and β receptors.

Chronotropes: drugs that alter heart rate.

This drug class includes:

- Negative chronotropes --> Decrease heart rate.
- Positive chronotropes --> Increase heart rate.

Inotropes: drugs or agents that the contraction of cardiac muscle

This drug class includes:

- Negative inotropes --> Weaken cardiac contractions.
- Positive inotropes --> Strengthen cardiac contractions.

Adrenergic Drugs Used in Cardiology

As discussed in the **Adrenergic Transmission module**, drugs that alter adrenergic transmission elicit a broad spectrum of physiological changes. Discussed below are the actions of adrenergic drugs most commonly used in cardiology. The effects described are limited to those on the cardiovascular system.

Certainly, a variety of drugs in addition to those that act on the sympathetic nervous system are used in cardiology, including **diuretics**, **calcium channel blockers**, etc. These drugs will be discussed later in the course and in subsequent courses such as the renal block. The principal goal of this module is to reinforce basic science principles discussed in prior lectures by discussing the actions of certain adrenergic drugs.

Sympathomimetics

Epinephrine

At low doses, epinephrine serves mainly as a positive inotrope and chrontrope. However, the doses of epinephrine usually provided pharmacologically are adequate to stimulate both α and β receptors. Hence, systemic injections of epinephrine elicit increases in heart rate and contractility *(by binding to cardiac β-1 receptors)* and vasoconstriction *(by binding to α-1 receptors in vascular smooth muscle)*. However, the increase in total peripheral resistance produced by epinephrine administration is only modest. This is because large doses of epinephrine activate both α-1 and β-2 receptors in muscle arterioles, and the physiological effects are offsetting (binding to α-1 receptors promotes vasoconstriction, while binding to β-2 receptors promotes vasodilation).

Systemic epinephrine is often administered prior to **cardiopulmonary resuscitation** *(when bradycardia is present; cardiac arrest)* or in patients with **anaphylactic shock**. It can also be used in patients with ventricular fibrillation.

Norepinephrine

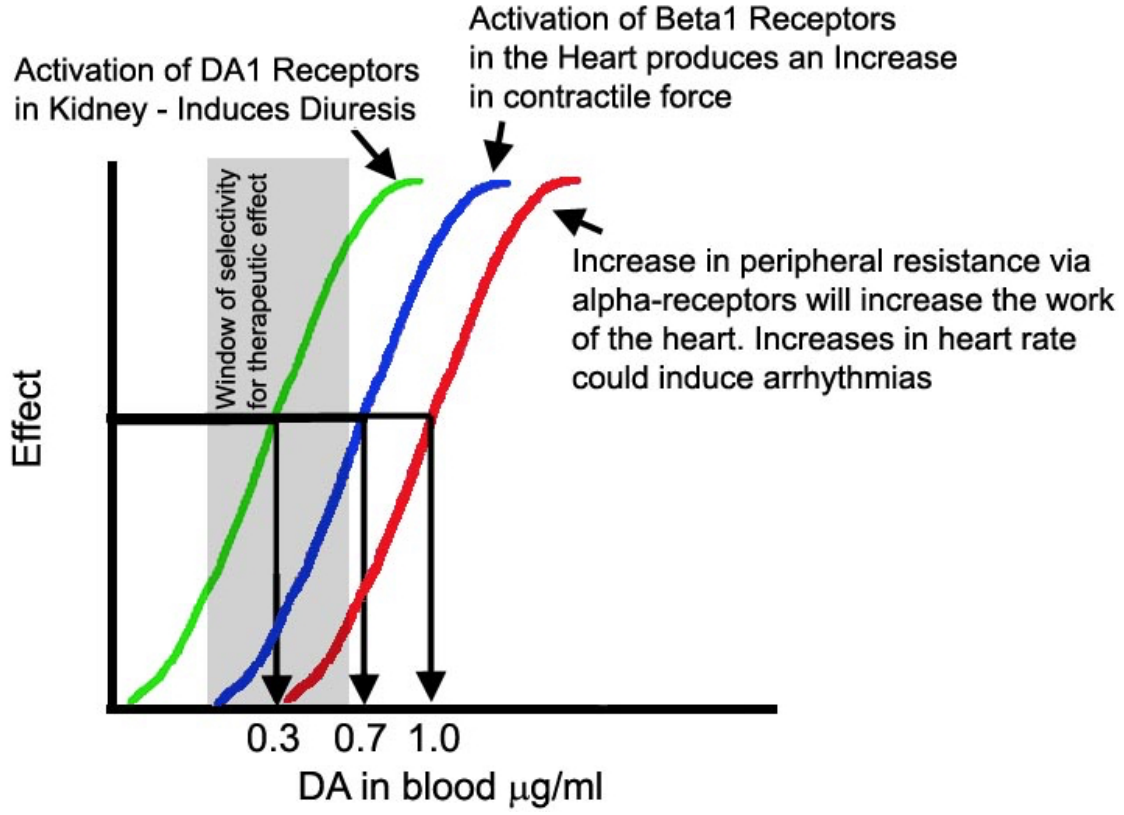
The main difference in the actions of pharmacological doses of norepinephrine and epinephrine is that epinephrine binds to β-2 receptors, whereas norepinephrine does not. Both of these drugs have chronotropic and inotropic effects, but norepinephrine elicits a much larger increase in total peripheral resistance. Since **afterload** increases precipitously following norepinephrine administration, increases in cardiac output can be limited despite the stimulatory effects of the drug on the heart.

