Activity 1

For each of the body systems listed describe the consequence of activation of the parasympathetic and sympathetic nervous systems, then describe a clinical symptom or condition that as a paramedic you may observe in someone with a highly activated PARASYMPATHETIC nervous system. (6 marks)

Body System	**Parasympathetic Activation**	**Sympathetic Activation**	**Clinical Symptom / Condition**
e.g.Heart - Rate	*Decreased heart rate*	*Increased heart rate*	*Bradycardia*
Heart – Force of Contraction	Force of myocardial contractility is decreased	Force of myocardial contractility is increased	Decreased blood pressure, heart failure
Pupil	Pupil of the eye is contracted	Pupil of the eye is dilated	Miosis
Lungs	Bronchial smooth muscles of lungs are contracted	Bronchial smooth muscles of lungs are relaxed	Pulmonary airway obstruction, broncho-constriction, breathlessness
Stomach	Muscle tone and peristaltic movement of stomach are increased	Muscle tone and peristaltic movement of stomach are decreased	Increased gastric emptying rate
	(2 marks)	(2 marks)	(2 marks)

Activity 2

For each drug, identify ONE paramedic indication, then in the subsequent columns list the molecular target, target tissue, type of interaction (i.e. agonist / antagonist / allosteric modulator / inhibitor) and briefly explain how the interaction of the drugwith the molecular targetaccounts forthe observed therapeutic effect for theparamedic indication identified in the first column.(24 marks)

Drug	Paramedic Indication	Molecular Target	Target Tissue	Type of interaction	Mechanism of Therapeutic Effect
e.g. Salbutamol	*Acute asthma*	*β_2-adrenoreceptor*	*Lungs*	*Agonist*	*Activation of β_2 adrenoceptors in the lung causes relaxation of the bronchiole smooth muscle, bronchodilation and increased airflow.*
Adrenaline	Mild asthma, wheezing, tightness of chest, shortness of breath	β_2-adrenoreceptor	Lungs	Agonist	Activation of β_2-adrenoreceptor in the lungs causes bronchodilation and relieves from breathlessness.[1]
Fentanyl	Intra-operative analgesia, breakthrough pain in patients receiving opioid therapy for chronic cancer pain	μ-receptor	Brain & Spinal cord. CNS	Agonist	Fentanyl binds with μ-receptors in brain & spinal cord, and then it blocks the release of some excitatory neurotransmitters which are responsible to produce pain.[2]
Ondansetron	Nausea & vomiting due to Gastroenteritis, Chemotherap	5-Hydroxytryptamine$_3$ receptor	Chemoreceptor trigger zone, vomiting center in	Antagonist	Ondansetron blocks the 5-HT$_3$ receptors at vomiting center and chemoreceptor trigger zone and thus it provides antiemetic action.[3]

	y/Radiotherapy induced Nausea & Vomiting		the medulla oblongata		
Midazolam	Convulsion, Insomnia, Sedation with amnesia; Sedation of ventilated patients in critical care units	$GABA_A$ receptor	Brain	Agonist	Midazolam binds with $GABA_A$ receptors in brain, as well as increases binding affinity of GABA to its receptors. Next, opening of chloride channels facilitate hyperpolarization, which ultimately inhibits action potential and firing of nerve.[4]
Ipratropium	Acute asthma, reversible Chronic obstructive pulmonary disease;	Muscarinic receptor	Lungs	Antagonist	Ipratropium blocks the muscarinic receptors in bronchial smooth muscles and decreased contractility of airway of lungs, secretion and bronchoconstriction.[5]
Adenosine	Inflammation	A_{2A} receptor	Inflamed cell	Agonist	By binding with A_{2A} receptors in inflamed cells it increases the intracellular cAMP level which produces anti-inflammatory effects, such as decreased secretion of tumour necrosis factor (TNF), interferon (IFN)-γ interleukin (IL)-12, IL-6, and inhibition of phagocytosis.[6]
Naloxone	Overdosage with opioids, Reversal of opioid-induced respiratory depression; reversal of neonatal	μ-receptor	Brain & Spinal cord, Brainstem respiratory centers,	Antagonist	Naloxone competitively inhibits μ-receptor in CNS causes reversal of coma due to opioid overdose and reversal of opioid-induced respiratory depression.[7]

	respiratory depression resulting from opioid administration to mother during labour;				
Aspirin	Anti-platelet, Prophylaxis of stroke or myocardial infarction, mild to moderate, fever	Cyclo-oxygenase-1 enzyme Cyclo-oxygenase-2 enzyme	Platelet Hypothalamus	Antagonist	By blocking COX-1 enzyme Aspirin inhibits Prostaglandin H2 synthesis in platelet as well as Thromboxane-A2 synthesis ultimately shows anti-platelet action. By inhibiting COX-2 enzyme in thermoregulating center in hypothalamus Aspirin provides antipyretic effect.[8]
	(4 marks)	(4 marks)	(4 Marks)	(4 marks)	(8 marks)

Activity 3

In pharmacodynamics, a drug can be thought of as 'selective' when it shows preference for interaction with one molecular target, even though it may be faced with many molecular targets to choose from. Indeed, salbutamol can act as an agonist at all β adrenergic receptors, but at therapeutic doses it 'selects' the β_2 adrenergic receptor subtype in preference to others.

