Introductory Pharmacology : Multiple Choice Questions : Bachelor Of Nursing : Southern Cross University

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MULTIPLE CHOICE QUESTIONS AND ANSWERS

WEEK 08

Q. Blood flow to the myocardium differs from blood flow to the rest of the cells of the body in that:

A. Blood perfuses the myocardial cells during diastole

Response Feedback:

Blood flow to the myocardium differs from blood flow to the rest of the cells of the body in that blood perfuses the myocardium during diastole, when the heart is relaxed. This has implications for some disorders, such as aortic valve regurgitation. In that disorder, since much of the blood stored in the aorta during diastole goes back into the chambers of the heart, there is little left for the heart itself.

Q. In the heart:

A. If the impulses from the SA node are blocked, the spontaneous depolarisation of the Atrioventricular (AV) node will occur about 40 times a minute

Response Feedback:

Impulses from the heart (not the brain) stimulate contraction of the heart muscle. Spontaneous depolarisation of the SA node will occur 60-100 times per minute. This is called normal sinus rhythm. If damaged, the impulses will be generated from the AV node at around 40 per minute.

Q. Cardiac cells differ from skeletal muscle cells in that:

A. They possess self-generating pacemaker potential that drives the self-generated rhythmic firing and the ability to conduct an electric current

Response Feedback:

Cardiac cells differ from skeletal muscle cells in that they have a self-generating pacemaker potential that drives the self-generated rhythmic firing and they have the ability to conduct an electric current (these are sometimes termed automaticity and conductivity respectively).

Q. The investigation that tests the electrical current through the heart is:

A. The ECG (sometimes called EKG)

Response Feedback:

The ECG measures flow of electrical current through the heart over time, as detected by electrodes attached to the surface of the skin. An ECG is used to measure the rate and regularity of heartbeats, as well as the size and position of the chambers, the presence of any damage to the heart, and the effects of drugs or devices used to regulate the heart. A myocardial infarction is normally caused by the development of a thrombus or an embolus that blocks the blood flow to an area of the heart.

A non-invasive technique that would more accurately predict the chances of a myocardial infarction is a doppler echocardiogram, which uses ultrasound technology to examine the heart and blood vessels. This measures the speed and direction of blood flow. To increase the accuracy of the flow-related measurement, contrast-enhanced ultrasound using gas-filled microbubble contrast media can also be used.

Question: It is possible for a person to have an electrocardiogram (ECG) with no abnormalities just before having a myocardial infarction. The explanation for this is:

The ECG only measures the flow of electrical current through the heart

The ECG is not related to heart problems

The ECG is not an accurate test

The ECG only reflects changes in cardiac output

Q. The rhythm of the heart is important because the atria contract just before the ventricular contraction and that gives optimal flow through the heart and into the system.

Dysrhythmias, or sometimes called arrhythmias, are an abnormality of the physiological rhythm of the heart. Think about what this would mean clinically. If a person had a dysrhythmia this would clinically result in:

A. Altered cardiac output that could affect all cells in the body

Response Feedback:

Dysrhythmias (arrhythmias) cause altered cardiac output that could affect all cells with the resulting hypoxia.

Q. The baroreceptors in the carotid sinus and aortic arch:

A. Are in an appropriate position to protect the brain

Response Feedback:

The baroceptors in the carotid sinus and aortic arch are in an appropriate position to protect the brain. When arterial blood pressure is increased, this increases the frequency of action potentials sent to the cardiovascular centre.

Q. One of the ways in which the body uses cholesterol is:

A. The formation of steroid hormones

Response Feedback:

One of the ways in which the body uses cholesterol is in the formation of steroid hormones. It is also an essential component of cell membranes and is important in the myelin sheath.

Q. A person with high lipid levels who cannot take fibrates or HMG-CoA reductase inhibitors should be prescribed:

A. Nicotinic acid

Response Feedback:

A person with high lipid levels who cannot take a statin (example, Simvastatin) or a fibrate (example: Fenofibrate) should be prescribed nicotinic acid.

Q. HMG-CoA reductase inhibitors work in the:

A. Process of cholesterol formation in the cell

Response Feedback:

HMG-CoA reductase inhibitors (or statins, example: Simvastatin) work in the process of cholesterol formation in liver cells. Statins act by competitively inhibiting HMG-CoA reductase. Specifically, they are very similar in molecular structure to HMG-CoA. This allows them to take the place of HMG-CoA in the enzyme HMG-CoA reductase, thereby reducing the rate by which it is able to produce mevalonate, a precursor to cholesterol. This results in less cholesterol synthesis in the liver, which is significant because humans generally produce more cholesterol than they absorb from the diet.

Q. Hyperlipidaemia is considered to be:

A. A treatable coronary artery disease (CAD) risk factor

Response Feedback:

Hyperlipidaemia is considered to be a treatable CAD risk factor. Hyperlipidaemia can be primary or secondary. Primary hyperlipidaemia is usually due to genetic causes (such as a mutation in a receptor protein), while secondary hyperlipidaemia arises due to other underlying causes (such as diabetes).

Other treatable risk factors of Coronary Heart Disease (atherosclerosis of the coronary artery) include smoking, diabetes, hypertension, sedentary lifestyle (or lack of exercise),

Other cause risk factors include increasing age and male gender.

Q. Which of the following would alert you that the person taking HMG-CoA reductase inhibitors is developing rhabdomyolysis?

A. Muscle pain and weakness

Response Feedback:

Rhabdomyolysis is a condition in which damaged skeletal muscle tissue breaks down rapidly. The breakdown product (myoglobin) is released into the bloodstream and can damage the kidneys. Symptoms include muscle pains, weakness, vomiting, confusion as well as symptoms consistent with acute renal failure.

Both fibrates (example, fenoFIBRATE) and statins (HMG CoA reductase inhibitors; simvaSTATIN) may precipitate rhabdomyolysis. Although this is a rare side effect, combining the two or one of the two with Niacin increases the risk greatly.

Q. Atheromas, which occur in atherosclerosis (hardening of the arteries) are involved in the development of:

A. Coronary artery disease

Response Feedback:

Atheromas and the process of atherosclerosis are involved in the development of coronary artery disease, which leads to myocardial infarction. They are also involved in cerebral vascular disease (which can lead to a stroke) and peripheral artery disease (which can lead to intermittent claudication, mesenteric arterial occlusion), and a number of other health complaints, depending on the location of the plaques.

Atherosclerosis cannot form on the venous vessels but can form on any of the arteries.

Intermittent claudication is a condition that causes cramping, pain and even skin changes in the legs, and is normally caused by atherosclerosis of the extremities. Mesenteric arterial occlusion is a condition in which the mesenteric artery occludes due to atherosclerosis. Both of these are considered to be under the umbrella term of peripheral arterial disease

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Q. The drugs that are considered bile acid sequestrants:

A. Prevent bile salts from being reabsorbed

Response Feedback:

The bile acid sequestrants like Cholestyramine prevent bile salts from being reabsorbed. The bile acid sequestrants are a group of resins used to bind certain components of bile in the GIT. They disrupt the enterohepatic circulation of bile acids by combining with bile constituents and preventing their reabsorption in the intestines.

Q. A woman who absolutely must go on a lipid lowering agent and is pregnant should be prescribed:

A. Bile acid sequestrants, even though they are normally contraindicated in pregnancy

Response Feedback:

Normally, we consider every lipid lowering drug to be contraindicated in pregnancy. BUT if a woman HAS TO take a lipid lowering agent during pregnancy should be prescribed bile acid sequestrants, as they are not absorbed and do not have systemic manifestations.

HMG-CoA reductase inhibitors (also known as statins) are Pregnancy Category X drugs and should not be taken by a woman with any chance of getting pregnant. Niacin is also

contraindicated during pregnancy and lactation, and the effect of fibrates during pregnancy has been inadequately studied.

Ideally, dietary and lifestyle changes without medication are recommended, as the growing foetus and infant needs cholesterol! Also, your pregnant patient on bile acid sequestrants may be binding fat soluble vitamins that are critical in the development of the foetus/infant (and medications important to the health of the mother)!

Q. The person taking statins should avoid the following:

A. Each of the choices are contraindicated in people taking statins

Response Feedback:

Combining any statin (example, Simvastatin) with a fibrate (example: Fenofibrate) or niacin increases the risks for rhabdomyolysis (a rapid breakdown of muscle that can lead to kidney failure). Consumption of grapefruit or grapefruit juice (or bitter oranges) inhibits the metabolism of certain statins (due to their inhibition of cytochrome P450 enzyme CYP3A4). Statins are contraindicated in pregnancy because of serious foetal adverse effects.

Q. The baroreceptors:

A. Sense pressure, immediately sending that information to the medulla in the brain

Response Feedback:

Baroreceptors are sensory neurons that are excited by stretch of the blood vessel. Increases in the pressure of the blood vessel triggers increased action potentials and provides information to the CNS. A specific area in the medulla oblongata (the nucleus tractus solitarii) recognises the firing rate of action potentials and influences cardiac output and systemic vascular resistance through the ANS.

Q. Essential hypertension is:

A. Associated with no single known cause

Response Feedback:

Essential (primary) hypertension makes up 90% of the cases of hypertension and is not associated with any one specific cause. It appears to have a number of risk factors, including genetics, lifestyle, diet and stress levels. Secondary hypertension is secondary to one other health problem, like renal arterial occlusion or a tumour in the adrenal gland. When that problem is eliminated, secondary hypertension is normally resolved.

Q. Hypertension is associated with:

A. Each of the health problems listed can be caused by long standing chronic hypertension

- Heart failure
- Renal failure
- Loss of vision

Response Feedback:

Hypertension is a major risk factor for aneurysms (including in the eye, resulting in loss of vision), stroke, myocardial infarction, heart failure, chronic kidney disease and peripheral arterial disease. Even moderate hypertension is associated with decreased life expectancy.

Q. Short term regulation of blood pressure includes:

A. Autonomic nervous system effects

Response Feedback:

This feedback is important for your understanding of blood pressure pharmacology.

*Short term regulation of blood pressure involves **autonomic nervous system** effects. For instance, as you stand up from a seated position, gravity forces a larger portion of the blood away from your head and towards lower portions of your body. The medulla immediately responds to baroreceptor information, triggering the SNS response. This immediately constricts peripheral blood vessels and increases the force and speed of the heart.*

*But after you have been standing for a while or the blood pressure is still decreasing, long term regulation of blood pressure must be used. This involves the kidneys and the effects of the **renin-angiotensin-aldosterone mechanism**. This works by several mechanisms to increase blood pressure, including the release of **ADH, the water saver and aldosterone, the salt saver**. Increased salt and fluid increases the blood pressure.*

*Did you notice that each of the **mechanisms we mention above** can be decreased by medications that treat high blood pressure?*

For instance, the short term regulation of blood pressure mainly uses the autonomic nervous system, so we can block the autonomic nervous system. Blocking the alpha 1 receptor with a selective alpha antagonist like prazosin or doxazosin or other AZOSIN drugs will essentially dilate the blood vessels. Blocking the beta 2 receptor with a non-selective beta 2 blocker like propranOLOL or a selective one like atenOLOL will decrease heart rate and contractility, decreasing afterload.

We can decrease the effects of the renin angiotensin aldosterone system with our SARTAN drugs that block angiotensin II or with our PRIL drugs that decrease ACE.

We can also affect aldosterone with some diuretics (some thiazide diuretics), which we discuss in the renal system.

Q. ACE inhibitors like captoPRIL and enalaPRIL block angiotensin converting enzyme (ACE) in the lung and often cause:

A. Unrelenting dry cough

Response Feedback:

A persistent dry cough is a relatively common adverse effect that may be due to the increases in bradykinin (a peptide that causes vasodilation) levels produced by ACE inhibitors like Captopril and Ramipril. Patients who experience this cough are often switched to angiotensin II receptor antagonists like CandeSARTAN.

***Question**: Which of the following acts on an enzyme? CandeSARTAN and other SARTAN drugs or Captopril and other PRIL drugs?*

***Answer**: the ACE inhibitors like caproPRIL work on the angiotensin converting enzyme (ACE), decreasing the conversion of angiotensin I to angiotensin II, while the SARTAN drugs block the binding of the Angiotensin II to its receptors. Ultimately BOTH decrease the actions of the potent stress hormone, angiotensin II. hint: an 'inhibitor' works on an enzyme, while agonists and antagonists work on receptors.*

***Question** 2: why do we have a hormone like angiotensin II if it is so bad?*

***Answer**: Angiotensin II is a potent stress hormone that we evolved to cope with dehydration or excessive bleeding. It is the hormone that orchestrates every blood pressure raising mechanism in our body to work at the same time. So it is great if we are bleeding to death. But we are not. The chronic diseases that humans are getting (because of their lifestyle and increasing longevity) ultimately results in too much Angiotensin II. So now, many people can benefit from ACE inhibitors or angiotensin II receptor blockers.*

Q. The drug of choice for a pregnant hypertensive woman is:

A. A calcium channel blocker

Response Feedback:

Calcium channel blockers like Verapamil are the most accepted choice during pregnancy, but they are not without their risks (see below if interested). ACE inhibitors (PRIL drugs) and angiotensin II receptor blockers (SARTAN drugs) are strictly contraindicated and barrier prophylactics should be used by the partner if the woman is of childbearing age.

The reduction of calcium in the heart cells leads to a decrease in contractility while the reduction of calcium in the smooth muscle of the blood vessels leads to vasodilation.

The following is from a study by the World Health Organisation and is not recommended reading. It is just out of interest. This review (1) included twenty-four trials in which the antihypertensive effect of different drugs for the management of very high blood pressure during pregnancy was compared. For only few outcomes in four of the 12 drug–drug comparisons in the review could inferences be drawn about comparative effect: (i) calcium channel blockers (nifedipine and isradipine) are associated with less risk of persistent hypertension compared with hydralazine (6% versus 18%); (ii) Ketanserin is associated with almost fivefold risk of persistent hypertension compared with hydralazine (27% versus 6%), though side-effects are less common; (iii) diazoxide tends to cause more hypotension compared with labetalol; and (iv) nimodipine and magnesium sulfate are both associated with high levels of persistent hypertension (47% versus 65%), though nimodipine is less likely to cause respiratory difficulties, postpartum haemorrhage and side-effects. Overall, there is insufficient evidence to conclude that any one antihypertensive drug is clearly better those others for the treatment of women with very high blood pressure in pregnancy. Duley, Lelia, Shireen Meher, and Leanne Jones. "Drugs for treatment of very high blood pressure during pregnancy." The Cochrane Library (2013)

Q. To inhibit the production of vitamin K clotting factors in the liver

Response Feedback:

Warfarin, an oral anticoagulant, acts by inhibiting vitamin K epoxide reductase, an enzyme that recycles oxidized vitamin K1 to its reduced (and active) form after it has participated in the making of a number of coagulation proteins including prothrombin. Warfarin does not antagonise vitamin K1 itself, but rather its recycling back to the active form. The result is inadequate active vitamin K and a decrease in clotting factors. This pharmacological action can be reversed by the administration of vitamin K, therefore altering consumption of vegetables (as well as a number of supplements) is contraindicated in people taking warfarin.