Because norepinephrine causes sharp increases in blood pressure, its administration activates the baroreceptor reflex. This diminishes the effects of the drug on the heart, so chronotropic effects are attenuated and the drug tends not to induce tachycardia.

Norepinephrine administration does not produce any of the physiological effects associated with β-2 agonists, such as dilation of airway smooth muscle. Systemic norepinephrine is used to treat profound hypotension.

Dopamine

Although dopamine is usually considered a neurotransmitter of the central nervous system, dopamine is also **produced and secreted by some renal cells**. The pharmacology of systemically administered dopamine is complex. At low does, the drug mainly binds to D1 receptors in the kidney, resulting in renal vasodilation and a decrease in total peripheral resistance. Increased renal blood flow will result in increased urine output and decreased fluid retention and decreased edema.



At higher doses, dopamine binds to β-1 receptors, producing cardiac effects. Interestingly, moderate doses of dopamine have an unusual action on the heart: a selective increase in the force of myocardial contraction occurs without a significant effect on heart rate. High doses of dopamine produce both inotropic and chronotropic effects. In addition, high doses of dopamine activate α-1 receptors, producing an increase in total peripheral resistance.

Dopamine has been used to treat heart failure patients, as it stimulates cardiac function while producing renal effects that aid to clearing the fluid accumulation resulting from the pumping mismatch between the left and right ventricles.

Isoproterenol

Isoproterenol is classified as a non-selective β-adrenergic agonist, as it binds well to both β-1 and β-2 receptors, but has higher sensitivity for β-1 receptors. Isoproterenol thus has both chronotropic and inotropic effects, and also reduces afterload by producing vasodilation of muscle arterioles *(through actions on β-2 receptors in vascular smooth muscle)*. Isoproterenol is thus an ideal drug to treat patients with poor myocardial contractility and low heart rate, but high peripheral resistance. Clinically, it is used most often for its chronotropic effects.

Dobutamine

Dobutamine was developed as a structural analogue of isoproterenol. At pharmacological doses, it is a β-1 agonist, but at very high doses it also binds to β-2 receptors. Thus, dobutamine increases heart rate and contractility, while producing less changes in peripheral resistance than isoproterenol.

Dobutamine is a useful drug to treat patients with low cardiac contractility due to organic disease or surgical procedures. Dobutamine is also commonly used in the hospital setting as a pharmacologic stress testing agent to identify coronary artery disease. However, its use is limited by propensity to produce tachycardia.

Clonidine

Clonidine is an α-2 receptor agonist that crosses the blood-brain barrier, and is particularly effective in blocking the subtype of α-2 receptors in the brainstem. As noted in the **Adrenergic Transmission module**, α-2 receptors are located on presynaptic terminals of noradrenergic neurons, including those of neurons projecting to the rostral ventrolateral medulla (RVLM). Binding of clonidine to these presynaptic receptors results in a decrease in norepinephrine release at the synapse, and thus less excitation of the postsynaptic neuron. Hence, clonidine results in reduced activity of RVLM neurons, reduced sympathetic nervous system activity, and a reduction in blood pressure. Clonidine is used to reduce blood pressure in patients that are resistant to other hypertensive treatments. Since clonidine acts in the central nervous system, it has also been used off-label to treat patients with a number of neurological and psychiatric problems. Clonidine has sedative effects due to its actions in the nervous system, which is a major side effect of the drug.

The classification of clonidine as a sympathomimetic drug can be questioned, as it does not fall neatly into this category. Although the drug is an agonist for adrenergic receptors, its administration results in a decrease in sympathetic nervous system activity. Some would classify clonidine as a sympatholytic. The terminology does not apply easily to this particular drug.

