

IMPORTANT MEDICAL FACTS

CARDIOLOGY

- Prominent U wave in ECG is seen in hypokalemia, inverted U wave is a subtle sign of myocardial infarction.
- Adults with mild pulmonic stenosis are usually asymptomatic. Unlike congenital aortic stenosis this condition usually does not progress.
- Coarctation of aorta usually occurs just distal to origin of left subclavian artery. If it arises above left subclavian, blood pressure is only raised in right arm.
- Adenosine decreases conduction in AV node; 6-12 mg IV dose terminates most SVTs.
- Angiotensin II and beta-agonists augment proto-oncogene expression, stimulate protein synthesis and induce synthesis of fetal forms of actin-myosin thereby causing cardiac hypertrophy.
- The gene responsible for familial hypertrophic cardiomyopathy is on chromosome-14.
- The vast majority of aortic aneurysms are due to atherosclerosis, 75% of them are located below renal arteries.
- Acute pericarditis is associated with ST segment elevation, PR segment depression. Reciprocal ST segment depression in opposite leads is characteristically absent.
- The AV node lies within triangle of Koch, the base of which is defined by annulus of tricuspid valve and the opening of coronary sinus.
- In pulmonary valve 2 cusps are anterior while in aortic valve 2 cusps are posterior. 19. Thebesian veins drain directly into right atrium and right ventricle.
- RCA supplies AV node, but in 10-15% cases the supply is from circumflex artery. SA node is supplied in 40-50% cases from circumflex and in the rest from RCA.
- Kugel's artery is an important collateral from the base of atrial septum to AV node and the posterior circulation. It may arise from LCA or RCA. 22...T.10 circle of Vieussens provides collateral circulation from left anterior descending to anterior right ventricle.
- Three venous drainages are present in heart (1) coronary sinus draining LV (2) anterior cardiac veins draining RV and (3) Thebesian system.
- 50-65% of pulmonary blood volume lies in thin walled capacitance vessels. Pulmonary vessels constrict in response to arterial hypoxemia and hypercapnea while systemic vessels dilate in response to such stimuli.
- The aorta functions as a reservoir chamber for the rapidly ejecting LV, converting pulsatile to a continuous flow (Windkessel effect). With aging this is reduced, resulting in higher pulse pressure and systolic hypertension.
- Myocardial lymphatic vessels are important in maintaining normal myocardial nutrition.
- The action potential of cardiac cell membranes is initiated by depolarisation related to sudden influx of sodium ions followed by slower influx of calcium ions.
- The initial transsarcolemmal influx of calcium ion triggers the release of calcium from sarcoplasmic reticulum.
- Calcium ions in sarcoplasm then bind to troponin C subunit which produces conformational changes in whole troponin complex that inhibits troponin I interaction with actin.
- This in turn allows tropomyosin to roll back into the grooves of the F-actin superhelix and allows the interaction of actin and myosin to produce a contraction.
- P cells constitute one of four types of cells involved in impulse formation and rapid conduction. These cells are present in sinus node and internodal pathways.
- The delay at AV node occurs at a latter time when atria are fully developed. There are minimum of 8 defined currents that contribute to adult cardiac action potential.
- Membrane conductance at the end of an action potential is determined primarily by the activities of two sets of potassium channels.
- The innerside of a heart cell during diastole is -60 to -90 mV, this negativity maintained by more pumping out of sodium than pumping in of potassium which is 3:2.
- Automatic cells of SA node demonstrate spontaneous diastolic depolarisation, responsible to initiate action-potential. This is brought about by decreased outward K^+ flux in SA node cells in comparison to Na^+ influx.
- Acetylcholine increases K^+ conductance and thus suppresses SA node. As heart rate increases, Na^+ flux inwards also increases.
- Cardiac dilatation, hypertrophy, anaerobic metabolism and tachycardia are the few mechanisms by which a beating heart meets increased circulatory demands.
- The four major determinants of myocardial oxygen consumption are—myocardial mass, wall stress (volume x pressure), inotropic state (contractility) and heart rate.
- The arterial pressure gradient (aortic-LV diastolic pressure) and duration of diastole are major determinants of coronary blood flow.
- During systole left ventricular intramyocardial pressure exceeds aortic root pressure leading to compression of epicardial coronary vessels that prevents forward coronary blood flow.
- Heart muscle has the highest fractional extraction of O_2 , to the extent of 70%. Reduced diastolic coronary flow limits O_2 availability and leads to myocardial acidemia due to predominant anaerobic metabolism.
- There are 5 major classes of lipids in plasma—the cholesterol, cholesterol esters, phospholipids, triglycerides, and unesterified fatty acids.
- LDL cholesterol is considered the most villain for atherosclerosis. The number of LDL receptors is the major determinant of LDL concentration in blood. In healthy humans 70% of circulating LDL is removed each day by these LDL receptors. A primary endothelial cell dysfunction plays the vital role in genesis of atherosclerosis.
- The pearly early atheromatous lesions are reversible but if fibrous plaque has formed, the lesions can be arrested by lowering of blood lipids but cannot be fully reversed.
- The smooth muscle proliferation in atheromatous lesion is secondary to subendothelial accumulation of lipids.
- Rise in diastolic pressure on standing indicates vulnerability

for developing hypertension. Obese people with small arm cuff show hypertension due to cuff-arm mismatch.