Warfarin is

An antagonist

An agonist

An enzymatic inhibitor

Yes, warfarin is an inhibitor. Most drugs work on cell receptors but inhibitors work by inhibiting AN ENZYME.

Simplistically warfarin inhibits an enzyme that rejuvenates vitamin K. If we stop rejuvenating vitamin K, the clotting factors that need vitamin K will not be able to participate in the clotting cascade.

Analogy: if clotting factors were a line of dominos all set up nicely so that they would all go off if one was pushed over (activated), warfarin in effect removes a few of those dominos. Without all of the clotting factors, the clotting cascade does not go all the way to the end (it does not produce fibrin strands necessary in clotting)

Q. Angina:

A. Is pain due to lack of oxygen supply to myocardial cells

Response Feedback:

Angina (angina pectoris) is NOT a disease but rather A SYMPTOM !! It is the pain due to lack of oxygen supply to myocardial cells. The main cause of angina is CAD (coronary artery disease AKA ischaemic heart disease, hardening of the arteries in the heart, atherosclerosis of the heart, and other names) . Once the ischaemia that causes angina actually results in cell death (about 20 minutes), it is called a myocardial infarction.

Angina is not the disease but rather the symptom, but it is often wrongly used to describe the disease by lay-people.

Q. Unstable angina:

A. Should be considered a warning that myocardial infarction is much more likely than with classic angina

Response Feedback:

"Angina" is a symptom (a pain in the heart) which is normally caused by coronary artery disease (ischaemic heart disease; hardening of the coronary artery). When the plaques on the coronary artery become very brittle or develop a partial thrombosis, the character of the

pain changes (see below) and THIS IS YOUR SIGNAL that there may be a heart attack in the next year. This dangerous condition is called unstable angina.

Most individuals with unstable angina have an atherosclerotic plaque with partial thrombosis and sometimes embolisation or vasospasm.

If the patient has (1) angina that has changed in onset, now occurring at rest or with minimal exertion, or (2) angina that has increased in intensity, duration or frequency, they have unstable angina.

Fifty percent of people with unstable angina will have evidence of myocardial necrosis based on elevated cardiac serum markers. People with unstable angina are often managed with nitroglycerine to decrease the preload on the heart, antiplatelet drugs such as aspirin to decrease thrombus formation in the arteries and an anticoagulant such as a low molecular weight heparin.

Q. The low-molecular-weight heparin that is recommended for DVT prevention after hip replacement is:

A. Enoxaparin

Response Feedback:

The low-molecular-weight heparin that is recommended for DVT prevention after hip replacement is Enoxaparin (Clexane). Note that all drugs in this group end in 'parin'.

Q. Which of the following is true about Heparin:

A. (all of the choices for this question are true about heparin)

- Uptake is variable if injected into the skin
- It can result in thrombocytopaenia
- It can result in dangerous bleeding

Response Feedback:

All of the choices are correct. Since heparin can result in dangerous bleeding, it is good to know that its effects can be reversed with administration of protamine sulfate.

Heparin is a naturally occurring anticoagulant produced by immune cells (basophils and mast cells). Heparin does not break down pre-formed clots, but rather activates the enzyme inhibitor antithrombin III (AT). The activated AT then inactivates thrombin.

Q. Coronary artery disease results in:

A. An imbalance in cardiac muscle oxygen supply and demand

Response Feedback:

Coronary artery disease (CAD; atherosclerotic heart disease, coronary heart disease [CHD], ischaemic heart disease [IHD]) results in an imbalance in cardiac muscle oxygen supply and demand. CAD is the most common type of heart disease and is the cause of most heart attacks. The disease is caused by the buildup of atherosclerotic plaques in the lumen of the arteries of the heart. Given the fact that decreasing the diameter of the vessel by ½ results in

just 1/16th the flow of blood, one can easily understand that this greatly reduces the oxygen supply to the heart at a time when other atherosclerotic vessels are causing more resistance or, in other words, causing a greater workload for the heart.

Question: how do we treat CAD?

Treatment includes decreasing platelet aggregation with aspirin (and sometimes the clotting cascade with warfarin). That helps with prevent thrombus formation, but be also need to decrease the progression of the disease, by decreasing the risk factors:

- *Hypertension*
- *Hyperlipidemia*
- *Lifestyle (stress, sedentary lifestyle, smoking, obesity...)*

Q. Verapamil is contraindicated for use with:

A. Anaesthetics

Response Feedback:

Verapamil is contraindicated with anaesthetics. Verapamil does not end in 'dipine' because it is one of the few calcium channel blockers that is not a dihydropyridine.

What are the indications for verapamil?

It is used predominantly to treat hypertension and arrhythmias

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Q. The most common side effect(s) of antihaemophilic agents is/are:

A. Immune reactions and the spread of viruses

Response Feedback:

The most common side effects of antihaemophilic agents are immune reactions and the spread of viral infections. There are a number of different types of bleeding disorders this broad group of agents treat. Some of them are made in mice, and the greatest risk is normally that of an immune reaction. Others are from human plasma donors, and despite screening and treatment, there is still a risk of transmission of viruses, including Hepatitis A. Contracting AIDS from these products is still possible with the agents sourced from humans, but the risk is very low.

Q. Variant angina occurs as a result of:

A. A spasm of a coronary vessel

Response Feedback:

Variant or Prinzmetal angina is a syndrome typically consisting of (the symptom of) angina that occurs at rest in cycles. Most cases of variant angina are caused by vasospasm in the coronary arteries and may occur in absence of atherosclerosis in those vessels. It occurs more in younger women. Beta-blockers are contraindicated in variant angina because they could cause vasospasm due to blocking of Beta-receptor sites.

Variant or Prinzmetal angina is one of the few types of angina that is not caused by ischaemic heart disease (coronary artery disease; hardening of the coronary artery)

Q. Nitrates act to:

A. Decrease venous return to the heart, decreasing the myocardial workload

Response Feedback:

Nitrates act to decrease venous return to the heart, decreasing the myocardial workload. Arteries that are undamaged will respond to nitrates, increasing flow of blood to the heart. However arteries that are badly damaged due to atherosclerotic plaques don't respond well to nitrates. If a patient is not getting relief from their nitrates, CHECK THE EXPIRATION DATE AND STORAGE METHODS they used, as these products can deteriorate in a relatively short period of time, especially if storage conditions are not ideal.

Q. A thrombolytic agent would be recommended in:

A. Acute MI within the last 3 hours

Response Feedback:

Thrombolytic agents are contraindicated in all choices given except the acute MI within the last 3 hours. Thrombolytic agents activate the natural anticlotting system (conversion of plasminogen to plasmin) and have a very narrow therapeutic index (having little difference between toxic and therapeutic doses).

Q. Blood coagulation involves:

A. Vasoconstriction, platelet aggregation, and a clotting cascade that ends in conversion of prothrombin to thrombin, which converts circulating fibrinogen to fibrin strands, which strengthen the platelet plug

Response Feedback:

Blood coagulation involves vasoconstriction, platelet aggregation, and a clotting cascade that ends in conversion of prothrombin to thrombin. The thrombin converts circulating fibrinogen to fibrin strands, which strengthen the platelet plug. Soon after formation, the clot dissolving substances increase in the area, with plasminogen being converted to plasmin, the main substance involved in fibrin dissolution.

Why is this important when studying pharmacology?

Because our drugs for reducing thrombi will target one of these mechanisms, especially

- *Platelet aggregation (antiplatelet drugs such as aspirin)*
- *The clotting cascade (drugs like warfarin)*
- *The fibrin strands (drugs like streptokinase)*

Q. Low dose aspirin (75-150mg/day) is effective:

A. In people with atherosclerotic vessels to help prevent strokes and myocardial infarction

Response Feedback:

Low dose aspirin (75-150mg/day) is used in people with atherosclerotic vessels to prevent strokes and myocardial infarction. Aspirin is an antiplatelet drug that non-competitively

inhibits cyclooxygenase (COX) that is needed to form TXA2, a pro-platelet prostaglandin. COX in cells will be affected as well, but they make more of that enzyme. Platelets cannot make more of that enzyme because they are just a cell fragment. Aspirin alone is not effective in reducing DVT risk and cannot break down pulmonary emboli.

Aspirin is antithrombotic in the

- *Veins*
- *Arteries*
- *Equally in the veins and arteries*

Q. ACE inhibitors are used in the early treatment of heart failure to:

A. Decrease blood volume

Response Feedback:

ACE inhibitors are used early in the treatment of heart failure to decrease blood volume, effectively decreasing the production of angiotensin II. This decreased angiotensin II effectively decreases aldosterone (the salt saver), decreases release of ADH (the water saver), decreases sympathetic stimulation and has other blood pressure lowering effects.

ACE inhibitors are the PRIL drugs (Ramipril, enalapril and others). These are extremely important for you to understand more about.

Q. A person taking the cardiogenic glycoside digoxin (trade name Lanoxin) for the treatment of congestive heart failure should do which of the following?

A. Report any changes in heart rate

Response Feedback:

A person taking Lanoxin (digoxin) for the treatment of congestive heart failure should report any changes in heart rate, as this may be the first sign of digoxin toxicity.

Q. Prior to the administration of the cardiogenic glycoside Digoxin (trade name Lanaxin), you take the patient's pulse and find that it is 50 beats per minute. You should:

A. Retake the pulse in one hour and withhold the drug if the pulse is still less than 60

Response Feedback:

If your patient's pulse is less than 60, it may indicate digoxin toxicity. Cardiogenic glycosides slow the rate of the heart (negative CHRONOtropic effect), increase the force of myocardial contraction (positive INOtropic effect), increase renal blood flow, which decreases the release of renin (renin-angiotensin-aldosterone mechanism) and increases urination.

Q. Cardiac contraction and relaxation are controlled by:

A. Spontaneous impulses arising within the heart

Response Feedback:

Cardiac contraction and relaxation are controlled by spontaneous impulses arising within the heart. Both arms of the autonomic nervous system affect the generation of these impulses.

The normal rhythm of the heart can be altered by a number of modifiable factors, including:

- *hypoxia from anaemia*
- *hyperkalemia (excess potassium slows depolarisation)*
- *fever*
- *alterations in thyroid hormone levels*
- *hypercalcaemia*
- *drugs (including caffeine)*
- *acidosis or alkalosis (as from hyperventilation).*
- *Structural damage from ageing and myocardial infarction can cause permanent damage.*

Q. In a case of heart failure (HF) you would expect the patient to have:

A. Pulmonary oedema and/or oedema of the extremities

Response Feedback:

In a case of Right-sided heart failure, the blood would back up into the venous system and push into the interstitial spaces, giving the patient ankle oedema, enlarged congested liver, congested gut (ascites) and in general, most areas would carry more fluid.

If the left side of the heart was involved, the individual would complain of a dry cough at first, and sleep on several pillows which would make the cough better. Later, the cough would become more productive and you could hear sounds in the chest with breathing.

These signs and symptoms of heart failure would get better with treatment, and the person may live 30 years or longer, so it may be best to use a softer term when describing it to the affected individual.

Q. Because antiarrhythmic drugs alter the action potential of cardiac cells, they:

A. Can cause new arrhythmias

Response Feedback:

Antiarrhythmic drugs alter the action potential of cardiac cells, so they can cause new arrhythmias. Because of this, people receiving antiarrhythmic drugs should be monitored closely for pulse, blood pressure, heart rate, and rhythm and should be assessed regularly for any abnormal sounds.

Q. Cardiac glycosides like DIGOXIN (trade name Lanoxin) which are used to treat congestive heart failure and dysrhythmias:

A. Affect the intracellular calcium levels in the heart muscle

Response Feedback:

Cardiac glycosides like digoxin affect the intracellular calcium levels in the heart muscle, leading to increased contractility. This is termed a positive inotropic effect (inos = fibre). The increased contraction strength leads to increased cardiac output per beat. The cardiac glycosides also increase the effect of the parasympathetic nervous system on the sinoatrial (SA) node, decreasing heart rate. This is termed a negative chronotropic effect (chrono =

time). Historically these were the main medicines used in the treatment of congestive heart failure, but they have largely been replaced by the ACE inhibitors due to their superior efficacy and safety.

Digoxin increases the force but slows down the heart

Digoxin therefore exerts a positive inotropic effect and a negative chronotropic effect

Q. The results of the Cardiac Arrhythmia Suppression Trial (CAST) study:

A. Have made Class I and III antiarrhythmic drugs reserved for use in cases of life-threatening arrhythmias.

Response Feedback:

The CAST study found that the long-term treatment of arrhythmias with Class I or III antiarrhythmic drugs INCREASED mortality instead of decreasing it. Therefore, these drugs are now indicated only for the short-term treatment of potentially life-threatening ventricular arrhythmias.

Q. Calcium is needed in the heart muscle:

A. To activate troponin

Response Feedback:

Calcium is needed in the heart to activate troponin.When the muscle cell is stimulated to contract by an action potential, calcium channels open in the sarcoplasmic membrane and release calcium into the sarcoplasm. Some of this calcium attaches to troponin, which causes it to change shape (activating it), exposing binding sites for myosin (active sites) on the actin filaments. Myosin's binding to actin causes crossbridge formation and contraction of the muscle begins. When troponin is released from calcium, the actin myosin crossbridges separate and the sarcomere slides apart (relaxation)

In both cardiac and skeletal muscles, muscular force production is controlled primarily by changes in intracellular calcium concentration. ***In general, when calcium rises, the muscles contract and, when calcium falls, the muscles relax.***

WHY IS THIS IMPORTANT TO US? This is the principle behind calcium channel blockers.

QUESTION*: Calcium channel blockers like nifedipine and verapamil, which decrease myocardial contraction and dilate the vasculature are associated with which of the following adverse effects?*

- *Dizziness, headaches*
- *Hypotension*
- *Tachycardia*

All of the above are possible with calcium channel blockers like nifedipine and verapamil

Q. A person who is receiving an antiarrhythmic drug needs:

A. Very frequent cardiac monitoring until stabilised

Response Feedback:

A person who is receiving an antiarrhythmic drug needs frequent cardiac monitoring until stabilised.

MULTIPLE CHOICE QUESTIONS AND ANSWERS

WEEK 09

Q. The diuretic(s) or diuretic like drugs that can cause HYPERkalaemia or increased levels of potassium include:

A. ACE inhibitors (like captopril and other pril drugs) and angiotensin II receptor blockers (like candesartan and other sartan drugs) and 'potassium sparing diuretics' like amiloride and spironolactone

Response Feedback:

ACE inhibitors (like captopril and other pril drugs) and angiotensin II receptor blockers (like candesartan and other sartan drugs) and 'potassium sparing diuretics' like amiloride and spironolactone which work at the same place as aldosterone works in the nephron will be able to cause hyperkalaemia, especially if combined with each other.

WHY IS THIS IMPORTANT?

Hyperkalaemia can cause life threatening dysrhythmias. These drugs are often combined with the diuretics that cause hypokalaemia (loop diuretics like frusemide and thiazide diuretics like hydrochlorothiazide.)

Q. Arteriolar blood flow to the nephron differs from blood flow to other tissues in that:

A. the diameter of afferent and efferent arterioles can be manipulated to increase or decrease glomerular filtration rate

Response Feedback:

Arteriolar blood flow to the nephron differs from blood flow to other tissues in that the diameter of afferent and efferent arterioles can be manipulated to increase or decrease glomerular filtration rate.

