BIOP211 – Pharmacology

Tutorial Session 10 Drugs affecting the PNS

- Students problem-solve case studies of given drug scenarios affecting the peripheral nervous system
- Students continue to work on the Drug Diary (Summary Booklet, as set out in detail in the Reading Guide
- Review questions on the Endeavour LMS website are also available

10.1 Discuss these medications acting in the Peripheral Nervous System, PNS.

- Adrenergic hormones as drugs, adrenaline (called epinephrine in the USA)
- Synthetic adrenergic agents e.g. isoprenaline
- Indirect acting sympathomimetic agents
- Alpha-selective antagonists
- Beta blockers (Will be covered in detail in Session 13)
- Neuromuscular blocking drugs
- Anticholinesterase drugs (also known as AChE-ase Inhibitors)

Your answer should cover the following

- Examples and indications
- Mechanism of action
- Efficacy and limitations or cautions / contra-indications
- Adverse effects and drug interactions with nutrients and herbs

Mark your own answers using the Pharmacology text or online resources. Alternatively, peer review each other’s answers, allocating 10 marks per drug class.

10.2 Case studies, drug scenarios, PNS

Case Study 1 Use your textbook, MIMSSOnline or other online electronic resource such as Medicines Complete (see LibGuides)

Gretchen, a 4 year old female, suffers from a peanut allergy and experiences a severe, anaphylactic reaction when she consumes them. She was accidently given a peanut paste sandwich at Kindy and the staff used the EpiPen™ on her.

a. What drug does the EpiPen™ contain?

b. How does the drug overcome a serious hypersensitivity reaction?

c. What are the adverse effects of this drug?

Case Study 2

Bill, 54 years, was having elective surgery to repair a hernia. Preoperatively he was given glycopyrrolate and, after the surgery, he had difficulty urinating.
a. Why was he given glycopyrrolate pre-operatively? What is its mechanism of action?

b. Why did Bill have difficulty passing urine after surgery and what medication could he be given to correct this condition?

10.3 Review questions. Feedback is available for some questions in the Review Quiz

Question 1

Autonomic Nervous System Drug, match with Pharmacodynamic action & indications.

- atropine
- hyoscine
- pindololol
- atenolol
- propranolol
- dopamine
- adrenaline
- noradrenaline
- isoprenaline
- neostigmine
- physostigmine
- bethanechol

- **Dose-related adrenergic receptor agonists**

- **Acetylcholinesterase Inhibitor ACh E I**

- **Anti-adrenergic drugs β-blockers**

- **Anti-muscarinic drugs blocking at receptor for acetylcholine**

- **Adjunct in surgery to reverse Neuromuscular blockade at motor end plate**

- **Adjunct in surgery to minimize salivary secretions as well as tracheal and pharyngeal mucous secretions**

- **Drug to treat urinary retention**
Question 2

Match the mode of action of the Peripheral Nervous System drug with its site of action:

(a) Selective α₁-adrenoreceptor antagonists e.g. prazosin to treat hypertension

(b) synthetic β agonist which is a direct-acting sympathomimetic, dobutamine to treat cardiogenic shock

(c) Indirect acting sympathomimetics which release NA e.g. metaraminol to treat hypotension

1. (a) Selective α₁-adrenoreceptor antagonists e.g. prazosin to treat hypertension

2. (b) synthetic β agonist which is a direct-acting sympathomimetic, dobutamine to treat cardiogenic shock

3. (c) Indirect acting sympathomimetics which release NA e.g. metaraminol to treat hypotension

α agonists
- Adrenaline
- Noradrenaline
- Dopamine

β-blockers
- Atenolol
- Metoprolol
- Propranolol
- Pindolol
- Oxprenolol
Question 3
Match the neurotransmitter with its correct description

The main neurotransmitter in the parasympathetic NS at post-ganglionic neurones is (i) ____________ while the main neurotransmitter at post-ganglionic neurones in the sympathetic NS is acetylcholine at sweat glands and (ii) _______________ at cardiac, smooth muscle and exocrine glands.
Textbook, Location of Readings

Research: Drugs Affecting the Peripheral Nervous System, Overview of the ANS, Cholinergic Transmission, Noradrenergic Transmission, Overview of the Somatic NS & Drugs Affecting Neuromuscular Transmission

Summary
In this lesson we look at drugs that affect the Peripheral Nervous System (PNS).

The Nervous system is divided into the central nervous system (CNS) and the peripheral nervous system (PNS). The peripheral nervous system is further subdivided into the autonomic nervous system (ANS) which is made up of the sympathetic nervous system (SNS) and the parasympathetic nervous system (PSNS) and the somatic nervous system.

Overview of the Autonomic Nervous System
Bryant & Knights (2011; 2015):
- See Unit “Drugs Affecting the Peripheral Nervous System”, Chapter on “Overview of the ANS….”
  - Section on Key Background, The autonomic nervous system up to Anatomical differences between the subdivisions of the ANS

Drugs affecting cholinergic transmission
These drugs involve the PSNS and affect acetylcholine (ACh) and can elicit either a cholinergic or anticholinergic response. Cholinergic drugs (muscarinic receptor agonists/parasympathomimetic) mimic the action of ACh on the PSNS. Anticholinergic drugs (muscarinic receptor antagonists, antimuscarinic, anticholinergic, parasympatholytic) antagonize or block the action of acetylcholine at the muscarinic receptor sites.

