**BHSC 5404 – Introduction to Pharmacology for Nuclear**

**Medicine**

**Module 4 Online**

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#### Style convention:

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| **Module Names** are in olive green, aligned left, encased in a box with light green background and olive green border of 1.5. Font: Arial RoundedMT, Bold, 16: (appears on top of every page within this module, spanning the entire page)    **Module name goes here**  **Unit Names** are in burgundy (red) – Arial, Bold and Italic, 14  **Headings and content** for the pages are in black. Headings as specified below, according to the style sheet and content will be Arial, normal, 12  **h1** is heading 1**, h2** is heading 2, **h3** is heading 3, **h4** is heading 4  **Quiz title** in blue (as quicklink in TOC)  **Discussion groups** are in orange  **Underlined text represents links to internal pages**  **Links to external pages are in purple**  Comments to D2L implementation team are in pink |

**5404 – Introduction to Pharmacology for Nuclear Medicine - TOC:**

* **Module 4** - Drugs Affecting the Cardiovascular and Renal Systems
  + Learning objectives
  + Learning Activities at a Glance
  + **Unit 1** – Inotropic Drugs
    - Use of dobutamine in nuclear medicine

**Unit 2** – Antiarrhythmic Drugs

* + - Class I
    - Class II
    - Class III
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  + **Unit 3** – Antianginal Drugs
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    - Classes of antihypertensive drugs
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  + **Unit 5** – Anticoagulants and Thrombolytics
    - Warfarin
    - Heparin and Low molecular weight heparins
    - EDTA and citrate anticoagulants
  + **Unit 6** – Diuretics
    - Classification of diuretics by mechanism of action
  + **Unit 7** – Fluids, Electrolytes and Insulin
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    - Reconstitution of Medications for Intravenous Use
    - Insulin
  + **Self-study quiz**

# (h1) Module 4: Drugs Affecting the Cardiovascular and Renal Systems

# (h2) Introduction

Call out box

The heart and kidneys work together to maintain blood perfusion of the organs, by a consistent and appropriate cardiac output and by maintaining fluid balance. Atherosclerosis and hypertension are common in our society, leading to heart disease that can result in myocardial infarction, heart failure, arrhythmias and death.

End call out box

In this module, you will learn about medications that affect the cardiovascular and renal systems:

* Drugs affecting the cardiovascular system may act on the heart’s conduction system, heart muscle, vascular smooth muscle or on the kidney. Antiarrhythmia drugs can control heart rate by influencing ion channels in cardiac muscle cells as well as the pacemaker cells of the SA and AV nodes.
* Blood pressure can be controlled by modifying vascular tone, reducing cardiac output or by reducing the pressure against which the heart has to pump.
* Remember from Physiology that the kidney has an important role in cardiovascular physiology. The kidney monitors its own perfusion, which usually reflects cardiovascular performance and blood oxigenation. Therefore, the kidney can control fluid balance by modifying salt and water retention. By producing erythropoietin, it can increase oxygen carrying capacity by stimulating red blood cell production. The kidney also produces renin when perfusion decreases, which, as you may recall from your Physiology coursework, starts the renin-angiotensin system, resulting in the production of the vasoconstrictive substance angiotensin II. You will learn about classes of drugs that can inhibit these actions of the kidney that tend to increase blood pressure, such as diuretics and ACE inhibitors.
* The autonomic nervous system also has a key role in heart function. By influencing heart rate and contraction force, the sympathetic and parasympathetic nervous systems control cardiac output so it is appropriate for the individual’s circumstances.

All of these systems **work in concert** so as to adjust for any changes in the demands placed on the cardiac system, such as the need to increase cardiac output under stress, illness or exercise. Stress testing in nuclear medicine mimics this increased demand with physical stress (exercise) or drugs, and monitors cardiac performance in response. Response will be suboptimal in the face of cardiovascular disease.

Finally, the clotting system is what we think of next considering that the heart’s job is to pump the oxygen-carrying blood around. We inhibit the clotting system if a patient is at risk for a thromboembolism (cardiac valve disease, certain interventional cardiac procedures, prior myocardial infarction, arrhythmias, and a variety of other disorders associated with excessive clot formation). We also anti-coagulate blood sampled from patients if we need to separate the blood plasma from the red blood cells for laboratory testing.

This is a large module with **seven units of study** that refer you to read a few chapters of your textbook, and so it is anticipated that it will require **2 weeks to complete this module**.

Review icon

Before you start your study, please **review basic cardiovascular physiology from BHSC 1106/2206** or from a college/university-level anatomy and physiology textbook (several are available at the BCIT library) before moving on with this module.

End review

(h2) Learning Activities at a Glance

Over the next **two weeks** you will study Module 4. As in previous modules, throughout your study you will work on a few learning activities. You will be introduced to these activities as your study goes along, but have a look at what lies ahead so that you can **plan your study time more effectively**. Enjoy your study!

Reading icon

# (h2) Textbooks

* *Pharmacology and Drug Administration for Imaging Professionals*

Read **Chapter 5 – Drug Classifications**, pages 54-46.

Don’t forget to **answer the review questions** at the end of the chapter (pp. 153-154). Only peek at the answers in the back of the book after you answered the questions yourself!

* *Pharmacology for Health Professionals*

Read the following **seven** **chapters**, in the order suggested below:

* **Chapter 14 – Drugs for Heart Conditions**, pp.199-214
* **Chapter 15 – Antianginal and Peripheral Vasodilating Drugs,** pp.217-223.
* **Chapter 16 – Antihypertensive Drugs,** pp.230-240, 241-242.
* **Chapter 18-Anticoagulant, Thrombolytic, and Antianemia Drugs,** pp. 255-265
* **Chapter 19-Diuretics,** pp. 275-286
* **Chapter 32- Fluids and Electrolytes,** pp.542-553.
* **Chapter 22-Antidiabetic Drugs,** pp. 323-329.

In your readings for Module 4, pay special attention to drugs used extensively in Nuclear Medicine Technology, such as:

1. Adenosine
2. Aminophylline
3. Atropine
4. Insulin
5. Dipyridamole
6. Dobutamine
7. ACD solution
8. Ascorbic acid
9. EDTA
10. Heparin

# (h2) Online

* Read the **online notes** in Units 1 - 7 of this module.
* Read the online **journal articles**:
  + Pharmacological Interventions in Nuclear Medicine Cardiac Perfusion Imaging ((Paul URl is <http://www.ualberta.ca/~csps/JPPS4(3)/G.Matte/perfusion.pdf> Please link to it from here.))
* Review the PowerPoint presentations which summarize the reading material:

1. Cardiotonic and anti-arrhythmic drugs

2. Anti-anginal drugs

3. Anticoagulants

4. Diuretics

5. Fluids and electrolytes

6. Insulin

* Visit the following **web resources**:
  + Society for Nuclear Medicine Procedure Guideline for Myocardial Perfusion Imaging 3.3. ((Paul URl is http://interactive.snm.org/docs/155.pdf Please link to it from here.))
  + Cardiac Action Potential website ((Paul URl is <http://www.upto11.net/generic_wiki.php?q=cardiac_action_potential> Please link to it from here.))
  + EKG signal pattern ((Paul URI is

<http://www.a-fib.com/EKGsignal.htm> Please link to it from here.))

* + MedScape website ((Paul URl is <http://www.medscape.com/content/2002/00/44/43/444378/444378_fig.html> Please link to it from here.))
  + Supplementary Blood Collection Tube Guide ((Paul URl is http://www.bd.com/vacutainer/pdfs/plus\_plastic\_tubes\_wallchart\_tubeguide\_VS5229.pdf Please link to it from here.))
  + Pharmamotion website ((Paul URl is <http://pharmamotion.com.ar/video-animation-on-renal-physiology-and-diuretics-mechanism-of-action/> Please link to it from here.))
  + Canadian Diabetes Association website: Lows and highs: blood glucose levels ((Paul URI is <http://www.diabetes.ca/about-diabetes/living/guidelines/lows-highs/> Please link to it from here))

Activity icon

# (h2) Learning Activities

During the 2 weeks allocated for the study of this fourth module, you will be required to complete a few learning activities, such as answering a few questions, taking online self-study quizzes, exploring relevant websites, etc. Make sure you complete all the activities and if you experience any difficulties, address them with your tutor or post any questions you may have in the Q&A discussion forum.