For instance, if the blood pressure is too high, the juxtaglomerular area autoregulates the pressure, constricting the afferent vessel and dilating the efferent vessel. This ensures that the pressure in the glomerulus is not high enough to damage the internal structures of the glomerulus. Unfortunately, about 5% of hypertensive individuals still develop glomerular dysfunction progressing to renal failure, because the high blood pressure exists too long or the blood pressure rises too high.

Q. Diuretics cause a loss of fluid volume. The decreased volume is sensed by:

A. the juxtaglomerular apparatus in the kidney, which releases renin. This activation of the renin-angiotensin aldosterone system results in increased ADH and aldosterone.

Response Feedback:

Diuretics cause a loss of fluid volume. The decreased volume is sensed by the juxtaglomerular apparatus in the kidney, which releases renin.

With the activation of the renin-angiotensin aldosterone system, ADH and aldosterone release is increased. ADH helps save water and aldosterone helps save salt. This increases the volume of fluid back to the pre-therapy treatment.

(ADH is also secreted in response to reduced plasma volume noted by pressure receptors in the carotid arteries and increases in plasma osmotic pressure sensed by osmoreceptors in the hypothalamus)

Q. Most diuretics cause:

A. loss of sodium

Response Feedback:

Most diuretics act to cause salt loss, and the water follows the salt.

The osmotic diuretics do not cause sodium loss because the diuretic agent is injected and acts as an osmotic particle pulling water into the tubule. With large amounts of osmotically active particles already present in the tubules, less salt is excreted. This can result in hypernatremia (excess salt in the blood).

Also, ADH antagonists prevent water reabsorption at the distal convoluted tubule. With less salt being wasted (as compared to other diuretics), they are the drug of choice in patients who have decreased plasma levels of salt.

Q. Hydrochlorothiazide and other thiazide diuretics are considered mild diuretics because:

A. they cause loss of sodium and chloride but little water

Response Feedback:

Thiazide diuretics cause an excretion of salt and chloride but this happens in the distal convoluted tubule which is impermeable to water, so there is little increase in the volume of urine.

Hydrochlorothiazide is frequently used for the treatment of hypertension, congestive heart failure and symptomatic oedema, and is often combined with other medications in the treatment of these disorders.

Hypokalemia, or low blood levels of potassium are an occasional side effect. It can be usually prevented by potassium supplements or by combining hydrochlorothiazide with a potassium-sparing diuretic. Other disturbances in the levels of serum electrolytes are frequently seen, especially low levels of magnesium

Hydrochlorothiazide is contraindicated in gout and may cause hyperuricemia, high levels of uric acid in the blood

Q. Loop diuretics such as Frusemide (Furosemide in some countries and textbooks) are the drug of choice for a person with:

A. pulmonary oedema

Response Feedback:

Loop diuretics are the drugs of choice when a rapid and extensive diuresis is needed, as in the case of pulmonary oedema.

Pulmonary oedema occurs in patients who have left-sided heart failure. The ailing left ventricle cannot pump fast enough, increasing the pressure in the lungs and forcing fluid into the interstitial spaces.

Loop diuretics allow a lot of water to be excreted from the kidneys. This causes a more hypertonic intravascular fluid. The hypertonic intravascular fluid then circulates back up to the lungs, osmotically pulling fluid from the interstitial spaces. The extra fluid is then taken to the kidneys and excreted. It can take hours for this process to be completed.

Frusemide (Furosemide) is primarily used for the treatment of hypertension and oedema. It is the first-line agent in most people with oedema caused by congestive heart failure. It is also used for liver cirrhosis, kidney impairment, nephrotic syndrome, in adjunct therapy for swelling of the brain or lungs where rapid diuresis is required (IV injection), and in the management of severe hypercalcemia in combination with adequate rehydration

Frusemide is considered ototoxic (it damages the ears) and may cause tinnitus (ringing of the ears), especially in large doses.

Frusemide can cause hypokalemia or low levels of potassium

WHY IS IT IMPORTANT TO KNOW THAT IT CAN CAUSE HYPOKALAEMIA?

Most people who take diuretics have heart problems, and hypokalaemia can cause dysrhythmias. Frequent electrolyte analysis should be performed and potassium supplements should be taken.

Q. Which of the following should be monitored most closely in a patient who is receiving a loop diuretic like frusemide (furosemide)?

A. potassium levels

Response Feedback:

potassium levels are most important as they can drop when the patient is on loop diuretics. Some of the first clinical manifestations of hypokalaemia include muscle weakness, muscle pain, muscle cramps and constipation. Sodium levels drop as well, however we are more tolerant of hypernatremia than hypokalaemia.

So if there is one thing that you need to remember about loop diuretics, it is that Frusemide can cause hypokalemia or low levels of potassium

WHY IS IT IMPORTANT TO KNOW THAT IT CAN CAUSE HYPOKALAEMIA?

Most people who take diuretics have heart problems, and hypokalaemia can cause dysrhythmias. Frequent electrolyte analysis should be performed and potassium supplements should be taken, because HYPOKALAEMIA IS A LIFE THREATENING CONDITION.

Possible MC Question: what are the first symptoms) of hypokalaemia:

muscle weakness, muscle pain, muscle cramps and constipation

(other symptoms)

(other symptoms...)

Q. Which of the following may cause hypokalaemia?

A. Hydrochlorothiazide and frusemide

Response Feedback:

Hydrochlorothiazide (a thiazide diuretic) and frusemide (a loop diuretic) can both cause hypokalaemia. Frusemide and other loop diuretics have the greatest possibility of decreasing potassium levels. Signs of hypokalaemia include muscle weakness, muscle cramps and cardiac arrhythmias.

Spironolactone is a potassium sparing diuretic that is an aldosterone antagonist, so it can cause hyperkalaemia. ACE inhibitors and ARBs (angiotensin receptor blockers can also cause HYPERkalaemia)

Q. If a patient lost kidney function, a practitioner would expect to find:

A. electrolyte disturbances

Response Feedback:

There are electrolyte disturbances when kidney function is lost. Other problems include acidosis as it becomes more difficult to excrete hydrogen ions and save bicarbonate, decreased red blood cells due to decreased longevity (toxins decrease lifespan of the cells) and decreased secretion of erythropoietin from the kidneys, INCREASED fluid volume and INCREASED blood pressure.

Q. Renal reabsorption is the process by which:

A. substances from the renal tubule are reabsorbed into the blood

Response Feedback:

Renal reabsorption is the process by which substances from the renal tubule are reabsorbed into the blood. If they had stayed in the renal tubule, they would have been eliminated.

Secretion is the process of the peritubular capillaries secreting substances into the tubule for excretion. No water is reabsorbed or secreted at the loop of Henle and glucose is only reabsorbed at the proximal tubule.

After these processes,the urine passes through the ureters by peristaltic actions to the urinary bladder. Blockage of the ureters or urethra damages the ability to engage in peristaltic actions and eventually damages the kidneys.

Q: Urine passes through the ureter by:

osmosis

air pressure

filtration

peristalsis

Q. Which of the following acts as an aldosterone (the salt saver from the adrenal cortex) antagonist?

A. Spironolactone

Response Feedback:

Spironolactone is a potassium sparing diuretic which acts as an aldosterone antagonist.and as such, is used for conditions of hyperaldosteronism and also as a diuretic. (we are blocking the salt saver OR wasting salt. If we waste salt we waste water)

Hydrochlorothiazide is a thiazide diuretic that is considered a weak diuretic.

Frusemide or furosemide (Lasix) is a Loop diuretic which is best when extensive diuresis is required.

Acetazolamide is a carbonic anhydrase inhibitor that is used for treatment of glaucoma, epileptic seizures and idiopathic (from no known cause) intracranial hypertension.

CAN SPIRONOLACTONE CAUSE HYPOKALAEMIA (LOW POTASSIUM)?

ANSWER; NO, it is a potassium sparing diuretic, so it can cause hyperkalaemia, especially if combined with ACE inhibitors.

Q. Antidiuretic hormone (ADH) is considered:

A. the water saver

Response Feedback:

Antidiuretic hormone (ADH) is considered water saver, as its presence at the collecting ducts opens the water channels and allows water to be reabsorbed into the blood. Alcohol inhibits ADH secretion - less water saving, less fluid saved, dehydration in the morning after a long night. Always drink plenty of water after consuming too much alcohol.

Aldosterone is the salt saver, and its presence at the distal convoluted tubule allows salt to be reabsorbed into the blood.

ACE inhibitors (pril drugs) and angiotensin II receptor blockers (sartan drugs) indirectly decrease release of ADH, the water saver and aldosterone the salt saver. They also result in less vasoconstriction and work by other mechanisms to decrease blood pressure.

Q. A person with severe glaucoma who is about to undergo eye surgery would be most likely to be administered:

A. an osmotic diuretic like mannitol or isosorbide

Response Feedback:

Acute situations that require decreasing intraocular pressure before eye surgery or during acute attacks of glaucoma normally require osmotic diuretics.

In less demanding situations, carbonic anhydrase inhibitors are used to treat glaucoma because the inhibition of carbonic anhydrase results in decreased secretion of aqueous humour of the eye. The carbonic anhydrase inhibitors are not as useful in acute situations, and you do not need to know about them.

WHAT DO I NEED TO KNOW ABOUT OSMOTIC DIURETICS?

A: not much. They are normally injected and used in a very controlled hospital setting. Know the least about these!

Q. Acid rebound is a condition that occurs when:

A. lowering gastric acid to an alkaline level stimulates the release of gastric acid

Response Feedback:

Acid rebound is a condition that occurs when the pH of the gastric contents is lowered to an alkaline level, which stimulates the release of gastric acid. It occurs most noticeably when the patient has taken antacids containing calcium carbonate. It can occur with proton pump inhibitors as well and there is some evidence to suggest that tapering off the drug helps prevent acid rebound.

Another potential problem with drugs that decrease the acidity of the stomach occurs while the patient is on the drugs. Small amounts of bacteria (that survive the stomach because the environment is more neutral than normal) in refluxed stomach juices can enter the trachea ("windpipe") and upper airways. This is thought to be the reason that people on anti-acid drugs are more likely to get pneumonia.

ANOTHER problem with drugs that decrease acidity is the fact that some nutrients and drugs will be affected.

Acid rebound is most likely to occur with which of the following antacids?

Sodium bicarbonate

Magnesium citrate

Aluminium hyrdoxide

Calcium Carbonate

Answer: 4

Q. Which of the following instructions is appropriate for enteric-coated proton pump inhibitors (the PRAZOLE drugs)?

A. swallow tablets or capsules whole

Response Feedback:

The enteric-coated proton pump inhibitors should not be chewed, although Omeprazole is available in a chewable form and enteric coated. Proton-pump inhibitors (PPIs) are a group of drugs whose main action is a pronounced and long-lasting reduction of gastric acid production. They are the most potent inhibitors of acid secretion available. The group followed and has largely superseded another group of pharmaceuticals with similar effects, but a different mode of action, called H2 receptor antagonists.

HOW DOES OMEPRAZOLE WORK?

Omeprazole is a selective and irreversible proton pump inhibitor. It suppresses stomach acid secretion by specific inhibition of the H+/K+-ATPase system found at the secretory surface of gastric parietal cells. Because this enzyme system is regarded as the acid / proton / H+ pump within the gastric mucosa, omeprazole inhibits the final step of acid production.

Omeprazole is indicated for the treatment of which of the following?

treatment of gastroesophageal reflux disease,

treatment of peptic ulcer disease

treatment of Zollinger–Ellison syndrome

all of the above

Q. GIT acid-neutralisers that are absorbed include:

A. calcium carbonate and sodium bicarbonate

Response Feedback:

GIT acid-neutralising agents THAT ARE ABSORBED include calcium carbonate and sodium bicarbonate.

Why is this important?

The antacids that are absorbed can change the pH of the system, potentially having more serious side effects than those not absorbed. Also, sodium bicarbonate is contraindicated for salt-sensitive individuals.

Aluminium hydroxide and magnesium hydroxide are neutralising agents that are not absorbed. They are often combined because aluminium hydroxide causes constipation and magnesium hydroxide causes diarrhoea.

Question: Which of the following antacids causes constipation?

Aluminium hydroxide

Calcium carbonate

magnesium citrate

sodium bicarbonate.

sodium bicarbonate.

...and Magnesium antacids cause diarrhoea! Sounds like a perfect match, but remember that there may be some rebound hyper-acidity. Also, a decrease in the pH of the gut results in alterations of drug and nutrient absorption.

Q. Patients receiving intravenous cimetidine (Tagamet) for an acute ulcer problem should be monitored for:

A. cardiac arrhythmias

Response Feedback:

Patients receiving intravenous cimetidine (Tagamet) for an acute ulcer problem should be monitored for cardiac arrhythmias.

Cimetidine is an H2 receptor antagonist and H2 receptors are also found in the heart: intravenous or high doses can cause arrhythmias!

Q. Which H2 antagonist would be ordered for a person with known liver dysfunction?

A. nizatidine (Nizac; Tazac)

Response Feedback:

Nizatidine is the newest drug in the class of H2 receptor antagonists, and is the safest drug for patients with liver dysfunction.

Q. Cimetidine and ranitidine are H2 receptor antagonists. H2 receptors are found throughout the body, including:

A. in the heart, CNS and stomach

Response Feedback:

H2 receptors are located in the parietal cells of the gut but also in the heart and the CNS

In the gut, H2 receptor antagonists suppress the normal secretion of acid by parietal cells by two mechanisms: Histamine released by ECL cells in the stomach is blocked from binding on parietal cell H2 receptors (these normally stimulate acid secretion). Other substances that promote acid secretion (such as gastrin and acetylcholine) have a reduced effect on parietal cells when the H2 receptors are blocked. Cimetidine and ranitidine are H2 receptor antagonists that block the H2 receptors and therefore decrease stomach acidity. Since there are H2 receptors on the heart, the H2 blockers may cause bradycardia.

H2 BLOCKERS ARE NOT CONSIDERED ANTIHISTAMINES - ANTIHISTAMINES BLOCK THE H1 RECEPTOR!!

Why do first generation H1 anti-histamines make your patient drowsy when H2 blockers do not? First, the first generation antihistamines break the blood brain barrier. Second, H1 is a mediator of "wakefulness" and its activity is necessary to maintain wakefulness, alertness, and reaction time. These activities can be impaired, especially by H1 antagonist capable of penetrating the blood-brain barrier.

Q. Misoprostol (Cytotec) is a prostaglandin analogue that is used to:

A. prevent NSAID-related gastric ulcers in people at high risk

Response Feedback:

Misoprostol is a prostaglandin analogue that is used to prevent NSAID-related gastric ulcers in people at high risk of ulceration. It is a second line therapy for decreasing stomach acid, behind the proton pump inhibitors (...prazole drugs)

Prostaglandin E1 stimulates gastric neck cells to produce more bicarbonate and mucus and simultaneously decreases the H+ ions released. Since NSAIDs decrease endogenous (internal) prostaglandins, Misoprostol is effective for those who need to take aspirin or other NSAIDs but are at risk of developing ulceration. Proton pump inhibitors are more effective in other applications so the use of Misoprostol is limited.

