LECTURE NOTES

ON

PHARMACOTHERAPEUTICS-1

(Subject Code: 17T00206)

2018 – 2019

II PHARM.D (JNTUA-R17)

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PHARM D-II YEAR

PHARMACOTHERAPEUTICS-1

UNIT-1: CARDIOVASCULAR SYSTEM

HYPERTENSION:

Hypertension (**HTN** or **HT**), also known as **high blood pressure** (**HBP**), is a long-term medical condition in which the blood pressure in the arteries is persistently elevatedHigh blood pressure usually does not cause symptoms Long-term high blood pressure, however, is a major risk factor for coronary artery disease, stroke, heart failure, atria fibrillation, peripheral vascular disease, vision loss, chronic kidney disease, and dementia.

High blood pressure is classified as either primary (essential) high blood pressure or secondary high blood pressure.[5] About 90–95% of cases are primary, defined as high blood pressure due to nonspecific lifestyle and genetic factors.[5][6] Lifestyle factors that increase the risk include excess salt in the diet, excess body weight, smoking, and alcohol use.[1][5] The remaining 5–10% of cases are categorized as secondary high blood pressure, defined as high blood pressure due to an identifiable cause, such as chronic kidney disease, narrowing of the kidney arteries, an endocrine disorder, or the use of birth control pills.

Blood pressure is expressed by two measurements, the systolic and diastolic pressures, which are the maximum and minimum pressures, respectively.[1] For most adults, normal blood pressure at rest is within the range of 100–130 millimeters mercury (mmHg) systolic and 60–80 mmHg diastolic.[7][12] For most adults, high blood pressure is present if the resting blood pressure is persistently at or above 130/80 or 140/90 mmHg.[5][7] Different numbers apply to children.[13] Ambulatory blood pressure monitoring over a 24-hour period appears more accurate than office-based blood pressure measurement.[5] [10]

Lifestyle changes and medications can lower blood pressure and decrease the risk of health complications.[8] Lifestyle changes include weight loss, decreased salt intake, physical exercise,

and a healthy diet.[5] If lifestyle changes are not sufficient then blood pressure medications are used.[8] Up to three medications can control blood pressure in 90% of people.[5] The treatment of moderately high arterial blood pressure (defined as >160/100 mmHg) with medications is associated with an improved life expectancy.[14] The effect of treatment of blood pressure between 130/80 mmHg and 160/100 mmHg is less clear, with some reviews finding benefit[7][15][16] and others finding unclear benefit.[17] [18] [19] High blood pressure affects between 16 and 37% of the population globally.[5] In 2010 hypertension was believed to have been a factor in 18% of all deaths (9.4 million globally)

Signs and symptoms

Hypertension is rarely accompanied by symptoms, and its identification is usually through screening, or when seeking healthcare for an unrelated problem. Some with high blood pressure report headaches (particularly at the back of the head and in the morning), as well as lightheadedness, vertigo, tinnitus (buzzing or hissing in the ears), altered vision or fainting episodes.[20] These symptoms, however, might be related to associated anxiety rather than the high blood pressure itself.[21]

On physical examination, hypertension may be associated with the presence of changes in the optic fundus seen by ophthalmoscopy.[22] The severity of the changes typical of hypertensive retinopathy is graded from I–IV; grades I and II may be difficult to differentiate.[22] The severity of the retinopathy correlates roughly with the duration or the severity of the hypertension.[20]

Secondary hypertension:

Hypertension with certain specific additional signs and symptoms may suggest secondary hypertension, i.e. hypertension due to an identifiable cause. For example, Cushing's syndrome frequently causes truncal obesity, glucose intolerance, moon face, a hump of fat behind the neck/shoulder (referred to as a buffalo hump), and purple abdominal stretch marks.[23] Hyperthyroidism frequently causes weight loss with increased appetite, fast heart rate, bulging eyes, and tremor. Renal artery stenosis (RAS) may be associated with a localized abdominal bruit to the left or right of the midline (unilateral RAS), or in both locations (bilateral RAS). Coarctation of the aorta frequently causes a decreased blood pressure in the lower

extremities relative to the arms, or delayed or absent femoral arterial pulses. Pheochromocytoma may cause abrupt ("paroxysmal") episodes of hypertension accompanied by headache, palpitations, pale appearance, and excessive sweating.

Hypertensive crisis

Severely elevated blood pressure (equal to or greater than a systolic 180 or diastolic of 110) is referred to as a hypertensive crisis. Hypertensive crisis is categorized as either hypertensive urgency or hypertensive emergency, according to the absence or presence of end organ damage, respectively.

In hypertensive urgency, there is no evidence of end organ damage resulting from the elevated blood pressure. In these cases, oral medications are used to lower the BP gradually over 24 to 48 hours.

In hypertensive emergency, there is evidence of direct damage to one or more organs.The most affected organs include the brain, kidney, heart and lungs, producing symptoms which may include confusion, drowsiness, chest pain and breathlessness. In hypertensive emergency, the blood pressure must be reduced more rapidly to stop ongoing organ damage,however, there is a lack of randomized controlled trial evidence for this approach.

CONGESTIVE HEART FAILURE:

Heart failure (**HF**), often referred to as **congestive heart failure** (**CHF**), is when the heart is unable to pump sufficiently to maintain blood flow to meet the body's needs.[9][10][11] Signs and symptoms commonly include shortness of breath, excessive tiredness, and leg swelling.[2] The shortness of breath is usually worse with exercise, while lying down, and may wake the person at night.[2] A limited ability to exercise is also a common feature.[12] Chest pain, including angina, does not typically occur due to heart failure.[13]

Common causes of heart failure include coronary artery disease including a previous myocardial infarction (heart attack), high blood pressure, atrial fibrillation, valvular heart disease, excess alcohol use, infection, and cardiomyopathy of an unknown cause.[2][3] These cause heart failure by changing either the structure or the functioning of the heart.[2] There are two main types of heart failure: *heart failure due to left ventricular dysfunction* and *heart failure with normal ejection fraction* depending on whether the ability of the left ventricle to contract is affected, or the heart's ability to relax.[2] The severity of disease is usually graded by the degree of problems with exercise.[5] Heart failure is not the same as myocardial infarction (in which part of the heart muscle dies) or cardiac arrest (in which blood flow stops altogether).[14][15] Other diseases that may have symptoms similar to heart failure include obesity, kidney failure, liver problems, anemia, and thyroid disease.[5]

The condition is diagnosed based on the history of the symptoms and a physical examination with confirmation by echocardiography.[4] Blood tests, electrocardiography, and chest radiography may be useful to determine the underlying cause.[4] Treatment depends on the severity and cause of the disease.[4] In people with chronic stable mild heart failure, treatment commonly consists of lifestyle modifications such as stopping smoking,[6] physical exercise,[16] and dietary changes, as well as medications.[6] In those with heart failure due to left ventricular dysfunction, angiotensin converting enzyme inhibitorsor angiotensin receptor blockers along with beta blockers are recommended.[4] For those with severe disease, aldosterone antagonists, or hydralazine with a nitrate may be used.[4] Diuretics are useful for preventing fluid retention.[6] Sometimes, depending on the cause, an implanted device such as a pacemaker or an implantable cardiac defibrillator may be recommended.[4] In some moderate or severe cases, cardiac resynchronization therapy (CRT)[17] or cardiac contractility modulation may be of benefit.[18] A ventricular assist device or occasionally a heart transplant may be recommended in those with severe disease that persists despite all other measures.[6]

Heart failure is a common, costly, and potentially fatal condition.[3] In 2015 it affected about 40 million people globally.[7] Overall around 2% of adults have heart failure[19] and in those over the age of 65, this increases to 6–10%.[3][8] Rates are predicted to increase.[19] In the year after diagnosis the risk of death is about 35% after which it decreases to below 10% each year.[2] This is similar to the risks with a number of types of cancer.[2] In the United Kingdom the disease is

the reason for 5% of emergency hospital admissions.[2] Heart failure has been known since ancient times with the Ebers papyrus commenting on it around 1550 BCE.[12]

Signs and symptoms:

Heart failure symptoms are traditionally and somewhat arbitrarily divided into "left" and "right" sided, recognizing that the left and right ventricles of the heart supply different portions of the circulation. However, heart failure is not exclusively *backward failure* (in the part of the circulation which drains to the ventricle).

There are several other exceptions to a simple left-right division of heart failure symptoms. Additionally, the most common cause of right-sided heart failure is left-sided heart failure.[24] The result is that patients commonly present with both sets of signs and symptoms.

Causes:

Heart failure may also occur in situations of "high output" (termed "high-output heart failure"), where the amount of blood pumped is more than typical and the heart is unable to keep up.[21] This can occur in overload situations (blood or serum infusions), kidney diseases, chronic severe anemia, beriberi (vitamin B_1/thiamine deficiency), hyperthyroidism, cirrhosis, Paget's disease, multiple myeloma, arteriovenous fistulae, or arteriovenous malformations.

Viral infections of the heart can lead to inflammation of the muscular layer of the heart and subsequently contribute to the development of heart failure. Heart damage can predispose a person to develop heart failure later in life and has many causes including systemic viral infections (e.g., HIV), chemotherapeutic agents such as daunorubicin, cyclophosphamide, and trastuzumab, and abuse of drugs such as alcohol, cocaine, and methamphetamine. An uncommon cause is exposure to certain toxins such as lead and cobalt. Additionally, infiltrative disorders such as amyloidosis and connective tissue diseases such as systemic lupus erythematosus have similar consequences. Obstructive sleep apnea (a condition of sleep wherein disordered breathing overlaps with obesity, hypertension, and/or diabetes) is regarded as an independent cause of heart failure.

Acute decompensation:

Kerley B lines in acute cardiac decompensation. The short, horizontal lines can be found everywhere in the right lung.

Chronic stable heart failure may easily decompensate. This most commonly results from an intercurrent illness (such as myocardial infarction(a heart attack), pneumonia), abnormal heart rhythms, uncontrolled hypertension, or a patient's failure to maintain a fluid restriction, diet, or medication.[25] Other well recognized factors that may worsen CHF include the following: anemia and hyperthyroidism which place additional strain on the heart muscle, excessive fluid or salt intake, and medication that causes fluid retention such as NSAIDs and thiazolidinediones.[26] NSAIDs in general increase the risk twofold.[27]

Medications:

A number of medications may cause or worsen the disease. This includes NSAIDS, a number of anesthetic agents such as ketamine, thiazolidinediones, a number of cancer medications, salbutamol, and tamsulosin among others.[28]

ANGINA PECTORIS:

Angina, also known as **angina pectoris**, is chest pain or pressure, usually due to not enough blood flow to the heart muscle.

Angina is usually due to obstruction or spasm of the coronary arteries.[1] Other causes include anemia, abnormal heart rhythmsand heart failure. The main mechanism of coronary artery obstruction is an atherosclerosis as part of coronary artery disease. The term derives from the Latin *angere* ("to strangle") and *pectus* ("chest"), and can therefore be translated as "a strangling feeling in the chest".

There is a weak relationship between severity of pain and degree of oxygen deprivation in the heart muscle (i.e., there can be severe pain with little or no risk of a myocardial infarction (heart attack) and a heart attack can occur without pain). In some cases, angina can be quite severe, and in the early 20th century this was a known sign of impending death.[2] However, given current medical therapies, the outlook has improved substantially. People with an average age of 62 years, who have moderate to severe degrees of angina (grading by classes II, III, and IV) have a 5-year survival rate of approximately 92%.[3]

Worsening angina attacks, sudden-onset angina at rest, and angina lasting more than 15 minutes are symptoms of *unstable angina* (usually grouped with similar conditions as the acute coronary syndrome). As these may precede a heart attack, they require urgent medical attention and are, in general, treated in similar fashion to myocardial infarction

SIGNS AND SYMPTOMS:

Angina pectoris can be quite painful, but many patients with angina complain of chest discomfort rather than actual pain: the discomfort is usually described as a pressure, heaviness, tightness, squeezing, burning, or choking sensation. Apart from chest discomfort, anginal pains may also be experienced in the epigastrium (upper central abdomen), back, neck area, jaw, or shoulders. This is explained by the concept of referred pain, and is due to the fact that the spinal level that receives visceral sensation from the heart simultaneously receives cutaneous sensation from parts of the skin specified by that spinal nerve's dermatome, without an ability to discriminate the two. Typical locations for referred pain are arms (often inner left arm), shoulders, and neck into the jaw. Angina is typically precipitated by exertion or emotional stress. It is exacerbated by having a full stomach and by cold temperatures. Pain may be accompanied by breathlessness, sweating, and nausea in some cases. In this case, the pulse rate and the blood pressure increases. Chest pain lasting only a few seconds is normally not angina (such as precordial catch syndrome).

Myocardial ischemia comes about when the myocardium (the heart muscle) receives insufficient blood and oxygen to function normally either because of increased oxygen demand by the myocardium or because of decreased supply to the myocardium. This inadequate perfusion of blood and the resulting reduced delivery of oxygen and nutrients are directly correlated to blocked or narrowed blood vessels.

Some experience "autonomic symptoms" (related to increased activity of the autonomic nervous system) such as nausea, vomiting, and pallor.

Major risk factors for angina include cigarette smoking, diabetes, high cholesterol, high blood pressure, sedentary lifestyle, and family history of premature heart disease.

A variant form of angina—Prinzmetal's angina—occurs in patients with normal coronary arteries or insignificant atherosclerosis. It is believed caused by spasms of the artery. It occurs more in younger women.[15]

Coital angina, also known as *angina d'amour*, is angina subsequent to sexual intercourse.[16] It is generally rare, except in patients with severe coronary artery disease.

CAUSES:

Major risk factors:

- Age (≥ 45 years for men, ≥ 55 for women)
- Smoking
- Diabetes mellitus
- Dyslipidemia
- Family history of premature cardiovascular disease (men <55 years, female <65 years old)
- Hypertension
- Kidney disease (microalbuminuria or GFR<60 mL/min)
- Obesity (BMI ≥ 30 kg/m2)
- Physical inactivity
- Prolonged psychosocial stress[17]

Routine counselling of adults to advise them to improve their diet and increase their physical activity has not been found to significantly alter behaviour, and thus is not recommended.[18]

Conditions that exacerbate or provoke angina

[19]

- Medications
  - Vasodilators
  - Excessive thyroid hormone replacement
- Vasoconstrictors

- Polycythemia, which thickens the blood, slowing its flow through the heart muscle
- Hypothermia
- Hypervolemia
- Hypovolemia

One study found that smokers with coronary artery disease had a significantly increased level of sympathetic nerve activity when compared to those without. This is in addition to increases in blood pressure, heart rate, and peripheral vascular resistance associated with nicotine, which may lead to recurrent angina attacks. In addition, the Centers for Disease Control and Prevention (CDC) reports that the risk of CHD (Coronary heart disease), stroke, and PVD (Peripheral vascular disease) is reduced within 1–2 years of smoking cessation. In another study, it was found that, after one year, the prevalence of angina in smoking men under 60 after an initial attack was 40% less in those having quit smoking compared to those that continued. Studies have found that there are short-term and long-term benefits to smoking cessation.[20][21][22][23]

Other medical problems[edit]

- Esophageal disorders
- Gastroesophageal Reflux Disease (GERD)
- Hyperthyroidism
- Hypoxemia
- Profound anemia
- Uncontrolled hypertension

Other cardiac problems[edit]

- Bradyarrhythmia
- Hypertrophic cardiomyopathy
- Tachyarrhythmia
- Valvular heart disease[24][25]

Myocardial ischemia can result from:

1. a reduction of blood flow to the heart that can be caused by stenosis, spasm, or acute occlusion (by an embolus) of the heart's arteries.
2. resistance of the blood vessels. This can be caused by narrowing of the blood vessels; a decrease in radius.[26] Blood flow is proportional to the radius of the artery to the fourth power.[27]
3. reduced oxygen-carrying capacity of the blood, due to several factors such as a decrease in oxygen tension and hemoglobin concentration.[28] This decreases the ability of hemoglobin to carry oxygen to myocardial tissue.[29]

Atherosclerosis is the most common cause of stenosis (narrowing of the blood vessels) of the heart's arteries and, hence, angina pectoris. Some people with chest pain have normal or minimal narrowing of heart arteries; in these patients, vasospasm is a more likely cause for the pain, sometimes in the context of Prinzmetal's angina and syndrome X.