Assignment icon

(h2) Term Assignment

Now it is also time to start working on your **Group Assignment**. This will involve writing a 2 page monograph on a drug used in nuclear medicine procedures. You will choose a drug from the list provided in the Group Assignment page, and prepare your monograph with one or two other members of your class. When it is complete, you will post it on the course website and will monitor the discussion for one week. It will be worth 10% of your course grade. **Due in Week 10**.

(Link underlined text to assignment instruction page)

You can now look at the learning objectives for this module, or you can move on to reading the notes for Unit 1. Enjoy your study!

# (h2) Learning Objectives

Insert learning objectives icon

At the end of this module, you will be able to:

1. Describe the purpose of inotropic drugs used in heart failure and in pharmacologic stress testing.
2. Outline the mechanism of action and adverse effects of antiarrhythmic drugs.
3. Describe the role of nitrates in relieving angina.
4. Describe the mechanisms of action and adverse effects of drugs for hypertension.
5. Describe how anticoagulants and thrombolytics work and give examples of drug interactions that may enhance or interfere with their action.
6. Explain the mechanism of action, adverse effects and uses of diuretics by pharmacological class.
7. Give examples of medical circumstances for which intravenous fluids may be necessary for treatment.
8. Discuss why there are so many insulin products available by describing their onset and duration of action.

(h1) Module 4 – Unit 1: Inotropic Drugs

# (h2) Introduction

Inotropic drugs **increase** (positive inotropes) or **decrease** (negative inotropes) the **force of myocardial contraction**. Chronotropic drugs increase or decrease heart rate. They are used in the treatment of heart failure and in nuclear medicine for determining myocardial viability and coronary artery disease.

Learning objectives icon

As you complete the study of this unit, you will be able to:

1. Describe the indications, mechanism of action and adverse effects of digitalis.
2. Describe the indications, mechanism of action and adverse effects of dobutamine.
3. Describe the use of inotropic and chronotropic drugs in pharmacological stress testing.
4. Explain drug interactions that may interfere with exercise stress testing or pharmacological stress testing.

End learning objectives

(h2) Use of Dobutamine in Nuclear Medicine

Dobutamine (or in some centers, arbutamine) is used in cardiac stress testing as a pharmacologic alternative to exercise stress testing. Please have a look at its use as described in the Society for Nuclear Medicine Procedure Guideline for Myocardial Perfusion Imaging 3.3.

Paul, URL for underlined text is: http://interactive.snm.org/docs/155.pdf

So why are stress tests done?

Reflection icon

To answer this question, reflect on the following quote, extracted from the article *Assessment of myocardial viability: review of the clinical significance.*

“The identification of myocardial viability in patients with coronary artery disease and left ventricular dysfunction (LVD) has important clinical and prognostic implications. Two terms commonly used to define clinical conditions of potentially reversible contractile dysfunction are stunned myocardium and hibernating myocardium. Stunned myocardium refers to transient depression of contractile function secondary to an acute ischemic insult. Hibernating myocardium is a form of contractile dysfunction of living myocytes in the setting of chronic ischemia or chronically reduced flow reserve …The use of noninvasive techniques to determine myocardial viability provides important information to guide clinicians in deciding which patients with LVD are likely to receive benefit from a revascularization procedure. Positron emission tomography, single-photon emission computed tomography, dobutamine echocardiography, and cardiac magnetic resonance imaging each have advantages and limitations.”

*(Ramos M, DePasquale E, Coplan NL. Assessment of myocardial viability: review of the clinical significance.Rev Cardiovasc Med. 2008 Fall;9(4):225-231)*

End reflection

Low-dose dobutamine (5–10 µg/kg/min)is infused into the patient and heart function is monitored by echocardiography. Low dose dobutamine increases contractility without much increase in heart rate in dysfunctional but viablemyocardium. Areas without viable myocardium do not show this “contractile reserve.” There are also protocols using a high-dose dobutamine infusion, which allows theassessment of ischemia as well.

Reading icon

Please read the following article to consolidate your learning of the use of dobutamine:

Pharmacological Interventions in Nuclear Medicine Cardiac Perfusion Imaging (Matte G and Barnes D. 2001, Journal of Pharmacy and Pharmaceutical Science 4(3): 255-262

Paul URL for underlined text is <http://www.ualberta.ca/~csps/JPPS4(3)/G.Matte/perfusion.pdf>

End reading

Activity icon

Based on the journal article you have just read, write down the answers to the following questions. To get feedback, simply click on the question. Now… don’t click for feedback before attempting to answer the questions yourself! ☺:

Paul, use the same format as in previous modules where learners click on the question to get feedback. Thanks!

* 1. What interventional drugs can be used in cardiac perfusion imaging to cause coronary vasodilation?
     1. **Feedback**: Adenosine and dipyridamole.
  2. What interventional drugs can be used in cardiac perfusion imaging to cause an increase in myocardial oxygen demand?
     1. **Feedback**: Dobutamine and arbutamine.
  3. What is the mechanism of action of dipyridamole?
     1. **Feedback**: Blocks adenosine re-uptake. Increases cardiac output and heart rate.
  4. Why should patients not have coffee, tea or other caffeinated beverages/foods prior to pharmacological stress testing with adenoside or dipyridamole?
     1. **Feedback**: Caffeine and other methylxanthines are competitive antagonists at the adenoside receptor, preventing the action of adenoside and dipyridamole.
  5. What are typical side effects of dipyridamole?
     1. **Feedback**: Arrhythmias, dizziness, arm/back/shoulder pain, headache, nausea/vomiting.
  6. How should dipyridamole adverse effects be managed?
     1. **Feedback**: Administration of aminophylline or caffeine.

End Activity

Well done! And with this activity you completed the study of Unit 1.

(h2) Summary

In this unit you learned that inotropic drugs **increase cardiac output by increasing contractility of the myocardium**. This is useful in heart failure to maintain perfusion of the organs. Inotropic drugs are also used in nuclear medicine to “stress” the heart and mimic exercise to determine how the heart responds, in order to aid in the diagnosis of heart diseases.

(h1) Module 4 – Unit 2: Antiarrhythmic Drugs

# (h2) Introduction

Antiarrhythmic drugs assist in regaining normal sinus rhythm when the atria or ventricles are beating too fast, too slowly or irregularly. A sustained irregular rate and rhythm can potentially damage the heart and may result in inefficient pumping. Poor perfusion due to reduced cardiac output has an effect on all the organ systems. Patients with arrhythmias are also at risk for thrombus formation, which has the potential for form a pulmonary embolism, stroke or infarction. Arrhythmias are also a cause of early death following a myocardial infarction.

Learning Objectives icon

As you complete the study of this second unit, you will be able to:

1. Describe the 5 phases of the cardiac action potential, identifying the ion channels that are responsible for those phases and the direction of ion current.
2. Indicate the mechanism of action for Classes 1-IV of anti-arrhythmic drugs, referring to the phases of the cardiac action potential.
3. Give examples of drugs in Classes I-IV of antiarrhythmic drugs.
4. Describe the typical dose ranges and adverse effects of the following antiarrhythmic drugs:

* Lidocaine,
* Disopyramide,
* Pocainamide,
* Propafenone,
* Acebutolol,
* Metoprolol,
* Propranolol,
* Sotolol,
* Esmolol,
* Bretylium,
* Amiodarone,
* Ibutilide,
* Dofetilide,
* Verapamil,
* Adenosine and
* Diltiazem.

End Learning Objectives

Reading Icon

To begin your study, read **Chapter 14 – Drugs for Heart Conditions,** pages 199-214 in the*Pharmacology for Health Professionals* textbook.

End Reading

(h2) Antiarrhythmic Drugs

Antiarrhythmic drugs control heart rate by controlling the manner in which the cardiac action potential is generated and propagated. The classic way these drugs are considered is the Vaughn-Williams classification (Class I-IV) based on where they act in the cycle of the action potential because they bind to and affect different kinds of ion channels – sodium, potassium or calcium. This in turn causes changes in the action potential itself, such as raising the threshold for action potential generation, reducing how fast the action potential rises, or making the action potential take longer to complete. These changes stop the arrhythmia.