- Complete disappearance of Korotkoff sound is the point of recording for diastolic BP in adults but muffling of sound is taken as end point in pediatric age group.
- Mean arterial BP is $(\text{systolic BP} - \text{diastolic BP})/3 + \text{diastolic BP}$. Pulse pressure is the difference between systolic and diastolic BP. Pulse pressure is increased when stroke volume is increased or peripheral vascular resistance is decreased.
- The post PVC beat in a patient IHSS or hypertrophic obstructive cardiomyopathy has increased pulse pressure due to enhanced contractility. This is called Brockenborough's sign.
- Pulsus alternans is defined as regular alteration of pulse pressure detected in peripheral artery where the systolic pressure variation exceeds 20 mmHg.
- The LV is normally palpated at the cardiac apex. The apical impulse is not necessarily the point of maximum cardiac impulse.
- A hyperkinetic pulse is characterised by rapid upstroke, brief summit and rapid downstroke. It is seen in patients with increased cardiac output due to decreased peripheral resistance.
- Kussmaul's sign refers to an increase in JVP on inspiration when there is resistance to right ventricular filling as in restrictive cardiomyopathy, constrictive pericarditis or RV infarction.
- 'a' wave of JVP is produced by right atrial contraction, 'y' descent is due to venous inflow into RV.
- In tricuspid stenosis 'y' descent is shallow but with regurgitation there is ventricularization of 'c' and 'v' waves resulting in a single positive systolic wave and an exaggerated 'y' descent.
- A grade 4 or greater murmur is accompanied by thrill. A palpable P2 implies pulmonary hypertension and can be plexogenic, thrombogenic or veno-occlusive.
- A palpable S4 implies vigorous atrial contraction and is associated with condition that restrict ventricular filling as in hypertension, hypertrophic cardiomyopathy.
- In 10% cases dorsalis pedis pulse is congenitally absent but absence of posterior tibial pulse is always abnormal.
- The venous filling time is determined by elevation of lower extremity until veins collapse and then promptly bringing the limb into dependent position. The veins normally fill in < 15 seconds. A delay in venous filling indicates arterial insufficiency.
- A ventricular septal defect is the most common manifestation of congenital heart disease.
- The chest pain of pulmonary hypertension is related to right ventricular ischaemia or pulmonary artery dilatation.
- Cheyne-Stokes respiration is a normal variation in newborn but in adults it is due to CVA or LV dysfunction.
- Osler's nodes are nonhaemorrhagic and tender lesions on palms and soles. Splinter haemorrhages are vertical, black linear haemorrhages located on distal third of finger nail.
- The centre of right atrium is approximately 5 cm below the sternal angle of Luis regardless of body position. Thus CVP is determined from addition of vertical height of oscillating venous column above sternal angle to 5 cm. It is commonly estimated in right internal jugular vein with 30° of body inclination and oblique lighting. External jugular vein since has valves is not suitable for CVP study.

- A third heart sound is normal finding in children and young adults. It is not synonymous with a gallop which is a pathological condition.
- A "cooing dove" sound is indicative of regurgitant murmur due to ruptured or retroverted aortic cusps. The systolic "whoop" or honk is heard in patients of mitral valve prolapse.
- Isometric handgrip increases peripheral resistance thus increasing the intensity of murmurs of MR and AR. It increases systolic murmur of HOCM and MVP due to ventricular dilatation.
- Valsalva maneuver results in increased intrathoracic pressure with decrease in venous return, and left ventricular volume thus accentuating murmur of HOCM and MVP.
- Squatting simultaneously increases venous return and peripheral vascular resistance. It decreases cyanosis of TOF by reducing right to Left shunt, and increasing flow across RVOT. It decreases murmur of MVP.
- A 'Q' wave is indicative of transmural myocardial infarction, but it may also occur in unstable angina, coronary spasm, Prinzmetal angina, and HOCM. 'Q' wave of myocardial infarction may disappear because of shrinking of zone of infarction, successful reperfusion, development of an intraventricular conduction delay, 'contracoup' LV infarction, or hypertrophy of adjacent myocardial fibers. Diffuse PR segment changes in association with large LV infarction is suggestive of atrial infarction, PR changes are evident in lead I and left chest lead with depression in right chest leads.
- LBBB may mask ECG features of myocardial infarction. However, presence of an anteroseptal infarction can be diagnosed from presence of small Q waves in leads I, V₅, V₆. Cabrera's sign refers to the notch in the ascending limb of the predominant negative deflection in leads V₃, V₄.
- A figure 3 sign and E sign in X-ray are features of coarctation. Figure 3 sign identifies the level of coarctation and marks the apex of enlarged LV. The E sign is of barium filled esophagus in coarctation.
- The heart defect in Noonan's syndrome is PS, in Turner syndrome is coarctation, pulmonary stenosis and in Marfan's syndrome is mitral valve prolapse, TR and aortic root dilatation with AR. 76. 50% of patients with coarctation have bicuspid aortic valve. Bicuspid aortic valves take decades to progress to point of severe aortic stenosis to warrant valve replacement.
- Atrial myxomas arise from interatrial septum and intermittently prolapse into inflow tracts to produce transient dizziness and dyspnoea mimicking TIA. MR/TR may occur due to repeated trauma to valve leaflets. High ESR and systemic embolisation (in left sided tumors) are frequent. Auscultatory findings may mimic mitral stenosis and the tumor plop occurring in diastole is frequently confused with opening snap or S3.
- Acute severe mitral regurgitation results from endocarditis, papillary muscle rupture/infarction and presents as intractable heart failure requiring vasodilator therapy or IABP.
- Continuous murmurs that begin in systole and continue into diastole through second heart sound are heard in PDA, coronary a-v fistula, rupture of sinus of Valsalva aneurysm.
- The earliest abnormalities in dilated cardiomyopathy are ventricular systolic dysfunction and ventricular enlargement. Causes include, alcohol, myocarditis, peripartum cardiomyopathy, anthracycline antibiotics, end stage ischaemic heart disease. Patients with high cardiac gallium 67 uptake have lymphocytic myocarditis.
- In hypertrophic cardiomyopathy the primary abnormality is diastolic stiffness with abnormal left ventricular filling. ECHO