Myocardial ischemia also can be the result of factors affecting blood composition, such as reduced oxygen-carrying capacity of blood, as seen with severe anemia (low number of red blood cells), or long-term smoking.

Treatment:

The most specific medicine to treat angina is nitroglycerin. It is a potent vasodilator that decreases myocardial oxygen demand by decreasing the heart's workload. Beta blockers and calcium channel blockers act to decrease the heart's workload, and thus its requirement for oxygen. Nitroglycerin should not be given if certain inhibitors such as sildenafil, tadalafil, or vardenafil have been taken within the previous 12 hours as the combination of the two could cause a serious drop in blood pressure. Treatments for angina are balloon angioplasty, in which the balloon is inserted at the end of a catheter and inflated to widen the arterial lumen. Stents to maintain the arterial widening are often used at the same time.Coronary bypass surgery involves bypassing constricted arteries with venous grafts. This is much more invasive than angioplasty.

The main goals of treatment in angina pectoris are relief of symptoms, slowing progression of the disease, and reduction of future events, especially heart attacks and death. Beta blockers (e.g., carvedilol, propranolol, atenolol) have a large body of evidence in morbidity and mortality

benefits (fewer symptoms, less disability and longer life) and short-acting nitroglycerin medications have been used since 1879 for symptomatic relief of angina.[34] Calcium channel blockers (such as nifedipine (Adalat) and amlodipine), isosorbide mononitrate and nicorandil are vasodilators commonly used in chronic stable angina.[*citation needed*] A new therapeutic class, called If inhibitor, has recently been made available: Ivabradine provides pure heart rate reduction[35] leading to major anti-ischemic and antianginal efficacy. ACE inhibitors are also vasodilators with both symptomatic and prognostic benefit. Statins are the most frequently used lipid/cholesterol modifiers, which probably also stabilize existing atheromatous plaque.[36] Low-dose aspirin decreases the risk of heart attack in patients with chronic stable angina, and was part of standard treatment. However, in patients without established cardiovascular disease, the increase in hemorrhagic strokeand gastrointestinal bleeding offsets any benefits and it is no longer advised unless the risk of myocardial infarction is very high.[37]

Exercise is also a very good long-term treatment for the angina (but only particular regimens - gentle and sustained exercise rather than intense short bursts),[38] probably working by complex mechanisms such as improving blood pressure and promoting coronary artery collateralisation.

Though sometimes used by patients, evidence does not support the use of Traditional Chinese Herbal Products (THCP) for angina.[39]

Identifying and treating risk factors for further coronary heart disease is a priority in patients with angina. This means testing for elevated cholesterol and other fats in the blood, diabetes and hypertension (high blood pressure), and encouraging smoking cessation and weight optimization.

The calcium channel blocker nifedipine prolongs cardiovascular event- and procedure-free survival in patients with coronary artery disease. New overt heart failures were reduced by 29% compared to placebo; however, the mortality rate difference between the two groups was statistically insignificant.[40]

MYOCARDIAL INFARCTION:

Myocardial infarction (**MI**), commonly known as a **heart attack**, occurs when blood flow decreases or stops to a part of the heart, causing damage to the heart muscle.[1] The most common symptom is chest pain or discomfort which may travel into the shoulder, arm, back, neck, or jaw.[1] Often it occurs in the center or left side of the chest and lasts for more than a few minutes.[1]The discomfort may occasionally feel like heartburn.[1] Other symptoms may include shortness of breath, nausea, feeling faint, a cold sweat, or feeling tired.[1] About 30% of people have atypical symptoms.[7] Women more often have atypical symptoms than men.[10] Among those over 75 years old, about 5% have had an MI with little or no history of symptoms.[11] An MI may cause heart failure, an irregular heartbeat, cardiogenic shock, or cardiac arrest.[2][3]

Most MIs occur due to coronary artery disease.[2] Risk factors include high blood pressure, smoking, diabetes, lack of exercise, obesity, high blood cholesterol, poor diet, and excessive alcohol intake, among others.[4][5] The complete blockage of a coronary artery caused by a rupture of an atherosclerotic plaque is usually the underlying mechanism of an MI.[2] MIs are less commonly caused by coronary artery spasms, which may be due to cocaine, significant emotional stress, and extreme cold, among others.[12][13] A number of tests are useful to help with diagnosis, including electrocardiograms (ECGs), blood tests, and coronary angiography.[6] An ECG, which is a recording of the heart's electrical activity, may confirm an ST elevation MI (STEMI) if ST elevation is present.[7][14] Commonly used blood tests include troponin and less often creatine kinase MB.[6]

Treatment of an MI is time-critical.[15] Aspirin is an appropriate immediate treatment for a suspected MI.[8] Nitroglycerin or opioidsmay be used to help with chest pain; however, they do not improve overall outcomes.[7][8] Supplemental oxygen is recommended in those with low oxygen levels or shortness of breath.[8] In a STEMI, treatments attempt to restore blood flow to the heart, and include percutaneous coronary intervention (PCI), where the arteries are pushed open and may be stented, or thrombolysis, where the blockage is removed using medications.[7] People who have a non-ST elevation myocardial infarction (NSTEMI) are often managed with the blood thinner heparin, with the additional use of PCI in those at high risk.[8] In people with blockages of multiple coronary arteries and diabetes, coronary artery bypass surgery (CABG) may be recommended rather than angioplasty.[16] After an MI, lifestyle

modifications, along with long term treatment with aspirin, beta blockers, and statins, are typically recommended.[7]

Worldwide, about 15.9 million myocardial infarctions occurred in 2015.[9] More than 3 million people had an ST elevation MI and more than 4 million had an NSTEMI.[17] STEMIs occur about twice as often in men as women.[18] About one million people have an MI each year in the United States.[2] In the developed world the risk of death in those who have had an STEMI is about 10%.[7] Rates of MI for a given age have decreased globally between 1990 and 2010.[19] In 2011, AMI was one of the top five most expensive conditions during inpatient hospitalizations in the US, with a cost of about $11.5 billion for 612,000 hospital stays.[20]

Signs and symptoms[edit]

Areas where pain is experienced in myocardial infarction, showing common (dark red) and less common (light red) areas on the chest and back.

Pain [edit]

Chest pain is the most common symptom of acute myocardial infarction and is often described as a sensation of tightness, pressure, or squeezing. Pain radiates most often to the left arm, but may also radiate to the lower jaw, neck, right arm, back, and upper abdomen.[24] The pain most suggestive of an acute MI, with the highest likelihood ratio, is pain radiating to the right arm and shoulder.[25] Similarly, chest pain similar to a previous heart attack is also suggestive.[26] The pain associated with MI is usually diffuse, does not change with position, and lasts for more than 20 minutes.[22] Levine's sign, in which a person localizes the chest pain by clenching one or both fists over their sternum, has classically been thought to be predictive of cardiac chest pain, although a prospective observational study showed it had a poor positive predictive value.[27] Pain that responds to nitroglycerin does not indicate the presence or absence of a myocardial infarction.[28]

Causes[edit]

The most prominent risk factors for myocardial infarction are older age, actively smoking, high blood pressure, diabetes mellitus, and total cholesterol and high-density lipoproteinlevels.[18] Many risk factors of myocardial infarction are shared with coronary artery disease, the primary cause of myocardial infarction,[15] with other risk factors including male sex, low levels of physical activity, a past family history, obesity, and alcohol use.[15] Risk factors for myocardial disease are often included in risk factor stratification scores, such as the Framingham risk score.[18] At any given age, men are more at risk than women for the development of cardiovascular disease.[34] High levels of blood cholesterol is a known risk factor, particularly high low-density lipoprotein, low high-density lipoprotein, and high triglycerides.[35]

Many risk factors for myocardial infarction are potentially modifiable, with the most important being tobacco smoking (including secondhand smoke).[15] Smoking appears to be the cause of about 36% and obesity the cause of 20% of coronary artery disease.[36] Lack of physical activity has been linked to 7–12% of cases.[36][37] Less common causes include stress-related causes such as job stress, which accounts for about 3% of cases,[36] and chronic high stress levels.

HYPERLIPIDAEMIAS:

Hyperlipidemia is abnormally elevated levels of any or all lipids or lipoproteins in the blood.[2] It is the most common form of dyslipidemia (which includes any abnormal lipid levels).

Lipids (water-insoluble molecules) are transported in a protein capsule. The size of that capsule, or lipoprotein, determines its density. The lipoprotein density and type of apolipoproteins it contains determines the fate of the particle and its influence on metabolism.

Hyperlipidemias are divided into primary and secondary subtypes. Primary hyperlipidemia is usually due to genetic causes (such as a mutation in a receptor protein), while secondary hyperlipidemia arises due to other underlying causes such as diabetes. Lipid and lipoprotein abnormalities are common in the general population and are regarded as modifiable risk factors for cardiovascular diseasedue to their influence on atherosclerosis. In addition, some forms may predispose to acute pancreatitis.

ELECTROPHYSIOLOGY OF HEART:

Cardiac electrophysiology is the science of elucidating, diagnosing, and treating the electrical activities of the heart. The term is usually used to describe studies of such phenomena by invasive (intracardiac) catheter recording of spontaneous activity as well as of cardiac responses to programmed electrical stimulation (PES). These studies are performed to assess complex arrhythmias, elucidate symptoms, evaluate abnormal electrocardiograms, assess risk of developing arrhythmias in the future, and design treatment. These procedures increasingly include therapeutic methods (typically radiofrequency ablation, or cryoablation) in addition to diagnostic and prognostic procedures. Other therapeutic modalities employed in this field include antiarrhythmic drug therapy and implantation of pacemakers and automatic implantable cardioverter-defibrillators (AICD).[1][2]

The cardiac electrophysiology study (EPS) typically measures the response of the injured or cardiomyopathic myocardium to PES on specific pharmacological regimens in order to assess the likelihood that the regimen will successfully prevent potentially fatal sustained ventricular tachycardia (VT) or ventricular fibrillation VF (VF) in the future. Sometimes a *series* of EPS drug trials must be conducted to enable the cardiologist to select the one regimen for long-term treatment that best prevents or slows the development of VT or VF following PES. Such studies may also be conducted in the presence of a newly implanted or newly replaced cardiac pacemaker or AICD.[1]

A specialist in cardiac electrophysiology is known as a cardiac electrophysiologist, or (more commonly) simply an electrophysiologist. Cardiac electrophysiology is considered a subspecialty of cardiology in most countries and usually requires two or more years of fellowship training beyond a general cardiology fellowship. In early 2011, the Centers for Medicare and Medicaid Services (CMS) promoted cardiac electrophysiology to its own specialty category in the United States. Cardiac electrophysiologists are trained to perform interventional cardiac electrophysiology studies (EPS) as well as surgical device implantations.[1]

Cardiac electrophysiology is a relatively young subdiscipline of cardiology and internal medicine. It was developed during the mid-1970s by Hein J. J. Wellens, professor of medicine at the University of Maastricht in the Netherlands and attending cardiologist at the Academic Hospital in Maastricht. In 1980 the first microprocessor based stimulator was developed there, which led to the foundation of the Maastricht-based company CardioTek.

Author of the definitive textbook in the field is by the late Mark E. Josephson, former Robinette Professor of Medicine and chief of cardiology at the University of Pennsylvania School of Medicine in Philadelphia, Pennsylvania, professor of medicine at Harvard Medical School, and attending cardiologist at Beth Israel Deaconess Medical Center in Boston, Massachusetts.[3] The most recent published edition of *Clinical Cardiac Electrophysiology: Techniques and Interpretations* is the 4th edition in 2008.

The Heart Rhythm Society, founded in 1979, promotes education and advocacy for cardiac arrhythmia professionals (including cardiac electrophysiologists) and patients. It is the largest society in the field.

Biosense-Webster, a subsidiary of Johnson & Johnson, produces a cardiac electrophysiology system called CARTO.[4] The system is designed to visualise the real-time calculated position and orientation of a specialised RF ablation catheter within the patient's heart in order to minimise radiation exposure during fluoroscopy, increase the accuracy of targeted RF ablation and reacquisition of pacing sites for re-ablation.[5] Its navigation system calculates the position and orientation of the catheter tip, using three known magnetic sources as references. The system uses static magnetic fields that are calibrated and computer controlled. Due to the nature of magnetic fields, the orientation may also be calculated while the tip is stationary. By calculating the strength and orientation of the magnetic fields at a given location, the x,y,z position may be calculated along with the roll, pitch, yaw orientation.

