The educational goal of these lectures is to gain an understanding of the uses and potential toxicities of specific drugs used in dental practice. It is also important to understand how drugs used in the medical management of patients can alter therapeutic planning. The foundation for this knowledge is an understanding of receptors in the sympathetic division of the autonomic nervous system at which these drugs act.

**Learning Objectives, Lecture I**

The student should be able to explain or describe;

1) The receptors at which epinephrine acts and its effects on the cardiovascular system.

2) The rationale for the use of epinephrine in dental and medical practice.

3) Potential drug interactions and toxicities associated with the use of epinephrine.

**Prototype drugs**
Epinephrine - Adrenalin
Norepinephrine- Levophed
Dental Uses, Cautions and Patient Variables of Epinephrine

1) Epinephrine is not orally active. Therefore, it must be given I.V., I.M., S.C., topically and in aerosolized sprays.

2) Epinephrine is used in combination with local anesthetics to prolong the duration of anesthetic action and can be absorbed systemically after intra-oral injection.

3) While the potential toxicities of epinephrine include an elevation of blood pressure, increases in heart rate and arrhythmias, it nonetheless can be used in hypertensive patients.

4) Dentally relevant drug interactions—Because of the risk of a significant increase in heart rate and/or blood pressure, epinephrine should be used cautiously in patients...
taking;

- tricyclic antidepressants
- nonselective beta blockers
- digoxin
- cocaine
- amphetamine-like drugs,
- drugs used to treat ADHD
- over the counter cough and cold preparations
- certain general anesthetics.

**Interactions to be discussed at the appropriate section of the course.**

**Understanding the Clinical Effects of Epinephrine**

1) The actions of epinephrine occur as a result of interaction at two discrete receptor types in the sympathetic division of the autonomic nervous system, beta adrenergic receptors (beta receptors) and alpha adrenergic receptors (alpha receptors).
THE BETA₂ ADRENERGIC RECEPTOR

Activation of the beta₂ receptor leads to vascular and nonvascular smooth muscle relaxation.

Activation of the Beta2 Receptor Results in--

- Bronchodilation and a decrease in airway resistance
- Relaxation of vascular and nonvascular smooth muscle
Implications of Drug Action at the Beta2-Receptor in Dental and Medical Practice

1) Nonselective beta blockers can potentiate the vasoconstrictor actions of epinephrine and prolong the duration of action of local anesthetics.

2) The major use of beta2 agonists is in the treatment of COPD, ie, asthma, emphysema or chronic bronchitis). In fact, epinephrine is used to provide acute relief of severe bronchoconstriction as in anaphylactic shock or asthma. Patients sensitive to bee stings carry an EPIPEN.

3) Selective beta2 receptor agonists can also be used to treat premature labor (by relaxing uterine smooth muscle).

Beta1 Receptor Systems

Physiologic consequences of beta1 receptor activation
Implications of Drug Action at the Beta1-Receptor in Dental and Medical Practice

1) Systemically absorbed epinephrine can increase the likelihood of arrhythmias as well as exacerbate ischemic heart disease by increasing myocardial oxygen consumption.

2) There are several types of drug interactions that could potentiate the arrhythmogenic or pro-ischemic actions of epinephrine. Patients taking any of the following are at greater risk of arrhythmias or ischemic attacks following systemic absorption of epinephrine.

   Digoxin
   Cocaine
   Amphetamine-like drugs
   Tricyclic antidepressants
3) Drugs that activate the beta\textsubscript{1} receptor can be used in heart failure to improve the contractile state of the failing heart. Arrhythmias are also a concern with these types of drugs.

**ALPHA RECEPTORS SYSTEMS**

**Postsynaptic Alpha\textsubscript{1} Receptors on Vascular Smooth Muscle:**

![Diagram of EPI or NE activation of the alpha1 receptor results in an increase in blood pressure](image)

1 Activation of the alpha\textsubscript{1} - adrenergic receptor by sympathetic nervous system transmission or drugs will result in vasoconstriction and an increase in peripheral resistance and systemic arterial blood pressure.

2) A large number of alpha\textsubscript{1} receptors are associated with vascular smooth muscle compared to beta\textsubscript{2} receptors. Therefore, the predominant effect of epinephrine will be vasoconstriction.

**Implications of Drug Action at the Alpha1-Receptor in Dental and Medical Practice**

1) Epinephrine is routinely formulated with local anesthetics to prolong the duration of anesthesia and decrease the systemic absorption of the anesthetic.
2) Epinephrine systemically absorbed after intra-oral injection can increase systemic arterial blood pressure. However, this action does not preclude the use of epinephrine in hypertensive patients.

3) Epinephrine is given systemically to raise blood pressure in treating shock syndromes. The EPIPEN

4) There are several types of drug interactions that could potentiate the vasoconstrictor actions of epinephrine. Patients taking any of the following could experience a prolonged local anesthetic response.

Cocaine
Amphetamine-like drugs
Tricyclic antidepressants
Over-the-counter cough and cold medications-ie, pseudoephedrine.

Presynaptic Alpha₂ Receptors
The alpha₂ receptor is expressed on presynaptic sympathetic nerve terminals. Activation of these receptors inhibits the release of norepinephrine.
REVIEW OF OBJECTIVES AND LECTURE SUMMARY

Objective # 1-- The receptors at which epinephrine acts and its effects on the cardiovascular system.

Epinephrine increases systemic arterial blood pressure by acting at alpha\textsubscript{1} adrenergic receptors. It increases contractile force and heart rate by acting at beta\textsubscript{1}-adrenergic receptors.

Objective # 2-- The rationale for the use of epinephrine in dental and medical practice.

**Dental Practice**
In dentistry epinephrine is used in combination with local anesthetics to limit the diffusion as well as the systemic absorption of the anesthetic prolonging its duration of action and limiting its systemic toxicity. This action is due to epinephrine acting at the alpha\textsubscript{1} receptor to produce vasoconstriction.

**Medical Practice**
Actions at the Beta\textsubscript{2} Receptor. Epinephrine is used in the emergency management of acute respiratory distress or bronchospasm caused by asthma (i.e. status asthmaticus) or anaphylaxis as a result of allergic responses. A particular note is made of the Epipen that can be carried by individuals prone to bronchospasm.

Actions at the Beta\textsubscript{1} Receptor.
Epinephrine is used to provide rapid inotropic support in cardiopulmonary resuscitation as well as in anaphylactic shock.
Actions at the \( \text{Alpha}_1 \) Receptor

Systemically, epinephrine-induced vasoconstriction results in increases in blood pressure making epinephrine useful in treating cardiogenic shock or anaphylactic shock.

Epinephrine can be used to reduce blood flow into surgical fields.

Objective # 3 -- Potential drug interactions and toxicities associated with the use of epinephrine.

Toxicities- Increases in blood pressure, heart rate and arrhythmias and the complications associated with these increases in susceptible patients such as hypertensives, those with ischemic heart disease or heart failure.

Drug interactions

<table>
<thead>
<tr>
<th>Drug</th>
<th>Interaction</th>
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<tbody>
<tr>
<td>Tricyclic antidepressants, cocaine, Amphetamine-like drugs, drugs used to treat ADHD</td>
<td>Potential EPI effects on HR and BP</td>
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<td>Nonselective beta blockers</td>
<td>Prolong the duration EPI vasoconstrictor action</td>
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