Atropine & Hyoscine
Muscarinic antagonists
- Summarize in your Drug Diary the indications, pharmacodynamics, pharmacokinetics, adverse effects, drug interactions and warnings and contraindications of these anti-muscarinic drugs

Bethanechol
Muscarinic receptor agonist
- Add Bethanechol to your summary (Drug Diary): the pharmacodynamics (Mode of Action, M of A), indications, ADR

- See Unit “Drugs Affecting the Peripheral Nervous System”, Chapter “Overview of the ANS and Drugs Affecting Cholinergic Transmission”
  - Section on Acetylcholine and Cholinergic Transmission up to and including Key Points

Drugs affecting noradrenergic transmission
These drugs involve the SNS and affect the sympathetic/adrenergic nervous system through the action of adrenaline, noradrenaline and dopamine.

Classes of adrenergic drugs:
- Direct acting sympathomimetic (agonists)
- Indirect-acting sympathomimetic
- Adrenoreceptor antagonists/sympatholytic (blockers)
Adrenaline (A)

Is used in the emergency treatment of acute anaphylactic shock and severe allergic reaction, as an adjunct to local anaesthetics, as a haemostatic agent to control superficial bleeding, in ocular surgery to prevent bleeding and to treat cardiac arrest

 Summarize in your Drug Diary the pharmacodynamics, pharmacokinetics, adverse effects, drug interactions and warnings and contraindications of adrenaline when used as a drug

Noradrenaline (NA)

Used to restore blood pressure in acute hypotensive states.

 Summarize in your Drug Diary the pharmacodynamics, pharmacokinetics, adverse effects, drug interactions and warnings and contraindications of noradrenaline when used as a drug

Isoprenaline

Synthetic catecholamine used as a cardiac stimulant and in the treatment of septic shock, hypovolaemic states, congestive heart failure (CHF) and cardiogenic shock

 Add isoprenaline to your summary (Drug Diary): pharmacodynamics, indications, ADR

Dopamine

Immediate precursor to NA and A and is used in the treatment of circulatory shock, haemodynamic imbalances caused by MI, open heart surgery and Congestive Heart Failure, CHF

 Add dopamine to your summary (Drug Diary): the pharmacodynamics, pharmacokinetics, adverse effects, drug interactions and warnings and contraindications of this drug

α-Selective antagonists (Prazosin)

Used for the treatment of hypertension and symptomatic relief of urinary obstruction in Benign Prostatic Hyperplasia, BPH

 Add the α-Selective antagonist prazosin to your summary (Drug Diary): pharmacodynamics, pharmacokinetics, adverse effects, drug interactions and warnings and contraindications of this drug

β-Blockers

Used in the treatment of hypertension, angina pectoris, myocardial infarct (MI) and glaucoma

 Summarize in your Drug Diary the pharmacodynamics, pharmacokinetics, adverse effects, drug interactions and warnings and contraindications of β-blockers (…..-olol) drugs

 See Unit “Drugs Affecting the Peripheral Nervous System” Chapter on “Overview of the Sympathetic Nervous System and Drugs Affecting Noradrenergic Transmission”

Somatic Nervous System

Division of the Peripheral NS that co-ordinates external respiration, posture and consciously controlled functions, including movement. Drugs may be used to block neuromuscular transmission as an adjunct to anaesthesia leading to muscle relaxation.

There are 2 types of neuromuscular blocking drugs. These are:

- non-depolarising (competitive)
- depolarising (nicotinic agonists)

 Summarize in your Drug Diary the mechanism of action of both of these types of neuromuscular blocking drugs

Anticholinesterase Agents
These are used to reverse the effects of the neuromuscular blocking drugs after anaesthesia

See Unit "Drugs Affecting the Peripheral Nervous System", Chapter on “Overview of the Somatic NS and Drugs Affecting Neuromuscular Transmission”

Revision Questions / Activities from the Reading Guide:

1. Which key neurotransmitter is involved in the Parasympathetic nervous system (PSNS) and which 2 types of receptors does it activate?
2. Name 1 cholinergic drug and outline its Mechanism of Action?
3. List 5 anticholinergic adverse effects
4. What are the 3 classes of adrenergic drugs?
5. Describe the cardiac effects of adrenaline.
6. What conditions is adrenaline contraindicated in?
7. How does noradrenaline differ from adrenaline in its actions? What is it therapeutically used for?
8. Compare and contrast alpha and beta blockers.
9. What receptors does ACh act upon?
10. Outline the 2 types of neuromuscular blocking drugs (Mechanism of Action, M o A).
11. What is the antidote for anticholinesterase agents?