Review icon

First review the cardiac action potential and the ion channels involved, which you learned in your prior Physiology coursework. You can review this material either in a Physiology reference textbook, or you may find this link useful.

* Focus on the 5 phases of the cardiac action potential (Phase 0, 1, 2, 3, 4), the main ion channels involved and the direction of ion flux that influences depolarization or repolarization.
* Review the absolute and relative refractory periods as well, where a new action potential cannot be generated (absolute refractory period) and when a much stronger than normal stimulus is needed to generate a new action potential (relative refractory period).

Paul, URL for underlined text: <http://www.upto11.net/generic_wiki.php?q=cardiac_action_potential>

End review

Now let’s consider what would happen if we were to **inhibit one of those ion channels**…

(h3) Class I Drugs

These anti-arrhythmia drugs **reduce the rate of the rapid rise in Phase 0 of the cardiac action potential**. The mechanism is inhibition of fast sodium channels. Anti-arrhythmia drugs are like anaesthetics also in that they reduce the degree of depolarization and reduce the rate of impulse transmission by “stabilizing” the myocardial cell membrane. They are presently used less often than other classes due to their adverse reactions, but are still used in certain situations, such as ventricular arrhythmias that do not respond to other agents.

Class IA drugs also prolong the action potential, which widens the Q-T interval (of the “PQRST” EKG tracing), predisposing some individuals to arrhythmias as electrical circuits in the heart become heterogeneous and conduction pathways are altered (not what we want in an anti-arrhythmia drug!). However, Class IA drugs effectively depress myocardial excitability and prolong the refractory period.

Paul, URSL for underlined text: http://www.a-fib.com/EKGsignal.htm

Example icon

Examples of these drugs include quinidine (not used as much now), disopyramide and procainamide.

End example

Class IB drugs shorten the action potential duration in non-diseased heart tissue. Class IB agents also act selectively on diseased/ischemic tissue to promote conduction block, preventing vicious circles of arrhythmias known as re-entry. This happens especially in the ventricles, therefore they are useful for ventricular tachycardia/arrhythmias. They raise the threshold required to generate an action potential.

Example icon

Examples of these drugs include lidocaine, mexiletine, tocainide.

End example

Class IA and IB drugs are used for **life-threatening ventricular arrhythmias**, such as ventricular tachycardia (VT).

Class IC drugs inhibit the fast sodium channel of Phase 0 of the cardiac action potential, prolong action potential duration by delaying inactivation of slow sodium channels and inhibit the rapid repolarizing current. These drugs are generally reserved for paroxysmal ventricular and supraventricular tachyarrhythmias that do not respond to other drugs, as Class IC agents are dangerously pro-arrhythmic.

Example Icon

Examples of these drugs include flecainide and propafenone.

End example

(h3) Class II Drugs

Class II are beta-blocker drugs, which means that they **inhibit the beta receptors of the autonomic nervous system** found in cardiac muscle (beta-1 receptors) and in vascular smooth muscle (beta-2 receptors). Thus, beta-blockers inhibit the chronotropic and inotropic effects of epinephrine and norepinephrine. They also indirectly inhibit calcium influx (we won’t go into the mechanism here), which is why they are **also antiarrhythmic**. Furthermore, they reduce heart rate by reducing SA and AV nodal conduction. These are the **safest anti-arrhythmic drugs**. With their broad spectrum of activity, they can be useful in combination with drugs from other classes in refractory cases.

Example Icon

Examples of these drugs: propranolol, acebutolol, sotolol and esmolol.

End example

Activity icon

Think about the role of beta blockers and answer the following question. Click on the question to obtain feedback and see if you are on the right track with your answer.

Paul use same functionality as before – click on question to get feedback. Thanks

Beta blockers must be discontinued prior to dobutamine or adenosine pharmacologic stress testing in myocardial perfusion imaging. Why?

**Feedback**: Because the beta blockers will prevent the increase in heart rate by the chronotropic or inotropic agent and the diagnostic test will not be possible.

End activity

(h3) Class III Drugs

These drugs **block slow potassium channels needed for repolarization** (and therefore prolong the relative refractory period). These agents are typically used only in serious arrhythmias that do not respond to other antiarrhythmics, as they are pro-arrhythmic themselves with some risk of mortality.

Example Icon

Examples of these drugs: procainamide, flecanide, bretyllium, encainide.

Amiodarone is primarily a Class III drug that also has some of the electrophysiological properties of Class I and IV. It also has some of the same effects as the beta-blockers; it binds noncompetitively to beta-adrenergic receptors and can be used with beta-blockers. Amiodarone **has serious side effects** (pulmonary fibrosis and thyroid problems), but it is a powerful antiarrhythmic, and it is coming back into more frequent use.

Sotolol has both beta-blocker and Class III effects and is the most widely used drug in this class. It is indicated for severe ventricular arrhythmias as well as atrial flutter and atrial fibrillation. It has some of the pro-arrhythmic effects of the Class III agents but not the toxicities of amiodarone.

Newer Class III drugs are ibutilide (IV) and dofetilide (oral), which are particularly useful in atrial flutter and atrial fibrillation. These are administered with constant cardiac monitoring in case of serious ventricular arrhythmias.

End example

(h3) Class IV Drugs

These drugs are calcium channel blockers. Calcium channel blockers slow conduction through the SA and AV nodes, hence increasing the refractory period of nodal tissue. These drugs prolong the plateau phase of the action potential and therefore the relative refractory period.

There are actually two varieties of calcium channel blockers, which differ in whether they affect vascular smooth muscle (dihydropyridines, which do not have electrophysiological effects on the heart; we will discuss these later in anti-hypertensive drugs) or not (the nondihydropyridine drugs, for example verapamil and diltiazem, which are anti-arrhythmic).

Also in this class is adenosine, a natural body substance which utilizes an adenosine-sensitive inward potassium rectifier channel. (Long name! You can just call it the “adenosine receptor”.) It acts like calcium channel blockers in that it depresses conduction at the AV node. Adenosine is used therapeutically and diagnostically for certain types of tachycardias such as supraventricular tachycardia. It has an extremely short duration of action due to its 10 second half-life, so it must be administered by rapid IV push, preferably in a central venous line (if present) rather than in a peripheral vein.

Adenosine is used in pharmacological cardiac stress testing in nuclear medicine. Its effects are antagonized by caffeine, which must be avoided prior to the test. Its use is also described in the Society for Nuclear Medicine Procedure Guideline for Myocardial Perfusion Imaging 3.3, website, as follows:

URL for underlined text: <http://interactive.snm.org/docs/155.pdf>

*The role of adenosine:* “Adenosine induces differential coronary hyperemia in normal coronary arteries versus coronary arteries with atherosclerosis, allowing single photon emission computed tomography (SPECT) imaging to identify reduced coronary flow in segments subtended by diseased coronary arteries. The potential attenuation of pharmacologic effects of adenosine in the presence of caffeine is why patients are routinely instructed to abstain from caffeine for 12 to 24 hours prior to administration of an adenosine stress test. Failure to abstain from caffeine results in cancellation or delaying of cardiac stress testing, resulting in procedural delays and its impact on patient throughput.”

*(Kovacs D, Pivonka R, Khosla PG, Khosla S. Effect of caffeine on myocardial perfusion imaging using single photon emission computed tomography during adenosine pharmacologic stress.Am J Ther. 2008 Sep-Oct;15(5):431-434.)*

Review Icon

To recapitulate what you have learned about new drugs, have a look at the **Summary Drug Table** for Antiarrhythmic Drugs in the textbook: *Pharmacology for Health Professionals,* p. 235-240 for adverse reactions and dose ranges.

End review

An easy way to study these drugs is to create flashcards. The following activity shows you how to do them.