Misoprostol is contraindicated in women of childbearing age, as it is also an abortifacient (Prostaglandin E1 is one of the prostaglandins released to commence labour).

Q. The exocrine functions of the pancreas include:

A. the secretion of enzymes that assist digestion and absorption of nutrients

Response Feedback:

The pancreas is an endocrine organ that secretes hormones into the blood and is also an exocrine digestive organ, secreting digestive enzymes that assist digestion and absorption of nutrients in the small intestine. These enzymes help to further break down the carbohydrates, proteins and lipids in the chyme.

After a pancreatectomy (removal of pancreas) or when deficiencies of pancreatic enzymes are noted, the patient will be prescribed pancreatic enzyme replacement therapy (pancrelipase) which is to be taken with meals and not chewed because the active ingredients are normally coated in a way to be released in the duodenum (as the pancreatic enzymes would be). Remember that some of the pancreatic enzymes break down proteins, so mouth or gastric ulcers are possible if taken incorrectly.

Q. The lining of the stomach is protected from the harsh environment of the stomach by:

A. bicarbonate rich mucus

Response Feedback:

The lining of the stomach is protected from the harsh environment of the stomach by mucus and bicarbonate. Both the mucus and bicarbonate are secreted from mucus neck cells in response to prostaglandin E1. The amount of bicarbonate that is secreted is just about 10% of the amount of H+ in the stomach, but it is effective because it is trapped beneath the "unstirred" mucus gel layer that adheres to the surface of the mucosa.

HOW DOES THIS RELATE TO PHARMACOLOGY?

Aspirin and other NSAIDs inhibit the synthesis of prostaglandins (therefore decreasing this protection) and permeate the "impermeable" cells of the stomach. This often damages the stomach lining and leads to ulceration (peptic ulcer; gastric ulcer)

Misoprostol is a synthetic prostaglandin E1 analogue that is used with NSAIDs to prevent gastric ulcers. Misoprostol inhibits the secretion of gastric acid. Because other classes of drugs, especially H2-receptor antagonists and proton pump inhibitors, are more effective for the treatment of acute peptic ulcers, misoprostol is only indicated for use by people who are both taking NSAIDs and are at high risk for NSAID-induced ulcers

Misoprostol is contraindicated in women of child bearing age. It is also used to induce labour.

Q. Which of the following is most accurate about the initiation of movement in the gastrointestinal tract?

A. it is primarily controlled by local nerve reflexes of the GI nerve plexus:

Response Feedback:

While some of the control of movement in the GIT emanates from connections between the digestive system and central nervous system, it is initiated and predominantly controlled from within the GIT by the local nervous system called the enteric nervous system.

The enteric nervous system has sensory neurons that receive information from sensory receptors in the mucosa and muscle. The sensory receptors respond to mechanical (stretch), thermal, osmotic, and chemical (acid, glucose and amino acids) stimuli.

The enteric nervous system responds to these stimuli with motor neurons that control gastrointestinal motility and secretion. Motor neurons act directly on a large number of effector cells, including smooth muscle, secretory cells (chief, parietal, mucous, enterocytes, pancreatic exocrine cells) and gastrointestinal endocrine cells.

The autonomic nervous system (ANS) can slow down (SNS) or speed up (PNS) movement but cannot initiate it. The two centrally controlled movements are swallowing and vomiting.

Q. Gastrin

A. stimulates acid secretion in the stomach

Response Feedback:

The presence of gastrin stimulates parietal cells of the stomach to secrete hydrochloric acid both directly on the parietal cell and indirectly by binding onto gastrin receptors on ECL cells in the stomach. The ECL cells then release histamine 2, which in turn acts in a paracrine manner on parietal cells stimulating them to secrete hydrogen ions.

Q. Histamine-2 antagonists:

A. selectively block specific histamine receptor sites, leading to a reduction in gastric acid secretion

Response Feedback:

Histamine 2 (H2) antagonists (or more accurately inverse agonists; an agent that binds to the same receptor as an agonist but induces a pharmacological response opposite to that agonist) bind to specific histamine receptor sites in parietal cells, leading to a reduction in

gastric acid secretion. This results in a decrease in acidity, but this group of drugs have been largely superseded by proton pump inhibitors.

H2 receptor antagonists include cimetidine (Taramet) and ranitidine (Zantac).

Q. The laxative of choice when mild stimulation is needed to prevent straining is:

A. bisacodyl

Response Feedback:

The laxative of choice when mild stimulation is needed to prevent straining is bisacodyl. Bisacodyl is an organic compound that has little action in the small intestine, but in the colon, it works by stimulating enteric nerves to cause contractions and to increase fluid and sodium chloride (NaCl) secretion. Because bisacodyl works mainly in the colon, it is effective as a suppository. When administered rectally, it is usually effective in 15 to 60 minutes. Despite being a "mild" stimulant, if taken at the maximum dosage, there will likely be a sudden, extremely powerful, uncontrollable bowel movement.

Senna glycosides (or sennosides) are used to increase gastric fluid secretion and bowel motility, producing laxative action. The products are only recommended for short-term use, and chronic use and abuse of senna has been associated with organ failure.

Magnesium salts are sometimes used as laxatives. They act as osmotic particles in the intestines, pulling in more water.

Castor oil is a vegetable oil obtained by pressing the seeds of the castor plant. Its major site of action is the small intestine but is seldom used in modern medicine.

Bisacodyl, senna and castor oil are all considered chemical stimulants and act on the enteric nervous system.

Q. Some antiemetics work to calm disturbances in the gut. Others work at the vestibular apparatus to decrease motion sickness. Others work at the central area to decrease nausea from emotional experiences. The final and largest group of antiemetics work with the CNS to decrease the activity of:

A. the CTZ

Response Feedback:

The largest group of antiemetic drugs work at the Chemoreceptor Trigger Zone (CTZ) in the medulla oblongata. The CTZ is outside the blood brain barrier and receives toxins from the GIT quite quickly. It responds by sending information to the vomiting centre. Drugs that work at the CTZ include phenothiazines like prochlorperazine (Stemetil), serotonin (5-HT3) receptor blockers like ondansetron (Zofran).

Drugs that act at the level of the vestibular apparatus are the anti-histamines that cause drowsiness (dymenhydrinate). Histamine is important in wakefulness and any antihistamine that breaks the blood brain barrier (BBB) will cause drowsiness.

Second generation anti-histamines like loratadine and fexofenadine have been designed to work peripherally only and will not enter the vestibular apparatus and will not relieve motion

sickness. Antihistamines that break the BBB are called "first-generation" antihistamines while newer anti-histamines that do not enter the BBB are "second-generation".

Q. Some antiemetics 'cause photosensitivity'. Which of the following instructions would you hypothesise to be most appropriate to give to a person to reduce the risk of photosensitivity related to the use of drug that can 'cause photosensitivity'?

A. wear protective clothing when in the sun

Response Feedback:

Patients who are taking drugs resulting in photosensitivity are advised to use sunscreens and protective garments if exposure cannot be avoided. Prochlorperazine can cause photosensitivity.

What is drug-induced photosensitivity?

Phototoxic reactions occur because of the damaging effects of light-activated compounds on cell membranes. Phototoxic reactions develop in most individuals if they are exposed to sufficient amounts of light and drug. Typically, they appear as an exaggerated sunburn response. These types of reactions normally require more drug than seen in a photoallergic reaction.

By contrast, photoallergic reactions are cell-mediated immune responses (delayed hypersensitivity type IV reactions that occur in 24 to 72 hours) to a light-activated compound. They look like allergic contact dermatitis.

Q. The neural pathways from the inner ear to the vomiting centre use the neurotransmitters Histamine 1 (H1) and Acetylcholine (Ach). From that, you would predict that the best antiemetics for motion induced vomiting are:

A. First generation H1 antagonists that break the blood brain barrier like Dimenhydrinate and acetylcholine receptor blockers that break the blood brain barrier like scopolamine

Response Feedback:

By knowing where the anti-emetic drugs work, you can understand why some types of nausea and vomiting are not soothed at all by one anti-emetic while another one is very effective.

The vomiting centre receives information from 4 different areas:

The GIT

The chemoreceptor trigger zone

The inner ear

The higher brain centres

IMPULSES FROM ANY ONE OF THOSE WILL INCREASE OUR NEED TO VOMIT.

Since the inner ear uses the neurotransmitters H1 and Ach, drugs that block either of those will have the best effect for motion sickness. First generation H1 antagonists or antihistamines that break the blood brain barrier have some inherent anticholinergic actions

and as such may be the best for motion induced vomiting. However, any anticholinergic agent that breaks the BBB is associated with increased risks of developing Alzheimer's disease. It is most effective to take antiemetics one hour before the motion begins.

Q. Cathartics or sometimes called stimulant laxatives are drugs that are used to:

A. accelerate defecation

Response Feedback:

By strict definition, a cathartic is a substance that accelerates defecation. A normal laxative is a substance which eases defecation, usually by softening feces.

There is little or no consensus on the definition between terms when used by different authors, so it is not necessary that you classify the drugs 'properly', Generally, drugs that are termed purgatives, cathartics, strong laxatives or osmotic stimulant laxatives can have more adverse effects than gentle laxatives. Those adverse effects include a dependence sometimes referred to as cathartic dependence. In addition, the stronger agents carry a risk of electrolyte imbalances and dehydration.

Stimulant laxatives or cathartics are to be used for short periods of time only.

Important safety question: which two laxatives should never be used together?

Answer: Docusate, also known as docusate salts or dioctyl sulfosuccinate, is a surfactant laxative, and as such, can allow MINERAL OIL (which is often used as a laxative) to be absorbed and made into internal granulomas.

Q. The 5-HT3 receptor blockers, including ondanstetron and other setron drugs, are particularly effective in decreasing the nausea and vomiting associated with:

A. cancer chemotherapy

Response Feedback:

By knowing where the anti-emetic drugs work, you can understand why some types of nausea and vomiting are not soothed at all by one anti-emetic while another one is very effective.

The vomiting centre receives information from 4 different areas:

- *The GIT*
- *The chemoreceptor trigger zone*
- *The inner ear*
- *The higher brain centres*

IMPULSES FROM ANY ONE OF THOSE WILL INCREASE OUR NEED TO VOMIT.

In the case of chemotherapeutic agents, they make an individual vomit due to irritation in two areas:

- *The GIT and the*
- *Chemoreceptor trigger zone*

Both of those areas use the neurotransmitter 5HT3. If we block 5HT3, it is the perfect antiemetic for chemotherapy induced vomiting.

NOTE: D2 or dopamine 2 also works at these two areas so why are the setron antiemetics preferred? D2 is used in many areas of the brain while 5HT3 is almost exclusively used in the GIT and chemoreceptor trigger zone. Result: D2 antagonists have long lists of adverse effects while 5HT3 antagonists (setron drugs) have few.

Q. Diarrhoea:

A. can be life threatening

Response Feedback:

Diarrhoea (as the presenting complaint or as a side effect of medications) can cause severe fluid and electrolyte abnormalities and, as such, can be life threatening. Worldwide, diarrhoea is the second most common cause of infant mortality.

Patients who are especially at risk include the very young, the very old, and those with predispositions for cardiac dysrhythmias or seizures. Diarrhoea can also result in decreased absorption of nutrients.

Diarrhoea is most commonly due to viral gastroenteritis, which accounts for 40% of cases in children under five. Viral gastroenteritis generally causes an inflammatory diarrhoea due to damage to the mucosal lining or brush border. Other types of diarrhoea include secretory diarrhoea in which there is an increase in the active secretions of the GIT, osmotic diarrhoea in which too much water is drawn into the GIT, and other types.

Oral rehydration solutions are appropriate for moderate diarrhoea, however in severe diarrhoea or in susceptible people; monitoring for fluid and electrolyte imbalances is appropriate.

Q. You would hypothesise that a D2 (dopamine 2) receptor antagonist like Prochlorperazine is the antiemetic of choice for which of the following?

A. nausea and vomiting after anaesthesia (which has a profound effect on the Chemoreceptor trigger zone that uses Dopamine 2 (D2))

Response Feedback:

Prochlorperazine (Stemetil) is the antiemetic of choice for nausea and vomiting after anaesthesia. Prochlorperazine is a dopamine (D2) receptor antagonist that belongs to the phenothiazine class of antipsychotic agents but is used for the treat nausea because it blocks the D2 receptors in the Chemoreceptor Trigger Zone (CTZ).

Interestingly, many pharmacological treatments which are effective for nausea and vomiting in some medical conditions may not be effective for motion sickness. For example, prochlorperazine, although widely used for nausea, is ineffective for motion-sickness prevention and treatment. Sedating anti-histamine medications such as dimenhydrinate work quite well for motion sickness, although they can cause significant drowsiness. (Some newer anti-histamines have been specially designed not to break the blood brain barrier so that they do not cause drowsiness. Those are not effective for motion sickness).

Q. The drug of choice for treating traveller's diarrhoea is:

A. loperamide

Response Feedback:

BUT WAIT, YOU NEED TO KNOW JUST A BIT ABOUT EACH OF THOSE.

- *Loperamide is an opioid receptor antagonist that has no CNS activity but rather works peripherally, in the myenteric plexus of the large intestine. Loperamide decreases the activity of the myenteric plexus, which in turn decreases the tone of the longitudinal and circular smooth muscles of the intestinal wall. This increases the amount of time substances stay in the intestine, allowing for more water to be absorbed out of the faecal matter.*
- *Travelan is another drug that is good for traveller's diarrhoea. It is made from bovine colostrum, following immunisation of the cow to certain strains of E. coli.*
- *Opium is the dried latex from an opium poppy. It contains the alkaloids morphine (used to produce heroin) and codeine. Both morphine and codeine act on the myenteric plexus of the GIT (similar to loperamide) to reduce gut motility, but these have CNS activity and are highly addictive.*
- *Peppermint oil is commonly used to soothe symptoms of irritable bowel syndrome and minor GIT discomfort.*
- *Bisacodyl is a stimulant laxative drug, which is obviously contraindicated in patients with diarrhoea.*

Q. Drugs that stimulate parasympathetic activity (dexpanthernol) are used to increase GI activity and secretions. For which of the following would this group be most likely used?

A. prevention of intestinal atony or loss of intestinal tone in postoperative situations

Response Feedback:

Drugs that stimulate parasympathetic activity (dexpanthenol) are used to increase GI activity and secretions as in the prevention of intestinal atony (loss of strength) or loss of intestinal tone in postoperative situations.

The use of drugs that stimulate parasympathetic activity (also called cholinergic agonists, parasympathomimetics or muscarinic agents) is limited due to the widespread parasympathetic activity they induce. More specific and less toxic drugs are now available and preferred for most applications.

Why do people experience GIT symptoms in postoperative situations?

Operations often involve a profound sympathetic nervous system response, which shuts down the motility and blood supply to the GIT. This is the reason we may need to stimulate the parasympathetic nervous system to get the GIT moving again.