features are left ventricular hypertrophy (symmetrical or asymmetrical) premature closure of aortic valve, and systolic anterior motion of anterior leaflet of mitral valve. HCM is the most frequent pathologic finding in young athletes who die suddenly. The development of ventricular arrhythmia in HCM is a poor prognostic sign.

- In restrictive cardiomyopathy diastolic ventricular filling is restricted but systolic function is relatively preserved. Maximum ventricular filling occurs in early diastole (the dip and plateau observed in ventricular pressure tracing). The two most common causes of it are—cardiac amyloidosis and endomyocardial fibrosis (nutritional).
- In cardiac amyloidosis endomyocardial biopsy is diagnostic. ^{99m}Tc pyrophosphate myocardial uptake is high and patients are likely to develop atrial fibrillation and high-grade a-v block.
- Patients of constrictive pericarditis typically have some degree of restriction in both ventricles but in restrictive cardiomyopathy left sided pressure exceeds right sided pressure by more than 5 mm.
- The echocardiographic features of cardiac tamponade are—right atrial and right ventricular early diastolic collapse. Among the malignant tumors, malignant melanoma has the highest propensity to involve pericardium with effusive-constrictive pericarditis.
- About one-third of normal patients develop ventricular ectopics during exercise testing which are usually uniform or unifocal. Multifocal VPBs, couplets or VT are indications of coronary artery disease. Presence of late potentials continuous with QRS complex and persisting into ST segment, thus indicating delayed and fragmented ventricular activation indicate high risk of myocardial infarction and VT.
- The combination of LV dysfunction and complex ventricular ectopics is associated with poor prognosis in patients following MI.
- First degree AV block may represent normal finding especially in trained athletes. Hyperthyroidism, adreno-cortical deficiency, TOF may often have it.
- Fusion beats result from simultaneous activation of atrium and ventricle by a spontaneous impulse or a paced impulse.
- Ventricular pacing rather than atrial pacing is generally used in patients of sick sinus syndrome, because of frequent association with disease of distal conduction system and atrial arrhythmias which make atrial pacing ineffective. In elderly patients with LV dysfunction, atrial pacing is helpful in improving CHF by providing atrial kick to ventricular filling.
- Digitalis action is mediated by its inhibiting effect on Na⁺/K⁺ ATPase. Patients of CHF with sinus rhythm with abnormalities in LV diastolic function do not benefit from digoxin.
- AV node is supplied by posterior descending branch of right coronary artery in 90% cases. Bundle of His is supplied by both AV nodal artery and first septal perforator of LAD. The vascular distribution to left anterior fascicle is same as that of right bundle branch, which accounts for occurrence of bifascicular block in acute anteroseptal myocardial infarction.
- Ablation of AV node for unmanageable SVT is by alcohol injection into AV nodal artery or electrical RF ablation of AV node.
- Torsade de pointis (twisting of points) is a particular form of polymorphic ventricular tachycardia with alternating polarity of QRS complexes around base line, and QT prolongation. 95% pacemakers are rarely indicated for first degree AV block. Occasionally H-V prolongation can lead to first degree block and a pacemaker in this situation is indicated.
- Wenckebach phenomenon is typically due to block proximal to bundle of His, usually within AV node. On the other hand type II, second degree AV block typically occurs at or below bundle of His. It commonly progresses to complete AV block, thus requiring pacemaker implantation.
- Complete heart block associated with inferior wall infarction is usually transient without haemodynamic consequence, thus rarely requiring pacing. On the other hand bifascicular block developed acutely during anterior myocardial infarction progresses frequently to complete heart block requiring pacing.
- Increased vagal tone leading to bradycardia and asystole are very common during anaesthesia and surgery. Atropine given IV may reverse the bradycardia, else IV epinephrine be given. Blows to sternum can terminate asystole. Temporary pacing should be done if asystole or bradycardia do not respond to above measures.
- During CPR, the mitral and tricuspid valves remain open both during compression and relaxation. Thus chest compression is no longer felt to move blood peripherally by simply squeezing blood out of ventricles. The ventricular refill is rather enhanced as ventricles recoil during release phase of chest compression. Thus the heart serves primarily as a passive conduit during CPR.
- An elderly patient with decreased cardiac reserve can easily develop CHF in presence of stress like fever, anaemia, or tachycardia. Myocardium in aged has increased lipofuscin or iron pigment.
- LV hypertrophy can be concentric or eccentric. In concentric hypertrophy ventricular chamber diameter is not increased as seen in pure AS. In eccentric hypertrophy, the internal diameter of ventricle increases proportionately as in athletes and patients of LV volume overload (MR, AR).
- The autonomic and neural reflex mechanisms called upon to adjust the circulatory system in shock include three major classes of receptors that moderate afferent neural impulses: (1) arterial baroreceptors (aortic arch and carotid body), (2) Cardiac receptors (posterior left ventricular wall) and (3) Chemoreceptors (aortic body and carotid body). The first two classes are inhibitory receptors, that when stimulated inhibit sympathetic response. In shock their activity is decreased, leading to sympathetic stimulation. Chemoreceptors are excitatory receptors that are stimulated by hypoxia and acidosis and thus increase sympathetic response.
- Sick sinus syndrome is associated with following pathologic abnormalities—(1) amyloid deposit in the node, (2) excessive loss for age of nodal cells, (3) atrophy or hypoplasia of the node, (4) no detectable abnormality. Sick sinus syndrome has been with loss of fibers in more distal conduction system as well as after open heart surgery.
- Parasystole is a 'protected' focus of automatic activity. It exhibits abnormal conduction into and out of the focus. The abnormal conduction into the focus is called entrance block and that out of the focus is called exit block; coupling intervals may be varying or fixed.
- The model of re-entry has 3 components—unidirectional block, a finite circuit, and slow conduction within one of the limbs. The limbs of finite circuit are named alpha and beta. The alpha limb conducts antegrade and beta limb conducts retrograde. Alpha pathway has slower conduction and longer refractory period. The mechanism for torsade-de-pointis is probably due to fusion of two colliding cycles of epicardial depolarisation and early afterdepolarisation (a form of re-entry).
- Triggered activity is one of the two potential abnormalities associated with impulse origination that may give rise to arrhythmia formation. The other mechanism is automaticity. Triggered activity requires a stimulus to provoke repetitive