Activity Icon

Flashcards! One way to get started learning new drugs is to make flashcards that you can use to study wherever you go (preferably not while driving, though!). Here is a suggestion with an example:

*Front of card:*

**Drug Name Classification Main Indications Dose Range**

Metoprolol beta-blocker hypertension, post-MI, 50-400mg as 1-2x/d

(Lopressor, Toprol XL) angina

*Back of card:*

**Adverse reactions Use in Nuc.Med. Other notes**

Bronchospasm in asthmatics (may prevent achieving cardioselective

Fatigue maximal heart rate in stress testing)

**Tips:**

* For drug names, include the generic and the brand names – sometimes we say one or the other interchangeably.
* “Main indications” means the usual uses for this medication, and the corresponding dose ranges for those indications. You will need to consult one of the drug references (print or online) discussed in Module 1, the reading material provided for the usual doses and your textbook *Pharmacology for Health Professionals*.
* For adverse reactions, there can be dozens listed in the CPS reference book! Just list the most common and the most serious.
* “Other notes” may include this drug’s claim to fame within its class, or other interesting tidbits.

End activity

There are also commercially available drug flashcards which you may find useful, although they may be more detailed. Learning about the drugs and how they differ within each drug class is an essential part of studying pharmacology. This will help you to understand some of the reasons why one agent is selected over another when they have similar-sounding names.

To keep you focused throughout the course, specific drugs used extensively in nuclear medicine will be listed within each Module. For those drugs, you will also be tested on the dosages, which are listed in your textbook Drug Tables, in their respective chapters.

(h2) Summary

As you conclude the study of antiarrhythmic drugs, go over the PowerPoint presentation Cardiotonic & Antiarrhythmic Drugs, which summarizes what you have been learning in Chapter 14 of the textbook *Pharmacology for Health Professionals*.

Paul, link to the PP presentation

Self-test icon

Now you are ready to take a short self-testing quiz to test your knowledge of inotropic and antiarrythmic drugs.

Paul, link to quiz

End self-test quiz

1. Match each type of arrhythmia with the respective description:
   1. Ventricular fibrillation
      1. Ans:1
   2. Atrial fibrillation
      1. Ans: 3
   3. Atrial flutter:
      1. Ans: 5
   4. Ventricular tachycardia
      1. Ans. 2
   5. Premature ventricular contractions
      1. Ans 4.

(descriptions)

1. Rapid, disorganized contractions of the ventricles such that cardiac output is low; not compatible with life if it continues. Called “V-fib.” for short.
2. Rapid heart rate >100 beats/min.
3. Irregular and rapid contraction of the atria, such that they are quivering rather than pumping; this results in inefficient ventricular filling and low cardiac output.
4. Beats originating in the ventricles rather than the SA node in the atria. The ventricles are made to contract *before* the atria so they are not filled efficiently, resulting in lower cardiac output. Also known as PVCs.
5. Rapid contraction of the atria (as much as 300bpm) which is conducted to the ventricles but too fast for the ventricles to pump efficiently.

Feedback for correct answers: Well done! That is the right match.

Feedback for wrong answers: If you’re stuck on this content, you may want to check out Table 14-1 “Common Types of Arrhythmias, p. 201 of your textbook *Pharmacology for the Health Professionals.*

1. True or false:

An ejection fraction of 70% means that the patient is in heart failure.

Answer: False

Feedback for true: A normal ejection fraction is >60%, so at 70%, this is normal.

Feedback for false: Correct! This is a false statement because a normal ejection fraction is >60%, so at 70%, this is normal.

1. Fill in the blank:

Two uses of cardiotonic drugs are\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_- and \_\_\_\_\_\_\_\_\_\_\_\_\_.

Ans: heart failure atrial fibrillation

1. Fill in the blank:

Quinidine, procainamide and disopyramide are examples of Class\_\_\_\_ antiarrhythmics.

Ans: IA

1. Fill in the blank:

Verapamil and diltiazem block\_\_\_\_\_\_\_\_\_\_\_\_channels.

Ans: calcium

1. Fill in the blank:

The class of antiarrhythmia drugs that decreases myocardial response to sympathetic neurotransmitters is \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_.

Ans: beta blockers OR Class II

1. Fill in the blank:

Miodarone is a Class III drug that prolongs this phase of the cardiac action potential:\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_.

Ans: refractory

Paul, not sure what to do about the feedback – perhaps just:

For incorrect: Hmmm… make sure your spelling is correct. If you are having trouble with the classes of drugs for heart conditions, review the section on antiarrhythmic drugs.

For correct: Well done! and Correct! and That’s right!

1. Examples of serious adverse reactions to antiarrhythmia drugs that warrant great concern include: (Select all that apply)
   1. Bradycardia
   2. Nausea and vomiting
   3. Severe hypotension
   4. Dry mouth and dizziness

Correct answer a b and c

Feedback for correct: Good job! You selected the right three serious adverse reactions to antiarrhythmia drugs.

Feedback for incorrect: Not quite. While dry mouth and dizziness are certainly bothersome, some side effects are to be expected and the patient will have to learn to manage them.

1. Two important contraindications to antiarrhythmia drugs include: (Select the two that apply).
   1. Pregnancy and lactation
   2. Hypersensitivity to the class of agents being considered
   3. History of myocardial infarction
   4. Asthma

Correct answer: a and b

Feedback for correct: Yes, pregnancy and lactation and hypersensitivity are important contraindications to antiarrhythmia drugs.

Feedback for incorrect: Not quite right…. A history of myocardial infarction is not a contraindication. In fact, antiarrhythmic therapy is important following a myocardial infarction as this is an important cause of early death.

The only class of drugs for which asthma is a concern is Class II, beta blockers. The use of beta blockers is contraindicated in asthma due to the potential for bronchospasm; beta-2 receptors in bronchial smooth muscle cause bronchoconstriction.

(h1) Module 4 – Unit 3: Antianginal Drugs

(h2) Introduction

Antianginal medications are used for **chest pain associated with myocardial ischemia**. They reduce coronary artery vasospasm and are vasodilating.

Learning objectives icon

As you complete the study of this unit, you will be able to:

1. Describe the mechanism by which nitrates relieve angina.
2. Describe the adverse effects of nitrates.
3. List the different forms of nitroglycerine by indicating which could be used for acute angina and which could be used for prevention.

End learning objectives

Reading icon

To begin your study of these types of drugs, read **Chapter 15 - Antianginal and Peripheral Vasodilating Drugs**, pp.217-277 in the *Pharmacology for Health Professionals* textbook.

End reading

(h2) Nitrates

If a patient who is known to have angina experiences chest pain during a nuclear medicine procedure he may have nitroglycerin with him. The physician would be notified and the antianginal medication would be administered to relieve the symptoms of coronary artery vasoconstriction. Typically this is in the form of sublingual tablets, a transmucosal tablet or a sublingual spray, with rapid onset of action. Anginal attacks deprive the heart muscle of oxygen, which reduces its efficiency. Nitrates cause coronary artery vasodilation, thereby relieving the discomfort as blood flow is restored. For prevention of angina, sometimes nitroglycerin tablets, capsules, patches or topical ointment are used regularly.

Calcium channel blockers prevent vasoconstriction of both peripheral and coronary arteries because calcium influx is essential for smooth muscle function. Dilation of arterioles increases blood flow to the heart muscle and reduces the work of the heart due to the peripheral vasodilating effect. This is also the reason calcium channel blockers also reduce blood pressure. However, this vasodilation can also cause edema, so sometimes vasodilating calcium channel blockers are used in combination with a diuretic.

It is typical to take calcium channel blockers with food if they cause GI upset. If a patient is supposed to be fasting for their nuclear medicine procedure, make sure they did not eat within the appropriate interval before the procedure.

Examples icon

Examples of calcium channel blockers used in ischemic heart disease include: verapamil, nifedipine, nicardipine, amlodipine and diltiazem. Verapamil and diltiazem are also anti-arrhythmic drugs.

End examples

Paul, In a call out box please

**Note**: older patients are particularly susceptible to orthostatic hypotension when taking anti-anginal drugs such as nitrates and calcium channel blockers. After a nuclear medicine procedure, they should get up slowly, and you may want to offer assistance if the patient complains of dizziness or seems unsteady.

End call out box

(h2) Summary

To see a summary of the key points on antianginal drugs, have a look at the PowerPoint presentation Antianginal Drugs, which highlights what you have learned in Chapter 14 of the textbook *Pharmacology for Health Professionals*.