MULTIPLE CHOICE QUESTIONS AND ANSWERS

WEEK 10

Q. The main underlying problem with Parkinson's disease seems to be a decrease in the neurotransmitter:

A. dopamine

Response Feedback:

The main underlying problem with Parkinson's disease seems to be a decrease in the neurotransmitter dopamine. Dopamine sets the effort- threshold for initiating behaviours. The higher the level of dopamine activity, the lower the impetus required to evoke a given behaviour. As a consequence, high levels of dopamine lead to high levels of motor activity and "impulsive" behaviour; low levels of dopamine lead to torpor (decreased temperature and metabolic rate) and slowed reactions.

The opposite is true as well, as the lower the level of dopamine activity, the higher the impetus required to evoke a given behaviour. Parkinson's disease, in which dopamine levels in the substantia nigra circuit are greatly reduced, is characterised by stiffness and greatly reduced movement—however, when people with the disease are confronted with strong stimuli such as a serious threat, their reactions can be as vigorous as those of a healthy person.

Q. A person who has been diagnosed with Parkinson's disease for many years and whose symptoms were controlled using the drug Sinemet has started to exhibit increasing signs of the disease. Possible treatment might include:

A. combination therapy with an anticholinergic drug

Response Feedback:

Sinemet is a combination of levodopa and carbidopa and is used to treat Parkinson's disease. It is sometimes combined with an anticholinergic drug after Sinemet itself is no longer effective.

Levodopa is converted to dopamine via the action of a naturally occurring enzyme called DOPA decarboxylase. This occurs both in the peripheral circulation and in the CNS after levodopa has crossed the blood brain barrier. Activation of central dopamine receptors improves the symptoms of Parkinson's disease; however, activation of peripheral dopamine receptors causes nausea and vomiting. For this reason, levodopa is usually administered in combination with a DOPA decarboxylase inhibitor, in this case carbidopa, which is very polar (and charged at physiologic pH) and cannot cross the blood brain barrier, however prevents peripheral conversion of levodopa to dopamine and thereby reduces the unwanted peripheral side effects of levodopa. Use of carbidopa also increases the quantity of levodopa in the bloodstream that is available to enter the brain.

The most important information in that feedback is below.

Q. Sinemet is a combination of levodopa and carbidopa and is used to treat Parkinson's disease. What does carbidopa do and what are the advantages of this combination as compared to levodopa alone?

A. Carbidopa inhibits the enzyme that converts the levodopa to dopamine in the periphery. It does not cross the BBB so the levodopa is still converted once it gets into the central nervous system. This has two advantages, the decreased amount of levodopa converting in the periphery leads to decreased side effects, and the increased amount of levodopa in the brain leads to increased dopamine in the brain where it is needed.

Q. Anticholinergic drugs are effective in early Parkinson's disease (only). They act:

A. to block stimulating effects of acetylcholine in the brain to bring activity back into balance

Response Feedback:

In the early stages of Parkinson's disease, there is a decrease in dopamine. Acetylcholine has the opposite effect to dopamine in this portion of the brain. Anticholinergics decrease the acetylcholine in the brain to restore the balance between acetylcholine and dopamine (both are then low). These drugs are only effective in the early stages of the disease and reduce the tremor associated with it.

Q. Parkinson's disease is a progressive, chronic neurological disorder that is usually:

A. known to affect people of all ages with no known cause in most cases

Response Feedback:

Parkinson's disease is the most common form of parkinsonism and is usually defined as "primary" parkinsonism, meaning parkinsonism with no external identifiable cause (idiopathic). In recent years, several genes that are directly related to some cases of Parkinson's disease have been discovered (5-15% of those with the disease). As much as this conflicts with the definition of Parkinson's disease as an idiopathic illness, genetic parkinsonism disorders with a similar clinical course to PD are generally included under the Parkinson's disease label. The terms "familial Parkinson's disease" and "sporadic Parkinson's disease" can be used to differentiate genetic from truly idiopathic forms of the disease. Familial Parkinson's disease often occurs much earlier in life.

Other types of parkinsonism include drug-induced parkinsonism.

Q. The glutamate receptor antagonist that is indicated for the treatment of mild to severe Alzheimer's disease is:

A. memantine

Response Feedback:

Memantine is the receptor antagonist that is used for treatment of Alzheimer's disease. It decreases the glutamate-regulated over excitation.

Donepezil is an acetylcholinesterase inhibitor that is used in Alzheimer's disease.

Levodopa and carbidopa combined are in the medication Sinemet, which is used in Parkinson's disease.

What is Donepezil, we covered it in the autonomic nervous system?

Donepezil binds and reversibly inactivates the cholinesterases, thus inhibiting hydrolysis of acetylcholine. This results in an increased acetylcholine concentrations at cholinergic synapses. Donepezil is used to improve cognition and behaviour of people with Alzheimer's, but does not slow the progression of or cure the disease.

Q. Replacing dopamine in the brain would seem to be the best treatment for Parkinson's disease. This is difficult because dopamine:

A. cannot cross the blood-brain barrier

Response Feedback:

Dopamine itself does not cross the blood brain barrier (BBB). L-DOPA crosses the BBB and is used to increase dopamine concentrations in the treatment of Parkinson's disease.

Using multivitamin and mineral supplements together with levodopa may decrease the effects of levodopa. This effect may be lessened by taking them separately. Using levodopa together with ethanol can increase nervous system side effects such as dizziness, drowsiness, and difficulty concentrating.

A person taking levodopa and over-the-counter megavitamins might experience:

cure from Parkinson's disease

return of Parkinson's disease symptoms

improved health and wellbeing

a resistance to viral infections

Q. Parkinson's disease reflects an imbalance between inhibitory and stimulating activity of nerves in the:

A. basal ganglia

Response Feedback:

Parkinson's disease reflects an imbalance between inhibitory and stimulating activity of nerves in the basal ganglia. The basal ganglia's primary function is to control and regulate activities of the motor and premotor cortical areas so that voluntary movements can be performed smoothly. This is important in understanding the manifestations of this movement disorder that results in a resting tremor, slowness of movement (bradykinesia) and rigidity.

Q. Anxiolytic drugs block the awareness of and reaction to the environment. This will NOT be beneficial:

A. in treating a person who must drive a vehicle for living

Response Feedback:

Anxiolytics may not be suitable for those driving or operating machinery, and taking those drugs often invalidates insurance claims.

Q. Barbiturates cause hepatic enzyme induction, which could lead to:

A. rapid metabolism and loss of effectiveness of other drugs metabolised by those enzymes

Response Feedback:

The cytochrome P450 superfamily of monooxygenases (CYP) are the major enzymes involved in drug metabolism, accounting for about 75% of the total metabolism. Most drugs undergo deactivation by CYPs, either directly or by facilitated excretion from the body. Also, many substances are bioactivated by CYPs to form their active compounds.

Drugs which induce hepatic enzymes may increase the bioavailability of drugs which require metabolism for their activation or may decrease the bioavailability of drugs which are metabolised by those enzymes. In the case of barbiturates, they lead to rapid metabolism and loss of effectiveness of other drugs metabolised by those enzymes.

Q. The benzodiazepines like alprazolam react with:

A. GABA-receptor sites in the RAS to cause inhibition of neural arousal

Response Feedback:

Benzodiazepines enhance the effect of the neurotransmitter gamma-aminobutyric acid (GABA), resulting in sedative, hypnotic (sleep inducing) anxiolytic, euphoric, anticonvulsant and muscle relaxant properties.

GABA is found on interneurons throughout the CNS - it is the chief inhibitory neurotransmitter in the mammalian central nervous system. Its principal role is reducing neuronal excitability throughout the nervous system. In humans, GABA is also directly responsible for the regulation of muscle tone.

Q. A child is prescribed phenobarbitone preoperatively to relieve anxiety and produce sedation. After giving the injection, you should assess the child for:

A. paradoxical excitement

Response Feedback:

Phenobarbital is a long-acting barbituate and the most widely used anticonvulsant worldwide, and the oldest still commonly used. It has sedative and hypnotic properties, but as with other barbiturates, it has been superseded by the benzodiazepines for these indications. Phenobarbital is indicated in the treatment of all types of seizures except absence seizures. It is no less effective at seizure control than more modern drugs such as phenytoin however it is significantly less well tolerated. Adverse effects such as dizziness, nystagmus and ataxia (lack of voluntary coordination of muscle movements) are also common. In elderly patients, it may cause excitement and confusion, while in children, it may result in paradoxical hyperactivity.

Q. A person who could benefit from an anxiolytic drug for short-term treatment of insomnia would not be prescribed:

A. buspirone

Response Feedback:

Buspirone is an anxiolytic psychoactive drug of the azapirone chemical class. It is primarily used to treat generalised anxiety disorder. Unlike most drugs predominately used to treat anxiety, buspirone's pharmacology is not related to benzodiazepines or barbituates, and so does not carry the risk of withdrawal symptoms that those drug classes are known for when discontinued. Azapirones are poorly absorbed and have a rapid onset of action, but they have only very short half-lives, ranging from 1–3 hours. The half-life of buspirone is about 2.5 hours.

Buspirone functions as a serotonin 5-HT1A receptor partial agonist and is the drug of choice when the patient needs to be alert, for instance, a student presentation in front of a large group of other students.

Q. A drug group known as a minor tranquilizer that is used to decrease anxiety for short periods of time is called:

A. anxiolytics

Response Feedback:

A drug used to treat anxiety is termed an anxiolytic. Anxiogenic drugs cause anxiety. Antiepileptics are anticonvulsives, whereas hypnotics are a class of psychoactive drugs that induce sleep.

Benzodiazepines are anxiolytics that are prescribed for short-term relief of severe and disabling anxiety. Benzodiazepines may also be indicated to cover the latent periods associated with the medications prescribed to treat an underlying anxiety disorder. They are used to treat a wide variety of conditions and symptoms and are usually a first choice when short-term CNS sedation is needed. There is a risk of a benzodiazepine withdrawal and rebound syndrome after continuous usage for longer than two weeks, and tolerance and dependence may occur if patients stay under this treatment for longer.

Benzodiazepines are the most common anxiolytics, as they are anxiolytic at doses much lower than those needed for sedation or hypnosis

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Q. You might question an order for an MAOI as a first step in the treatment of depression, remembering that these drugs are reserved for use in cases in which there has been no response to other agents because:

A. MAOIs are associated with potentially serious drug-food interactions

Response Feedback:

Because of potentially lethal dietary and drug interactions, MAOIs have historically been reserved as a last line of treatment, used only when other classes of antidepressant drugs (for example selective serotonin reuptake inhibitors and tricyclic antidepressants) have failed.

However two studies claim that much of the concern over their dangerous dietary side effects stems from misconceptions and misinformation, and that despite proven effectiveness of this class of drugs, it is underutilised and misunderstood in the medical

profession. Some research also questions the validity of the perceived severity of dietary reactions, which has historically been based on out-dated research.

Conclusion: while there is emerging evidence that we may see decreasing restrictions on MAOIs in the future, they are still considered the last line of treatment at this time.

Q. Venlafaxine (Efexor) is a relatively new antidepressant that might be very effective for use in people who:

A. have not responded to other antidepressants and would benefit from once-a-day dosing

Response Feedback:

Venlafaxine is a relatively new SSRI used primarily for the treatment of depression, generalised anxiety disorder, social phobia, panic disorder and vasomotor symptoms.

Many doctors are starting to prescribe venlafaxine "off label" for the treatment of diabetic neuropathy and migraine prophylaxis (in some people, however, venlafaxine can exacerbate or cause migraines).

It has been associated with substantial weight loss in patients with major depression, but the manufacturer does not recommend use as an anorectic.

Q. Jane, a 23 year old female is being treated for depression and is started on a regimen of Prozac (fluoxetine). She calls you 10 days after the drug therapy has started to report that nothing has changed and she wants to try a different drug. You should:

A. ensure that she is not suicidal, and if not, encourage her to keep taking the drug as prescribed because it usually takes up to 4 weeks to see the full antidepressant effect

Response Feedback:

Antidepressants may increase the risk of suicide in people younger than 25!

The brain concentration of fluoxetine and its metabolites keeps increasing through at least the first five weeks of treatment. That means that the full benefits of the current dose a patient receives are not realised for at least a month since its initiation.

Q. When teaching a person receiving tricyclic antidepressants (TCAs), it is important to remember that TCAs are associated with many anticholinergic adverse effects. Teaching about these drugs should include anticipation of:

A. urinary retention, arrhythmias and constipation

Response Feedback:

The TCAs were first discovered in the early 1950s and were subsequently introduced later in the decade. In recent times, the TCAs have been largely replaced in clinical use in most parts of the world by newer antidepressants which typically have more favourable side-effect profiles, such as the selective serotonin reuptake inhibitors (SSRIs), selective noradrenaline reuptake inhibitors (SNRIs) and others.

Many of the side effects of TCAs may be related to the antimuscarinic properties of the TCAs. It is easiest to remember antimuscarinic effects by thinking "against the muscarinic

receptors of the parasympathetic nervous system >> Against the rest and digest system >> Sympathetic nervous system (fight or flight dominates!!)"

Such side effects are relatively common and may include dry mouth (we shut down the GIT when we need to flee), dry nose, blurry vision (pupils dilate, making photophobia and sometimes blurring vision), lowered gastrointestinal motility or constipation (we need to flee, not digest) , urinary retention (we need to flee, not pee), cognitive and/or memory impairment, and increased body temperature. There are many other side effects of these medications.

Q. Adverse effects may limit the usefulness of TCAs with some people. Care interventions that could alleviate some of the unpleasant aspects of these adverse effects include:

A. taking the major portion of the dose at bedtime to avoid experiencing drowsiness and the unpleasant anticholinergic (antimuscarinic) effects

Response Feedback:

Many of the side effects of the TCAs are not as intolerable if taken at bedtime.

Q. Depression is an affective disorder that is:

A. characterised by overwhelming sadness, despair and hopelessness

Response Feedback:

However patients with major depressive disorder may not initially present with a complaint of low mood, anhedonia, or other typical symptoms. In the primary care setting, where many of these patients first seek treatment, the presenting complaints often can be somatic (e.g. fatigue, headache, abdominal distress, or change in weight). Patients may complain more of irritability or difficulty concentrating than of sadness or low mood.

Children with major depressive disorder may also present with initially misleading symptoms such as irritability, decline in school performance, or social withdrawal. Elderly persons may present with confusion or a general decline in functioning; they also experience more somatic complaints, cognitive symptoms, and fewer complaints of sad or dysphoric mood.