activity. Triggered activity is effectively suppressed by verapamil but automaticity is not. Triggered activity exhibits warm-up, a term signifying gradual increase in rate.

- The presence of a new right bundle branch block in the setting of acute myocardial infarction has serious consequences. The right bundle receives its vascular supply in one of two ways. In 50%, it is first septal perforator of anterior descending which is the sole supplier and in rest the supply is from AV nodal artery or right coronary and first septal perforator.
- Complications of cardioversion are related to 3 categories—(1) electrical cardioverter is not synchronised to R wave, thus often delivered within vulnerable period of cardiac cycle producing ventricular fibrillation (2) systemic embolization (3) appearance of postcardioversion arrhythmias.
- Syncope with effort is a major symptom of aortic stenosis, hypertrophic obstructive cardiomyopathy and pulmo-nary hypertension secondary to congenital heart disease.
- Four major characteristics associated with increased risk of sudden cardiac death in patients of coronary artery disease or hypertension are (1) ventricular electrical instability (2) extensive coronary artery narrowing (3) abnormal LV function and (4) conduction/repolarisation abnormalities.
- Epinephrine is the most crucial drug used during resuscitation effort. It increases arterial and coronary perfusion, stimulates spontaneous contraction during asystole, makes fine ventricular fibrillation more responsive to defibrillation, and acts as inotropic agent. It prevents carotid artery collapse, and enhances responsiveness to external cardiac compression.
- Amrinone is a noncatecholamine, nonglycoside bipyridine derivative that acts as a phosphodiesterase inhibitor. When used IV it reduces systemic and pulmonary vascular resistance and LV filling pressure unaffected heart rate (similar to dobutamine). Its vasodilator property predominates over positive inotropic characteristic. Enoximone and piroximone are also phosphodiesterase inhibitors but are imidazolone derivatives.
- In total anomalous pulmonary venous return, all the pulmonary veins unite to form a common chamber superior to left atrium. An intra atrial communication is necessary to transport partially oxygenated blood to the left side of heart and to sustain life until surgical correction is made.
- Postinfarction rupture of septal wall occurs within 24 hours of chest pain in upto 1/3 of patients and presents with a loud, harsh holosystolic murmur.
- Aneurysm of sinus of valsalva occurs due to congenital absence of media in the aortic wall. Its rupture most commonly occurs in young males. There is acute onset of chest pain accompanied by continuous murmur as the rupture is commonly to right atrium/ventricle.
- Only 50% cases of mitral stenosis recall a history of acute rheumatic fever. Mitral annulus calcification can rarely cause mitral stenosis but usually causes mitral regurgitation or heart block due to calcific encroachment of conduction system.
- Mitral regurgitation after myocardial infarction can be due to ischaemia/infarction of papillary muscle or the adjacent myocardium. The posteromedial set of muscles are more commonly involved than the anterior set by a ratio of 4:1. Severity of mitral regurgitation depends upon whether an entire set or only isolated heads are involved.
- Causes of tricuspid stenosis can be due to rheumatic fever, endocardial fibroelastosis, endomyocardial fibrosis, SLE, carcinoid syndrome, right atrial myxoma/thrombus and tumor metastasis. In a patient of mitral stenosis relief of dyspnoea,

PND in the face of worsening systemic venous hypertension 1341 indicates onset of tricuspid stenosis.