Paul, link to the PP presentation

Self-test icon

Try your hand at a few review questions about drugs for angina: See p. 229 at the end of Chapter 15 in the textbook *Pharmacology for Health Professionals*

End self-test

(h1) Module 4 – Unit 4: Antihypertensive Drugs

(h2) Introduction

Antihypertensive drugs may differ in their mechanisms of action, but the goal is the same: **reduce blood pressure to reduce the potential for organ damage**. Untreated hypertension causes accelerated atherosclerosis, increased cardiac workload, renal damage, damage to retinal blood vessels in the eye, and carries a risk of myocardial infarction and stroke.

Learning objectives icon

As you complete the study of this unit, you will be able to:

1. Give examples while describing the mechanisms of action of antihypertensive drugs that are beta blockers, vasodilators, diuretics and calcium channel blockers.
2. Explain why multiple drugs may be used to treat hypertension.
3. Describe the typical adverse effects of antihypertensive drugs, including those directly related to their mechanism of action against high blood pressure.

End learning objectives

Reading Icon

Now you should read **Chaper 16 – Antyhypertensive Drugs**, pp. 230-240, 242 in the textbook *Pharmacology for Health Professionals*.

End reading

(h2) Classes of Antihypertensive Drugs

Classes of antihypertensive drugs include:

* [**Diuretics**](http://www.cvpharmacology.com/diuretic/diuretics.htm) (*These will be discussed in Unit 6-Diuretics*)  
  -  [thiazide diuretics](http://www.cvpharmacology.com/diuretic/diuretics.htm)  
  -  [loop diuretics](http://www.cvpharmacology.com/diuretic/diuretics.htm)  
  -  [potassium-sparing diuretics](http://www.cvpharmacology.com/diuretic/diuretics.htm)
* [**Cardioinhibitory drugs**](http://www.cvpharmacology.com/cardioinhibitory/Cardioinhibitory.htm)  
  -  [beta-blockers](http://www.cvpharmacology.com/cardioinhibitory/beta-blockers.htm)  
  -  [calcium-channel blockers](http://www.cvpharmacology.com/vasodilator/CCB.htm)
* [**Vasodilators**](http://www.cvpharmacology.com/vasodilator/vasodilators.htm)  
  -  [alpha-adrenoceptor antagonists (alpha-blockers)](http://www.cvpharmacology.com/vasodilator/alpha.htm)  
  -  [angiotensin converting enzyme inhibitors (ACE inhibitors)](http://www.cvpharmacology.com/vasodilator/ACE.htm)  
  -  [angiotensin receptor blockers (ARBs)](http://www.cvpharmacology.com/vasodilator/ARB.htm)  
  -  [calcium-channel blockers](http://www.cvpharmacology.com/vasodilator/CCB.htm)  
  -  [direct acting arterial dilators](http://www.cvpharmacology.com/vasodilator/direct.htm)  
  -  [ganglionic blockers](http://www.cvpharmacology.com/vasodilator/Ganglion.htm)  
  -  [nitrodilators](http://www.cvpharmacology.com/vasodilator/nitro.htm)  
  - [potassium-channel openers](http://www.cvpharmacology.com/vasodilator/K-openers.htm)  
  -  [renin inhibitors](http://www.cvpharmacology.com/vasodilator/renin.htm)
* [**Centrally acting sympatholytics**](http://www.cvpharmacology.com/vasodilator/Central-acting.htm)

Example icon

To see some examples of medications in these different classes of antihypertensive drugs, take a look at the list of examples on p. 232 of the textbook *Pharmacology for Health Professionals*.

End example

The diuretics primarily cause loss of sodium from the body, which reduces blood pressure. The other agents reduce cardiac output, cause vasodilation or reduce CNS sympathetic signals.

(h2) Beta blockers, Diuretics and Calcium Channel Blockers

Often, if weight reduction, diet and exercise fail to control blood pressure, a medication may be added to **prevent the long-term consequences of hypertension**. Usually a diuretic is first-line therapy as diuretics are well tolerated and efficacious for mild hypertension.

Some drugs work well in some patients and not so well in others. Still other patients may require combination therapy to achieve a normal blood pressure. There are commercially available combinations of diuretics with antihypertensive drugs in a single dosage form as well. Figure 16-1 on p. 233 of your textbook *Pharmacology for Health Professionals* illustrates an algorithm for therapeutic choices in the management of hypertension. **Diuretics and beta blockers are front-line drugs**. Hydrochlorothiazide, for example, is a diuretic that is often used in combination with beta blockers in products marketed for hypertension. If not successful, calcium channel blockers may be tried or ACE inhibitors, until a successful regimen is devised.

The table below lists examples of cardioinhibitory drugs used in the treatment of hypertension:

Paul, please use the “background” colour for the tables below. Thanks

|  |  |
| --- | --- |
| **Cardioinhibitory Drugs**  **-Beta Blockers** | **Description and Effects** |
| |  | | --- | | *Non-selective β1/β2* | | * carteolol\* | | * carvedilol | | * labetalol\* | | * nadolol | | * penbutolol\* | | * pindolol\* | | * propranolol | | * sotalol | |  | | *β1-selective* | | * acebutolol\* | | * atenolol | | * betaxolol | | * bisoprolol | | * esmolol | | * metoprolol | | \*has intrinsic sympathomimetic activity (partial agonist), reduces normal and elevated sympathetic tone while still giving some baseline sympathetic stimulation | |  | | Beta-blockers are drugs that bind to beta-adrenoceptors and thereby block the binding of [norepinephrine and epinephrine](http://www.cvpharmacology.com/norepinephrine.htm) to these receptors. This inhibits normal sympathetic effects that act through these receptors. (“sympatholytic”). Beta blockers also reduce the work of the heart and are antiarrhythmic, which is cardioprotective.  **Cardiac Effects**   * Decrease contractility (negative intropy) * Decrease relaxation rate (negative lusitropy) * Decrease heart reat (negative chronotropy) * Decrease conduction velocity (negative dromotropy)   **Vascular Effects**   * Smooth muscle contraction (mild vasoconstriction)   *Note: patients on beta blockers will not be able to reach their maximal heart rate on an exercise stress test because of the negative inotropic and negative chronotropic effects of beta blockers.* |
| **Cardioinhibitory Drugs**  **-Calcium Channel Blockers** | **Description and Effects** |
| Dihydropyridines: (mainly vascular effect):   * amlodipine * felodipine * isradipine * nicardipine * nifedipine * nimodipine * nitrendipine   Non-dihydropyridines (cardiac effect):   * diltiazem * verapamil | By blocking calcium entry into cardiac and vascular smooth muscle cells, calcium channel blockers cause:   * vascular smooth muscle relaxation (vasodilation), * decreased myocardial force generation (negative inotropy), * decreased heart rate (negative chronotropy), and * decreased conduction velocity within the heart (negative dromotropy), particularly at the [atrioventricular node](http://cvphysiology.com/Arrhythmias/A004.htm).   These drugs may cause flushing, headache, hypotension, edema and reflex tachycardia.  Not combined with beta blockers or used in patients with bradycardia to avoid beta-blocker-induced AV node block or decreased myocardial contractility. |

Adapted from: http://www.cvpharmacology.com/antihypertensive/antihypertensive.htm

(h2) Vasodilators

Vasodilators **reduce the force against which the heart has to pump** by reducing peripheral vascular resistance.

If you have a given volume of water flowing through a garden hose, and you block some of the flow with your thumb, what happens? The pressure of the water flow increases at the outlet, resulting in a more forceful spray. Now imagine moving your thumb away from the outlet, thereby enlarging the opening, and what happens? The pressure drops and the flow is less forceful. With vasodilators, we are enlarging the channels through which blood flows, and so blood pressure is reduced.

In considering how these drugs work, it is important to know that:

* **Mean arterial blood pressure = stroke volume *x* total peripheral resistance**

To reduce blood pressure, we can reduce either factor in the equation.

* **Cardiac Output = Heart Rate *x* Stroke Volume** - Latter is dependent on:
* **Preload** = Left ventricular end diastolic volume i.e. amount of stretch of left ventricle = volume overload. Dilating veins reduces preload because there is less return to the heart.
* **Afterload** = Total peripheral resistance; if it increases = pressure overload. Reducing afterload reduces the work of the heart and blood pressure.
* **Contractility** = Capacity of myocardium to 'respond to' preload and afterload. Reducing contractility reduces cardiac output.