Q. The biogenic amine theory of depression states that depression is a result of:

A. a deficiency of 5-hydroxytryptamine (5-HT; serotonin), noradrenaline, and/or dopamine in key areas of the brain

Response Feedback:

However there are several flaws in this hypothesis (and you would be justified in wondering why it is still our main hypothesis):

1. *Reducing levels of norepinephrine, serotonin and dopamine does not actually produce depression in humans, even though it appeared to do so in animals.*
2. *The theory cannot explain why there are drugs that alleviate depression despite the fact that they have little or no effect on either serotonin or norepinephrine.*
3. *Drugs that raise serotonin and norepinephrine levels, such as amphetamine and cocaine, do not alleviate depression.*

4. *No one has explained why it takes a relatively long time before antidepressant drugs produce any elevation of mood. Antidepressants produce their maximum elevation of serotonin and norepinephrine in only a day or two, but it often takes several weeks before any improvement in mood occurs.*
5. *Although some depressed patients have low levels of serotonin and norepinephrine, the majority do not. Estimates vary, but a reasonable average from several studies indicates that only about 25 percent of depressed patients actually have low levels of these metabolites.*
6. *Some depressed patients actually have abnormally high levels of serotonin and norepinephrine, and some patients with no history of depression at all have low levels of these amines.*
7. *Although there have been claims that depression may be caused by excessive levels of monoamine oxidase (the enzyme that breaks down serotonin and norepinephrine), this is only true in some depressed patients and not in others.*
8. *Antidepressants produce a number of different effects other than increasing norepinephrine and serotonin activity that have not been accounted for when considering their activity on depression.*

Q. The drug of choice for a person with a documented obsessive-compulsive disorder who is also suffering from depression and occasional panic disorder would be:

A. Paroxetine (Aropax; Paxil among others)

Response Feedback:

Paroxetine is an antidepressant of the SSRI type. Paroxetine is used to treat major depression, obsessive-compulsive disorder, panic disorder, social anxiety, posttraumatic stress disorder, generalised anxiety disorder and vasomotor symptoms (e.g. hot flushes and night sweats) associated with menopause.

As with all antidepressants there may be an increased risk of suicidality in patients receiving paroxetine, although the only solid evidence regarding this is with regard to children and young adults under the age of 25.

Differences between newer antidepressants are usually fairly subtle and mostly confined to side effects. Paroxetine shares the common side effects and contraindications of other SSRIs, with high rates of nausea, insomnia, and sexual side effects. Paroxetine is associated with weight gain. Discontinuing paroxetine is associated with a high risk of withdrawal syndrome.

Paroxetine is the only SSRI proven to be associated with an increased risk of birth defects.

Q. Adverse effects associated with antipsychotic drugs are related to the drugs' effects on receptor sites and can include:

A. dry mouth, hypotension and glaucoma

Response Feedback:

Antipsychotics are associated with a range of side effects including dry mouth, hypotension and glaucoma. It is well-recognised that many people stop taking them (around two-thirds even in controlled drug trials) due in part to adverse effects.

More than one antipsychotic drug should not be used at a time except under unusual circumstances. One of the reasons for this is the increased number and harm from adverse effects of the drug when multiple drugs are used.

Q. Lithium toxicity can be dangerous. Individual assessment to evaluate for appropriate lithium levels would look for:

A. Tinnitus (ringing in ears), tremor, ataxia (lack of coordination of movements), dysarthria (abnormal or difficult movement)

Response Feedback:

Lithium compounds are used as mood-stabilising drugs, primarily in the treatment of bipolar disorder (people who alternate between depression and mania or extremely elevated mood). As a mood stabilizer, lithium is probably more effective in preventing mania than depression, and reduces the risk of suicide in bipolar patients.

In depression alone (unipolar disorder), lithium can be used to augment other antidepressants. Overdosage, usually with plasma concentrations over 1.5 mmol Li/l, may be fatal, and toxic effects include tremor, ataxia (lack of coordination of movements), dysarthria (abnormal or difficult movement), nystagmus, renal impairment, confusion, and convulsions. If these potentially hazardous signs occur, treatment should be stopped, plasma lithium concentrations redetermined, and steps taken to reverse lithium toxicity.

Q. Antipsychotic drugs are also known as neuroleptic drugs because:

A. they are major tranquilizers tending to reduce nervous tension by depressing nerve functions

Response Feedback:

Antipsychotics are often called neuroleptics because they are major tranquilizers used to manage psychosis including delusions, hallucinations and disordered thought. The word neuroleptic originates from the Greek word lepsis ("seizure" or "fit").

First-generation antipsychotics, known as typical antipsychotics, were discovered in the 1950s. Most second-generation drugs, known as atypical antipsychotics, have been developed more recently. Both generations of medication tend to block receptors in the brain's dopamine pathways but atypicals tend to act on serotonin receptors as well.

Notable and relatively common adverse effects of antipsychotics include extrapyramidal symptoms (which involve motor control).

Q. Haloperidol is a potent antipsychotic that is associated with:

A. severe extrapyramidal effects

Response Feedback:

Haloperidol is a high potency, typical antipsychotic that tends to produce significant extrapyramidal side effects

EXTRA what?? Extrapyramidal refers to motor symptoms. 80% of movement does not go through the pyramids. They are associated with the gross movement. The other 20% of

motor pathways go through the pyramids, and include pathways involving fine movement (mediated by the cerebellum) and the initiation of movement (that pathway involves the basal ganglion). The extrapyramidal symptoms associated with Haloperidol include dystonia (a state of abnormal muscle tone resulting in muscular spasm and abnormal posture), muscle rigidity, akathisia (unpleasant sensations of inner restlessness that manifests itself with an inability to sit still or remain motionless) and parkinsonism (a syndrome characterised by a resting pill-rolling tremor, rigidity, and postural instability)

Q. Antipsychotic drugs are basically:

A. dopamine-receptor blockers

Response Feedback:

The primary target for antipsychotic medication has been the dopamine (DA) neurotransmitter system, and the clinical efficacy correlates with affinity for D2 receptors. Traditionally, antipsychotic drugs have been categorized based on their specificity and can be divided into two basic families, typical and atypical. The typical antipsychotic category includes the phenothiazines (e.g. chlorpromazine) while the atypical antipsychotic category includes the tricyclic antipsychotics (e.g. clozapine). Atypical antipsychotics are more selective and have been found to be associated with fewer extrapyramidal side effects.

Q. Certain mental disorders are thought to be caused by a dysfunction within the brain that leads to abnormal thought processes and responses. They include:

A. schizophrenia

Response Feedback:

Schizophrenia is a mental disorder characterised by a breakdown in thinking and poor emotional responses. Schizophrenia is not a disorder of dual personalities as many people believe. People affected by schizophrenia often have stimuli coming in and respond inappropriately to the stimulus. For instance, they may hear that a relative has just passed away and begin to laugh uncontrollably. They may watch a video of a popular musician and fully believe that the song was written for them.

Common symptoms include delusions such as paranoia, hearing voices or noises that are not there; disorganised thinking, a lack of emotion and lack of motivation. Schizophrenia causes significant social and work problems. Symptoms begin typically in young adulthood and about 0.3–0.7% of people are affected during their lifetime.

Q. Methylphenidate is used to control an attention-deficit disorder for those over 6 years of age. Family teaching should include which of the following?

A. this drug may cause insomnia, weight loss and GI upset

Response Feedback:

Methylphenidate is a psychostimulant drug approved for treatment of attention-deficit hyperactivity disorder (ADHD). Prescribed to patients beginning in 1960, the drug became heavily prescribed in the 1990s, when the diagnosis of ADHD itself became more widely accepted.

ADHD and other similar conditions are believed to be linked to sub-performance of the dopamine and noradrenaline functions in the brain, primarily in the prefrontal cortex responsible for inhibition, motivation, memory and concentration, organisation, solving and planning. Methylphenidate is a dopamine reuptake inhibitor and has some noradrenaline reuptake inhibition.

Methylphenidate produces such effects as increasing or maintaining alertness, combating fatigue, and improving attention. The short-term benefits and cost effectiveness of methylphenidate are well established, although long-term effects are unknown. The long-term effects of methylphenidate on the developing brain are unknown. Methylphenidate is not approved for children under six years of age. It is sometimes used off-label for the treatment of obesity as it often causes weight loss and GI upset.

Q. Attention-deficit disorders (the inability to concentrate or focus on an activity) and narcolepsy (sudden episodes of sleep) are both most effectively treated in some individuals with the use of:

A. CNS stimulants

Response Feedback:

Attention-deficit disorders (the inability to concentrate or focus on an activity) and narcolepsy (sudden episodes of sleep) are both most effectively treated with the use of CNS stimulants.

Guidelines recommend that medications and behavioural therapy be used together as a first-line therapy, except in preschool-aged children. Stimulant medication therapy is not recommended as a first-line therapy in preschool-aged children in either guideline. Treatment with stimulants is effective for up to 14 months; however, its long term effectiveness is unclear. Adolescents and adults tend to develop coping skills which make up for some or all of their impairments.

Methylphenidate primarily acts as a norepinephrine–dopamine reuptake inhibitor (NDRI) is often the CNS stimulant of choice in ADD.

Q. The drug of choice for a person experiencing severe muscle spasms and pain precipitated by anxiety is:

A. diazepam

Response Feedback:

Diazepam is the treatment of choice for patients experiencing muscle spasms and pain precipitated by anxiety. Diazepam was first marketed as Valium. The pharmacological action of diazepam enhances the effect of the neurotransmitter GABA by binding to the benzodiazepine site on the GABA receptor leading to CNS depression.

Q. Which of the following is a type of generalised seizure?

A. all of the seizures listed in these choices are generalised seizures

- tonic seizures
- petit mal seizures

- grand mal seizures

Response Feedback:

There are six main types of generalized seizures: grand mal (or tonic-clonic), tonic, clonic, myoclonic, petit mal (or absence), and atonic seizures. Tonic-clonic seizures present with a contraction of the limbs followed by their extension along with arching of the back, which lasts 10–30 seconds. A cry may be heard due to contraction of the chest muscles. This is then followed by a shaking of the limbs in unison. After the shaking has stopped it may take 10–30 minutes for the person to return to normal. Tonic seizures produce constant contractions of the muscles. A person often turns cyanotic as breathing is stopped.

In clonic seizures, there is shaking of the limbs in unison. Myotonic seizures involved spasms of muscles in either a few areas or all over. Petit mal seizures (or absence seizures) are characterized by a brief loss and return of consciousness not followed by a period of lethargy (post-ictal state). Atonic seizures involve the loss of muscle activity for greater than one second. This typically occurs on both sides of the body.

Q. Epilepsy is:

A. the most prevalent neurological disorder

Response Feedback:

Epilepsy is the most prevalent neurological disorder, affecting about 1% of people worldwide (65 million). The word epilepsy comes from the ancient Greek verb ἐπιλαμβάνειν meaning "to seize, possess, or afflict". Epilepsy is the umbrella term used to denote a group of neurological disorders characterised by epileptic seizures. These seizures are episodes that can vary from brief and nearly undetectable to status epilepticus, which involves one seizure followed by another.

In most cases, the cause of epilepsy is unknown, although some people develop epilepsy as the result of brain injury, stroke, brain cancer, and drug and alcohol misuse, among others. Epilepsy cannot be cured, but seizures are controllable with medication in about 70% of cases. Not all cases of epilepsy are lifelong, and a substantial number of people improve to the point that medication is no longer needed.

Patients who have epilepsy should wear or carry a MedicAlert identification

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Q. One drug that is used alone in the treatment of partial seizures is:

A. carbamazepine

Response Feedback:

Carbamazepine can be used alone in partial seizures. Carbamazepine is an anticonvulsant and mood-stabilising drug used primarily in the treatment of epilepsy, bipolar disorder and trigeminal neuralgia. Carbamazepine stabilises the inactivated state of voltage-gated sodium channels, making fewer of these channels available to subsequently open. This leaves the affected cells less excitable. Carbamazepine has also been shown to potentiate the inhibitory GABA receptors.

Q. Dantrolene (Dantrium) differs from the other skeletal muscle relaxants because:

A. it acts directly within the skeletal muscle fibre and not within the CNS

Response Feedback:

Dantrolene sodium is a muscle relaxant that works at the muscle cells, by abolishing the excitation-contraction coupling within them. Despite this, central nervous system side effects are quite frequently noted and encompass speech and visual disturbances, mental depression and confusion, hallucinations, headache, insomnia and exacerbation or precipitation of seizures, and increased nervousness. Infrequent cases of respiratory depression or a feeling of suffocation have been observed. Dantrolene often causes sedation severe enough to incapacitate the patient to drive or operate machinery.

Q. Dantrolene is associated with potentially fatal cellular damage. If a person's condition is being managed with dantrolene, the person should:

A. be monitored for signs of liver damage and have liver function tests done regularly

Response Feedback:

Dantrolene is associated with potentially fatal cellular damage in the liver. The risk of hepatitis is associated with the duration of treatment and the daily dose. Interestingly, no liver toxicity has been reported in patients being treated for malignant hyperthermia.

Q. Signs and symptoms of tetanus, which includes severe muscle spasm, are best treated with:

A. botulinum toxin A

Response Feedback:

Tetanus is a highly fatal disease, with mortality rates reported varying from 40% to 78%. The disease stems from a potent neurotoxin (tetanus toxin or tetanospasmin) from Clostridium tetani. Clostridium tetani is found in soil, especially heavily-manured soils, and in the intestinal tracts and faeces of various animals.

The toxin is produced during cell growth, sporulation and lysis. In the human body; it migrates through the peripheral nerves to the CNS; or is transferred by lymphocytes from a local wound to the CNS. The clinical pattern of generalized tetanus consists of severe painful spasms and rigidity (AN INCREASE IN MUSCLE TONE) of the voluntary muscles. The characteristic symptom of "lockjaw" involves spasms of the masseter muscle. It is an early symptom, which is followed by progressive rigidity and violent spasms of the trunk and limb muscles.

Tetanus toxin is one of the three most poisonous natural substances known, the other two being the toxins of botulism and diphtheria. The toxin is produced by growing cells and released only on cell lysis

Botulism is mainly food borne intoxication, when botulinum toxin is ingested with food in which spores have germinated. The toxin passes into the blood stream, by which it reaches the peripheral neuromuscular synapses. The toxin binds to the presynaptic stimulatory terminals and blocks the release of the neurotransmitter acetylcholine, which is required for

a nerve to simulate the muscle. This causes the so-called flaccid paralysis, or REDUCED MUSCLE TONE.

The botulinum toxins are very similar in structure and function to the tetanus toxin, but differ dramatically in their clinical effects. In fact the pharmacological equivalent of the toxin from Clostridium botulinum is the best therapy for the toxin from Clostridium tetani.

Q. Drugs that are commonly used to treat grand mal seizures include:

A. barbiturates (like phenobarbital and other barbital drugs), benzodiazepines (like diazepam, alprazolam and oxazepam) and hydantoins (like phenytoin)

Response Feedback:

Drugs that are commonly used to treat grand mal seizures include barbiturates, benzodiazepines and hydantions.

Barbiturates (like phenobarbital and other barbital drugs), are drugs that increase the inhibitory neurotransmitter GABA in the central nervous system. This CNS depressant activity makes them effective as sedatives, anxiolytics, hypnotics and anticonvulsants.

Benzodiazepines (like diazepam, alprazolam and oxazepam) also enhance the effect of the neurotransmitter gamma-aminobutyric acid (GABA) resulting in sedative, hypnotic, anxiolytic, and anticonvulsant properties.

Hydantions such as phenytoin protect against seizures by causing voltage-dependent blockages of voltage-gated sodium channels.

Q. The use of neuromuscular junction blockers may sometimes cause a condition known as malignant hyperthermia. The drug of choice for prevention or treatment of this condition is:

A. dantrolene

Response Feedback:

Malignant hyperthermia is best treated with dantrolene. The typical symptoms of malignant hyperthermia are due to a hypercatabolic state, and present with a very high temperature, increased heart and breathing rates, acidosis (from excess carbon dioxide), rigid muscles and rhabdomyolysis (rapid breakdown of muscles).