Considering the drugs used in your clinical practice as a paramedic:

- In the first column, list FOUR receptors from different classes,thenin the second column, list their endogenous agonist(s).(2 marks)
- In the third column give an example of ONE drug that is a clinically relevant SELECTIVE agonist OR antagonist for each of the receptors.(2 marks)

Receptor	Endogenous agonist	Selective drug agonist or antagonist
κ-receptor	Dynorphin A	Naltrexone - Antagonist
Epidermal growth factor receptor	Growth factor	Cetuximab - Antagonist
$GABA_B$ receptor	GABA	Baclofen - Antagonist
Dihydrofolate reductase	Folic acid	Folic acid - Agonist

Activity 4

Antagonists at receptors for neurotransmitters or hormones are often used clinically.

- Use a diagram to explain how β-adrenoceptors antagonists produce clinically useful effects. (2 marks)

1. By blocking β_1-adrenoceptors these reduce tachycardia.
2. By blocking β_1-adrenoceptors these reduce myocardial contractility
3. By blocking β_1-adrenoceptors these reduce renin release which is helpful for hypertensive patients
4. By blocking β_1-adrenoceptors in heart these reduce the demand of oxygen of heart muscle and reduce the risk of myocardial infarction
5. By blocking β_2-adrenoceptors these reduce glucagon release which is helpful for diabetic patients
6. By blocking β_2-adrenoceptors in eye these reduce intraocular pressure of eye which is effective for Glaucoma
7. By inhibiting peripheral conversion of thyroxine to triiodothyronine these reduce severe hyperthyroidism

Ref.:

Book: Lippincott's Illustrated Reviews: Pharmacology. 4th Edition. By Richard Finkel Pharm.D. Chapter 7 Adrenergic Antagonists

- Considering the actions of β-adrenoceptors throughout the body, would it be the most appropriate treat uncomplicated hypertension in 68yo patient with moderate asthma and renal impairment with atenolol, metoprolol or propranolol? Briefly explainthe reasons for your decision. (4 marks)

Drug	Decision and explanation
Metoprolol	Metoprolol is highly selective for β_1- adrenoreceptor in heart. It has least affinity for β_2-adrenoceptor in lungs. So, it mainly blocks the β_1-adrenoreceptor in heart. That's why it is not worsen the asthma condition of patient. Also, it does not affect the kidney function of renal impaired patients. So, no dose reduction is needed in renal impaired patients. **Considering the above discussion, Metoprolol would be the appropriate drug for that patient.**
Atenolol	Atenolol is also highly selective for β_1- adrenoreceptor in heart and has least affinity for β_2-adrenoceptor in lungs. So, it is not worsen the asthma condition of patient also. But, it is mainly excreted through urine. And, it affects the kidney function of renal impaired patients. So, dose of Atenolol should be reduced in renal impaired patients otherwise drug will be accumulated inside the body that may cause severe hypotension. **Considering the above discussion, Atenolol would be the 2nd choice of drug for that patient.**
Propranolol	Propranolol is a non-selective β_1 & β_2 adrenoreceptor antagonist. That's why, it blocks both β_1- adrenoreceptor in heart as well as β_2 –adrenoreceptor in lungs. In that case, it will be worsen asthma condition of that patient. And that is hazardous for that patient. Also, dose of Propranolol should be reduced in that renal impaired patient. **Considering the above discussion, Propranolol would not be used in that patient.**

Ref.:

1. Goodman & Gilman's Manual of Pharmacology and Therapeutics. Eleventh Edition. By Laurence L. Brunton, PhD. CHAPTER 6 Neurotransmission: The Autonomic and Somatic Motor Nervous Systems. Page: 90.
2. Goodman & Gilman's Manual of Pharmacology and Therapeutics. Eleventh Edition. By Laurence L. Brunton, PhD. CHAPTER 10 Adrenergic Agonists and Antagonists. Page: 152.
3. Basic & Clinical Pharmacology, Tenth Edition. By Bertram G. Katzung, MD, PhD. Chapter-31: Opioid Analgesics & Antagonists
4. Lippincott's Illustrated Reviews: Pharmacology. 4th Edition. By Richard Finkel Pharm.D. Chapter 28 Gastrointestinal and Antiemetic Drugs
5. Lippincott's Illustrated Reviews: Pharmacology. 4th Edition. By Richard Finkel Pharm.D. Chapter 9 Anxiolytic and Hypnotic Drugs
6. Goodman & Gilman's Manual of Pharmacology and Therapeutics. Eleventh Edition. By Laurence L. Brunton, PhD. CHAPTER 7 Muscarinic Receptor Agonists and Antagonists-Page-122.
7. Goodman & Gilman's Manual of Pharmacology and Therapeutics. Eleventh Edition. By Laurence L. Brunton, PhD. CHAPTER 34 Antiarrhythmic Drugs-Page-592

8. Goodman & Gilman’s Manual of Pharmacology and Therapeutics. Eleventh Edition. By Laurence L. Brunton, PhD. CHAPTER 21 Opioid Analgesics, Page-353
9. Lippincott's Illustrated Reviews: Pharmacology. 4th Edition. By Richard Finkel Pharm.D.Chapter 41Anti-inflammatory Drugs
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11. Lippincott's Illustrated Reviews: Pharmacology. 4th Edition. By Richard Finkel Pharm.D.
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13. Goodman & Gilman’s Manual of Pharmacology and Therapeutics. Eleventh Edition. By Laurence L. Brunton, PhD. CHAPTER 10 Adrenergic Agonists and Antagonists. Page: 178