Answer the following

From Bryant & Knights (2011; 2015)

Review questions: Overview ANS, Drugs acting at muscarinic receptors, Drugs affecting noradrenergic transmission, Overview Somatic NS & Drugs Affecting Neuromuscular Transmission
Below is a review of the Session 4 tutorial material on

- Neurotransmitters involved in both the Sympathetic Nervous System and Parasympathetic Nervous System
- The Somatic Nervous System and the Neuromuscular Junction (NMJ)

<table>
<thead>
<tr>
<th>Hormone Exogenous Xeno-biotic or drug</th>
<th>Receptor</th>
<th>Site of Action</th>
<th>Action</th>
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</table>
| Acetylcholine, ACh                    | **Muscarinic**
  - M1,4,5 (CNS)
  - M2 (cardiac and presynaptic)
  - M3 (glandular or smooth muscle)
  **Nicotinic**
  **Overview:**
  - CNS receptors (muscarinic and nicotinic)
  - Autonomic receptors (muscarinic and nicotinic)
  - Neuromuscular (nicotinic)
| Bind to presynaptic receptors: presynaptic activation or inhibition
Bind to postsynaptic receptors: activation of these receptors by acetylcholine leads to cholinergic response | Postsynaptic **nicotinic receptors** on the motor end-plate of the muscle fibre, leading to muscular contraction
Overall intended action (movement, depolarization) |

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<tr>
<th>Anticholinergics</th>
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<tbody>
<tr>
<td>Atropine</td>
<td>muscarinic antagonist</td>
<td>Antimuscarinic agents operate on the muscarinic acetylcholine receptors. The majority of anticholinergic drugs are antimuscarinics.</td>
<td>Inhibit parasympathetic nerve impulses by selectively blocking the binding of the neurotransmitter acetylcholine to its receptor in nerve cells.</td>
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<tr>
<th>Neuromuscular Blocking Drugs</th>
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<tr>
<td><strong>Non-depolarising</strong> (competitive)</td>
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<tr>
<td>Example: Tubocurarine</td>
<td>nicotinic receptors</td>
<td>Block the action of ACh at post and presynaptic cleft</td>
<td>Blocks the normal feedback loop that increases the release of ACh under conditions of enhanced stimulation.</td>
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### Depolarising drugs (nicotinic agonists)

**Example:** Suxamethonium (is a paralytic drug used to induce muscle relaxation and short-term paralysis, usually to facilitate tracheal intubation)

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<tr>
<th>Nicotinic receptors</th>
<th>Post synaptic cleft</th>
<th>Maintain the depolarised state of the motor end-plate, thus preventing transmission of another muscle action potential</th>
</tr>
</thead>
</table>

### Acetylcholinesterase (AChE) inhibitors

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<th>Inhibits the break down acetylcholine</th>
<th>Between the synaptic cleft</th>
<th>Neostigmine and physostigmine are used to reverse the effects of the neuromuscular blocking drugs (non-depolarising) after anaesthesia. Pesticides and poisons have AChE I actions</th>
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### Adrenaline, A

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<th>Stimulates both alpha and beta receptors.</th>
<th>Primary action is beta receptors of the heart, smooth muscle of bronchi and blood vessels. At high doses stimulates alpha receptors</th>
<th>Increases contraction of the heart. Increases cardiac rate. Improves conduction. Large doses activates alpha receptor and increases BP. Bronchodilator. Increases metabolism.</th>
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<td>Examples of Drug</td>
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</table>
| Isoprenaline             | Stimulates $\beta_1$ and $\beta_2$ receptors. | Heart   | - $\beta_1$ receptors – leads to ↑ force of myocardial contraction and heart rate  
                             |          |          | - $\beta_2$ receptors – leads to relaxation of smooth muscle of bronchi, skeletal muscle, GIT and blood vessels of the splanchnic bed. |
| Noradrenaline, NA        | High affinity for Alpha receptors          | Found all over the body | - Increased heart rate, increased blood pressure, dilation of pupils and dilation of air passages in the lungs and narrowing of blood vessels in non-essential organs.  
                             |          |          | - Vasoconstriction of the vessels in the skin and mucous membranes |
| Dopamine, DA             | Dopaminergic receptors, since DA is a direct precursor of NA and A, $\beta_1$ receptors, and in high doses, $\alpha_1$ and $\alpha_2$ receptors | Primarily in the CNS Also found in the cardio-pulmonary and renal and smooth muscles. | At low doses - Vasodilation of renal and mesenteric arterioles  
                             |          |          | - Renal vasodilation with increased Na $^+$ excretion At low to moderate doses - Direct effect on $\beta_1$ receptors and stimulates release of NA - Increase heart rate and stroke volume so therefore also cardiac output At high doses - Increased peripheral resistance - May reduce urine output |

**Adrenoreceptor Antagonists**

| $\alpha$-adrenoreceptor antagonists | $\alpha$-receptor sites and inhibit sympathetic stimulation. | Prazosin, terazosin, doxazocin, tamsulosin | Effects are dose dependent but intended effect is - ↓ in peripheral vascular resistance, decrease in blood pressure |