ARRHYTHMIAS:

Heart arrhythmia (also known as **arrhythmia**, **dysrhythmia**, or **irregular heartbeat**) is a group of conditions in which the heartbeat is irregular, too fast, or too slow.[2] A heart rate that is too fast – above 100 beats per minute in adults – is called tachycardia and a heart rate that is too slow – below 60 beats per minute – is called bradycardia.[2] Many types of arrhythmia have no symptoms.[1] When symptoms are present these may include palpitations or feeling a pause between heartbeats.[1] In more serious cases there may be lightheadedness, passing out, shortness of breath, or chest pain.[1] While most types of arrhythmia are not serious, some predispose a person to complications such as stroke or heart failure.[2][3] Others may result in cardiac arrest.[3]

There are four main types of arrhythmia: extra beats, supraventricular tachycardias, ventricular arrhythmias, and bradyarrhythmias.[3] Extra beats include premature atrial contractions, premature ventricular contractions, and premature junctional contractions.[3] Supraventricular tachycardias include atrial fibrillation, atrial flutter, and paroxysmal supraventricular tachycardia.[3] Ventricular arrhythmias include ventricular fibrillation and ventricular tachycardia.[3][7] Arrhythmias are due to problems with the electrical conduction system of the heart.[2] Arrhythmias may occur in children; however, the normal range for the heart rate is different and depends on age.[3] A number of tests can help with diagnosis including an electrocardiogram(ECG) and Holter monitor.[5]

Most arrhythmias can be effectively treated.[2] Treatments may include medications, medical procedures such as inserting a pacemaker, and surgery.[6] Medications for a fast heart rate may include beta blockers or agents that attempt to restore a normal heart rhythm such as procainamide.[6] This latter group may have more significant side effects especially if taken for a long period of time.[6] Pacemakers are often used for slow heart rates.[6] Those with an irregular heartbeat are often treated with blood thinners to reduce the risk of complications.[6] Those who have severe symptoms from an arrhythmia may receive urgent treatment with a controlled electric shock in the form of cardioversion or defibrillation.[6]

Arrhythmia affects millions of people.[4] In Europe and North America, as of 2014, atrial fibrillation affects about 2% to 3% of the population.[8] Atrial fibrillation and atrial flutter resulted in 112,000 deaths in 2013, up from 29,000 in 1990.[9] Sudden cardiac death is the cause of about half of deaths due to cardiovascular disease or about 15% of all deaths globally.[10] About 80% of sudden cardiac death is the result of ventricular arrhythmias.[10] Arrhythmias may occur at any age but are more common among older people.[4]

It is also appropriate to classify by site of origin:

Atrial[edit]

- Sinus bradycardia
- Premature atrial contractions (PACs)
- Wandering atrial pacemaker
- Atrial tachycardia

- Multifocal atrial tachycardia
- Supraventricular tachycardia (SVT)
- Atrial flutter
- Atrial fibrillation (Afib)

Junctional arrhythmias[edit]

- AV nodal reentrant tachycardia
- Junctional rhythm
- Junctional tachycardia
- Premature junctional contraction

Ventricular[edit]

- Premature ventricular contractions (PVCs), sometimes called ventricular extra beats (VEBs)
  - Premature ventricular beats occurring after every normal beat are termed "ventricular bigeminy"
  - PVCs that occur at intervals of 2 normal beats to 1 PVC are termed "PVCs in trigeminy"
  - Three premature ventricular grouped together is termed a "run of PVCs" in general, runs lasting longer than three beats are referred to as ventricular tachycardia
- Accelerated idioventricular rhythm
- Monomorphic ventricular tachycardia
- Polymorphic ventricular tachycardia
- Ventricular fibrillation
- Torsades de pointes

Heart blocks[edit]

These are also known as AV blocks, because the vast majority of them arise from pathology at the atrioventricular node. They are the most common causes of bradycardia:

- First degree heart block, which manifests as PR prolongation
- Second degree heart block
  - Type 1 Second degree heart block, also known as Mobitz I or Wenckebach

    - Type 2 Second degree heart block, also known as Mobitz II
- Third degree heart block, also known as complete heart block.

First, second and third degree block also can occur at the level of the sinoatrial junction. This is referred to as sinoatrial block typically manifesting with various degrees and patterns of sinus bradycardia.

Sudden arrhythmic death syndrome[edit]

Sudden arrhythmic death syndrome (SADS), is a term used as part of *sudden unexpected death syndrome* to describe sudden death due to cardiac arrest brought on by an arrhythmia in the presence or absence of any structural heart disease on autopsy. The most common cause of sudden death in the US is coronary artery disease specifically because of poor oxygenation of the heart muscle, that is myocardial ischemia or a heart attack [11] Approximately 180,000 to 250,000 people die suddenly of this cause every year in the US. SADS may occur from other causes. There are many inherited conditions and heart diseases that can affect young people which can subsequently cause sudden death without advance symptoms.[12]

Causes of SADS in young people include viral myocarditis, long QT syndrome, Brugada syndrome, Catecholaminergic polymorphic ventricular tachycardia, hypertrophic cardiomyopathy and arrhythmogenic right ventricular dysplasia.[13][14]

Signs and symptoms[edit]

The term cardiac arrhythmia covers a very large number of very different conditions.

The most common symptom of an arrhythmia is an awareness of an abnormal heartbeat, called palpitations. These may be infrequent, frequent, or continuous. Some of these arrhythmias are harmless (though distracting for patients) but some of them predispose to adverse outcomes.

Some arrhythmias do not cause symptoms, and are not associated with increased mortality. However, some asymptomatic arrhythmias *are* associated with adverse events. Examples include a higher risk of blood clotting within the heart and a higher risk of insufficient blood being transported to the heart because of weak heartbeat. Other increased risks are of embolisation and stroke, heart failure and sudden cardiac death.

If an arrhythmia results in a heartbeat that is too fast, too slow or too weak to supply the body's needs, this manifests as a lower blood pressure and may cause lightheadedness or dizziness, or syncope (fainting).

Some types of arrhythmia result in cardiac arrest, or sudden death.

Medical assessment of the abnormality using an electrocardiogram is one way to diagnose and assess the risk of any given arrhythmia.

Differential diagnosis[edit]

Normal electrical activity[edit]

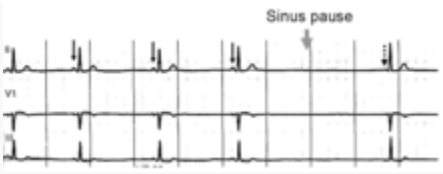
Main article: Electrical conduction system of the heart

Each heart beat originates as an electrical impulse from a small area of tissue in the right atrium of the heart called the sinus node or Sino-atrial node or SA node. The impulse initially causes both atria to contract, then activates the atrioventricular (or AV) node, which is normally the only electrical connection between the atria and the ventricles (main pumping chambers). The impulse then spreads through both ventricles via the Bundle of His and the Purkinje fibres causing a synchronised contraction of the heart muscle and, thus, the pulse.

In adults the normal resting heart rate ranges from 60 to 90 beats per minute. The resting heart rate in children is much faster. In athletes, however, the resting heart rate can be as slow as 40 beats per minute, and be considered as normal.

The term sinus arrhythmia [15] refers to a normal phenomenon of alternating mild acceleration and slowing of the heart rate that occurs with breathing in and out respectively. It is usually quite pronounced in children and steadily decreases with age. This can also be present during meditation breathing exercises that involve deep inhaling and breath holding patterns.[16]

Bradycardias[edit]



Normal sinus rhythm, with solid black arrows pointing to normal P waves representative of normal sinus node function, followed by a pause in sinus node activity (resulting in a transient

loss of heart beats). Note that the P wave that disrupts the pause (indicated by the dashed arrow) does not look like the previous (normal) P waves — this last P wave is arising from a different part of the atrium, representing an escape rhythm.

A slow rhythm (less than 60 beats/min) is labelled bradycardia. This may be caused by a slowed signal from the sinus node (sinus bradycardia), by a pause in the normal activity of the sinus node (sinus arrest), or by blocking of the electrical impulse on its way from the atria to the ventricles (AV block or heart block). Heart block comes in varying degrees and severity. It may be caused by reversible poisoning of the AV node (with drugs that impair conduction) or by irreversible damage to the node. Bradycardias may also be present in the normally functioning heart of endurance athletes or other well-conditioned persons. Bradycardia may also occur in some types of seizures.

Tachycardias[edit]

In adults and children over 15, resting heart rate faster than 100 beats per minute is labelled tachycardia. Tachycardia may result in palpitation; however, tachycardia is not *necessarily* an arrhythmia. Increased heart rate is a normal response to physical exercise or emotional stress. This is mediated by the sympathetic nervous system on the sinus node and called sinus tachycardia. Other conditions that increase sympathetic nervous system activity in the heart include ingested or injected substances, such as caffeine or amphetamines, and an overactive thyroid gland (hyperthyroidism) or anemia.

Tachycardia that is not sinus tachycardia usually results from the addition of abnormal impulses to the normal cardiac cycle. Abnormal impulses can begin by one of three mechanisms: automaticity, re-entry or triggered activity. A specialised form of re-entry which is both common and problematic is termed fibrillation.

Although the term "tachycardia" has been known for over 160 years, bases for the classification of arrhythmias are still being discussed.

RESPIRATORY SYSTEM

PULMONARY FUNCTION TESTS:

„ PFTs can be roughly divided into 5 basic components,

Spirometry

volumes

diffusing capacity

arterial blood gas

and flow-volume loops.

„ SPIROMETRY : The first component of a PFT report is spirometry which mainly provides a measure of flow. This defines whether or not the person is obstructed. We define obstruction as an FEV1/FVC ratio of less than the 5th percentile of the values obtained for normals

LUNG VOLUMES: „ We define restriction (decreased lung volume) as a reduction in the total lung capacity (TLC) to values less than the 5th percentile of the predicted value for normals „

DIFFUSION CAPACITY:In the simplest sense, the diffusing capacity is the ability of gas to

FLOW VOLUME LOOPS: „ The greatest value of the flow-volume loop is to assess for upper airway obstruction (for example, a laryngeal cancer

PLETHYSMOGRAPHY: „ Plethysmography is an alternative means of measuring lung volume which is performed by having the patient sit in a closed box and measuring the degree of intrathoracic gas compression during inhalation and exhalation plus the amount of air displaced from the box during ventilation. Lung Volumes and Capacities „ There are four basic lung volumes: „

Inspiratory reserve volume (IRV) „

Tidal volume (TV) „

Expiratory reserve volume (ERV) „

Residual volume (RV) „

In various combinations, these lung volumes then form lung capacities.

E.g., Vital capacity = IRV + TV + ERV

Indications for Pulmonary Function Testing :„

- Patients 45 years old and older who have ever smoked.
- „ Patients with prolonged or excessive cough or sputum production.
- „ Patients with a history of exposure to lung irritants.

„

Detecting pulmonary disease „

- Pulmonary symptoms – chest pain, orthopnea, cough, phlegm production, dyspnea, wheezing
- „ Physical findings – Chest wall problems, cyanosis, clubbing, decreased breath sounds „
- Abnormal labs/x-rays – ABG, Chest X-Ray
- „ Assessing disease severity and progression
- „ Pulmonary disease – COPD, Cystic fibrosis, Interstitial lung disease, Sarcoidosis „
- Cardiac disease – CHF, Congenital heart disease, Pulmonary hypertension „
- Neuromuscular disease – Amyotrophic lateral sclerosis, Guillain-Barre syndrome, Multiple sclerosis, Myasthenia gravis

Actual PFT Performance Technique:

- „ Prepare the equipment –
- find a nurse who knows (or is that nose?) what to do. „
- Patient should be seated with nose clip in place. „
- The patient needs to practice the exercise before actually performing the test. Have the patient breath in and out deeply several times. „
- Ask the patient to breath in as deeply as they can.
- The patient should place their mouth completely over the mouthpiece, not inside it.

- „ Ask the patient to blow out as fast and as quick as they can for at least six seconds. Enthusiastically coach the patient – jump, shout, get down, hoot and holler…
- "Blow, blow, come on, blow more, you can do it!"
- „ Once the patient has blown out as much as they can, ask them to then inhale as deeply as they can. „
- Repeat the whole test three times. The goal is to get a reproducible result that is consistent.
- You may need to repeat the test more than three times in order to obtain an internally valid test.

  Normal Values:
  - „ FVC is the total amount of air a person can exhale, usually measured in six seconds. „
  - 80 – 120% of predicted is a normal value „
  - 70 – 80% demonstrates mild reduction/restriction „
  - 50 – 70% demonstrates moderate reduction
  - FEF25-75 reflects small airway function „
  - >80% is normal „
  - 60 – 80% reflects mild obstruction in the small airways „
  - 40 – 60% reflects moderate obstruction „

PFT Interpretation:

„ Three steps in interpretation „

- Is the test valid? „
- Interpret the test „
- Classify severity of disease if present

Validity:

- „ The test is valid is you have good patient effort and the three tests performed are internally consistent. „

- You may notice a learning curve in that the latter tests are better performed than the former. „ Make sure that the tests are maximal effort.
- You need to be really aggressive in coaching your patient.

PFT Interpretation:

- „ Assess FVC, FEV 1, and FEV 1/FVC ratio. „
- FVC and FEV 1 normal, with a normal FEV 1/FVC ratio:
- „ Normal Test … „
- FVC decreased, FEV 1 low or normal, and a normal to high FEV 1/FVC ratio: „
- Restrictive lung disease „
- FVC normal or low, FEV 1 low, and a low FEV 1/FVC ratio: „
- Obstructive lung disease

Special Techniques:

- ✓ „ Beta Agonist Challenge „
- ✓ Methacholine Challenge „
- ✓ DLCO

Beta Agonist Challenge:

- „ Perform this when there is a suspicion that the obstructive defect may be reversible –> asthma.
- „ Give the patient a beta agonist treatment (two puffs of an albuterol MDI or an albuterol nebulizer) and repeat the PFTs several minutes later. If you notice a 12% or more increase in FEV 1, then you have diagnosed reversible airway disease/asthma.

  ASTHMA:

- „ Perform this when there is a suspicion that the obstructive defect may be reversible –> asthma. „
- Give the patient a beta agonist treatment (two puffs of an albuterol MDI or an albuterol nebulizer) and repeat the PFTs several minutes later. If you notice a 12% or more increase in FEV 1, then you have diagnosed reversible airway disease/asthma.

  Symptoms:

  - Common symptoms of asthma include:
  - Coughing
  - Wheezing
  - Tightness in the chest
  - Shortness of breath

  Causes:

  - Parents with asthma
  - Atopy
  - Childhood respiratory infections
  - Exposure to allergens or infections while the immune system is developing

  Diagnosis:

  - Based on:
  - Medical history
  - Physical examination
  - Test results

Asthma Triggers:

- A variety of things can cause asthma symptoms to appear:
  - Allergens

- Irritants
- Food and drinks
- Medicines
- Physical activity
- Upper respiratory infections (viral)

Asthma prevalence:

- In the United States:
  - More females than males have asthma.
  - Blacks and American Indian/Alaska natives have higher percentages of asthma than Whites, Hispanics, and Asians.

Asthma disparities:

- Death from asthma is 3 times more likely to occur among Blacks than Whites.
- Among adults, women of all races have higher rates of illness and death from asthma than men.
- Rates of hospitalization for asthma for Blacks are almost triple those for Whites.

Increasing rates:

- Asthma rates have been increasing in the United States for both adults and children, males and females, and in the different races and ethnicities.
- It is estimated that the number of people with asthma worldwide will increase by 25% in the next 15 years.

Worldwide Burden of Asthma:

- 300 million people suffer from asthma worldwide.

- 255,000 asthma deaths in 2005.
    - ~3,500 in the United States.
- Over 80% of asthma deaths occur in low and lower-middle income countries.