- A positive exercise ECG response for CAD in a young woman has predictive accuracy of 50%, while in middle aged man the predictive accuracy is 70-80%.
- Diffuse esophageal spasm may produce chest pain that is very similar to angina in quality, location and radiation, but it occurs after meal and is not related to physical exertion.
- Patients of unstable angina carry a high risk of sudden death and myocardial infarction within the first 3-months of onset of symptoms. The most powerful predictors of outcome in the early postinfarction period are the degree of LV dysfunction and objective evidence of ischaemia during exercise testing.
- Asymptomatic ischaemia (silent ischaemia) has a prevalence of 2-4% in men over 40 years of age. These patients have lower risk of developing myocardial infarction or sudden death.
- Even after successful thrombolysis, the incidence of reocclusion of the infarct affected artery is 25%. Hence, coronary angiography after 24-48 hours of thrombolysis with PTCA of the occluded artery is advisable.
- Patients with exercise induced ischaemia and single vessel disease have approximately 2% annual mortality while those with tripple vessel disease have 6% annual mortality.
- In variant angina (coronary spasm) ST depression occurs as commonly as ST elevation. Subendocardial ischaemia causing ST depression may be in part due to subtotal coronary occlusion, involvement of smaller branch vessels or due to presence of major collaterals. Variant angina frequently occurs at same time of the day and there is no increase in heart rate.
- The pathophysiology of mild essential hypertension is different from that of moderate or severe hypertension. Increased beta adrenergic activity and reduced parasympathetic activity results in increased myocardial contractility and heart rate in mild hypertension.
- Patients of moderate and severe hypertension either have low renin, normal or high plasma renin. Orthostatic hypertension is evidence of increased nor adrenergic activity.
- Diagnosis of pheochromocytoma should be considered in patients of episodic hypertension. 10% of these tumor are extra-adrenal, 10% are bilateral and 10% are malignant. Failure of plasma norepinephrine to fall with oral clonidine is an indirect indicator. Plasma volume is usually reduced but plasma renin activity is usually increased. Preoperative volume expansion and alpha receptor blockade are essential.
- Diastolic dysfunction may be the earliest manifestation of hypertensive heart disease. LV hypertrophy is associated with reduced compliance and impaired LV filling. Prolongation of isovolumetric relaxation correlates positively with LV mass index. The length of pre-ejection period reflects systolic function. Peak velocity of early filling is reduced while that of later filling is increased.
- Urinary excretion of metanephrine is the most sensitive test for adrenal pheochromocytoma, A urinary metanephrine-creatinine ratio above 22 is highly predictive. CT and NMR have replaced adrenal venography for diagnosis of pheochromocytomas.
- Renovascular hypertension is the most common curable cause of secondary hypertension. It should be considered in patients of abdominal bruit, those below 35 years of age, those with severe resistant hypertension and in whom renal function deteriorates following antihypertensive therapy. The two most common causes of renovascular hypertension are atherosclerosis and fibromuscular dysplasia of renal artery. The former benefit more from surgical revascularisation and the latter from balloon

angioplasty. Complications of balloon angioplasty include acute renal failure, renal infarction and renal artery dissection.

- Reduced plasma potassium in a patient of hypertension may indicate hyperaldosteronism. Primary aldosteronism can result from adenoma or bilateral hyperplasia of zona glomerulosa. Patients with bilateral hyperplasia are better treated with spironolactone.
- Elevation of serum lipid and potassium may accompany use of betablockers in hypertension and renal failure.
- The indications for venous interruption in pulmonary embolism are (1) recurrent emboli on adequate anticoagulation (2) contraindication of anticoagulants (3) persistent disease state leading to emboli (4) septic embolization from below heart (4) certain patients with massive emboli in whom a further embolus would be fatal. Thrombolytic therapy does not reduce long-term mortality when compared to heparin anticoagulation alone.

12 MCQs in Medicine

- Fat embolization usually occurs following fracture of midfemur or pelvic bones. Patient has acute respiratory distress with altered consciousness, seizure, delirium, coma and development of petechiae, Heparin is not beneficial and may even be detrimental in that the lipase activity might increase the toxic fatty acids in the lungs.
- The most sensitive indicator of pulmonary hypertension is enlargement of pulmonary arteries. RV enlargement is often difficult to demonstrate when emphysema causes a vertical heart shadow. Patients of sleep apnoea syndrome develop general alveolar hypoventilation and hypoxia leading to pulmonary hypertension. The symptoms of sleep apnoea are morning headache, day time somnolence, loud snoring and periodic apnoea during sleep and personality disorder.
- In dilated cardiomyopathy, atrial fibrillation and left bundle branch block are common rhythm disturbances caused by replacement of myocardial cells with fibrosis as well as myocytolysis. Abnormal thallium perfusion scan is common in long-standing dilated cardiomyopathy.
- Approximately 55% of the anterior surface of heart is by right ventricle, 20% by left ventricle and 10% by left atrium. Nonpenetrating trauma, hence is more likely to involve right ventricle. ECG in such patients is similar to infarction.
- The most common site of aortic rupture following blunt chest trauma is at the level of ligamentum ductus arteriosus. Survival is higher in distal aortic rupture and in those forming a false aneurysm initially at the site of rupture.
- The prevalence of cerebral infarction is 3%. Heart failure, atrial arrhythmias, anterolateral infarction and ven-tricular aneurysm all predispose to cerebral embolism. Cerebral infarction occurs in upto 17% of patients with cyanotic congenital heart disease. TOF and TGA account for most of these patients. Patients with congenital heart disease and right to left shunt are at increased risk of developing brain abscess.
- Patients of ostium primum atrial septal defect have left axis deviation with mitral regurgitation and enlargement of left atrium. Complete heart block may appear immediately after ASD closure or months later. Banding of pulmonary arteries may be needed in patients of ASD with large Lt to Rt shunt, to prevent pulmonary vascular disease. ASD children with severe MR or increased pulmonary vascular resistance must be repaired early since survival to age 5 without surgical correction occurs in only 4%.
- The normal aortic valve area is 2-3 cm². Chest pain, syncope, heart failure, and sudden death occur in critical aortic stenosis. Survival averages 5 years from development of exertional chest pain; 3-4 years from that of syncope and 2 years from