The mechanisms by which these antihypertensive drugs cause vasodilation and therefore influence preload and afterload are tabulated below:

|  |  |
| --- | --- |
| **Vasodilator Class** | **Mechanism of Action and Effects** |
| Angiotensin converting enzyme inhibitors (ACE inhibitors):   * captopril * enalapril * fosinopril * lisinopril * moexipril * quinapril * ramipril | Block conversion of angiotensin I🡪angiotensin II.  Angiotensin II is a potent vasoconstrictor. ACE inhibitors dilate veins and arteries.  Less angiotensin II also means less production of aldosterone, resulting in less sodium retention and therefore increased fluid loss.  Blocking angiotensin II reduces sympathetic tone on veins and arteries as well, causing vasodilation. |
| Angiotensin receptor blockers (ARBs):   * candesartan * eprosartan * irbesartan * losartan * olmesartan * telmisartan * valsartan | Antagonism of angiotensin II receptors.  Effects (like ACE inhibitors):   * Dilate arteries and veins and thereby reduce arterial pressure as well as [preload](http://cvphysiology.com/Cardiac%20Function/CF007.htm) and [afterload](http://cvphysiology.com/Cardiac%20Function/CF008.htm) on the heart. * Down regulate sympathetic adrenergic activity by blocking the effects of angiotensin II on sympathetic nerve release and reuptake of norepinephrine. * Promote renal excretion of sodium and water (natriuretic and diuretic effects) by blocking the effects of angiotensin II in the kidney and by blocking angiotensin II stimulation of aldosterone secretion. * Inhibit cardiac and vascular remodeling associated with chronic hypertension, heart failure, and myocardial infarction.   Avoids some of the adverse effects of ACE inhibitors such as cough and angiodedema. |
| Calcium-channel blockers:   * *Dihydropyridines* (primarily vascular effect,used for hypertension rather than arrhythmias): * amlodipine * felodipine * isradipine * nicardipine * nifedipine * nimodipine * nitrendipine * *Nondihydropyridine*: * verapamil * diltiazem | Cardiac effects of calcium channel blockers:  * Decrease contractility (negative inotropy) * Decrease heart rate (negative chronotropy) * Decrease conduction velocity (negative dromotropy)  Vascular effects of calcium channel blockers:  * Smooth muscle relaxation (vasodilation) |
| Direct acting arterial dilators:   * hyralazine | Cause relaxation of arteriolar smooth muscle, reduce systemic vascular resistance and arterial pressure (reflex tachycardia also occurs). |
| Ganglionic blockers:   * trimethaphan camsylate | Block impulse transmission at the sympathetic ganglia, reducing vasoconstriction. |
| Nitrodilators:   * isosorbide dinitrate * isosorbide mononitrate * nitroglycerin * erythrityl tetranitrate * pentaerythritol tranitrate * sodium nitroprusside | Mimic the actions of endogenous nitrous oxide (NO) by releasing NO or forming NO within tissues. These drugs act directly on the vascular smooth muscle to cause relaxation and therefore serve as endothelial-independent vasodilators. *Nitroglycerin* is used for angina because it is very fast acting (within 2 to 5 minutes) when administered sublingually. Its effects usually wear off within 30 minutes.  *Isosorbide compounds* have a longer onset of action and duration of action than nitroglycerin, therefore more useful than nitroglycerin for long-term use. *Sodium nitroprusside*, which is used to treat severe hypertensive emergencies and severe heart failure, has a rapid onset of action.  It is only available as an intravenous preparation, and because of its short half-life, continuous infusion is required. Effects:Systemic vasculature:  * vasodilation     (venous dilation > arterial dilation) * decreased venous pressure * decreased arterial pressure (small effect)  Cardiac:  * reduced preload and afterload     (decreased wall stress in veins and arteries) * decreased oxygen demand  Coronary:  * prevents/reverses vasospasm * vasodilation (primarily epicardial vessels) * improves subendocardial perfusion * increased oxygen delivery |
| Potassium-channel openers:   * minoxodil | Dilation of small arteries and arterioles by altering potassium current and calcium flux in vascular smooth muscle.  Not first line. Reflex tachycardia and orthostatic hypotension are common. Used with diuretics to avoid edema. (And, yes, this is the same drug used in the hair-growth product Rogaine, but the route of administration and dosage are quite different!) |
| Renin inhibitors:   * aliskiren (U.S.; still investigational in Canada) | Block actions of renin, so less angiotensin is produced.  **Effects:**   * Vasodilation (arterial & venous) - reduce arterial & venous pressures - reduce ventricular afterload & preload * Decrease blood volume - natriuretic (sodium loss) - diuretic * Depress sympathetic activity * Inhibit cardiac and vascular hypertrophy   New class, fewer side effects than ACEI, ARBs. |
| Alpha blockers:   * prazosin * terazosin * doxazosin * trimazosin | Antagonism of alpha adrenergic receptors, thereby reducing vasoconstriction. α1-adrenoceptor antagonists cause vasodilation of arteries and veins by blocking the binding of norepinephrine to the smooth muscle receptors  Also cause orthostatic hypotension and reflex tachycardia. Used with diuretics to avoid edema. |
| Centrally-acting sympatholytics:   * clonidine * guanabenz * guanfacine * α-methyldopa | Centrally acting sympatholytics block sympathetic activity as agonists of alpha2 (α2)-adrenoceptors, reducing sympathetic outflow to the heart. Cardiac output is lowered by decreasing heart rate and contractility. Reduced sympathetic output to the blood vessels decreases sympathetic vascular tone🡪 vasodilation,reduced systemic vascular resistance, decreased arterial pressure.  Not first-line!  Used with diuretics to avoid edema. Good for hypertensive patients with poor renal function because they do not adversely affect renal blood flow.  After administration, α-methyldopa is converted to α-methynorepinephrine, which then serves as the α2-adrenoceptor agonist in the medulla to decrease sympathetic outflow. |

Adapted from: http://www.cvpharmacology.com/antihypertensive/antihypertensive.htm

**Note:** ACE inhibitors are also used in nuclear medicine in renal function studies to assess whether or not hypertension is due to renovascular causes. Although only about 5% of hypertension is renal in origin, renal hypertension is the most common cause of secondary hypertension. Through activation of the rennin-angiotensin system (RAS) by the affected kidney(s), blood pressure becomes elevated. Diagnosis allows for cure by surgery or angioplasty of the vessels responsible. Renal scans are performed before and after administration of an ACE inhibitor (such as captopril), and if renal hypertension is present, blocking production of angiotensin II will result in a decrease of glomerular filtration pressure and a decrease in glomerular filtration rate.

Activity Icon

* Study the Drug Table for Antihypertensive Drugs starting on p.235 of the textbook *Pharmacology for Health Professionals*.
* Make a list of the most common adverse reactions for each class of drugs for your notes.

End activity

Review Icon

At this point, you may want to return to the PowerPoint presentation Adrenergics, introduced in Module 3, to review the effects of drugs influencing the sympathetic and parasympathetic nervous systems. This time consider in particular the impact on the cardiovascular system: heart rate, contractility, vascular tone and blood pressure.

Paul, link to presentation in Module 3

End review

Self-test

You are now ready to answer the review questions on Antihypertensive Drugs, at the end of Chaper 16 of the textbook *Pharmacology for Health Professionals*.

* Have a look at the Case Study on p. 242
* Answer the questions on p. 243
* Check your answers against the answer key at the end of the Chapter

End self-test

(h1) Module 4 – Unit 5: Anticoagulants and Thrombolytics

(h2) Introduction

Patients with arrhythmias, prosthetic heart valves, prior myocardial infarction and clotting disorders require treatment with anticoagulants to avoid the potentially devastating effects of coronary thromboembolism, pulmonary embolism or cerebral infarction (stroke).

Thrombolytics are used to eliminate clots that have already formed, and these are often used in the acute phase of myocardial infarction, following a stroke or during interventional cardiac procedures.

Also in this unit, you will learn about the anticoagulants used in blood collection tubes for laboratory diagnostics or ex vivo nuclear medicine red cell/white cell labelling procedures.

Learning objectives icon

By the end of this unit, you will be able to:

1. List the indications, contraindications and adverse effects of warfarin.
2. Give examples of uses of heparin and fractionated (low molecular weight) heparins.
3. Describe the adverse effects of heparin and its management.
4. Explain how EDTA prevents blood from clotting in a collection tube.
5. Explain the importance of choosing the correct blood collection tube (no additive, heparin, EDTA) with regard to coagulation requirements.
6. Distinguish the thrombolytic actions of tPA vs. streptokinase.