Treatment:

- Medication
    - Long term
        - Inhaled corticosteroid
        - Leukotriene modifiers
        - Long-acting beta agonists
        - Combination inhalers
    - Quick relief (rescue) medications
        - Short-acting beta agonists
        - Ipratropium
        - Oral and intravenous corticosteroids
    - Bronchial thermoplasty
    - Recognizing, tracking, and avoiding triggers

CHRONIC OBSTRUCTIVE AIRWAYS DISEASE:

Chronic obstructive pulmonary disease (**COPD**) is a type of obstructive lung disease characterized by long-term breathing problems and poor airflow.[1][8] The main symptoms include shortness of breath and cough with sputum production.[1] COPD is a progressive disease, meaning it typically worsens over time.[9] Eventually everyday activities,

such as walking or getting dressed, become difficult.[3] **Chronic bronchitis** and **emphysema** are older terms used for different types of COPD.[3][10] The term "chronic bronchitis" is still used to define a productive cough that is present for at least three months each year for two years.[1]

Tobacco smoking is the most common cause of COPD, with factors such as air pollution and genetics playing a smaller role.[2]In the developing world, one of the common sources of air pollution is poorly vented heating and cooking fires.[3] Long-term exposure to these irritants causes an inflammatory response in the lungs, resulting in narrowing of the small airways and breakdown of lung tissue.[5] The diagnosis is based on poor airflow as measured by lung function tests.[4] In contrast to asthma, the airflow reduction does not improve much with the use of a bronchodilator.[3]

Most cases of COPD can be prevented by reducing exposure to risk factors.[11] This includes decreasing rates of smoking and improving indoor and outdoor air quality.[3] While treatment can slow worsening, no cure is known.[3] COPD treatments include smoking cessation, vaccinations, respiratory rehabilitation, and often inhaled bronchodilators and steroids.[2] Some people may benefit from long-term oxygen therapy or lung transplantation.[5] In those who have periods of acute worsening, increased use of medications and hospitalization may be needed.[2]

As of 2015, COPD affected about 174.5 million (2.4%) of the global population.[6] It typically occurs in people over the age of 40.[3] Males and females are affected equally commonly.[3] In 2015, it resulted in 3.2 million deaths, up from 2.4 million deaths in 1990.[7][12] More than 90% of these deaths occur in the developing world.[3] The number of deaths is projected to increase further because of higher smoking rates in the developing world, and an aging population in many countries.[13] It resulted in an estimated economic cost of $2.1 trillion in 2010.

Signs and symptoms

The most common symptoms of COPD are sputum production, shortness of breath, and a productive cough.[15] These symptoms are present for a prolonged period of time[16] and typically worsen over time.[5] It is unclear whether different types of COPD exist.[2] While previously divided into emphysema and chronic bronchitis, emphysema is only a description of lung

changes rather than a disease itself, and chronic bronchitis is simply a descriptor of symptoms that may or may not occur with COPD.

Cough[edit]

A chronic cough is often the first symptom to develop. When it persists for more than three months each year for at least two years, in combination with sputum production and without another explanation, it is by definition chronic bronchitis. This condition can occur before COPD fully develops. The amount of sputum produced can change over hours to days. In some cases, the cough may not be present or may only occur occasionally and may not be productive. Some people with COPD attribute the symptoms to a "smoker's cough". Sputum may be swallowed or spat out, depending often on social and cultural factors. Vigorous coughing may lead to rib fractures or a brief loss of consciousness. Those with COPD often have a history of "common colds" that last a long time.[15]

Shortness of breath[edit]

Shortness of breath is often the symptom that most bothers people.[17] It is commonly described as: "my breathing requires effort," "I feel out of breath," or "I can't get enough air in".[18] Different terms, however, may be used in different cultures.[15] Typically the shortness of breath is worse on exertion of a prolonged duration and worsens over time.[15] In the advanced stages, or end stage pulmonary disease it occurs during rest and may be always present.[19][20] It is a source of both anxiety and a poor quality of life in those with COPD.[15] Many people with more advanced COPD breathe through pursed lips and this action can improve shortness of breath in some.[21][22]

Other symptoms[edit]

In COPD, breathing out may take longer than breathing in.[23] Chest tightness may occur,[15] but is not common and may be caused by another problem.[17] Those with obstructed airflow may have wheezing or decreased sounds with air entry on examination of the chest with a stethoscope.[23] A barrel chest is a characteristic sign of COPD, but is relatively uncommon.[23] Tripod positioning may occur as the disease worsens.[16]

Advanced COPD leads to high pressure on the lung arteries, which strains the right ventricle of the heart.[5][24][25] This situation is referred to as cor pulmonale, and leads to symptoms of leg

swelling[15] and bulging neck veins.[5] COPD is more common than any other lung disease as a cause of cor pulmonale.[24] Cor pulmonale has become less common since the use of supplemental oxygen.[16]

COPD often occurs along with a number of other conditions, due in part to shared risk factors.[2] These conditions include ischemic heart disease, high blood pressure, diabetes mellitus, muscle wasting, osteoporosis, lung cancer, anxiety disorder, sexual dysfunction, and depression.[2][26] In those with severe disease, a feeling of always being tired is common.[15] Fingernail clubbing is not specific to COPD and should prompt investigations for an underlying lung cancer.[27]

Exacerbation[edit]

An acute exacerbation of COPD is defined as increased shortness of breath, increased sputum production, a change in the color of the sputum from clear to green or yellow, or an increase in cough in someone with COPD.[23] They may present with signs of increased work of breathing such as fast breathing, a fast heart rate, sweating, active use of muscles in the neck, a bluish tinge to the skin, and confusion or combative behavior in very severe exacerbations.[23][28] Crackles may also be heard over the lungs on examination with a stethoscope.

SMOKING:

The primary risk factor for COPD globally is tobacco smoking.[9] Of those who smoke, about 20% will get COPD,[31] and of those who are lifelong smokers, about half will get COPD.[32] In the United States and United Kingdom, of those with COPD, 80–95% are either current smokers or previously smoked.[31][33][34] The likelihood of developing COPD increases with the total smoke exposure.[35] Additionally, women are more susceptible to the harmful effects of smoke than men.[34] In nonsmokers, secondhand smoke is the cause of about 20% of cases.[33] Other types of smoke, such as, marijuana, cigar, and water-pipe smoke, also confer a risk.[9] Water-pipe smoke appears to be as harmful as smoking cigarettes.[36] Problems from marijuana smoke may only be with heavy use.[37] Women who smoke during pregnancy may increase the risk of COPD in their child.[9] For the same amount of cigarette smoking, women have a higher risk of COPD than men.

Air pollution[edit]

Poorly ventilated cooking fires, often fueled by coal or biomass fuels such as wood and dung, lead to indoor air pollution and are one of the most common causes of COPD in developing countries.[39] These fires are a method of cooking and heating for nearly 3 billion people, with their health effects being greater among women due to more exposure.[9][39] They are used as the main source of energy in 80% of homes in India, China and sub-Saharan Africa.[11]

People who live in large cities have a higher rate of COPD compared to people who live in rural areas.[40] While urban air pollution is a contributing factor in exacerbations, its overall role as a cause of COPD is unclear.[9] Areas with poor outdoor air quality, including that from exhaust gas, generally have higher rates of COPD.[11] The overall effect in relation to smoking, however, is believed to be small.

Occupational exposures[edit]

Intense and prolonged exposure to workplace dusts, chemicals, and fumes increases the risk of COPD in both smokers and nonsmokers.[41] Workplace exposures are believed to be the cause in 10–20% of cases.[42] In the United States, they are believed to be related to more than 30% of cases among those who have never smoked and probably represent a greater risk in countries without sufficient regulations.[9]

A number of industries and sources have been implicated, including[11] high levels of dust in coal mining, gold mining, and the cotton textile industry, occupations involving cadmiumand isocyanates, and fumes from welding.[41] Working in agriculture is also a risk.[11] In some professions, the risks have been estimated as equivalent to that of one-half to two packs of cigarettes a day.[43] Silica dust and fiberglass dust exposure can also lead to COPD, with the risk unrelated to that for silicosis.[44][45] The negative effects of dust exposure and cigarette smoke exposure appear to be additive or possibly more than additive.[43]

Genetics:

Genetics play a role in the development of COPD.[9] It is more common among relatives of those with COPD who smoke than unrelated smokers.[9] Currently, the only clearly inherited risk factor is alpha 1-antitrypsin deficiency (AAT).[46] This risk is particularly high if someone

deficient in alpha 1-antitrypsin also smokes.[46] It is responsible for about 1–5% of cases[46][47] and the condition is present in about three to four in 10,000 people.[16] Other genetic factors are being investigated,[46] of which many are likely

Drug-induced pulmonary disease:

Drug-induced pulmonary disease is lung disease brought on by a bad reaction to a medicine. Pulmonary means related to the lungs.

Causes

Many types of lung injury can result from medicines. It is usually impossible to predict who will develop lung disease from a medicine.

Types of lung problems or diseases that may be caused by medicines include:

- Allergic reactions -- asthma, hypersensitivity pneumonitis, or eosinophilic pneumonia
- Bleeding into the lung air sacs, called alveoli (alveolar hemorrhage)
- Swelling and inflamed tissue in the main passages that carry air to the lungs (bronchitis)
- Damage to lung tissue (interstitial fibrosis)
- Drugs that cause the immune system to mistakenly attack and destroy healthy body tissue, such as drug-induced lupus erythematosus
- Granulomatous lung disease -- a type of inflammation in the lungs
- Inflammation of the lung air sacs (pneumonitis or infiltration)
- Lung vasculitis (inflammation of lung blood vessels)
- Lymph node swelling
- Swelling and irritation (inflammation) of the chest area between the lungs (mediastinitis)
- Abnormal buildup of fluid in the lungs (pulmonary edema)
- Buildup of fluid between the layers of tissue that line the lungs and chest cavity (pleural effusion).

Many medicines and substances are known to cause lung disease in some people. These include:

- Antibiotics, such as nitrofurantoin and sulfa drugs
- Heart medicines, such as amiodarone
- Chemotherapy drugs such as bleomycin, cyclophosphamide, and methotrexate
- Street drugs

Symptoms

Symptoms may include any of the following:

- Bloody sputum
- Chest pain
- Cough
- Fever
- Shortness of breath
- Wheezing

Exams and Tests

The health care provider will perform a physical exam and listen to your chest and lungs with a stethoscope. Abnormal breath sounds may be heard.

Tests that may be done include:

- Arterial blood gases
- Blood test to check for an autoimmune disorder
- Blood chemistry
- Bronchoscopy
- Complete blood count with blood differential
- Chest CT scan
- Chest x-ray

- Lung biopsy (in rare cases)
- Lung function tests
- Thoracentesis (if pleural effusion is present)

Treatment

The first step is to stop the medicine that is causing the problem. Other treatments depend on your specific symptoms. For example, you may need oxygen until the drug-induced lung disease improves. Anti-inflammatory medicines called corticosteroids are most often used to quickly reverse the lung inflammation.

Outlook (Prognosis)

Acute episodes usually go away within 48 to 72 hours after the medicine has been stopped. Chronic symptoms may take longer to improve.
Some drug-induced lung diseases, such as pulmonary fibrosis, may never go away and can worsen, even after the medicine or substance is stopped.

Possible Complications

Complications that may develop include:

- Diffuse interstitial pulmonary fibrosis
- Hypoxemia (low blood oxygen)
- Respiratory failure

When to Contact a Medical Professional

Call your provider if you develop symptoms of this disorder.

Prevention

Note any past reaction you have had to a medicine, so that you can avoid the medicine in the future. Wear a medical alert bracelet if you have known drug reactions. Stay away from street drugs.

ENDOCRINE SYSTEM

DIABETIS:

Diabetes is a chronic disease that occurs when the pancreas does not produce enough insulin (a hormone that regulates blood sugar) or alternatively, when the body cannot effectively use the insulin it produces.

The overall risk of dying among people with diabetes is at least double the risk of their peers without diabetes.

DIABETES Type 1 diabetes is characterized by a lack of insulin production. Without daily administration of insulin, type 1 diabetes is rapidly fatal.

- Type 2 diabetes results from the body's ineffective use of insulin.
- About 90% of people with diabetes around the world have type 2.
- It is largely the result of excess body weight and physical inactivity.
- More than 220 million people worldwide diabetes had in 2004.

• WHO projects that diabetes deaths will double between 2005 and 2030.

• Almost half of diabetes deaths occur in people under the age of 70 years.

• Almost 80% of diabetes deaths occur in low and middle-income countries. Health implications Elevated blood sugar is a common effect of uncontrolled diabetes, and over time can damage the heart, blood vessels, eyes, kidneys, and nerves.

Some health complications from diabetes include:

• Diabetic retinopathy is a significant cause of blindness, and occurs as a result of long- term accumulated damage to the small blood vessels in the retina. After 15 years of diabetes about 10% of patients develop severe visual impairment.

• Diabetic neuropathy is damage to the nerves as a result of diabetes, and affects up to 50% of people with diabetes. Common symptoms are tingling, pain, numbness, or weakness in the feet and hands.

• Combined with reduced blood flow, neuro- pathy in the feet increases the chance of foot ulcers and eventual limb amputation.

• Diabetes is among the leading causes of kidney failure; 10-20% of people with diabetes die of kidney failure.

• Diabetes increases the risk of heart disease and stroke; 50% of people with diabetes die of cardiovascular disease (primarily heart disease and stroke).

The Economic Implications:

Diabetes and its complications impose significant economic consequences on individuals, families, health systems and countries.

• People living with diabetes and their families feel the impact of diabetes most directly, often through the expenses of diabetes treatment and loss of family income when diabetes interferes with work.

Prevention Without urgent action, diabetes-related deaths will increase by more than 50% in the next 10 years. To help prevent type 2 diabetes and its complications, people should:

• Achieve and maintain healthy body weight.

• Be physically active - at least 30 minutes of regular, moderate-intensity activity on most days.

• Early diagnosis can be accomplished through relatively inexpensive blood testing.

• Treatment of diabetes involves lowering blood sugar and the levels of other known risk factors that damage blood vessels.

• Tobacco cessation is also important to avoid complications.

Control of diabetes

• People with type 1 diabetes require insulin; people with type 2 diabetes can be treated with oral medication, but may also require insulin.

• Blood pressure control

• Foot care Other cost saving interventions include:

• Screening and treatment for retinopathy (which causes blindness);

• Blood lipid control (to regulate cholesterol levels);

• Screening for early signs of diabetes-related kidney disease and treatment. These measures should be supported by a healthy diet, regular physical activity, maintaining a normal body weight and avoiding tobacco use.

WHO aims to stimulate and support the adoption of effective measures for the surveillance, prevention and control of diabetes and its complications, through a primary health care approach, particularly in low-and middle-income countries.

The WHO Global Strategy on Diet, Physical Activity and Health complements WHO's diabetes work by focusing on population-wide approaches to promote healthy diet and regular physical activity, thereby reducing the growing global problem of overweight and obesity.

THYROID DISEASES:

The WHO Global Strategy on Diet, Physical Activity and Health complements WHO's diabetes work by focusing on population-wide approaches to promote healthy diet and regular physical activity, thereby reducing the growing global problem of overweight and obesity.

FUNCTION OF THYROID GLAND:

The WHO Global Strategy on Diet, Physical Activity and Health complements WHO's diabetes work by focusing on population-wide approaches to promote healthy diet and regular physical activity, thereby reducing the growing global problem of overweight and obesity.