date of CHF. Sudden death occurs in 15-20% of patients with symptomatic aortic stenosis. Elderly patients with calcific aortic stenosis have a faster downhill course.

- The means by which hypertension induces atherosclerosis is not clear. Increased renin levels may induce cellular changes that lead to atherosclerosis. Altered characteristics of flow including eddy currents and back flow of blood at selected anatomic sites within arterial tree may result in focally altered endothelium and the development of atherosclerotic lesion.
- Cholesterol is a strong independent predictor of coronary mortality. Patients with serum cholesterol of 250-275 mg% have twice the risk of myocardial infarction as in patients with a serum cholesterol level of <175 mg%. The incidence of coronary artery disease appear to be inversely related to HDL level. The ratio HDL to LDL is a better predictive index for CAD than absolute HDL level.
- Glucose intolerance doubles the occurrence of CAD in men and triples or quadruples the incidence in women particularly prior to 50 years of age. Diabetes may predispose to atherosclerotic CAD by a number of mechanisms including increased lipid levels, hypertension, obesity. Control of hyperglycemia alone does not eliminate coronary risk. However, improved glucose tolerance is associated with increase in HDL value.
- Oral contraceptives increase body weight, and blood pressure, elevate triglyceride level, reduce glucose tolerance and reduce HDL levels. Their use is associated with higher risk of myocardial infarction, cerebrovascular and thromboembolic diseases. They are relatively safe for women below 35 years who do not smoke, are normotensive with normal lipid profile and no history of thromboembolic disease.
- Aspirin 325 mg daily on long-term intake reduces chances of myocardial infarction in general population by 50% in some studies. Betablockers started before hospital discharge in patients of myocardial infarction also reduces future sudden death by 26-39%.
- Exercise thallium scintigraphy is significantly superior to exercise ECG alone in both specificity and sensitivity. Multiple perfusion defects can be seen in 50% of patients with triple vessel disease and in 2/3 of patients with left main disease.
- The status of LV function is a more important prognostic variable than the extent of angiographic narrowing. Patients of 3 vessel disease and normal ventricular function have a four-year survival of 80% compared to less than 60% in those with TVD and impaired LV function.
- The most important determinants of survival in patients after myocardial infarction are infarct size and degree of LV dysfunction.
- Most patients of ischaemic cardiomyopathy die of dysrhythmias rather than of congestive failure or infarction. Fifty per cent of patients with CAD and severe LV dysfunction die within 3-year of presentation and about 80% die within 5-years.
- Diltiazem When given within 72 hours of non Q wave infarction, will reduce chances of reinfarction in 50%.
- The most common pattern of anomalous aortic origin of a coronary artery is that of left circumflex arising from right sinus of valsava and courses between aorta and pulmonary artery, there is an increased incidence of exercise induced sudden death. Anomalous origin of LCA from pulmonary artery presents in infancy with angina, infarction or CHF.
- Systolic compression of epicardial vessel due to intramyocardial bridging is a relatively rare arteriographic finding occurring in less than 1% cases studied for chest pain. Left anterior descending is commonly involved with systolic lumen < 25% of diastolic diameter of vessel.