Q. A muscle spasm often results from:

A. injury to the musculoskeletal system

Response Feedback:

A muscle spasm is a sudden, involuntary contraction of a muscle or group of muscles. It is often referred to as a 'muscle cramp' and is usually accompanied by a sudden burst of pain. Muscle spasms are usually harmless and cease after a few minutes. Rarely, a spasm may lead to muscle strains or tears of tendons and ligaments, if the force of the spasm exceeds the tensile strength of the underlying connective tissues, such as with a particularly forceful spasm, or in the case of weakened connective tissues.

There are a variety of causes of involuntary muscle contractions. Among these are muscle overload, muscle damage and any imbalance of electrolytes (as from insufficient hydration or loss of electrolytes).

Muscle spasms are not synonymous with muscle spasticity.

Q. Focal or partial seizures:

A. involve only part of the brain

Response Feedback:

Partial or focal seizures are generated in and affect just one part of the brain – the whole hemisphere or part of a lobe. Symptoms will vary according to where the seizure occurs. In the frontal lobe, symptoms may include a wave-like sensation in the head; in the temporal lobe, a feeling of déjà vu; in the parietal lobe, numbness or tingling; and in the occipital lobe, visual disturbances or hallucinations. Conversely, a complex partial seizure affects a larger part of the hemisphere than a simple partial seizure and the person may lose consciousness. In a generalised seizure, both hemispheres are involved and consciousness is lost because the brain uses all the all the oxygen and glucose being delivered to it.

Q. Treatment of epilepsy is directed at:

A. stabilising overexcited nerve membranes

Response Feedback:

Treatment of epilepsy is aimed at stabilising over-excited neurons by affecting the GABA or its receptors. GABA is the main inhibitory neurotransmitter.

In effect, medications for epilepsy increase the negative ion influx into brain cells, making it more difficult to depolarise. This reduces most neural activity in the central nervous system.

Q. Muscle spasticity is the result of:

A. damage to neurons within the CNS

Response Feedback:

Muscle spasticity or hyperreflexia involves increased tone of muscles and mostly occurs in disorders of the central nervous system. In general, spasticity develops when an imbalance occurs in the excitatory and inhibitory input to α motor neurons caused by damage to the spinal cord and/or central nervous system. The damage causes a change in the balance of signals between the nervous system and the muscles, leading to increased excitability in the muscles.

Q. The drug of choice for the treatment of absence seizures is:

A. ethosuximide

Response Feedback:

Ethosuximide is considered the first choice drug for treating absence seizures in part because it lacks the idiosyncratic hepatotoxicity of the alternative anti-absence drug, valproic acid.

Phenytoin is an antiepileptic drug that is is useful for treating partial seizures and generalised tonic-clonic seizures but not primary generalised seizures such as absence seizures or myoclonic seizures. Clonazepam is a benzodiazepine drug that has anxiolytic and anticonvulsant properties but it is not used for absence seizures.

MULTIPLE CHOICE QUESTIONS AND ANSWERS

WEEK 11

Q. A person has been receiving ibuprofen for many years to relieve the pain of osteoarthritis. Assessment of the person should include:

A. renal evaluation

Response Feedback:

Ibuprofen blocks both COX-1 and COX-2 enzymes.

COX-1 is associated with protective prostaglandins in the kidney and gut. Eliminating protective prostaglandins will increase susceptibility to other substances. NSAIDs are particularly problematic in patients concurrently taking other nephrotoxic agents.

Q. Treating fevers remains a controversial subject because:

A. higher temperatures act as catalysts to many of the body's chemical reactions

Response Feedback:

Fever has many benefits including:

- *Increased temperature kills many micro-organisms*
- *Increased temperature has adverse effects on the growth and replication of others*
- *Higher body temperatures decrease serum levels of iron, zinc and copper needed for bacterial replication*
- *Increased temperature prevents viral replication in infected cells*
- *Fever is one of the inflammatory factors that promotes liver to produce acute-phase proteins*
- *Heat binds cations necessary for bacterial reproduction*
- *Heat increases lymphocytic transformation*
- *Heat increases motility of polymorphonuclear neutrophils*
- *Phagocytosis is enhanced during fever*
- *Production of antiviral interferon may be augmented during fever*

Cold compresses to the head will help reduce the possibility of complications in those with a fever.

Q. An antipyretic is a drug that can:

A. block fever

Response Feedback:

The word 'antipyretics' originates from the Greek anti, against, and pyreticus, pertaining to fever. Antipyretics are drugs that reduce fever.

The cytokines (especially interleukins and tumour necrosis factor released from leukocytes and other cells) cause the hypothalamus to change its 'set point', thus telling the hypothalamus to increase the body temperature. Taking an antipyretic agent causes a blockage of this message, reversing the cytokine-induced increase in body temperature.

Therefore, taking an antipyretic agent when the temperature is normal or when it has been increased from environmental factors rather than cytokines will not decrease the temperature.

Q. According to the gate control theory, pain:

A. can be blocked or intensified by gates in the CNS

Response Feedback:

The gate control theory suggests that the spinal cord contains a neurological "gate" that either blocks pain signals or allows them to continue on to the brain. Unlike an actual gate, which opens and closes to allow things to pass through, the "gate" in the spinal cord operates by differentiating between the types of fibres carrying pain signals. Pain signals traveling via small nerve fibres are allowed to pass through, while signals sent by large nerve fibres are blocked. Gate control theory is often used to explain phantom or chronic pain. Descending pathways from the brain close the gate by inhibiting the projector neurons and diminishing pain perception.

Congenital analgesia is a rare genetic disorder where the individual is unable to feel pain. You might think this sounds like a good thing, but it's actually a life-threatening condition. Pain serves as a warning against injury, so people who don't feel it can be severely injured hurt by things that most of us would react quickly to. For example, a child could get third-degree burns on her knees by climbing on a hot radiator. There would be no signal for her to stop.

Q. Chronic or excessive activity by the inflammatory response can lead to:

A. tissue destruction due to fibrosis or release of lysosomal enzymes

Response Feedback:

Chronic activity by the inflammatory response leads to accumulation and activation of fibroblasts, with resultant fibrosis (scarring) of the tissues involved. Conversely, severe acute activity of the inflammatory response leads to the release of lysosomal enzymes that directly kill host cells, while decreased blood supply due to the severely inflamed tissues impinging on the blood supply add to the injury.

Many authors use a set time period to denote the word 'chronic'. This is often 3 or 6 months. However, I argue that the cellular responses that inevitably occur in 'chronic' inflammation should be considered for each type of disorder and therefore "chronic" is not only time-dependant. In the liver, "chronic" hepatitis C may not manifest significant fibrosis for years,

while tuberculosis manifests in fibroblast activation and scarring in two weeks. Regardless, eventually inflammation will in itself decrease the function of the tissues that are inflamed.

Q. People taking prescribed NSAIDS should be taught to avoid the use of OTC medications without checking with their prescriber or pharmacist because:

A. many of the OTC preparations contain NSAIDs, and inadvertent toxicity could occur

Response Feedback:

One should never combine analgesics, as it could lead to analgesic nephropathy. Analgesic nephropathy is irreversible injury to the kidney (not the glomerulus like most injury, but rather to the interstitial and tubular areas). The specific kidney injuries induced by analgesics are renal papillary necrosis and chronic interstitial nephritis. They are due to decreased blood flow to the kidney, rapid consumption of antioxidants and oxidative damage to the kidney. Kidney cells do not regenerate. Once a nephron is destroyed, it will remain destroyed until stem cell therapy is advanced enough to help replace the cells (sometime in the next 30 years or so).

It should be noted that analgesic nephropathy is much less prevalent since phenacetin was banned in the mid 1980's. Phenacetin is an analgesic widely used from its introduction in 1887. It is metabolized to paracetemol, which replaced it in some over-the-counter medications following the ban on phenacetin.

The first known case of analgesic nephropathy (renal papillary necrosis) was that of Ludwig van Beethoven who died of it in 1827. Beethoven was known to consume large amounts of willow bark (Salix alba et. spp.) which contains large amounts of salicin (metabolised to salicic acid; aspirin).

Q. Normal NSAIDS affect the COX-1 and COX-2 enzymes.

Blocking COX-2 enzymes enables the NSAIDS to block the production of inflammatory mediators at the site of inflammation.

By blocking COX-1 enzymes, these drugs block prostaglandins that protect the stomach and kidney.

Therefore, selective COX-2 inhibitors like celecoxib were introduced, but celecoxib and other COX-2 inhibitors dramatically increase the risk of:

A. cardiovascular events

Response Feedback:

Blocking COX - 1 results in many of the adverse effects of NSAIDs. Selectivity for COX-2 is the main feature of celecoxib and other members of this drug class. Because COX-2 is usually specific to inflamed tissue, there is much less gastric irritation associated with COX-2 inhibitors, with a decreased risk of peptic ulceration.

But one of the most important adverse effects of celecoxib and other COx- 2 specific NSAIDs is the increased risk of MI and stroke.

Q. A drug could be classified as an analgesic if it:

A. reduces pain

Response Feedback:

The word analgesic derives from Greek ἀν-, "without", and ἄλγος, "pain". It is the name we use to describe painkillers.

Q. Opioid receptors are found throughout the body:

A. to incorporate pain perception and blocking

Response Feedback:

Opioid receptors are involved in pain perception and blocking.

Opioid receptors are distributed widely in the brain, and are found in the spinal cord and digestive tract. The endogenous (within the body) are dynorphins, enkephalins, endorphins and others. Morphine and other opioid drugs act on an endogenous opioidergic system, which is not only involved in setting pain (nociceptive) threshold and controlling nociceptive processing but also participates in modulation of gastrointestinal, endocrine and autonomic function, as well as a possible role in cognition.

The receptors were named using the first letter of the first ligand that was found to bind to them. Morphine was the first chemical shown to bind to mu receptors. The first letter of the drug morphine is m, rendered as the corresponding Greek letter μ. In similar manner, a drug known as ketocyclazocine was first shown to attach itself to κ receptors, while the δ receptor was named after the mouse vas deferens tissue in which the receptor was first characterised.

Q. Codeine is:

A. (All of the choices given are correct)

- An opiate used to treat mild to moderate pain, as a cough medicine, and for diarrhea
- Associated with drowsiness and constipation, and can cause respiratory depression.
- Ineffective for 10% of people, as they do not have the enzyme to metabolise the drug to the active form.

Response Feedback:

On 1 February, 2018, it became necessary to have a prescription in order to obtain analgesics containing codeine.

Q. Which of the following narcotics has a prolonged duration of action?

A. Methadone.

Response Feedback:

Because it is an acyclic analogue of morphine, methadone acts on the same opioid receptors as these drugs, and thus has many of the same effects. Methadone is also used in managing severe chronic pain, owing to its long duration of action (half-life of about 40 hours rather than 2-4), extremely powerful effects, and very low cost. In Australia, methadone abuse results in hundreds of overdose deaths per year.

Over the last few years in Australia, there has been a steady increase in the number of deaths attributed to methadone toxicity. This mainly involves patients recently commencing this treatment, often within the first week. A series of deaths were investigated by the Coroner in the southern state of Victoria.

An account of these deaths was published in an international forensic journal and a letter to the Lancet. The Coroner was very critical of training methods of medical practitioners prescribing methadone. Subsequently, a number of deaths attributed to methadone have occurred in New South Wales. Coronial enquiries are underway. It is likely that the majority of cases will be confirmed as methadone deaths. Why has this happened? In Victoria, it was obvious that most of the deaths involved medical practitioners who had received little if any advice about the unusual pharmacology of methadone. Many patients were started on unrealistically high doses (e.g. 70 mg) or were prescribed increments which were too large (e.g. 10 mg) or too frequent (e.g. more than twice a week). Guidelines were produced and these have become more conservative over time. All guidelines now recommend starting at 40 mg or less and also warn against increments greater than 10 mg per week or more than 5 mg twice a week. New guidelines are expected to recommend an initial starting dose of 35 mg or even 30 mg. Another problem has been that of disseminating these guidelines. Prescribers who have been practising in this field for some years without problems continue to prescribe doses which are now realised to be hazardous. However, some fatal cases have occurred even among prescribers who have attended courses where the dangers of excessive starting doses of methadone have been discussed. Another problem has been that liberal take-away policies, intended to encourage rehabilitation, improve the attractiveness of treatment and reduce the costs of unnecessary bureaucracy, unfortunately resulted in substantial diversion. Some of the deaths have been attributed to 'grey market' methadone. An additional cause of death was young children unscrewing bottles of parental methadone and dying from an overdose. Most take-away methadone in Australia is now provided in special screw top bottles which cannot be opened by infants. As always in drugs and drug policy, a sense of balance is of critical importance but difficult to achieve. All of us working in this field need no reminders about the immense benefits which can accrue to individuals and their communities when heroin dependent drug users can readily obtain treatment in well run methadone programmes. Few of us would have realised, until recently, that these programmes are not without cost. There can be little doubt that the balance of benefits and costs in Australia, as elsewhere, remains strongly favourable. However, as committed harm reductionists, we must all do what we can to ensure that deaths from methadone are reduced to an absolute minimum. What is even harder is ensuring that this is achieved without making methadone programmes so rigid and unattractive that our patients prefer the street heroin programme run by criminals and disgraced ex-policemen.

Alcohol & Drug Services

St. Vincent's Hospital Sydney

Q. The opioid tramadol should be avoided in clients with:

A. epilepsy

Response Feedback:

Tramadol is a centrally-acting atypical opioid analgesic with additional serotonin-noradrenaline reuptake-inhibiting effects used to treat moderate to severe pain. Its analgesic effects take about one hour to come into effect and 2-4 hours to peak after oral administration with an immediate-release formulation. Tramadol does not produce the euphoria effects that most narcotics do, and is therefore has a lower potential for dependence.

On a dose-by-dose basis tramadol has about one-tenth the potency of morphine and is approximately equally potent when compared to pethidine and codeine. Compared to other opioids respiratory depression and constipation is considered less of a problem with tramadol, although increased vulnerability to epileptic seizures is common in experimental animals, and is a rare occurrence in humans. Tramadol should not be taken with other drugs that increase the possibity of causing seizures.

The following is an example of the type of question that could be asked to test your knowledge of the feedback. Obviously it is not the only important point in the feedback.

When administering tramadol, it should not be given with drugs that:

A) affect coagulation.

B) affect blood vessel vasculature.

C) are largely metabolised renally.

D) increase seizure tendencies.

Q. Which of the following is not a characteristic of oxycodone? (which is incorrect?)

A. It has a shorter half-life than morphine.

Response Feedback:

Oxycodone has a half-life of 2-4 hours compared to the 2-3 hour half-life of morphine. All other statements about Oxycodone in the choices are correct. What were they?

Q. Most narcotics are controlled substances because they:

A. can be addictive

Response Feedback:

Schedule 8 Controlled Drug (Possession without authority is illegal)

Schedule 8 (S8) drugs and poisons, otherwise known as Controlled Drugs, are substances and preparations for therapeutic use which have high potential for abuse and addiction.