Phenylephrine

Phenylephrine is an α-1 receptor agonist. Phenylephrine is commonly used as a vasopressor to increase the blood pressure in unstable patients with hypotension. Since the drug produces a sudden increase in blood pressure, it can activate the baroreceptor reflex, thereby causing a reflexive decrease in heart rate and contractility.

Sympatholytics

Prazosin / Doxazocin / Terazosin / Tamsulosin

These drugs are α-1 receptor antagonists. They all lower blood pressure by causing peripheral vasodilation and reducing total peripheral resistance. However, as discussed in the **Adrenergic Transmission module**, the initial drop in blood pressure produced by an α-1 receptor antagonist induces a baroreceptor reflex-mediated increase in heart rate and contractility, thereby increasing myocardial oxygen demand. Hence, these drugs are second-line treatments for hypertension, but are commonly used for other medical conditions such as **benign prostatic hyperplasia**.

Phenoxybenzamine / Phentolamine

These drugs are antagonists for both α-1 and α-2 receptors. They have the same vasodilatory effects as selective α-1 receptor antagonists, but also block presynaptic α-2 receptors in the periphery, including those on sympathetic efferent fibers in the heart. As a consequence, norepinephrine release from sympathetic nerve terminals increases, since the normal presynaptic feedback inhibition mediated through the α-2 receptor is blocked. As noted above, vasodilators induce a baroreceptor reflex-mediated increase in heart rate and contractility. The reflex-mediated increases in heart rate and contractility are larger following the administration of a combined α-1 / α-2 antagonist than a selective α-1 antagonist, as more norepinephrine is released from sympathetic postganglionic terminals in the heart.

Other Drugs

β receptor antagonists (β blockers) are commonly used in cardiology to treat hypertension, as they decrease cardiac output by producing negative chronotropic and inotropic effects. These drugs will be discussed in great detail later in the course.

Review

The table below summarizes the actions of the drugs discussed in this module.

Drug	Agonist or Antagonist	Receptors Affected	Effect on Total Peripheral Resistance	Chronotropic Effect	Inotropic Effect	Other Information
Epinephrine	Agonist	β1 = β2 > α	Decrease with low dose; Modest increase with high dose	Positive	Positive	Less increase in TPR than norepinephrine
Norepinephrine	Agonist	β1 > α >> β2	Increase	Positive	Positive	Produces a large increase in afterload; chronotropic effects are attenuated by the baroreceptor reflex; less risk of tachycardia than other beta-agonists
Dopamine--low dose	Agonist	Dopamine > β > α	Decrease	Little	Little	Mainly acts in kidney to increase renal blood flow
Dopamine--moderate dose			Decrease	Little	Positive	
Dopamine--high dose			Increase	Positive	Positive	
Isoproterenol	Agonist	β1 > β2 No α	Decrease	Positive	Positive	
Dobutamine	Agonist	β1 >> β2 > α	Little, but a decrease at high dose	Positive	Positive	
Phenylephrine	Agonist	Selective α1	Increase	Decrease	Decrease	Effects on heart are due to baroreceptor reflex
Clonidine	Agonist	Selective α2 *(acts in brainstem)*	Decrease	Decrease	Decrease	Acts in the central nervous system; decreases activity of RVLM neurons
Prazosin	Antagonist	Selective α1	Decrease	Increase	Increase	Chronotropic and inotropic effects are via baroreceptor reflex mechanisms
Phenoxybenzamine	Antagonist	Selective α	Decrease	Increase	Increase	Produces larger chronotropic and inotropic effects than Prazosin

Adrenergics Module

Part 4: Hypercalcemia & Hypocalcemia

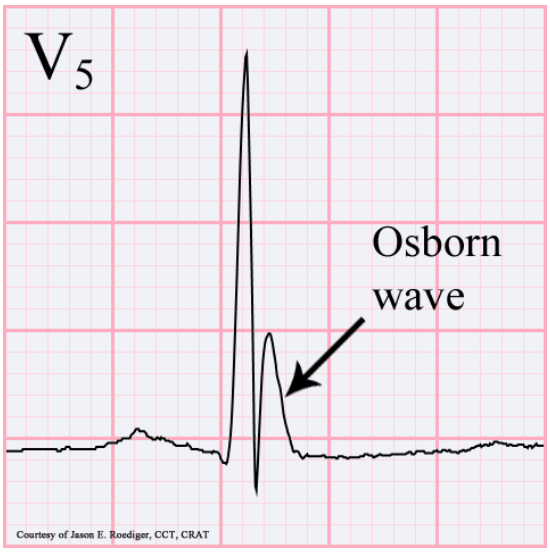
Introduction

Conditions that alter plasma calcium levels affect the characteristics of the electrocardiogram. This module provides information on changes in the ECG when plasma calcium levels are altered.