DIAGNOSIS OF THYROID DISEASE:

The WHO Global Strategy on Diet, Physical Activity and Health complements WHO's diabetes work by focusing on population-wide approaches to promote healthy diet and regular physical activity, thereby reducing the growing global problem of overweight and obesity.

TESTS USED TO DIAGNOSE THYROID DISEASES:

- Blood tests
- Ultrasound exam of thyroid
- Thyroid scan

Signs and symptoms

Symptoms of the condition vary with type: hypo- vs. hyperthyroidism, which are further described below.

Possible symptoms of hypothyroidism are:[12][13]

- Tiredness

- Unexplained weight gain
- Slow movement
- Muscle cramps
- Slow heart rate (bradycardia)
- Sensitivity to cold temperatures
- Constipation
- Depressed mood
- Memory difficulty

Possible symptoms of hyperthyroidism are:[14]

- Difficulty sleeping (insomnia)
- Unexplained weight loss
- Tremors
- Fast heart rate (tachycardia) or palpitations
- Sensitivity to hot temperatures, excess sweating
- Diarrhea
- Anxiety, irritability

Note: certain symptoms and physical changes can be seen in both hypothyroidism and hyperthyroidism —fatigue, fine / thinning hair, menstrual cycle irregularities, muscle weakness / aches (myalgia), and different forms of myxedema.

ORAL CONTRACEPTIVES:

Oral contraceptives, abbreviated **OCPs**, also known as **birth control pills**, are medications taken by mouth for the purpose of birth control.

Female[edit]

Two types of female oral contraceptive pill, taken once per day, are widely available:

- The combined oral contraceptive pill contains estrogen and a progestin
- The progestogen-only pill
- Ormeloxifene is a selective estrogen receptor modulator which offers the benefit of only having to be taken once a week.

Emergency contraception pills ("morning after pills") are taken at the time of intercourse, or within a few days afterwards:

- Levonorgestrel, sold under the brand name **Plan B**
- Ulipristal acetate
- Mifepristone and misoprostol, when used in combination, are more than 95% effective during the first 50 days of pregnancy. The combination is administered by a physician, and is only used as a last resort

Male[edit]

- Male oral contraceptives are currently not available commercially, although several possibilities are in various stages of research and development.

HORMONE REPLACEMENT THERAPY:

Hormone replacement therapy (**HRT**), also known as **menopausal hormone therapy** (**MHT**) or **postmenopausal hormone therapy** (**PHT**, **PMHT**), is a form of hormone therapywhich is used to treat symptoms associated with menopause in women.[1][2] These symptoms can include hot flashes, vaginal atrophy and dryness, and bone loss, among others, and are caused by diminished levels of sex hormones in the menopausal period.[1][2] The main hormonal medications used in HRT for menopausal symptoms are estrogens and progestogens.[3] A progestogen is usually used in combination with an estrogen in women with intact uteruses because unopposed estrogen therapy is associated with endometrial hyperplasia and cancer and progestogens prevent these risks.[3][4][5] Androgens like testosterone are sometimes used in HRT as well.[6] HRT medications are available in various forms and for use by a variety of different routes of administration.[3]

The 2002 Women's Health Initiative (WHI) of the National Institutes of Health (NIH) found disparate results for all cause mortality with HRT, finding it to be lower when HRT was begun earlier, between age 50 to 59, but higher when begun after age 60. In older patients, there was an increased incidence of breast cancer, heart attacks and stroke, although a reduced incidence of colorectal cancer and bone fracture.[7] Some of the WHI findings were again found in a larger national study done in the United Kingdom, known as the Million Women Study (MWS). As a

result of these findings, the number of women taking HRT dropped precipitously.[8] The WHI recommended that women with non-surgical menopause take the lowest feasible dose of HRT for the shortest possible time to minimize associated risks.[7]

The current indications for use from the United States Food and Drug Administration (FDA) include short-term treatment of menopausal symptoms, such as vasomotor hot flashes or vaginal atrophy, and prevention of osteoporosis.[9] In 2012 and 2017, the United States Preventive Task Force (USPSTF) concluded that the harmful effects of combined estrogen and progestin therapy are likely to exceed the chronic disease prevention benefits in most women.[10][11][12] A consensus expert opinion published by The Endocrine Society stated that when taken during perimenopause, or the initial years of menopause, HRT carries significantly fewer risks than previously published, and reduces all cause mortality in most patient scenarios.[13] The American Association of Clinical Endocrinologists (AACE) also released a position statement in 2009 that approved of HRT in appropriate clinical scenarios.

Medical uses[edit]

HRT is used to treat or prevent menopausal symptoms in postmenopausal, perimenopausal, and surgically menopausal women, including the following:[1][2]

- Hot flashes (vasomotor symptoms)
- Vulvovaginal atrophy (atrophic vaginitis; including vaginal dryness)
- Dyspareunia (painful sexual intercourse, due to vaginal atrophy and lack of vaginal lubrication)
- Bone loss (decreased bone mineral density, which can eventually lead to osteopenia, osteoporosis, and associated bone fractures)
- Decreased sexual desire
- Defeminization (e.g., diminished feminine fat distribution, worsened skin appearance and accelerated skin aging)[14][15]
- Additional symptoms such as sleep disturbances, joint pain, and possibly others

It is also used for health benefits, such as reduced risk of dementia, colorectal cancer, endometrial cancer, and others. However, this may be counterbalanced by various health risks, like an increased risk of cardiovascular disease and breast cancer.

HRT is often given as a short-term relief (often one or two years, usually less than five) from menopausal symptoms (such as hot flashes, irregular menstruation). Such treatments aren't usually recommended to women who are perimenopausal or for at least 12 months after the last menstrual period.[16] Younger women with premature ovarian failure or surgical menopause may use HRT for many years, until the age that natural menopause would be expected to occur.

Contraindications[edit]

Absolute contraindications[edit]

- Undiagnosed vaginal bleeding
- Severe liver disease
- Pregnancy
- Coronary artery disease
- Well-differentiated and early endometrial cancer (once treatment for the malignancy is complete, is no longer an absolute contraindication). Progestogens alone may relieve symptoms if the patient is unable to tolerate estrogens.
- Recent deep vein thrombosis or stroke

Relative contraindications[edit]

- Migraine headaches
- Personal history of breast cancer
- Personal history of ovarian cancer
- Venous thrombosis
- History of uterine fibroids
- Atypical ductal hyperplasia of the breast
- Active gallbladder disease (cholangitis, cholecystitis)

Side effects[edit]

Common symptoms

- Headache

Uncommon symptoms

- Double vision

- Upset stomach, stomach cramps or bloating
- Diarrhea
- Appetite and weight changes
- Changes in sex drive or performance
- Nervousness
- Brown or black patches on the skin
- Acne
- Swelling of hands, feet, or lower legs due to fluid retention
- Changes in menstrual flow
- Breast tenderness, enlargement, or discharge
- Sudden difficulty wearing contact lenses
- Severe abdominal pain
- Yellowing of skin or eyes
- Severe depression
- Unusual bleeding
- Loss of appetite
- Skin rash
- Lassitude
- Fever
- Dark-colored urine
- Light colored stool
- Chorea[37]

Health effects[edit]

A 2017 pooled analysis of data from five observational cohort studies in Swedish women found a reduction in risk of stroke among women who started hormone replacement therapy within five years of onset of menopause.[38] Demographically, the vast majority of data available is in postmenopausal American women with concurrent pre-existing conditions, and with a mean age of over 60 years.[39]

The North American Menopause Society (NAMS) 2016 annual meeting mentioned that HRT may have more benefits than risks when it comes to females under the age of 60 years old.[40]

In 2002 the WHI was published. That study looked at the effects of hormonal replacement therapy in postmenopausal women. Both age groups had a slightly higher incidence of breast cancer, and both heart attack and stroke were increased in older patients, although not in younger participants. In fact, the use of HRT in the United States has actually dropped greatly since 2002.[41] Breast cancer was increased in women treated with estrogen and a progestin, but not with estrogen and progesterone or estrogen alone.[42][43][44]Treatment with unopposed estrogen (i.e., an estrogen alone without a progestogen) is contraindicated if the uterus is still present, due

to its proliferative effect on the endometrium. The WHI also found a reduced incidence of colorectal cancer when estrogen and a progestogen were used together, and most importantly, a reduced incidence of bone fractures. Ultimately, the study found disparate results for all cause mortality with HRT, finding it to be lower when HRT was begun during ages 50–59, but higher when begun after age 60.[7]Some findings of the WHI were reconfirmed in a larger national study done in the United Kingdom, known as MWS. Coverage of the WHI findings led to a reduction in the number of postmenopausal women on HRT.[45] The authors of the study recommended that women with non-surgical menopause take the lowest feasible dose of HRTHRT, and for the shortest possible time, to minimize risk.[7]

The data published by the WHI suggested supplemental estrogen increased risk of venous emboli and breast cancer but was protective against osteoporosis and colorectal cancer, while the impact on cardiovascular disease was mixed.[46] These results were later confirmed in trials from the United Kingdom, but not in more recent studies from France and China. Genetic polymorphism appears to be associated with inter-individual variability in metabolic response to HRT in postmenopausal women.[47][48]

These recommendations have not held up with further data analysis, however. Subsequent findings released by the WHI showed that all cause mortality was not dramatically different between the groups receiving CEEs, those receiving estrogen and a progestogen, and those not on HRT at all. Specifically, the relative risk for all-cause mortality was 1.04 (confidence interval 0.88–1.22) in the CEEs-alone trial and 1.00 (CI, 0.83–1.19) in the estrogen plus progestogen trial.[49] Further, in analysis pooling data from both trials, postmenopausal HRT was associated with a significant reduction in mortality (RR, 0.70; CI, 0.51–0.96) among women ages 50 to 59. This would represent five fewer deaths per 1,000 women per 5 years of therapy.

Sexual dysfunction[edit]

See also: Testosterone (medication) § Women

Menopause is the permanent cessation of menstruation resulting from loss of ovarian follicular activity.[5] Menopause can be divided into early and late transition periods, also known as perimenopause and postmenopause. Each stage is marked by changes in hormonal patterns, which can induce menopausal symptoms.[5] It is possible to induce menopause prematurely by surgically removing the ovary or ovaries (oophorectomy). This is often done as a consequence of

ovarian failure, such as ovarian or uterine cancers. The most common side effects of the menopausal transition are: lack of sexual desire or libido, lack of sexual arousal, and vaginal dryness.[5] The modification of women's physiology can lead to changes in her sexual response, the development of sexual dysfunctions, and changes in her levels of sexual desire.[62]

It is commonly perceived that once women near the end of their reproductive years and enter menopause that this equates to the end of her sexual life.[5] However, especially since women today are living one third or more of their lives in a postmenopausal state, maintaining, if not improving, their quality of life, of which their sexuality can be a key determinant, is of importance.[63] A recent study of sexual activities among women aged 40–69 revealed that 75% of women are sexually active at this age; this indicates that the sexual health and satisfaction of menopausal women are an aspect of sexual health and quality of life that is worthy of attention by health care professionals.[5]

A major complaint among postmenopausal women is decreased libido, and many may seek medical consultation for this.[6] Several hormonal changes take place during the menopausal period, including a decrease in estrogen levels and an increase in follicle-stimulating hormone. For most women, the majority of change occurs during the late perimenopausal and postmenopausal stages.[5] Decrease in other hormones such as the sex hormone-binding globulim (SHBG) and inhibin (A and B) also take place in the postmenopausal period. Testosterone, a hormone more commonly associated with males, is also present in women. It peaks at age 30, but declines with age, so there is little variation across the lifetime and during the menopausal transition.[5] However, in surgically induced menopause, instead of the levels of estrogens and testosterone slowly declining over time, they decline very sharply, resulting in more severe symptoms.[5]

In menopausal women, sexual functioning can impact several dimensions of a woman's life, including her physical, psychological, and mental well-being.[64] During the onset of menopause, sexuality can be a critical issue in determining whether one begins to experience changes in their sexual response cycle.[65] Both age — and menopause-related events can affect the integrity of a woman's biological systems involved in the sexual response cycle, which include hormone environment, neuro-muscular substrates, and vascular supplies.[65] Therefore, it can be

appropriate to make use of HRT, especially in women with low or declining quality of life due to sexual difficulties.

Cardiovascular effects[edit]

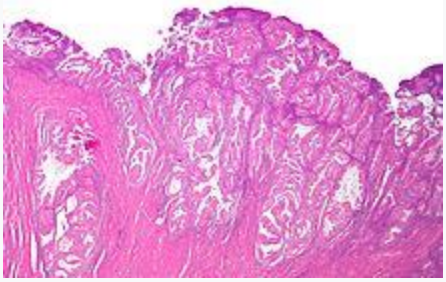
The impact of HRT on cardiovascular morbidity is a subject of much controversy in the medical literature. The reduced risk of cardiovascular diseases associated with HRT, reported in observational studies, has not been subsequently confirmed in randomized clinical trials. The increased risk of cardiovascular disease in the WHI was not statistically significant, and only found in the oldest women, and those who started HRT late after menopause began.[68] The increase in risks of coronary heart disease in the treatment arm of the study varied according to age and years since onset of menopause. Women aged 50 to 59 using HRT showed a trend towards lower risk of coronary heart disease,[69] as did women who were within five years of the onset of menopause.[70]

A Cochrane review came to the result that in women starting HRT less than 10 years after menopause have a lower mortality and lower rate of coronary heart disease compared to placebo or no treatment, without any strong evidence of an effect on the risk of stroke. Those starting therapy more than 10 years after menopause have little effect on mortality and coronary heart disease, but have an increased risk of stroke. Overall, however, taking the increased risk of venous thromboembolism into account, it came to the conclusion that has HRT has little if any benefit for primary or secondary prevention of cardiovascular disease.[71]

The adverse cardiovascular outcomes may only apply to oral dosing with CEEs and progestins in oral systemic therapy, while transdermal estradiol and estriol may not produce the same risks, due to the absence of anabolic effects of hepatic vitamin K dependent clotting factors.[67]

On a molecular level, HRT at the time of menopause has effects on the lipid profile. Specifically, HDL decreases, while LDL, triglycerides and lipoprotein a increase. Supplemental estrogen improves the lipid profile by reversing each of these effects. Beyond this, it improves cardiac contractility, coronary artery blood flow, metabolism of carbohydrates, and decreases platelet aggregation and plaque formation. At the molecular level HRT may promote reverse cholesterol transport (RCT) via the induction of cholesterol ABC transporters.[72]

Endometrial effects[edit]



Endometrial tumor on histology. Most commonly, the tumor is *in situ*with minimal morbidity; patients still have lower all-cause mortality than those not on HRT.

While combined estrogen–progestogen supplementation has been linked to an increased incidence of endometrial cancer, the specific subtype is usually stage I, or *in situ*, and has extremely low morbidity and mortality, and studies in American women have shown the tumor to not have propensity for growth into the myometrium or parametrial soft tissues. When seen in the context of all cause mortality, women who take estrogen and develop endometrial cancer have higher survival rates than women who do not take hormonal therapy at all, which was due to the preventive effect of HRT on hip fractures.