End learning objectives

Reading icon

To begin your study of anticoagulants, read **Chapter 18 - Anti-coagulant, Thrombolytic and Antianemia Drugs,** p. 255-263. In the textbook *Pharmacology for Health Professionals*

End reading

(h2) Warfarin

Warfarin is a commonly prescribed anticoagulant for patients who are at **risk for developing dangerous blood clots** which can result in a heart attack, stroke, pulmonary embolism or deep vein thrombosis. Because it depletes prothrombin by blocking the synthesis of Vitamin K-dependent clotting factors, patients are also at risk of bleeding complications. Vitamin K containing foods must be limited or avoided (e.g. leafy green vegetables). The equilibrium between anticoagulation and normal clotting must be kept in careful balance. This is an example of a drug with a “narrow therapeutic index” where high drug levels cause adverse effects and low drug levels are subtherapeutic (as you learned in Module 1). Therefore, patients are **monitored with laboratory tests** to ensure that they will not bleed excessively. However, even when these tests appear to be in the desired range, patients are still at risk for bleeding and the nuclear medicine technologist should be aware of this, particularly when drawing blood or giving an injection. **Excessive bleeding** after normal procedures **should be reported to the physician**.

(h2) Heparin and Low Molecular Weight Haparins

Heparin has a different mechanism of action from warfarin. It **inhibits the conversion of fibrinogen to fibrin** in the formation of a blood clot.

Low molecular weight heparins (LMWHs) are newer alternatives to unfractionated heparin. They do not require as much monitoring as heparin because they are more predictable and less likely to cause bleeding complications. Their “therapeutic index” is greater.

Example icon

Enoxaparin and daltaparin are the most common examples of low molecular weight heparins.

End example

Aspirin also has anti-platelet actions at low doses, and low-dose aspirin is often used chronically in patients with cardiovascular disease at risk of a myocardial infarction.

Reflection icon

Why do you think this would be prophylactic? Think about it for a moment then click on the question.

**Feedback**: By reducing clotting tendency, a patient with cardiovascular disease such as atherosclerosis is less likely to develop a thrombus (blood clot) that may get loose and travel to the coronary arteries. Blocking a coronary artery with a blood clot will cause ischemia to the myocardium supplied by that artery and eventually infarction, or tissue death 🡪 myocardial infarction or heart attack.

End reflection

Activity Icon

Now, take a moment to review the clotting cascade and how a blood clot forms. Go to the MedScape website for an illustration of the mechanism by which warfarin and heparin interfere with blood clot formation.

Then answer the following couple of questions. (Click on each question to obtain feedback).

* + - 1. With which factors of the clotting cascade does warfarin bind?

**Feedback**: Prothrombin and Factor X; Prothrombin is not converted to thrombin.

* + - 1. What is heparin doing in the clotting cascade?

**Feedback**: Blocking the action of thrombin on the conversion of fibrinogen to fibrin.

URL for underline text: <http://www.medscape.com/content/2002/00/44/43/444378/444378_fig.html>

End activity

(h2) EDTA and Citrate Anticoagulants

In the case of anticoagulation of blood collected from patients into tubes, for example to do laboratory testing on the blood (clinical chemistry and haematology, drug analysis, DNA studies, etc.), red blood cell or white blood cell labelling studies, platelet labelling studies, etc., the choice of anticoagulant will be **one that does not interfere with the analytical methodology**, or **does not damage the cells if they are to be reinfused**. Some of the anticoagulant choices for these clinical scenarios include:

* **Heparin**: is a very common anticoagulant that comes as sodium heparin or lithium heparin.
* **EDTA** is a common anticoagulant used when heparin interferes with the analysis to be done. It chelates calcium ions that are essential for blood to clot.
* **Citrate** also binds calcium ions (reversibly) and is used as an anticoagulant in blood collection tubes and during procedures like platelet plasmapheresis.
* Another anticoagulant and blood preservative is **ACD solution**, which stands for **a**cid **c**itrate **d**extrose solution. It would be used to maintain healthy blood cells and clotting factors that are to be reinfused into the patient. It comes in 2 forms (A and B) which differ slightly in their additives, so it is important to use the correct one for the intended procedure.

Reading Icon

If you are interested in learning more about anticoagulation of blood collected into tubes, have a look at the following website:

Supplementary Blood Collection Tube Guide

(**Note**: this is not a required reading. It’s simply for your interest!)

URL for the underlined text: <http://www.bd.com/vacutainer/pdfs/plus_plastic_tubes_wallchart_tubeguide_VS5229.pdf>

End reading

(h2) Summary

A major goal of anticoagulant drugs is the prevention of heart attack and stroke by drugs that act on the clotting cascade. Warfarin is an example of an anticoagulant that may be used chronically. It has many drug interactions and requires patient monitoring. Prevention of blood clot formation during medical procedures is often achieved with heparin or its related fractions, the low molecular weight heparins. All anticoagulants have the risk of serious bleeding complications.

In vitro anticoagulants in blood collection tubes must be chosen carefully according to the intended analytical or diagnostic purpose to avoid interference with the test or procedure.

Go over the PowerPoint presentation Anticoagulant Drugs, which summarizes what you have learned in this unit about anticoagulants.

Paul, link to the PP presentation

Self-test

* To test your knowledge of anticoagulants, answer questions 1-4 on page 274 of the textbook *Pharmacology for Health Professionals*.
* Then think of a single word to answer the following questions. Click on the question to see if you got it right!

Paul – use the same functionality – click on question to get answer

1. Which anticoagulant is used to maintain IV lines?

**Answer**: Heparin

2. Which anticoagulant should NOT be used in measures of blood calcium levels?

**Answer**: EDTA or Citrate. Both are correct.

3. Which anticoagulant would be reversed by administration of Vitamin K?

**Answer**: Warfarin

4. What drug may be used to reverse the effects of heparin overdose?

**Answer**: Protamine

Well done!

End self-test

(h1) Module 4 – Unit 6: Diuretics

(h2) Introduction

Diuretics **reduce fluid volume in the body**. This may be done by promoting water loss or by causing sodium loss because water will follow sodium out with the urine.

Learning Objectives Icon

By the end of this unit you will be able to:

1. Describe the mechanism of action, uses and adverse reactions of carbonic anhydrase inhibitors, loop diuretics, aldosterone antagonists (potassium-sparing diuretics) thiazides and osmotic diuretics.
2. Give examples within each of the classes of diuretics.
3. Describe the signs and symptoms of electrolyte imbalances that can occur with diuretic use.

End Learning Objectives

(h2) Classification of diuretics by mechanism of action

In this unit, you will learn about how drugs in each of the diuretic classes cause fluid loss through specific interactions with receptors on the renal tubules or collecting ducts. There are **5 main classes** of diuretics:

* **Carbonic anhydrase inhibitors**: block the actions of the enzyme carbonic anhydrase, which generates hydrogen ions that are normally exchanged for sodium. Sodium is not reabsorbed and water follows out with the urine.
* **Loop diuretics**: block reabsorption of sodium and chloride in the proximal and distal regions of the Loop of Henle of the nephron, thereby water is lost in the urine.
* **Thiazides**: block reabsorption of sodium and chloride in the ascending limb of the Loop of Henle, and so water is not reabsorbed.
* **Aldosterone antagonists** (also known as potassium-sparing diuretics): block the actions of aldosterone on reabsorption of sodium, and so sodium (and water) are lost in the urine while potassium is retained.
* **Osmotic diuretics**: osmotic diuretics are a little different in that by increasing the osmolarity of the blood, water is pulled into the blood from the extracellular fluid, which is then eliminated as excess fluid by the kidney.

Reading icon

Let’s begin by reading **Chapter 19 – Diuretics**, pp. 275-286 in the textbook *Pharmacology for Health Professionals*.

* **Reading details**: Start by reading p.275-276, Summary Drug Table, skip carbonic anhydrase inhibitors (p.276, 279), resume with loop diuretics p.280-285. See Key Points on p. 286.