- The exact etiology of primary pulmonary hypertension is unknown. Atherosclerotic plaques in large elastic pulmonary arteries and medial hypertrophy of small muscular arteries are relatively specific pathologic findings, but fibrinoid medial necrosis is a nonspecific finding.
 - The pulmonary circulation must remain as a low pressure, low resistance conduit to preserve the cardiac output. This is maintained because pulmonary arteries are thin walled, with little resting muscle tone, autonomic nervous system has very little effect on pulmonary vessels, and there are many small arteries and capillaries that are not utilized at rest but are perfused with exercise. Hypoxia causes a rise in pulmonary vascular resistance. In COPD, PA pressure is related to level of hypoxemia and is usually decreased by O₂ administration.
 - Cardiac myxoma is the most common benign cardiac tumor. The most frequent location for cardiac myxoma is left atrium (75%), right atrium 18%, right ventricle 4% and left ventricle 4%. They usually arise from fossa ovalis.
 - In ASD the mean LA pressure is usually less than 3 mm higher than RA pressure. The larger the ASD, less is the resistance and so minimal is the pressure difference between two atria. Atrial distensibility, atrioventricular valve distensibility and ventricular compliance contribute to the flow across the defect. 166. Features of a patient with single atrium are similar to those of a large ASD with fixed split S₂, hyperdynamic right ventricular lift and holo systolic murmur of mitral regurgitation. Clubbing and mild cyanosis that increase with crying differentiate it from ASD.
 - There is higher incidence of PDA among female children, in children with birth asphyxia/respiratory distress syndrome and in children with maternal exposure to rubella. Commonly associated defects include VSD and coarctation of aorta. The magnitude of shunt is determined by cross sectional area and length of ductus. Indications for PDA closure include uncontrollable congestive failure in neonate or growth retardation. Persistence of ductus beyond six months of age is also an indication for closure as endocarditis is a danger.
 - In aortic stenosis a measured pulse pressure $s' 30$ mmHg suggests severe aortic stenosis. Absence of systolic thrill indicates systolic gradient $5 30$ mmHg. Paradoxical splitting of S₂ is due to severe aortic obstruction or LV dysfunction. Patients of severe AS show in ECG absence of R wave in V₁ V₂, loss of Q wave in V₆ and ST-T changes anterolaterally.
 - Aortic stenosis can be valvular, subvalvular or supra-valvular. An ejection click in the apex is the hallmark of valvular aortic stenosis. Half of the patients of subvalvular stenosis have aortic regurgitation. In postvalvular stenosis patients have characteristic facies, hypercalcemia and mental retardation (William's syndrome). Poststenotic dilatation is common in valvular aortic stenosis but concentric LV hypertrophy is common to all forms.
 - One-third of patients with supra-valvular pulmonic stenosis have unilateral stenosis while 2/3 have bilateral peripheral pulmonic stenosis. 2/3 of these patients have associated anomalies like VSD, coarctation, TOF, supra-valvular aortic stenosis.
 - Patients with Noonan syndrome have a dysplastic pulmonary valve that causes pulmonary stenosis.
- complications arising from arrhythmia (atrial fibrillation), embolic manifestation (LA clot), and haemoptysis. Less common presentations are hoarseness, chest pain.
- The mid-diastolic rumble of mitral stenosis can be heard in other conditions like vsrt, PDA, due to increased flow across mitral valve. Austin flint murmur of aortic regurgitation is due to aortic jet impinging upon anterior leaflet of mitral valve. Left atrial myxoma, ball valve thrombus can also cause mitral mid-diastolic murmur.
 - Acute mitral regurgitation is more sinister as the receiving left atrium is not dilated with normal compliance. Hence pulmonary edema occurs easily. A holosystolic murmur is more common to chronic mitral regurgitation. Dyspnoea and fatigue occur late in chronic mitral regurgitation. Once LV dysfunction occurs in chronic MR, valve replacement may not bring full relief. 176. Occlusion of circumflex or right coronary branch produces papillary muscle infarction and resultant regurgitation, either due to rupture of the muscle or its malalignment.
 - Coronary fistula arise more frequently from right coronary than left coronary. History may include recent or remote chest trauma, and chest pain compatible with coronary steal phenomena. Physical examination reveals a continuous murmur. X-ray and ECG are unrewarding.
 - Kawasaki's disease is characterised by non-purulent cervical adenopathy, desquamation of extremities, pharyngeal erythema and sterile conjunctivitis. In 20% cases, vasculitis of vasavosorum leads to coronary arteritis, aneurysm, stenosis and occlusion. Syphilis causes coronary osteal stenosis in 25% of patients with tertiary leucic cardio-vascular disease. Other infections that rarely affect coronary arteries are salmonellosis, tuberculosis and leprosy.
 - Hypertrophic cardiomyopathy may be determined by an aberration of catecholamine function as it is associated with pheochromocytoma, systemic hypertension, Friedreich's ataxia and neurofibromatosis and LV function improves with betablocker therapy but worsens with isoproterenol.
 - Amyloid heart disease is a form of restrictive cardiomyopathy characterised by normal systolic function, normal cavity dimensions, and reduced LV diastolic function. Amyloid deposits can be seen in over 50% of patients above 60 years of age and most of the lesions are limited to atria, only one-third involving the valves and ventricles.
 - Sarcoidosis may cause pericarditis and restrictive cardiomyopathy. Sudden death due to dysarrhythmia or heat block is a common presentation. Thallium study shows myocardial perfusion defects due to sarcoid granulomas.
 - 4 electrocardiographic stages have been described in acute pericarditis. Stage I-diffuse ST elevation with PR depression. This ST elevation is less than 5 mm and is without monophasic patterns. There is reciprocal ST depression with corresponding PR elevation in aVR and V₁ Stage II-phase of normalization; stage III-diffuse T wave inversion; Stage IV-abnormal T waves may remain or revert to normal. Absence of Q waves, concavity of ST segment upwards and absence of associated T wave inversion differentiate it from myocardial infarction.
 - Chronic constrictive pericarditis in developing countries is largely due to tuberculosis. Pericardial involvement occurs in 30% cases of rheumatoid arthritis but it is subacute and seldom calcified.
 - Syphilitic, aortic aneurysm occurs most commonly in ascending aorta and tends to be saccular or fusiform. Coronary osteal stenosis does not extend distally beyond 1 cm. Atherosclerosis on the contrary usually spares ascending aorta, except in diabetes.