Unopposed estrogen can also result in endometrial hyperplasia, a precursor to endometrial cancer. The extensive use of high-dose estrogens for birth control in the 1970s is thought to have resulted in a significant increase in the incidence of this type of cancer.[73]

Musculoskeletal effects[edit]

HRT is effective at reversing the effects of aging on muscle.

OSTEOPOROSIS:

Osteoporosis is a disease where increased bone weakness increases the risk of a broken bone.[3] It is the most common reason for a broken bone among the elderly.[3] Bones that commonly break include the vertebrae in the spine, the bones of the forearm, and the hip.[8] Until a broken bone occurs there are typically no symptoms.[3] Bones may weaken to such a degree

that a break may occur with minor stress or spontaneously.[3] Chronic pain and a decreased ability to carry out normal activities may occur following a broken bone.[3]

Osteoporosis may be due to lower than normal maximum bone mass and greater than normal bone loss.[3] Bone loss increases after menopause due to lower levels of estrogen.[3] Osteoporosis may also occur due to a number of diseases or treatments
including alcoholism, anorexia, hyperthyroidism, kidney disease, and surgical removal of the ovaries.[3] Certain medications increase the rate of bone loss including some antiseizure medications, chemotherapy, proton pump inhibitors, selective serotonin reuptake inhibitors, and glucocorticosteroids.[3] Smoking and too little exercise are also risk factors.[3] Osteoporosis is defined as a bone density of 2.5 standard deviations below that of a young adult.[4] This is typically measured by dual-energy X-ray absorptiometry.[4]

Prevention of osteoporosis includes a proper diet during childhood and efforts to avoid medications that increase the rate of bone loss.[3] Efforts to prevent broken bones in those with osteoporosis include a good diet, exercise, and fall prevention.[3] Lifestyle changes such as stopping smoking and not drinking alcohol may help.[3] Biphosphonate medications are useful in those with previous broken bones due to osteoporosis.[5][6] In those with osteoporosis but no previous broken bones they are less effective.[5][6][9] A number of other medications may also be useful.[3][10]

Osteoporosis becomes more common with age.[3] About 15% of white people in their 50s and 70% of those over 80 are affected.[7] It is more common in women than men.[3] In the developed world, depending on the method of diagnosis, 2% to 8% of males and 9% to 38% of females are affected.[11] Rates of disease in the developing world are unclear.[12] About 22 million women and 5.5 million men in the European Union had osteoporosis in 2010.[13] In the United States in 2010, about eight million women and one to two million men had osteoporosis.[11][14] White and Asian people are at greater risk.[3] The word osteoporosis is from the Greek terms for "porous bones"

Signs and symptoms[edit]

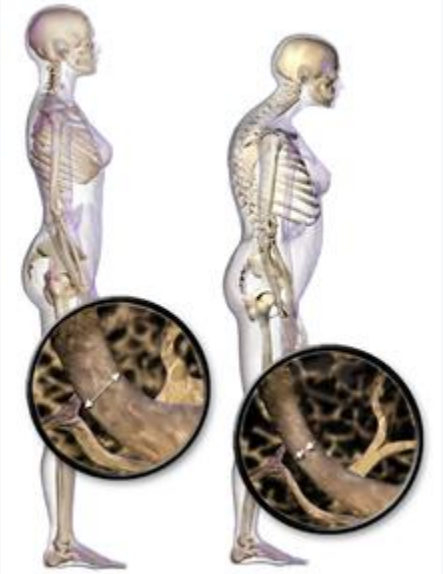


Illustration depicting normal standing posture and osteoporosis

Osteoporosis itself has no symptoms; its main consequence is the increased risk of bone fractures. Osteoporotic fractures occur in situations where healthy people would not normally break a bone; they are therefore regarded as fragility fractures. Typical fragility fractures occur in the vertebral column, rib, hip and wrist.

Fractures[edit]

Fractures are the most dangerous aspect of osteoporosis. Debilitating acute and chronic pain in the elderly is often attributed to fractures from osteoporosis and can lead to further disability and early mortality.[16] These fractures may also be asymptomatic. The most common osteoporotic fractures are of the wrist, spine, shoulder and hip. The symptoms of a vertebral collapse ("compression fracture") are sudden back pain, often with radicular pain (shooting pain due to nerve root compression) and rarely with spinal cord compression or cauda equina syndrome. Multiple vertebral fractures lead to a stooped posture, loss of height, and chronic pain with resultant reduction in mobility.[17]

Fractures of the long bones acutely impair mobility and may require surgery. Hip fracture, in particular, usually requires prompt surgery, as serious risks are associated with it, such as deep vein thrombosis and pulmonary embolism, and increased mortality.

Fracture risk calculators assess the risk of fracture based upon several criteria, including bone mineral density, age, smoking, alcohol usage, weight, and gender. Recognized calculators include FRAX[18] and Dubbo.

The term "established osteoporosis" is used when a broken bone due to osteoporosis has occurred.[19] Osteoporosis is a part of frailty syndrome.

Falls risk[edit]

The increased risk of falling associated with aging leads to fractures of the wrist, spine, and hip. The risk of falling, in turn, is increased by impaired eyesight due to any cause (e.g. glaucoma, macular degeneration), balance disorder, movement disorders (e.g. Parkinson's disease), dementia, and sarcopenia (age-related loss of skeletal muscle). Collapse(transient loss of postural tone with or without loss of consciousness) leads to a significant risk of falls; causes of syncope are manifold, but may include cardiac arrhythmias (irregular heart beat), vasovagal syncope, orthostatic hypotension (abnormal drop in blood pressure on standing up), and seizures. Removal of obstacles and loose carpets in the living environment may substantially reduce falls. Those with previous falls, as well as those with gait or balance disorders, are most at risk.[20]

Risk factors[edit]

Risk factors for osteoporotic fracture can be split between nonmodifiable and (potentially) modifiable. In addition, osteoporosis is a recognized complication of specific diseases and disorders. Medication use is theoretically modifiable, although in many cases, the use of medication that increases osteoporosis risk may be unavoidable. Caffeine is not a risk factor for osteoporosis.[21]

It is more likely in females than males

Medication[edit]

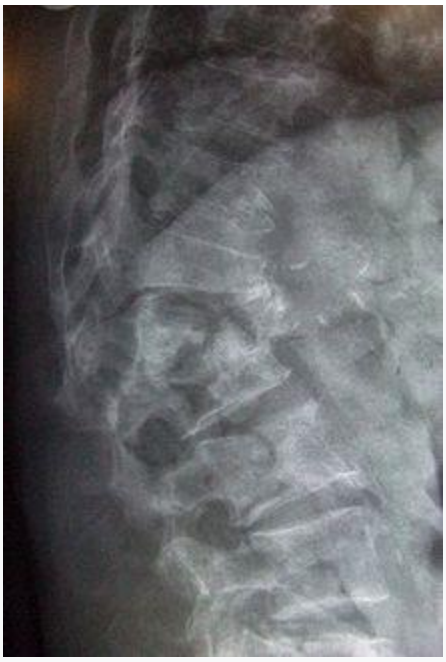
Certain medications have been associated with an increase in osteoporosis risk; only glucocorticosteroids and anticonvulsants are classically associated, but evidence is emerging with regard to other drugs.

- Steroid-induced osteoporosis (SIOP) arises due to use of glucocorticoids – analogous to Cushing's syndrome and involving mainly the axial skeleton. The synthetic glucocorticoid

prescription drug prednisone is a main candidate after prolonged intake. Some professional guidelines recommend prophylaxis in patients who take the equivalent of more than 30 mg hydrocortisone (7.5 mg of prednisolone), especially when this is in excess of three months.[64] Alternate day use may not prevent this complication.[65]

- Barbiturates, phenytoin and some other enzyme-inducing antiepileptics – these probably accelerate the metabolism of vitamin D.[66]
- L-Thyroxine over-replacement may contribute to osteoporosis, in a similar fashion as thyrotoxicosis does.[54] This can be relevant in subclinical hypothyroidism.
- Several drugs induce hypogonadism, for example aromatase inhibitors used in breast cancer, methotrexate and other antimetabolite drugs, depot progesterone and gonadotropin-releasing hormone agonists.
- Anticoagulants – long-term use of heparin is associated with a decrease in bone density,[67] and warfarin (and related coumarins) have been linked with an increased risk in osteoporotic fracture in long-term use.[68]
- Proton pump inhibitors – these drugs inhibit the production of stomach acid; this is thought to interfere with calcium absorption.[69] Chronic phosphate binding may also occur with aluminium-containing antacids.[54]
- Thiazolidinediones (used for diabetes) – rosiglitazone and possibly pioglitazone, inhibitors of PPARγ, have been linked with an increased risk of osteoporosis and fracture.[70]
- Chronic lithium therapy has been associated with osteoporosis.

- Diagnosis[edit]

- 
- Multiple osteoporotic wedge fractures demonstrated on a lateral thoraco-lumbar spine X-ray
- The diagnosis of osteoporosis can be made using conventional radiography and by measuring the bone mineral density (BMD).[77] The most popular method of measuring BMD is dual-energy X-ray absorptiometry.
- In addition to the detection of abnormal BMD, the diagnosis of osteoporosis requires investigations into potentially modifiable underlying causes; this may be done with blood tests. Depending on the likelihood of an underlying problem, investigations for cancer with metastasis to the bone, multiple myeloma, Cushing's disease and other above-mentioned causes may be performed.
- **Conventional radiography**[edit]
- Conventional radiography is useful, both by itself and in conjunction with CT or MRI, for detecting complications of osteopenia (reduced bone mass; pre-osteoporosis), such as fractures; for differential diagnosis of osteopenia; or for follow-up examinations in specific clinical settings, such as soft tissue calcifications, secondary hyperparathyroidism, or osteomalacia in renal osteodystrophy. However, radiography is relatively insensitive to detection of early disease and requires a substantial amount of bone loss (about 30%) to be apparent on X-ray images.

- The main radiographic features of generalized osteoporosis are cortical thinning and increased radiolucency. Frequent complications of osteoporosis are vertebral fractures for which spinal radiography can help considerably in diagnosis and follow-up. Vertebral height measurements can objectively be made using plain-film X-rays by using several methods such as height loss together with area reduction, particularly when looking at vertical deformity in T4-L4, or by determining a spinal fracture index that takes into account the number of vertebrae involved. Involvement of multiple vertebral bodies leads to kyphosis of the thoracic spine, leading to what is known as dowager's hump.

GENERAL PRESCRIBING GUIDELINES FOR PEDIATRIC PATIANTS:

- Children, and particularly neonates, differ from adults in their response to drugs.
- Special care is needed in ensuring the drug prescribed is appropriate and that the correct dosage is given, especially in the neonatal period.
- Factors affecting drug disposition in children:
- Oral absorption:
- Variable gastric and intestinal transit time: in young infants, gastric emptying time is prolonged and only approaches adult values at around 6 months of age.
- In older infants, intestinal hurry may occur.

  Distribution:

  ◦ Increased total body water: as a percentage of total body weight, the total body water and extracellular fluid volume decrease with increasing age.

  Neonates require higher doses of water-soluble drugs, on an mg/kg basis, than adults.

  • Metabolism:

  ◦ Enzyme systems mature at different times and may be absent at birth, or present in considerably reduced amounts.

  ◦ Altered metabolic pathways may exist for some drugs.

  Excretion:

◦ Complete maturation of renal function is not reached until 6-8 months of age. Route of administration and drug regimes: y Compliance in children is influenced by the formulation, taste, appearance and ease of administration of a preparation.

Prescribed regimens should be tailored to the child's daily routine. Where possible, treatment goals should be set in collaboration with the child.

Product licence:

Where possible, medicines for children should be prescribed within the terms of the marketing authorisation (product licence). However, many children may require medicines not specifically licensed for paediatric use.

The Medicines Act 1968 and European legislation make provision for doctors to use medicines in an off-label capacity or to use unlicensed medicines. However, individual prescribers are always responsible for ensuring that there is adequate information to support the quality, efficacy, safety and intended use of a drug before prescribing it.

Prescription writing:

Inclusion of age is a legal requirement in the case of prescription-only medicines for children under 12 years of age, but it is preferable to state the age for all prescriptions for children. It is particularly important to state the strengths of capsules or tablets. y Although liquid preparations are particularly suitable for children, they may contain sugar which encourages dental decay. Sugar-free medicines are preferred for long-term treatment. Many children are able to swallow tablets or capsules and may prefer a solid dose form; involving the child and parents in choosing the formulation is help

Dosages:

Children are not mini-adults. Paediatric doses should be obtained from a paedia y tric dosage reference text and not extrapolated from the adult dose. y When considering drug use in children, the following age groups should be used: neonate (birth to 1 month), infant (1 month to 2 years), child (2 to 12 years) and adolescent (12 to 18 years).

DOSE CALCULATION:

Children's doses may be calculated from adult doses by using age, body-weight, or body-surface area, or by a combination of these factors. The most reliable methods are those based on body-surface area.

Body-weight may be used to calculate doses expressed in mg/kg. Young children may require a higher dose per kg than adults because of their higher metabolic rates.

Adverse drug reactions:

Adverse drug reaction profiles in children may differ from those seen in adults. Doctors and pharmacists should report suspected adverse drug reactions to the Medicines and Healthcare products Regulatory Agency (MHRA), even if the product is being used in an off-label manner or is an unlicensed product. The identification and reporting of adverse reactions to drugs in children is particularly important because:

The action of the drug and its pharmacokinetics in children (especially in the very young) may be different from that in adults.

Safety in the home:

- Patients must be warned to keep all medicines out of the reach of children. All solid dose and all oral and external liquid preparations must be dispensed in a child-resistant container unless:
- The medicine is in an original pack or patient pack such as to make this inadvisable.
- The parent will have difficulty in opening a childresistant container.
- A specific request is made that the product shall not be dispensed in a child-resistant container.

GENERAL PRESCRIBING GUIDELINES FOR GERIATRIC PATIENTS:

About a fifth of the population in the United Kingdom is 60 years or older,[1] yet people in this age group receive 59% of dispensed prescriptions and account for more than half of NHS drug costs.[2] Older people often have several coexisting medical problems and take multiple drugs. Increasing age is associated with changes in pharmacokinetics and pharmacodynamics, so prescribing in this age group can be problematic.[3]

Many randomised controlled trials involving older patients focus on managing a single disease state, such as hypertension or osteoporosis, but people in this age group often have many interacting conditions and are taking many drugs, so guidance on their treatment often has to be

based on consensus and involves extrapolating data derived from healthier patients. This review highlights some of the difficulties in prescribing in older patients and offers guidance for appropriate prescribing.

Sources and selection criteria

We searched the National Library for Health, PubMed, and Embase databases using the keywords “elderly” and “prescribing”, including synonyms by the MeSH or major descriptor headings. Our search was limited to studies undertaken in humans that were published in English during the past five years. We displayed abstracts of interest using Abstract Plus before obtaining the full text of articles of interest. In addition, we searched the Cochrane Library and our own personal archives of references.