Hypercalcemia

High Ca2+ levels can block sodium movement through voltage-gated sodium channels, retarding sodium entry into excitable membranes. Thus, generation of action potentials is altered in neurons as well as skeletal and cardiac muscle cells.

The reduced depolarization of cardiac myocytes shortens repolarization time, so the Q-T interval is reduced. In addition, Ca2+ entry during phase 2 of the cardiac action potential is facilitated during hypercalcemia. This affects the closing kinetics of the L-type Ca2+ channel, such that the plateau phase of the cardiac action potential is abbreviated and repolarization occurs earlier.



Hypercalcemia may also cause a positive deflection in the ECG at the junction between the QRS complex and the ST segment. This deflection is called an **Osborn wave**, or *J wave*. The biophysical mechanisms responsible for generation of this wave are unclear.

Hypocalcemia

Low Ca2+ levels facilitate sodium transport, as the normal inhibition of sodium movement by Ca2+ is lost. Thus, low Ca2+ levels result in hyper-excitability of excitable tissues, including cardiac myocytes. The increased depolarization of cardiac myocytes lengthens repolarization time, so the Q-T interval increases. In addition, Ca2+ entry during phase 2 of the cardiac action potential is reduced during hypercalcemia. This affects the closing kinetics of the L-type Ca2+ channel, such that the plateau phase of the cardiac action potential is lengthened and repolarization occurs later.

Summary

The table below summarizes the effects of alterations in plasma Ca2+ on cardiac activity:

State	Plateau Phase of Cardiac Action Potential	Change in Q-T interval
Hypercalcemia	Shorter; May be Followed by Osborn Wave (J Wave)	Reduced
Hypocalcemia	Longer	Increased

Adrenergics Quiz

Test your proficiency in cardiovascular pharmacology by completing this quiz.

A patient with hyperparathyroidism has increased serum calcium levels. Observation of the patient's electrocardiogram could show: *

- Lengthened R–R interval
- Lengthened Q–T interval
- Presence of a J–wave
- Both lengthened Q–T interval and the presence of a J–wave

A moderate dose of dopamine: *

- Produces a positive chronotropic effect with little inotropic effect
- Produces a large increase in total peripheral resistance
- Acts as a sympatholytic
- Produces a positive inotropic effect with little chronotropic effect

Binding of agonist to which of the following receptors activates phospholipase C? *

- Alpha–1
- Alpha–2
- Beta–1
- Beta–2

Clonidine: *

- Raises blood pressure by causing an increase in norepinephrine release from sympathetic efferent fibers
- Lowers blood pressure by activating presynaptic alpha–2 receptors in the brain
- Raises blood pressure by increasing the activity of RVLM neurons
- Lowers blood pressure by blocking presynaptic alpha–2 receptors in the brain

Which of the following drugs produces a marked DECREASE in total peripheral resistance? *

- Norepinephrine
- High dose of dopamine
- Low dose of dobutamine
- Prazosin

Which of the following drugs produces the largest INCREASE in total peripheral resistance? *

- Norepinephrine
- Epinephrine

- Dopamine--small dose
- Phentolamine

Administration of a selective beta-2 agonist would produce: *

- Vasodilation and a reflex-mediated positive inotropic effect
- Less norepinephrine release from sympathetic efferent fibers in the heart
- Vasoconstriction and a reflex-mediated negative inotropic effect
- Vasodilation without any effects on the heart

Which of the following drugs DECREASES myocardial oxygen demand? *

- Isoproterenol
- Prazosin
- Beta-1 receptor antagonist
- Dopamine--high dose

A selective antagonist for ganglionic nicotinic receptors like Trimetaphan: *

- Increases both sympathetic and parasympathetic postganglionic activity
- Depresses epinephrine release into the bloodstream
- Decreases sympathetic efferent activity, but has no effect on the parasympathetic system
- Decreases parasympathetic efferent activity, but has no effect on the sympathetic system

Adrenergics Module

Winter 2024

Answers to Self Assessment Questions

A patient with hyperparathyroidism has increased serum calcium levels. Observation of the patient's electrocardiogram could show:

- Lengthened R-R interval
- Lengthened Q-T interval
- **Presence of a J-wave**
- Both lengthened Q-T interval and the presence of a J-wave

Hypercalcemia results in a shortening of the Q-T interval. A J-wave may also be present (along with a shortened Q-T interval). Heart rate is not generally altered unless hypercalcemia is very severe, and if there are changes heart rate would increase (the R-R interval is shortened).