In some states, all drugs on schedule 8 require a doctor to have an S8 permit before prescribing treatment.

Q. Proper administration of an ordered narcotic:

A. should be done promptly to prevent increased pain and the need for larger doses

Response Feedback:

Delaying the administration of pain killers can result in more being needed. In fact, as pain becomes chronic, there are changes that occur which in effect, magnify the pain. Chronic pain is considered a disease in its own right.

Q. The reason(s) that methadone is used to help wean people off heroin is that:

A. (All of the reasons given in these choices are correct)

- methadone has a much longer half-life, which contributes to weaker withdrawal symptoms.
- methadone is administered orally, reducing syringe use.
- methadone binds to opioid receptors leaving few receptors available for a heroin 'high'.

Response Feedback:

All three of the choices are reasons why methadone is used to help wean people off heroin.

What are the reasons again? Exam questions can be worded, for instance,

Which of the following is true about methadone:

- *It is normally administered by syringe*
- ***methadone has a much longer half-life than heroin, which contributes to weaker withdrawal symptoms and is therefore used to help wean people off of heroin***
- *There is no risk of respiratory depression with methadone*
- *Methadone causes opioid dependency*

Each of the answers above is incorrect except the one that is bolded.

Q. Which of the following is a non-competitive opioid receptor antagonist?

A. naloxone

Response Feedback:

Naloxone is a non-competitive opioid receptor antagonist while the other drugs in the answers are opioid narcotic analgesics.

Naloxone is a medication used to block the effects of opioids, especially in overdose. Naloxone may be combined within the same pill as an opioid to decrease the risk of misuse. The effects of naloxone last about half an hour to an hour, so multiple doses may be required

Administration to opioid-dependent individuals may cause symptoms of opioid withdrawal, including restlessness, agitation, nausea, vomiting, tachycardia, and sweating. To prevent this, small doses every few minutes can be given until the desired effect is reached.

Q. The opioid receptors most involved in mediating analgesia are:

A. mu and kappa.

Response Feedback:

There are four types of opiod receptors, Delta (δ1, δ2), kappa (κ1, κ2, κ3) mu (μ1, μ2, μ3)and epsilon. Mu and kappa have the greatest effect on pain while delta has some effect on pain. You will run across tables that describe opioids by their affinity for various receptors.

Q. What is the equivalent dose of pethidine when compared with 10 mg of morphine?

A. 75-100 mg of pethidine.

Response Feedback:

Pethidine is a synthetic opiod analgesic that was originally synthesized in 1939 and is just about 1/8th as potent as morphine. Pethidine is indicated for the treatment of moderate to severe pain. For much of the 20th century, pethidine was the opioid of choice for many physicians; because it was first toted as being safer.

It was later discovered that pethidine is more dangerous and more addictive than morphine.

Q. Local anaesthetics are used to block feeling in specific body areas. If given in increasing concentrations, local anaesthetics can cause loss, in order, of the following:

A. temperature sensation, touch sensation, proprioception and skeletal muscle tone

Response Feedback:

If given in increasing concentrations, local anaesthetics can cause loss in the order of temperature sensation, touch sensation, proprioception and skeletal muscle tone.

Q. One topic that we did not get time to cover in our lecture series on analgesics was relief of pain from migraines.

Triptans are a family of tryptamine-based drugs used in the treatment of migraines and cluster headaches. This drug class was first introduced in the 1990s. While effective at treating individual headaches, they do not provide preventative treatment and are not considered a cure. They are not effective for the treatment of tension headache or other kinds of pain.

The drugs of this class act as agonists for serotonin 5-HT1B and 5-HT1D receptors at blood vessels and nerve endings in the brain. The first clinically available triptan was sumatriptan, which has been marketed since 1991 and is the only triptan that has been approved for use in treating cluster headaches as well as migraines.

The only triptan that has been approved for use in treating cluster headaches as well as migraines is:

A. sumatriptan

Response Feedback:

Q. While a person is receiving a general anaesthetic, he or she must be continually monitored because:

A. generalised CNS depression affects all body functions

Response Feedback:

Physiologic monitoring during anaesthesia is continuous - CNS depression affects all body functions.

Monitoring involves the use of several technologies to allow for a controlled induction of, maintenance of and emergence from general anaesthesia. Monitoring includes the following:

1. *Continuous Electrocardiography (ECG): The placement of electrodes that monitor heart rate and rhythm. This may also help the anaesthetist to identify early signs of heart ischaemia.*
2. *Continuous pulse oximetry (SpO2): The placement of this device (usually on one of the fingers) allows for early detection of a fall in a patient's haemoglobin saturation with oxygen (hypoxaemia).*
3. *Blood Pressure Monitoring (NIBP or IBP): There are two methods of measuring the patient's blood pressure. The first, and most common, is called non-invasive blood pressure (NIBP) monitoring. This involves placing a blood pressure cuff around the patient's arm, forearm or leg. A blood pressure machine takes blood pressure readings at regular, pre-set intervals throughout the surgery. The second method is called invasive blood pressure (IBP) monitoring. This method is reserved for patients with significant heart or lung disease, the critically ill, major surgery such as cardiac or transplant surgery, or when large blood losses are expected. The invasive blood pressure monitoring technique involves placing a special type of plastic cannula in the patient's artery - usually at the wrist or in the groin.*
4. *Agent concentration measurement: Common anaesthetic machines have monitors to measure the percentage of inhalational anaesthetic agent used (e.g. sevoflurane, isoflurane, desflurane, halothane etc.). The monitors also usually measure nitrous oxide and oxygen percentages and could give a MAC level.*
5. *Low oxygen alarm: Almost all circuits have a backup alarm in case the oxygen delivery to the patient becomes compromised. This warns if the fraction of inspired oxygen drops lower than minimum alarm setting and allows the anaesthetist to take immediate remedial action.*
6. *Circuit disconnect alarm or low-pressure alarm: indicates failure of the circuit to achieve a given pressure during mechanical ventilation.*
7. *Carbon dioxide measurement (capnography): measures the amount of carbon dioxide expired by the patient's lungs in per cent or mmHg, mmHg is usually used to allow the anaesthesia provider to see more subtle changes in CO2. It allows the anaesthetist to assess the adequacy of ventilation*
8. *Temperature measurement: used to discern hypothermia or fever, and to aid early detection of malignant hyperthermia.*
9. *EEG or other systems to verify depth of anaesthesia may also be used. This reduces the likelihood that a patient will be mentally awake, although unable to move because of the paralytic agents. It also reduces the likelihood of a patient receiving significantly more amnesic drugs than are actually necessary to do the job.*

Q. Wait a minute, prostaglandins 'mediators' that we affect with our NSAIDs, right? ...then what are cytokines again?

Correct, prostaglandins are the LIPID MEDIATORS that we indirectly decrease with our NSAIDs. Prostaglandins act on platelets, endothelium, uterine and mast cells.

In contrast, cytokines are small PROTEIN MEDIATORS released by cells and they communicate between cells. Recall when we were talking about hepatocytes infected by the Hepatitis C virus secreted cytokines (interleukins) to the adjacent cells to WARN THEM AND PREPARE THEM FOR THE VIRUS. Then we made these interleukins into a therapy for Hepatitis.

Which of the following is not a cytokine?

A. Antibody

Response Feedback:

Cytokines are small proteins that are important in cell signalling. They are released by cells and affect the behaviour of other cells, and sometimes the releasing cell itself. Cytokines include

- Chemokines
- Interferons
- Interleukins
- Lymphokines
- Tumour necrosis factor

Cytokines are produced by a broad range of cells, including immune cells like macrophages, B cells, T cells and mast cells, as well as endothelial cells, fibroblasts and other cells.

Cytokines are especially important in the immune system. They modulate the balance between humoral and cell-based immune responses, and they regulate the maturation, growth, and responsiveness of particular cell populations. Some cytokines enhance or inhibit the action of other cytokines in complex ways.

They are different from hormones, which are also important cell signalling molecules, in that hormones circulate in much lower concentrations and hormones tend to be made by specific kinds of cells.

Many cytokines are used as drugs.

Q. Some Tricyclic Antidepressants show efficacy in the clinical treatment of a number of different types of chronic pain, notably neuralgia or neuropathic pain and fibromyalgia. These tricyclic antidepressants that yield this effect include:

A. amitriptyline and nortriptyline

Response Feedback:

Amitriptyline and nortriptyline are tricyclic antidepressants that have been approved for neuropathic and chronic pain. Their primary site of action seems to be in the spinal cord, near the 'gate'.

Recall that phenelzine and tranylcypromine are MAOI antidepressants and that Sertraline (Zoloft) is a SSRI antidepressant, and none of which are approved for chronic or neuropathic pain.

Carbamazepine is approved for neuropathic pain but is an anti-seizure medication.

Q. Triptans, a drug class used to treat migraine headaches, decrease migraine pain by at least three modes of action. These antimigraine mechanisms are:

1.vasoconstriction of pain producing intra cranial extracerebral vessels by a direct effect on vascular smooth muscle.

2.inhibition of vasoactive neuropeptide release in the brain.

3.inhibition of nociceptive neurotransmission within the brainstem and upper cervical spinal column.

The triptans are a class of drugs that bind to selective serotonin receptor sites and cause:

A. cranial vascular constriction

Response Feedback:

The triptans work by a few mechanisms including vasoconstriction.

Q. Which of the following local anaesthetics has a relatively long duration of action?

A. Bupivacaine

Response Feedback:

The half-life of bupivacaine is 3.5 hours, compared to 60 seconds for procaine. Compared to other local anaesthetics, bupivacaine is markedly cardiotoxic. However, ADRs are rare when it is administered correctly. Most adverse drug reactions (ADRs) are caused by accelerated absorption from the injection site, unintentional intravascular injection, or slow metabolic degradation.

Q. The drug that acts as a selective antagonist of the NMDA receptor and is a medication mainly used for starting and maintaining anesthesia but is also useful in many cases of chronic pain is:

A. Ketamine

Response Feedback:

The drug that acts as a selective antagonist of the NMDA receptor and is a medication mainly used for starting and maintaining anesthesia but is also useful in many cases of chronic pain is ketamine. It induces a trance-like state while providing pain relief, sedation, and memory loss.

Methadone is an opioid used to treat pain and as maintenance therapy or to help with tapering in people with opioid dependence. Due to its activity at the NMDA receptor, it may be more effective against neuropathic pain than the other opioids, which are generally relatively ineffective.

Gabapentin and Pregabalin are anticonvulsants that are effective in some types of neuropathic pain.

Q. The most dangerous period for many people undergoing general anaesthesia is during which stage?

A. Stage 2, when systemic stimulation occurs

Response Feedback:

Stage 2 is the most dangerous.

Stage 1

Stage 1 anaesthesia, also known as the "induction", is the period between the initial administration of the induction agents and loss of consciousness. During this stage, the patient progresses from analgesia without amnesia to analgesia with amnesia. Patients can carry on a conversation at this time.

Stage 2

Stage 2 anaesthesia, also known as the "excitement stage", is the period following loss of consciousness and marked by excited and delirious activity. During this stage, respirations and heart rate may become irregular. In addition, there may be uncontrolled movements, vomiting, breath holding, and pupillary dilation. Since the combination of spastic movements, vomiting, and irregular respirations may lead to airway compromise, rapidly acting drugs are used to minimise the amount of time in this stage and reach stage 3 as fast as possible.

Stage 3

Stage 3, "surgical anaesthesia". During this stage, the skeletal muscles relax, vomiting stops, and respiratory depression occurs. Eye movements slow, then stop, the patient is unconscious and ready for surgery. It has been divided into 4 planes:

1. *eyes initially rolling, then becoming fixed*
2. *loss of corneal and laryngeal reflexes*
3. *pupils dilate and loss of light reflex*
4. *intercostal paralysis, shallow abdominal respiration*

Stage 4

Stage 4 anaesthesia, also known as "overdose", is the stage where too much medication has been given relative to the amount of surgical stimulation and the patient has severe brain stem or medullary depression. This results in a cessation of respiration and potential cardiovascular collapse. This stage is lethal without cardiovascular and respiratory support.

MULTIPLE CHOICE QUESTIONS AND ANSWERS WEEK 12

Q. Patients taking OTC and complementary medication may:

A. all of the choices given here are correct

- attempt self-diagnosis and treatment prior to consulting their doctor.

- have adverse drug interactions if they are also taking prescription medications.
- not discuss the OTC or complementary medicines with their health provider as they do not consider them important.

Response Feedback:

Always consider OTC medications and complementary medicine use when taking a patient history.

Q. A key feature of polypharmacy is:

A. the excessive or unnecessary use of medicines

Response Feedback:

The term polypharmacy lacks a universally consistent definition, but normally refers to the patient taking 4-5 or more medications at the same time, some of which are or may be unnecessary. Polypharmacy is most common in the elderly, affecting about 40% of older adults living in their own homes. Polypharmacy is often associated with a decreased quality of life, decreased mobility and cognition.

It is well accepted in pharmacology that it is impossible to accurately predict the side effects or clinical effects of a combination of drugs without studying that particular combination of drugs in test subjects. Knowledge of the pharmacologic profiles of the individual drugs in question does not assure accurate prediction of the side effects of combinations of those drugs.

In the first year after a myocardial infarction, a perfectly legitimate treatment regimen could include a statin, an ACE inhibitor, a beta-blocker, aspirin, paracetamol, and an antidepressant. So this is not to say that a person should not be on more than x amount of drugs, but rather to draw your attention to the fact that more is not always better and in fact is often worse for the patient.

Q. Which of the following health professionals can decrease the incidence of polypharmacy?

A. All health professionals including nurses, midwifes and osteopaths should do their part in helping to reduce polypharmacy

Response Feedback:

All health professionals including nurses, midwifes and osteopaths should do their part in helping to reduce polypharmacy.

Q. Jack B. has Parkinson's disease that has been controlled for several years with levodopa. After he begins a health food and diet supplementation program with high levels of B vitamins, his tremors return, and he develops a rapid heart rate, hypertension, and anxiety. This is because vitamin B6 can speed the conversion of levodopa to dopamine in the periphery, leading to these problems. This type of problem is common and is termed:

A. a drug-drug interaction

Response Feedback:

Drug-drug interactions and drug-nutrient reactions are quite common, and it is important to include questioning about vitamin and herbal supplementation when trying to determine the cause of adverse effects and when prescribing additional drugs. For some drugs like warfarin, altering the diet can result in plasma levels of the drug falling out of therapeutic range or into a dangerous range.

Q. The use of a contraindicated medicine may have the following effect(s) EXCEPT:

A. safely curing the disorder

Response Feedback:

The use of a contraindicated medicine may exacerbate the disorder, cause an allergic reaction or cause a toxic reaction. It will not safely cure a disorder.

Q. When trying to determine why the desired therapeutic effect is not being seen with an oral drug, one should consider:

A. food altering the makeup of gastric juices

Response Feedback:

Diet is an important factor in the pharmacokinetics of many drugs. Food can alter the gastric acids, leading to altered absorption. Foods like grapefruit juice can affect the liver enzyme production, thereby altering the excretion of the substance. Foods containing high amounts of vitamins can affect the efficacy of many drugs.

Diet is an important factor in the pharmacokinetics of many drugs.