What physiological changes occur with ageing?

Pharmacokinetic and pharmacodynamic changes

With age the body undergoes several changes that can affect the distribution, metabolism, and excretion of drugs. These changes included a reduction in renal clearance, liver size, and lean body mass.[4] Hepatic enzyme activity and serum albumin may also be reduced in the presence of chronic disease. The most clinically important of these changes is the reduction in renal clearance, which results in reduced excretion of water soluble drugs. This is especially important for drugs with a narrow therapeutic window (ratio of desired effect to toxic effect), such as digoxin, lithium, and gentamicin.

As well as changes in pharmacokinetics, older people are also more sensitive to the effects of some drugs, especially those that act on the central nervous system, such as benzodiazepines, which are associated with an increase in postural sway and risk of falls.

Multiple pathology and polypharmacy

Polypharmacy is common in older people—around 20% of people over 70 take five or more drugs.[5] In the past decade, the average number of items prescribed to people aged 60 and over has almost doubled from 21.2 to 40.8 items for each person each year.[6] Previously,

polypharmacy implied inappropriate prescribing, but this is not necessarily true, because all of the prescribed drugs may have an appropriate indication.

Polypharmacy is associated with increases in many adverse outcomes, including drug interactions, adverse drug reactions, falls, hospital admissions, length of hospital stay, readmission rate soon after discharge, and mortality rate.[5 7 8] However, these effects may result from polypharmacy acting as a marker of multiple pathology or frailty, as opposed to being an independent risk factor.

What is inappropriate prescribing?

Inappropriate prescribing for older patients encompasses all of the normal indicators of inappropriate prescribing for adults in general, but the problem is especially relevant to older patients because they often take a large number of drugs. Not only does this increase their chance of having an adverse event, but it means that unnecessary drugs may be obscured by the large number of necessary ones. Dose, formulation, and delivery need to be adjusted according to the age and frailty of the patient, and some drugs are best avoided altogether. This is familiar territory to general practitioners, who also see very young patients and routinely adjust drug dose according to the *British National Formulary for Children*—perhaps we need an equivalent publication for older patients to highlight the importance of taking age into account. Problems arise when older patients are assumed to respond to drugs in the same way that an average adult does.[9] In addition, as patients grow older, it is easy to forget to adjust drug doses appropriately. This is where a review by someone other than the usual prescriber can be particularly helpful.

Which drugs should we avoid in older patients?

Some adverse drug reactions occur at a similar prevalence regardless of age, such as cough induced by angiotensin converting enzyme inhibitors. However, a greater prevalence of adverse drug reactions may be seen as a result of the pharmacokinetic or pharmacodynamic changes seen with ageing. An American consensus guideline known as the Beers criteria—first published in 1991 and last updated in 2003—provides a list of drugs that the panel of experts thought to be particularly problematic for older patients.[10]The tabletable gives examples from this list that are especially relevant to prescribing in the United Kingdom.

Drugs that pose a particular risk for older people[10]

Drug	Adverse drug reactions
Long term non-steroidal anti-inflammatory drugs	Gastrointestinal haemorrhage, renal impairment, hypertension
Benzodiazepines	Falls caused by impaired balance
Anticholinergic drugs	Unmasking Alzheimer's disease, urinary retention
Tricyclic antidepressants	Orthostatic hypotension, sedation
Chlorpropramide	Hypoglycaemia
Doxazosin	Orthostatic hypotension, dry mouth, urinary problems

What drugs should we routinely consider in older patients?

Older people have been under-represented in clinical trials of new drugs, but there is a solid evidence base using some newer treatments in this population. Warfarin reduces strokes in patients with atrial fibrillation, with no significant increase in the risk of bleeding, and it is recommended for most patients over 75 years with atrial fibrillation.[11] [12]

Recent reviews also provide convincing evidence for the use of angiotensin converting enzyme inhibitors and β blockers in left ventricular systolic dysfunction, statins in hypercholesterolaemia, and bisphosphonates in osteoporosis in older patients.[13 14 15 16] These drugs were well tolerated in older people, but few studies included patients who were taking several drugs at the same time.[11 13 14 15 16] We therefore advise monitoring the introduction of new agents carefully, often starting with low doses and titrating upwards.

How can inappropriate prescribing in older people be reduced?

Good prescribing practice

Box 1 offers some guidelines to aid prescribing in older patients. Some of these guidelines, such as using as few prescribers as possible, are evidence based,[17] but because of the paucity of evidence in this area, most are consensus opinion.

Box 1 Guidelines for good prescribing in elderly patients

- Carry out a regular medication review and discuss and agree all changes with the patient
- Stop any current drugs that are not indicated
- Prescribe new drugs that have a clear indication
- If possible, avoid drugs that have known deleterious effects in elderly patients, such as benzodiazepines, and recommend dosage reduction when appropriate
- Use the recommended dosages for elderly patients
- Use simple drug regimens and appropriate administration systems
- Consider using once daily or once weekly formulations and using fixed dose combinations when possible
- Consider non-pharmacological treatments if appropriate
- Limit the number of people prescribing for each patient if possible
- Where possible, avoid treating adverse drug reactions with further drugs

GENERAL PRESCRIBING GUIDELINES FOR PREGNANCY AND BREAST FEEDING:

A creditable and unusual aspect was the inclusion of data related to drug ingestion by fathers, in the three month period prior to conception. It is largely unknown how highly teratogenic drugs

such as isotretinoin (which was taken by 13 men in this study) affect offspring. The study showed that around 25% of fathers had a prescription medicine, with around 12% taking one drug only. By comparison, around 39% of women had a prescription during this period, which dropped to around 30% for each of the first to third trimesters, and rose to 57% for the three month post-partum period (presumably excluding drugs given at the time of delivery). The changing pattern of drug ingestion in the relevant periods was interesting, and generally reflected what might be regarded as good medical practice in a developed country. The extent of drug ingestion around the time of conception remains a concern, especially related to unplanned pregnancies.

Our knowledge about the safety of drugs in the immediate pre-pregnant period is scanty, yet the ova and sperm about to make contact are subject to possible effects at this time. Methotrexate, a folate antagonist and potential teratogen and abortifacient, may adversely affect developing sperm and ova, and it is recommended that pregnancy should be avoided for at least 3 months after cessation of treatment in males, and for at least 1 ovulatory cycle in females. However, proof of this is lacking [2]. Pharmacokinetic considerations are also important at this time. Drugs with very long half-lives will continue to have influence long after they have been ‘stopped’. Patients are very likely not to declare such drugs at the time of a drug history (if indeed asked!). Fortunately there is a short window of relative safety between conception and implantation, where the conceptus is relatively spared of drug in the maternal circulation [3].

Pregnancy and the post-partum period have historically been largely excluded from drug trials, for obvious reasons. Koren [4] has stated that the best way to achieve better knowledge of effects of drugs during pregnancy is collection and follow-up of observational data. More countries should follow Norway's example in their data collection strategies. Interestingly, I have tried to establish a database related to pregnancy and drugs in our local region in New Zealand, but persistently struck resistance (largely from medical colleagues) related to privacy issues. This is political correctness gone mad.

Transporters and the placenta

Transporters seem to be a flavour of our times, so it is not surprising that they have been looked for, and found, in the human placenta. Transporters often serve a useful Darwinian purpose of

protection, which, in the case of the placenta, is of the foetus. Inhibitors of transporters are therefore of great importance, because they potentially increase exposure.

Sudhakaran *et al.*[5] investigated the effect of P-glycoprotein (P-gp) inhibition on maternal to foetal transfer of indinavir. They had previously shown that indinavir was subject to efflux transport (i.e. foeto-protective) in the isolated human placenta, which was presumed to be via P-gp [6]. In the study in this issue of the journal, a P-gp inhibitor PSC833 enhanced maternal to foetal transfer of indinavir, but not of ritonavir. The differential effect was considered to be due to clinically relevant concentrations in relation to different binding affinities of indinavir and ritonavir.

Since P-gp has a large number of substrates and inhibitors, one can only speculate as to how many other drug interactions may occur at this level.

From pregnancy to lactation

A cooperative study involving researchers from Western Australia and Papua New Guinea, (Law *et al.*[7]), investigated the transfer of chloroquine and desethylchloroquine (the primary active metabolite) across the placenta, and into milk, in Melanesian mothers. In Papua New Guinea chloroquine is recommended for prophylaxis of malaria during pregnancy, and many women are routinely prescribed this drug at the time of delivery.

In this study foetal cord and maternal serum samples were collected at delivery, and milk samples were collected over 3 weeks after delivery. It was commendable that the active metabolite was measured as well as the parent drug. Results showed that during pregnancy concentrations were similar on the infant and maternal sides, while the relative infant dose of the 2 compounds (as chloroquine equivalents) was around 3.2%, and therefore compatible with breastfeeding. It is generally accepted that for drugs without excessive toxicity, a relative infant dose of <10% is considered ‘safe’ for full term infants.

This study nicely confirms the most common situation related to drugs in pregnancy and lactation – that in pregnancy the infant is usually exposed to similar concentrations as is the mother, while during lactation the relative exposure is much lower. It is amazing how often this comes as a surprise to many people.

A second paper from Western Australia, from Ilett *et al.*[8], examined the use of a sparce sampling design to assess transfer of tramadol and its active o-desmethyl metabolite, into transitional milk. This paper was interesting for 2 reasons. Firstly it provided the first detailed data on tramadol in lactation, when used as postoperative analgesia on days 2-4 after Caesarian section. The combined relative infant dose of parent and metabolite drugs was 2.9%, indicating that short term use in this setting is compatible with breastfeeding.

The other point of interest in this paper is the use of a sparce sampling study technique. Most studies of drugs in human milk involve few woman/child pairings (usually ≤6), with intensive sampling across a dosing interval. In this study, data were provided on 73 women, with 3 milk samples and one plasma sample taken in each woman, distributed across a dosing interval. The authors believed that this was the first time such an approach has been used in this field. Such an approach could lend itself to population pharmacokinetic modelling, and I know the authors are interested in pursuing this approach further.

OPTHAMOLOGY

GLAUCOMA:

Glaucoma is a group of related eye disorders that cause damage to the optic nerve that carries information from the eye to the brain.

In its early stages, glaucoma usually has no symptoms, which is what makes it so dangerous — by the time you notice problems with your sight, the disease has progressed to the point that irreversible vision loss has already occurred and additional loss may be difficult to stop.

In most cases, glaucoma is associated with higher-than-normal pressure inside the eye — a condition called ocular hypertension. But it also can occur when intraocular pressure (IOP) is normal. If untreated or uncontrolled, glaucoma first causes peripheral vision loss and eventually can lead to blindness.

According to the American Academy of Ophthalmology, the most common type of glaucoma — called primary open-angle glaucoma — affects an estimated 2.2 million people in the United States, and that number is expected to increase to 3.3 million by 2020 as the U.S. population ages.

And because most cases of glaucoma have few or no early symptoms, about half of Americans with glaucoma don't know they have it.

Types Of Glaucoma

The two major categories of glaucoma are open-angle glaucoma (OAG) and narrow angle glaucoma. The "angle" in both cases refers to the drainage angle inside the eye that controls the outflow of the watery fluid (aqueous) that is continually being produced inside the eye.

If the aqueous can access the drainage angle, the glaucoma is known as open angle glaucoma. If the drainage angle is blocked and the aqueous cannot reach it, the glaucoma is known as narrow angle glaucoma.

Variations of OAG include: primary open angle glaucoma (POAG), normal-tension glaucoma (NTG), pigmentary glaucoma, pseudoexfoliation glaucoma, secondary glaucoma and congenital glaucoma.

Variations of narrow angle glaucoma include include acute angle closure glaucoma, chronic angle closure glaucoma, and neovascular glaucoma.

- **Primary open-angle glaucoma.** This common type of glaucoma gradually reduces your peripheral vision without other symptoms. By the time you notice it, permanent damage already has occurred.
  If your IOP remains high, the destruction caused by POAG can progress until tunnel vision develops, and you will be able to see only objects that are straight ahead. Ultimately, all vision can be lost, causing blindness.

- **Acute angle-closure glaucoma.** Also called narrow-angle glaucoma, acute angle-closure glaucoma produces sudden symptoms such as eye pain, headaches, halos around lights, dilated pupils, vision loss, red eyes, nausea and vomiting.
  These signs constitute a medical emergency. The attack may last for a few hours, and then return again for another round, or it may be continuous without relief. Each attack can cause progressively more vision loss.

- **Normal-tension glaucoma.** Like POAG, normal-tension glaucoma (also called normal-pressure glaucoma, low-tension glaucoma or low-pressure glaucoma) is a type of open-angle glaucoma that can cause visual field loss due to optic nerve damage. But in normal-tension glaucoma, the eye's IOP remains in the normal range.
  Also, pain is unlikely and permanent damage to the eye's optic nerve may not be noticed until symptoms such as tunnel vision occur.
  The cause of normal-tension glaucoma is not known. But many doctors believe it is related to poor blood flow to the optic nerve. Normal-tension glaucoma is more common in those who are Japanese, are female and/or have a history of vascular disease.

- **Pigmentary glaucoma.** This rare form of glaucoma is caused by clogging of the drainage angle of the eye by pigment that has broken loose from the iris, reducing the rate of aqueous outflow from the eye. Over time, an inflammatory response to the blocked angle damages the drainage system.
  You are unlikely to notice any symptoms with pigmentary glaucoma, though some pain and blurry vision may occur after exercise. Pigmentary glaucoma most frequently affects white males in their mid-30s to mid-40s.

- **Secondary glaucoma.** Symptoms of chronic glaucoma following an eye injury could indicate secondary glaucoma, which also may develop with presence of eye infection, inflammation, a tumor or enlargement of the lens due to a cataract.

- **Congenital glaucoma.** This inherited form of glaucoma is present at birth, with 80 percent of cases diagnosed by age one. These children are born with narrow angles or

some other defect in the drainage system of the eye.

It's difficult to spot signs of congenital glaucoma, because children are too young to understand what is happening to them. If you notice a cloudy, white, hazy, enlarged or protruding eye in your child, consult your eye doctor. Congenital glaucoma typically occurs more in boys than in girls.

Who Is At Risk?

Open-angle glaucoma is three times more likely to affect African-Americans, compared with non-Hispanic whites in the United States, and blindness from glaucoma is at least six times more prevalent among African-Americans than non-Hispanic whites.

Conjunctivitis-viral and bacterial:

All forms of conjunctivitis — including bacterial, viral, allergic and other types — involve inflammation of the transparent, mucous membrane (conjunctiva) covering the white part of the eye or sclera.

Infectious causes of an inflamed eye and conjunctivitis include bacteria, viruses and fungi. Non-infectious causes include allergies, foreign bodies and chemicals.

The phrase "pink eye" is commonly used to refer to conjunctivitis, because pinkness or redness of the conjunctiva is one of the most noticeable symptoms.