A moderate dose of dopamine:

- Produces a positive chronotropic effect with little inotropic effect
- Produces a large increase in total peripheral resistance
- Acts as a sympatholytic
- **Produces a positive inotropic effect with little chronotropic effect**

Moderate doses of dopamine activate D1 receptors in the kidney as well as β-1 receptors. Moderate doses of dopamine produce a selective increase in the force of myocardial contraction without a significant effect on heart rate. Thus, there is a modest decrease in total peripheral resistance (due to renal vasodilation), a positive inotropic effect, but little chronotropic effect. Since the drug activates β-1 receptors, it would be classified as a sympathomimetic.

Binding of agonist to which of the following receptors activates phospholipase C?

- **Alpha-1**
- Alpha-2
- Beta-1
- Beta-2

Binding of agonist to an α-1 receptor activates phospholipase C. Binding of agonist to other adrenergic receptors affects cAMP.

Clonidine:

- Raises blood pressure by causing an increase in norepinephrine release from sympathetic efferent fibers
- **Lowers blood pressure by activating presynaptic alpha-2 receptors in the brain**
- Raises blood pressure by increasing the activity of RVLM neurons
- Lowers blood pressure by blocking presynaptic alpha-2 receptors in the brain

Clonidine is an α-2 receptor agonist, which selectively activates α-2 receptors in the brainstem. This causes a decrease in the activity of RVLM neurons, resulting in reduced sympathetic nervous system activity and lowered blood pressure.

Which of the following drugs produces a marked **DECREASE** in total peripheral resistance?

- Norepinephrine
- High dose of dopamine
- Low dose of dobutamine
- **Prazosin**

Prazosin is an α-1 receptor antagonist, and thus causes widespread vasodilation and reduced total peripheral resistance. Norepinephrine and high doses of dopamine are α-1 receptor agonists, and thus INCREASE total peripheral resistance. A low dose of dobutamine is a β-1 agonist, and does not directly affect the vasculature. However, dobutamine raises blood pressure, and could cause a baroreceptor reflex-mediated decrease in total peripheral resistance. However, the effect would not be a drastic as that produced by Prazosin.

Which of the following drugs produces the largest **INCREASE** in total peripheral resistance?

- **Norepinephrine**
- Epinephrine
- Dopamine--small dose
- Phentolamine

Norepinephrine produces large increases in total peripheral resistance by acting on α-1 receptors. Epinephrine also binds to β-2 receptors, causing simultaneous vasodilation and vasoconstriction, and thus moderate changes in total peripheral resistance. Small doses of dopamine increase renal blood flow, thus lowering total peripheral resistance. Phentolamine is an α-receptor antagonist, and thus lowers total peripheral resistance.

Administration of a selective beta-2 agonist would produce:

- **Vasodilation and a reflex-mediated positive inotropic effect**
- Less norepinephrine release from sympathetic efferent fibers in the heart
- Vasoconstriction and a reflex-mediated negative inotropic effect
- Vasodilation without any effects on the heart

β-2 agonists cause vasodilation of muscle arterioles, thereby lowering total peripheral resistance and blood pressure. As a result, there is a baroreceptor-mediated increase in both

heart rate and contractility.

Which of the following drugs **DECREASES** myocardial oxygen demand?

- Isoproterenol
- Prazosin
- **Beta-1 receptor antagonist**
- Dopamine--high dose

Isoproterenol and high doses of dopamine directly produce positive chronotropic and inotropic effects, thereby increasing myocardial oxygen demand. Prazosin produces vasodilation, and thus baroreceptor-mediated positive chronotropic and inotropic effects. In contrast a β-1 receptor antagonist blocks sympathetic effects on the heart, causing negative chronotropic and inotropic effects.

A selective antagonist for ganglionic nicotinic receptors like Trimetaphan:

- Increases both sympathetic and parasympathetic postganglionic activity
- **Depresses epinephrine release into the bloodstream**
- Decreases sympathetic efferent activity, but has no effect on the parasympathetic system
- Decreases parasympathetic efferent activity, but has no effect on the sympathetic system

Trimetaphan would block nicotinic receptors on both sympathetic and parasympathetic postganglionic neurons, suppressing activity of both parasympathetic and sympathetic efferent fibers. It also would depress epinephrine release from the adrenal medulla, as medullary chromaffin cells have the same receptors as sympathetic postganglionic neurons.