End reading

Web resources icon

After reading the Chapter 19 pages specified above, visit the Pharmamotion website to see a video animation of renal physiology and diuretics mechanism of action:

* Scroll down until you see the video window.
* Click on the play button in the video window.
* The video will take approximately 10 minutes to complete.
* While you watch, note where each class of diuretics acts on the renal tubule, and which channel type or receptor is inhibited.

URL for underlined text: <http://pharmamotion.com.ar/video-animation-on-renal-physiology-and-diuretics-mechanism-of-action/>

End web resources

Patients on diuretics are at **risk for fluid and electrolyte imbalances**. If a patient who is taking diuretics is to be fasting for a nuclear medicine test, be aware for signs of fluid deficit (dehydration), such as fatigue, weakness, dizziness and confusion. Electrolyte imbalances tend to occur over a longer period of time and include hyponatremia (low blood sodium) and hypokalemia (low blood potassium), which can lead to cardiac arrhythmias.

In addition to the use of diuretics in the management of heart failure and hypertension, diuretics are used in nuclear medicine in **renal imaging;** forexample, to differentiate between a dilated, obstructed collecting system and a normal one. In this case, the obstructed kidney will not increase flow rate after administration of the diuretic, such as furosemide, as observed by functional imaging with radionuclides as a prolonged washout period of the radioactivity.

(h2) Summary

To summarize the key points about diuretics that you learned in your readings, go to the PowerPoint presentation Diuretics.

Link to PowerPoint presentation

Self-test icon

* You are now ready to test your knowledge of diuretics. To do that:
  + Answer Case Study questions 2-4 on page 287 of the textbook *Pharmacology for Health Professionals*.
* Then take this short mini, online self-test.

Paul, link to the self-test.

Questions for self-test

1. What are the main adverse effects of furosemide? (Select all that apply).
   1. Postural or orthostatic hypotension
   2. Nausea and vomiting
   3. Photosensitivity
   4. Glucose in the urine

Correct answer: a b c and d

Feedback for correct: You chose all of the options. Well done! They are all main adverse effects of furosemide.

Feedback for incorrect: Hmmm… You should have selected all the options, as they are all main adverse effects of furosemide.

1. What are the main adverse effects of spironolactone?
   1. Hyperkalemia
   2. Sleepiness, lethargy
   3. Diarrhea
   4. Rash

Correct answer: a b c and d

Feedback for correct: You chose all of the options. Well done! They are all main adverse effects of spironolactone.

Feedback for incorrect: Hmmm… You should have selected all the options, as they are all main adverse effects of spironolactone.

End self-test

(h1) Module 4 – Unit 7: Fluids, Electrolytes and Insulin

(h2) Introduction

Administration of intravenous fluids provides not only hydration but also a means to administer parenteral drugs. There are a variety of standardized solutions used in hospitals, typically consisting of sodium chloride or dextrose, or combinations thereof. They are isotonic with the blood. It is very important to choose the correct IV solution not only to meet the medical needs of the patient but also to avoid incompatibilities with drugs.

In this unit you will learn about insulin, which is necessary for diabetic patients to be able to utilize glucose. You will also learn what is in total parenteral nutrition, which is intravenous food given to patients who cannot eat (for example, patients unconscious for an extended period of time or those with limited amount of intestine due to prior surgery). Sometimes TPN is given to those who should not eat due to gastrointestinal disease.

Learning Objectives Icon

By the end of this unit you will be able to:

1. Give examples of standard intravenous fluids, while explaining the reasons why they may be administered.
2. Explain the importance of choosing the right solution for drug dilution and administration.
3. Describe the common signs and symptoms of electrolyte imbalances for calcium, magnesium, potassium and sodium.
4. Explain the role and therapeutic use of bicarbonate, calcium, magnesium, potassium and sodium.
5. Describe the adverse reactions that may occur upon administration of bicarbonate, calcium, magnesium, potassium and sodium.
6. Explain the meaning of total parenteral nutrition (TPN) by outlining the components used to provide energy, amino acids, fat and electrolytes.
7. Describe the actions of insulin as well as its adverse reactions.
8. Give examples of insulin preparations that are rapid, intermediate and long-acting.
9. Describe actions to take when a patient is hyperglycemic or hypoglycemic.

End learning Objectives

Reading icon

It is now time to read **Chapter 32 – Fluids and Electrolytes**, pp. 542-553 in the textbook *Pharmacology for Health Professionals.*

End reading

(h2) Standard IV Solutions and Electrolytes

Intravenous fluids are often administered to hospital patients for a variety of reasons, such as:

1. Hydration.
2. An intravenous line for administration of medications.
3. Parenteral nutrition, which is nutrition given intravenously in patients who cannot eat.
4. Correcting or preventing electrolyte imbalances (such as high or low levels of: Na+, K+, Mg+, Ca2+,Cl-, HCO3-).
5. Treatment of acidosis.

There are several **standard IV solutions** that are used routinely in hospitals. These are:

1. **Normal saline** also known as NS, N.S. or N/S, which is 0.9% sodium chloride and isotonic with blood.
2. **Dextrose 5% in water**, also known as D5W, also isotonic.
3. Combinations of **NS and D5W** such as D5 1/2NS, D5 1/4NS where the normal saline component is half or quarter-strength.
4. **Ringer’s Lactate** – also known as RL or LR (Lactated Ringer’s), is a complex mixture of sodium chloride, potassium chloride, sodium lactate and calcium chloride, isotonic with blood. RL is used in fluid resuscitation therapy after blood loss from surgery, trauma or burns. It is useful the lactate is metabolized in the liver to byproducts that counteract acidosis, which is an imbalance that occurs with acute fluid loss or renal failure.

(h2) Reconstitution of Medications for Intravenous Use

Regarding reconstitution of medications for intravenous use, either by infusion or by rapid IV administration (“IV push”) it is very important that the solution used for infusion or dilution is **compatible with the drug**. If the wrong solution is used, drug precipitation may occur, which is dangerous. Always follow the package insert instructions or protocol exactly regarding which solution to use. If you have questions about the proper solution to use, contact the pharmacy department.

(h2) Insulin

Insulins come in a variety of forms that are short, intermediate or long acting (See the Summary Drug Table “Insulin Preparations” on p. 326 of the textbook *Pharmacology for Health Professionals*) to help the patient maintain the best control over their blood glucose throughout the day, as they eat, exercise, work, rest etc. Different levels of insulin are required for these different activities to avoid hyper and hypoglycemia.

Hospitalized patients may have different requirements than when they are healthy, for example, and will require more intensive monitoring than usual.

For very long procedures in the nuclear medicine department, it may be necessary for the patient or caregiver to administer insulin during that time according to the schedule they have established.

Reading icon

To begin your study of insulin, read **Chapter 22 - Antidiabetic Drugs**, in the textbook *Pharmacology for Health Professionals.*

* Reading details: Read the section on insulin (starting on p. 323).
* Stop at p. 329.

End reading

Reflection icon

After reading the insulin section in your textbook, reflect on the following questions:

* What causes hyperglycemia? (p.325)
* What causes hypoglycemia? (p.325)
* What should be done if a patient has a hypoglycemic reaction? (p.327)
* Have you encountered any situations like this in your practice?

End reflection

Some drugs used in nuclear medicine procedures may alter the effects of insulin, such as:

* beta blockers
* diuretics
* corticosteroids
* dobutamine.

The nuclear medicine technologist should be aware of the signs of hyperglycemia and hypoglycemia for those patients with diabetes who may undergo procedures using these medications.

(h2) Summary

The key points about the uses of intravenous fluids are summarised in the Fluids and Electrolytes PowerPoint presentation.

Also, take the time to review Table 22-1 “Hypoglycemia vs Hyperglycemia” on p. 327 of the textbook *Pharmacology for Health Professionals* and go over the important points about insulin for nuclear medicine technologists in the PowerPoint presentation Insulin.

Paul, please link to the PP presentation files

Insert self-test icon

Well done! You have now completed the study of Module 4. To verify your knowledge of drugs that affect the cardiovascular and renal systems, take this self-test. If you are having difficulties with this content, do not hesitate to contact you tutor. Also, don’t forget to use the Q&A forum to post any specific questions you may have. Good luck!

End self-test icon

Paul, link underlined words to the end of module test