Types Of Conjunctivitis

Bacterial conjunctivitis is a common type of pink eye, caused by bacteria that infect the eye through various sources of contamination. The bacteria can be spread through contact with an infected individual, exposure to contaminated surfaces or through other means such as sinus or ear infections.

The most common types of bacteria that cause bacterial conjunctivitis include Staphylococcus aureus, Haemophilus influenzae, Streptococcus pneumoniae and Pseudomonas aeruginosa.

Bacterial conjunctivitis usually produces a thick eye discharge or pus and can affect one or both eyes.

As with any bacterial infection, antibiotics are required to eliminate the bacteria. Treatment of bacterial conjunctivitis is typically accomplished with topical antibiotic eye drops and/or eye ointments. The treatment usually takes from one to two weeks, depending on the severity of the infection.

Viral conjunctivitis is another common type of pink eye that is highly contagious, because airborne viruses can be spread through sneezing and coughing. Viral conjunctivitis also can accompany common viral upper respiratory infections such as measles, the flu or the common cold.

Viral conjunctivitis usually produces a watery discharge. Typically the infection starts in one eye and quickly spreads to the other eye.

Unlike with bacterial infections, antibiotics will not work against viruses. No eye drops or ointments are effective against the common viruses that cause viral conjunctivitis. But viral conjunctivitis is self-limited, which means it will go away by itself after a short time.

Typically with viral conjunctivitis, the third through the fifth days are the worst. After that, eyes begin to improve on their own.

Treatment of viral conjunctivitis usually involves supportive therapies, such as eye drops, that help reduce the symptoms: for example, vasoconstrictors to whiten the eye, decongestants to reduce the surface swelling and antihistamines to reduce occasional itching. Treatments usually are continued for one to two weeks, depending on the severity of the infection.

Gonococcal and chlamydial conjunctivitis are bacterial forms related to infections from sexually transmitted diseases including gonorrhea and chlamydia. Newborn babies may be exposed when they pass through the birth canal of an infected mother. Trachoma is a form of chlamydial infection that causes scarring on the eye's surface. Trachoma is the world's leading cause of preventable blindness.

Neonatal conjunctivitis found in newborn babies can cause blindness when left untreated. Up to 10 percent of all pregnant women in the United States have a sexually transmitted chlamydial infection. If these infections are untreated in mothers, the possibility that a newborn infant will develop a related eye infection ranges from 10 percent to 20 percent.*

Another type of sexually transmitted disease related to the herpes simplex virus type 2 found in the genital area can infect eyes of infants as they are born. Herpes simplex virus type 1, a cause of cold sores on the mouth, also can cause a type of eye herpes that results in pink eye.

If you are pregnant and suspect you may have a sexually transmitted disease, you need to be checked and possibly treated for any infection before the birth of your baby.

In the United States, an antibiotic ointment often is applied as a basic standard of care for newborn infants, to help prevent the possibility of certain eye infections.

Allergic conjunctivitis caused by eye allergies is very common. Eye allergies, like other types, can be triggered by allergens including pollen, animal dander and dust mites.

The most common symptom of allergic conjunctivitis is itchy eyes, which may be relieved with special eye drops containing antihistamines to control allergic reactions. These eye drops are available both over the counter and by prescription.

Avoiding the allergen is also important in the treatment of allergic conjunctivitis. Allergic conjunctivitis can be seasonal or perennial (year-round), depending on the allergen causing the reaction.

Giant papillary conjunctivitis (GPC) usually involves both eyes and often affects soft contact lens wearers. This condition may cause contact lens intolerance, itching, a heavy discharge, tearing and red bumps on the underside of the eyelids.

You'll need to stop wearing your contact lenses, at least for a little while. Your eye doctor may also recommend that you switch to a different type of contact lens, to reduce the chance of the conjunctivitis coming back.

For example, you might need to switch from soft contacts to gas permeable ones or vice versa. Or you might need to try a type of lens that you replace more frequently, such as disposable contact lenses. GPC can also result from artificial eyes (prosthetics), stitches and more. Your eye doctor will decide if removal is appropriate.

Non-infectious conjunctivitis from eye irritation causing pink eye symptoms that can result from many sources, including smoke, diesel exhaust, perfumes and certain chemicals. Some forms of conjunctivitis also result from sensitivity to certain ingested substances, including herbs such as eyebright and turmeric.**

Certain forms of pink eye, including giant papillary conjunctivitis, can be caused by the eye's immune responses, such as a reaction to wearing contact lenses or ocular prosthetics (artificial eyes). A reaction to preservatives in eye drops or ointments also can cause toxic conjunctivitis.

RATIONAL DRUG USE

DEFINITION:

The rational use of drugs requires that patients receive receive medications appropriate to their clinical needs, in needs, in doses that meet their own individual requirements for an adequate period of time, and at the and at the lowest cost to them and their community.

ROLE OF PHARMACIST:

Physicians are often highlighted as the final pathway for nearly all professional decisions about the use of health resources. Yet with respect to drugs, pharmacists and other dispensers are in many cases the final link between the medication and the patient. Community pharmacies have always been a major location for health care worldwide. Pharmacy employees are consulted for health advice on problems of all kinds, and remedies are sold or dispensed with almost every transaction. Some of the remedies are safe and effective when used correctly but otherwise can be dangerous; others are ineffective no matter how they are used.

The purpose of this session is to identify important factors that influence the dispenser's behavior and consequently, his or her impact on a patient's compliance with drug therapy.

OBJECTIVES

To develop your ability to:

1. Identify who can be dispensers.

2. Describe the dispensing process.

3. Identify factors that influence decisions dispensers make.

4. Describe methods that enhance dispenser/patient communications.

5. Identify ways to influence a dispenser's behavior.

PREPARATION

Read Session Notes and Trainers Guide and review visual aids.

Read Chapter 32 of Managing Drug Supply, "Ensuring Good Dispensing Practices."

Read article by Ross-Degnan, et al, "The Impact of Face to Face Educational Outreach Diarrhea Treatment in Pharmacies," *Health Policy and Planning*, vol. 11, no. 3, Sept. 1996.

Note: This module has been developed by a number of people including Drs. Kumud Kafle, Farai Chinyanganya and Sri Suryawati. Photographs have been provided by Dr. Edelisa Carandang (Philippines), Fatima Suleman (South Africa), Prof. Willy Anockobongo (Uganda), and Dr. Farai Chinyanganya (Zimbabwe).

THE DISPENSING PROCESS:

As shown below, there are eight important steps to assure the proper delivery of drugs to the patient from the dispenser. Notice that each step carries with it a number of important responsibilities and/or considerations. For our purposes, we make the assumption that (1) the

prescriber has made the correct diagnosis and has selected the correct drug, dosage and quantity, and (2) the patient has access to the dispensary (pharmacy).

1. The dispenser receives the correct prescription from the patient or prescriber (written or oral).

- information on patient
- • therapeutic appropriateness
- • economic consideration
- • communicate with prescribers for dubious or unclear instructions
- 2. The dispenser correctly interprets the prescription or instructions on the prescription.
- • check the name of drugs

• check the dosages, administration,

• check the availability of drugs

• retrieve from storage area.

. The prescribed therapy is available at the pharmacy in a usable form (not expired or damaged).

 ensure proper drug storage

 check and double check (if possible) the drug product for accuracy of identity, strength, and dose form.

4. The dispenser has true knowledge of the medication and its proper use.

• precise preparation of products

• re-check drugs and dosages.

5. The dispenser communicates the correct way to take the medication to the patient.

• label with patient's name, drug name, directions for use, date of dispensing, identity of prescriber, and identity of dispenser

• symbolic instructions in case of illiteracy

• use of auxiliary labels.

6. The patient understands the instructions from the dispenser.

• repeat orally the labeled instruction, if possible in laymen's terms

• patient should repeat the instructions back to the dispenser

• emphasize the need for compliance

• provide warnings and cautions

• give special attention to certain cases,

e.g.:

- pregnant women

- those with visual or hearing impairment

- functional illiterates

- children and elderly patients

- those taking multiple medications

7. The patient complies with the instructions for therapy.

8. The dispenser keeps accurate records of operations.

- enter details of encounter on patient profile card
- enter record in prescription register
- complete inventory records.

POTENTIAL FOR ERROR PROBLEMS:

During any of the above activities there is potential for errors to be made and problems to occur. A few of these have been identified below. See if you can think of others.

- Wrong interpretation of the prescription (or diagnosis)
- Retrieval of the wrong drug from stock
- Wrong dosages
- Inadequate packaging/labeling of proprietary drugs
- Inaccurate counting, compounding
- Inadequate or nonexistent labeling
- No knowledge of proper drug compliance
- Insufficient knowledge of the disease process
- Insufficient time to talk with patients about their drugs
- Inability to communicate to patients about therapy

PROPER DISPENSING TAKES TIME:

There are many factors that influence dispenser behavior:

- Training and knowledge
- Professional compensation (salary, prestige, etc.)

• Economic incentives (markup and volume of sales)

• Supply (cannot dispense what is not in stock)

• Available product information

• Availability of dispensing equipment (counting trays, vials, bottles, syringes, labels, etc.).

• Public vs. private sector promotional and marketing techniques.

• The social status of a dispenser and his or her role in the health care system.

• Dispenser-prescriber relationship.

• Lack of communication skills.

C. DISPENSING PRACTICES TO ENHANCE RATIONAL DRUG USE

Below are a series of questions designed to help assess dispensing practices in a drug delivery system

• What conditions exist at dispensing points? How are drugs handled? How accurately and cleanly are drugs dispensed? How concerned are health officials and health workers about the quality of compounding and dispensing practices?

• How long is normally spent for dispensing? How do dispensers communicate with patients?

• How often are patients improperly treated because their medicines have been improperly compounded or dispensed, or because drugs have deteriorated in inadequate packaging?

• At each level in the health care system, who is responsible for the compounding and dispensing of drugs? What training do these individuals have in the principles and practices of drug compounding and dispensing? How much supervision do these individuals receive?

• What types of pharmaceutical training are available in the country? Are there standardized education curricula for pharmacy personnel? Are training requirements for dispensers spelled out and reasonable, given the numbers and geographical distribution of individuals meeting, or eligible for meeting, these requirements?

• What resources exist to attract individuals to pursue dispenser training and to what extent can these individuals expect satisfactory remuneration for the services they provide?

• Are wages and salaries adequate to effectively discourage dispensers from engaging in the illegal sale and distribution of pharmaceuticals?

• What kinds of packaging are used to dispense drugs to patients? Is there any mechanized repackaging into course-of-therapy packets? In light of losses from poor packaging and the costs of proper packaging, are there cost-effective alternatives to present packaging methods? Could more expensive containers be recycled?

ESSENTIAL DRUG CONCEPT:

The Alma-Ata declaration during the International Conference on Primary Health Care in 1978 reaffirms that health is a fundamental human right and the attainment of the highest possible level of health is a most important worldwide social goal.(1) The Alma Ata declaration has outlined the eight essential components of primary health care and provision of essential medicines is one of them.(1) Medicines are integral parts of the health care and the modern health care is unthinkable without the availability of necessary medicines. They not only save lives and promote health, but prevent epidemics and diseases too. The medicines are undoubtedly one of the weapons of mankind to fight disease and illness. Accessibility to medicines is too the fundamental right of every person.

Concept of Essential Medicines

World Health Organization (WHO) introduced the concept of essential medicines in 1977.(2) Essential medicines are those that satisfy the priority health care needs of the population. They are selected with due regard to public health relevance, evidence on efficacy and safety, and comparative cost-effectiveness. Essential medicines are intended to be available within the

context of functioning health systems at all times in adequate amounts, in the appropriate dosage forms, with assured quality and adequate information, and at a price the individual and the community can afford. The implementation of the concept of essential medicines is intended to be flexible and adaptable to many different situations; exactly which medicines are regarded as essential remains a national responsibility. Experience has shown that careful selection of a limited range of essential medicines results in a higher quality of care, better management of medicines (including improved quality of prescribed medicines), and a more cost-effective use of available health resources. The WHO has developed the first essential medicines list in 1977 and since then the list has been revised every 2 years. The current one is the 15th model list released in 2007.(2) The essential medicine list contains limited cost-effective and safe medicines, while the open pharmaceutical market is flooded with large number of medicines many of which are of doubtful value. The model list of WHO serves as a guide for the development of national and institutional essential medicine list. The concept of essential medicines has been worldwide accepted as a powerful tool to promote health equity and its impact is remarkable as the essential medicines are proved to be one of the most cost-effective elements in health care.

Selection of Essential Medicine List

The process by which medicines are selected is critical. An essential medicines list which is imposed from above will not reflect the need of the users or be accepted by them. It is therefore very important that the process be consultative and transparent, selection criteria be explicit, selection of the medicines be linked to evidence-based standard clinical guidelines, clinical guidelines and the list be divided into levels of care, and are regularly reviewed and updated. A review of the clinical guidelines and the list should be carried out at least every second year, and their use and the impact should be monitored.

Strategies to promote rational use of medicines

A mandated multi-disciplinary national body to coordinate medicine use policies

Clinical guidelines

Essential medicines list based on treatments of choice

Drugs and therapeutics committees in districts and hospitals

Problem-based pharmacotherapy training in undergraduate curricula

Continuing in-service medical education as a licensure requirement

Supervision, audit and feedback

Independent information on medicines

Public education about medicines

Avoidance of perverse financial incentives

Appropriate and enforced regulation

Sufficient government expenditure to ensure availability of medicines and staff

This concept of essential medicines is relatively new to India and Tamil Nadu is the first state to develop the essential medicine list as early as in 1994. Then government of Delhi too had developed its own list. The government of India and many other individual states have their own essential medicines list, and the current national list was compiled during 2003. Unfortunately, the list is not regularly up dated except for Tamil Nadu. As the list needs to be developed locally and should be based on evidence not merely on individual's experience, it is necessary first to develop clinical guidelines, called standard treatment guidelines (STG). Then based on STG the list is compiled. Delhi took the lead in developing a comprehensive Drug Policy in 1994 and was the only Indian state to have such a comprehensive policy.(6) The policy's main objective is to improve the availability and accessibility of quality essential drugs for all those in need.(6) Now many state governments too have developed STG for use within the state government health facilities. The Armed Forces Medical College (AFMC) has developed STGs for quite large number of common conditions and the treatment cost is also calculated.

Usage of Essential Medicine List

The concept of essential medicines has also been adopted by many international organizations, including the United Nations Children's Fund (UNICEF) and the Office of the United Nations High Commissioner for Refugees (UNHCR), as well as by non-governmental organizations and international non-profit supply agencies. Many of these organizations base their medicine supply system on the Model List. Lists of essential medicines also guide the procurement and supply of medicines in the public sector, schemes that reimburse medicine costs, medicine donations and local medicine production, and, furthermore, are widely used as information and education tools by health professionals. Health insurance schemes too are increasingly using national lists of essential medicines for reference purposes. The model list serves as a baseline for further modification (addition and deletion of new medicines), correct dosage strength, and form depending upon the national priority and available evidence.