Sympatholytics: Drugs that bind to beta or alpha receptors or act through other mechanisms to block the actions of endogenous neurotransmitters or other sympathomimetics.

Learning Objectives Lecture III
The student should be able to explain or describe

1. The pharmacologic properties and therapeutic uses of alpha and beta blockers.
2. How the presence of sympathomimetics alters the dental management of patients.

Prototype Drugs
Metoprolol-Toprol XL - Lopressor - Various formulations in the top 50 leading prescription drugs in the US in 2010
Clonidine - Catapres,- 109th leading prescription drug in the US in 2010
MAO Inhibitors
Phentolamine – Ora Verse
Propranolol - Inderal - various trade names
Terazosin - Hytrin
Tamsulosin-Flomax - 37th leading prescription drug in the US in 2010

* A more complete list of sympatholytics and their trade names can be found in the Yagiela text.
BETA ADRENERGIC RECEPTOR BLOCKERS

1. These drugs are competitive antagonists of the beta adrenergic receptor.

2. The beta blockers used are referred to as either selective, that is blocking the beta\textsubscript{1} receptor, or nonselective, blocking both the beta\textsubscript{1} and beta\textsubscript{2} receptor. \textit{Propranolol} is the prototype nonselective beta blocker while \textit{metoprolol} is a prototype selective beta\textsubscript{1} blocker.

3. There are over 15 beta blockers available for clinical use. In addition to selective and non selective antagonists, many of these drugs have novel effects unrelated to beta blockade.
Basic Properties of Beta Blockers

Blockade of the Beta\textsubscript{1} Receptor Produces Therapeutic Benefit

- Force and rate of myocardial contraction and renin secretion

Beta blockers can be used to treat:
- Hypertension
- Ischemic heart disease
- Supraventricular tachyarrhythmias
- Heart failure
- Following an MI

Blockade of the Beta\textsubscript{2} Receptor Produces Side effects

- Bronchospasm and increases in airways resistance
- Exacerbation of peripheral vascular disease

Implications in Dental Practice

Nonselective beta-blockers increase the risk of a hypertensive episode following systemic absorption of epinephrine. In addition, they could prolong the duration of local anesthetic action.
Implications in Medical Practice
Beta blockers are used to treat a variety of medical conditions including;

1) **Ischemic heart disease**: Decrease myocardial oxygen consumption by decreasing the force and rate of contraction.

2) **Hypertension**: Decrease in blood pressure due in part to a decrease in cardiac output and heart rate and a decrease in renin levels.

3) **Post myocardial infarction**: Beta blockers are given in the immediate peri-infarct period to decrease oxygen consumption and prevent reinfarction.

4) **Heart failure**: Certain beta blockers, such as metoprolol, and carvedilol, have been shown in clinical trials to be effective in treating heart failure.

5) **Supraventricular tachyarrhythmias**: Certain arrhythmias are due to excess stimulation of the beta1-receptors. Thus beta blockers are useful in treating SVT arrhythmias due to excess sympathetic drive. Esmolol is an ultrashort acting beta blocker useful for this purpose.
6) There are many indications for beta blockers unrelated to cardiovascular therapeutics including migraines, glaucoma, and “stage fright”.

Side Effects
1) Nonselective beta blockers - Blockade of beta\textsubscript{2} receptors associated with airway or vascular smooth muscle exacerbates:

- airway diseases (asthma, emphysema, chronic bronchitis)
- peripheral vascular disease (Raynaud’s Disease)

2) Sedation, fatigue, and impairment of mental function - common to all beta blockers

3) Hypotension and bradycardia - common to all beta blockers

\textbf{ALPHA\textsubscript{1}-ANTAGONISTS}
Mechanism: blockade of the smooth muscle alpha\textsubscript{1}-receptor

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\textbf{Selective antagonists}
1) \textbf{Terazosin} and analogs (*FYI* - prazosin, doxazosin)
- All analogs have similar actions, differing only in pharmacokinetic parameters
- Block the alpha1-receptor associated with arteries and veins resulting in a decrease in systemic arterial blood pressure
- Block the alpha1 receptor associated with prostate tissue increasing urine output in BPH
2) **Tamsulosin**
- selectively blocks the alpha1 receptor associated with prostate tissue
  increasing urine output in BPH

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**Implications in Dental Practice**

1) Orthostatic hypotension is a problem with terazosin analogs and to a lesser extent tamsulosin.

2) FYI---Orthostasis can be seen with any vasodilator that affects the tone on venous smooth muscle. This would include organic nitrates, hydralazine, clonidine, minoxidil and the many drugs (Viagra, Cialis) used to treat impotence.

**Nonselective antagonists**

1) **Phentolamine** is a well-known nonselective antagonist recently introduced in the form of Ora Verse to reduce the duration of local anesthetic action.
**ALPHA$_2$ AGONISTS**

1) **Clonidine** reduces blood pressure by stimulating alpha$_2$ receptors in the nucleus tractus solitarius (NTS) to decrease sympathetic outflow to the heart and blood vessels leading to a decrease in blood pressure.

**Implications in Dental Practice and Drug Therapy**
The use of clonidine has been associated with an increased incidence of xerostomia.

1) Clonidine is used in dental practice in the management of chronic pain. It can be given orally or in patch form.

2) Clonidine is a second-line antihypertensive that has many other uses including opiate withdrawal, nicotine withdrawal, vascular headaches, diabetic diarrhea, glaucoma, ulcerative colitis and Tourette's syndrome.

**MAO Inhibitors**

1) Blocks the breakdown of catecholamines and serotonin

**Implications in Dental Practice and Drug Therapy**
A complete discussion will be held in the CNS section.
1) Used to treat depression and Parkinson’s disease (selegiline)
2) These drugs can cause a variety of side effects and drug interactions that are relevant to dentistry including **xerostomia and orthostatic hypotension**

**REVIEW OF OBJECTIVES AND LECTURE SUMMARY**

**Objective # 1-- The pharmacologic properties and therapeutic uses of alpha and beta blockers**

Beta blockers – **propranolol, metoprolol**
Both selective and nonselective beta blockers - Used to treat hypertension, ischemic heart disease, following an MI, heart failure, arrhythmias as well as non-cardiovascular uses.

Alpha-blockers
**Terazosin**- Selective alpha1-receptor blocker. Useful in treating BPH and hypertension.

**Tamsulosin**- Selectively blocks those alpha1-receptors associated with the prostate. Useful in treating BPH.

**Phentolamine**- Nonselective alpha blocker. Used to reverse the actions of locally administered epinephrine.

**Clonidine**- Management of chronic pain. Hypertension.

**MAOI**-Blocks MAO. Used to treat depression.

**Objective # 2-- The precautions for sympatholytic drugs in dental practice**

**Nonselective beta blockers**- prolongation of local anesthetic response. An enhanced pressor response to absorbed epinephrine.

Alpha-blockers
**Terazosin** and **Tamsulosin** - Orthostatic hypotension (less likely with Tamsulosin)

**Clonidine** - Xerostomia

**MAOI** - Xerostomia and orthostatic hypotension