14 MCQs in Medicine

- In corrected transposition pulmonary artery arises from left sided morphologic right ventricle. In addition to ventricular inversion there is inversion of A-V valves. A VSD is present in most patients and 50% have Ebstein's anomaly of inverted left sided pulmonary valve.
- The most prominent complaint in mitral stenosis is dyspnea due to pulmonary edema. Patient may also present with

1344 • The major manifestations of cardiovascular syphilis are aortic regurgitation, aortic aneurysm and coronary ostial stenosis. To begin with there is involvement of vasa vasorum of aorta.

• The term mycotic aneurysm is a misnomer, since the invading organism is not always a fungus but can be bacteria.

• In osteogenesis imperfecta, there is aortic root dilatation but no regurgitation. Inheritance is autosomal dominant; bones are fragile and sclera is bluish.

• Thiazide diuretics cause a rise in serum triglyceride and LDL cholesterol. It also reduces insulin secretion leading to glucose intolerance.

• Peaked or tented T waves, which are the earliest electrocardiographic manifestation of hyperkalemia occur when plasma potassium exceeds 5.5 mEq/lit but are only seen in 20% of patients. Subendocardial ischaemia and cerebro-vascular accidents also cause tall peaked T waves.

• Depression of intra-atrial conduction at plasma greater than 7 mEq/lit results in broad and low amplitude P waves. When potassium level is greater than 9 mEq/liter the QRS widens. Acidosis, hyponatremia, and hypocalcemia potentiate ECG manifestations and cardiotoxic effects of hyperkalemia.

• Hypocalcemia is associated with prolonged QTc interval but there is no correlation between serum calcium level and QTc. Despite primary role of calcium in contraction, heart failure as a complication of hypocalcemia is rare.

• ECG manifestation of hypomagnesemia include narrow QRS complex and tall peaked T waves. Patients predisposed to magnesium depletion are those on diuretics, patients of gastrointestinal disease, diabetes mellitus, patients of heart failure and secondary aldosteronism. Hypomagnesemia potentiates digitalis induced arrhythmia.

• Severe hypophosphatemia may be associated with depression of myocardial contractility. Prolonged respiratory alkalosis, nutritional recovery from starvation, alcohol withdrawal and recovery phase of diabetic ketoacidosis are associated with hypophosphatemia.

• The immediate cardiac effects of electric shock include asystole or ventricular fibrillation. Apnoea and hypoxia induced by shock can lead to cardiac arrest which takes longer time to recover. Myocardial infarction can also result from electric shock.

• Week end 'angina' occurs in workers involved in ammunition making that uses nitroglycerol. This compound is 180 times more volatile than nitroglycerin and is thus easily absorbed from lungs and skin. Chest pain and sudden death can occur in these workers on withdrawal from prolonged nitroglycerin or nitrate exposure.

• Chronic use of vibrating tools predispose to cardiovascular changes similar to those seen in endurance athletes with increased ejection fraction and left ventricular end diastolic dimension with a decreased resting heart rate.

• Beta-blockers cross placenta, can cause low birth weight and induce premature labor but they still be used cautiously in pregnant ladies with hypertrophic obstructive cardiomyopathy. In young hypertensives beta-blockers should be tried but in older age group vasodilators because in the latter beta-blocker induced vasodilatory response is minimal.

• SLE can cause pancarditis with involvement of pericardium, endocardium, myocardium and coronary arteries. The pericardium is most frequently involved and pericardial effusion occurs in over 50% cases. Fibrofibrinous sterile vegetations known as Libman-Sacks vegetations occur but do not produce any valve dysfunction.

• Aortic root dilatation occurs in rheumatoid arthritis, psoriatic arthritis, Reiter's syndrome, and ankylosing spondylitis. This aortic root inflammation is clinically silent until aortic regurgitation occurs. While corticosteroids can be useful in iritis associated with these diseases, it is not helpful in aortic root disease.

• Tricyclic antidepressants may cause mild tachycardia and also orthostatic hypertension. They also have a quinidine like property, hence antiarrhythmic. In overdose they cause sinus tachycardia, prolongation of PR, QRS, and QT intervals, bundle branch block.

• Doxorubicin may cause cardiomyopathy in dose (total) exceeding 430 mg/m². Vincristine is reported to cause myocardial infarction. Among general anesthetics, halothane, enflurane and nitrous oxide are rarely used alone because of dysarrhythmia and cardiac depression. Ketamine may also cause post-operative psychosis and dysphoria. Pancuronium maintains sympathetic tone by inhibition of catecholamines at nerve terminal which leads to tachycardia and hypertension.

• Naloxone may reverse the depressant effects of narcotic analgesics, but may be dangerous in a patient of coronary artery disease as it produces sympathetic stimulation.

• In younger persons the endsystolic volume diminishes with exercise, reflecting a betasympathomimetic effect that enhances inotropic state and promotes effective arterial vasodilation. Elderly persons however, lack this response.

• Atrial natriuretic factor is formed and stored in granules in atrial tissue, to be released under conditions of atrial stretch. It increases GFR and decreases hypertonicity of renal medulla. It inhibits vasopressin and aldosterone.

• The earliest haemodynamic response to isotonic exercise is vasodilatation of resistance vessels in exercising muscles with fall in systemic vascular resistance, increase venous return, increase in end diastolic volume and increase in cardiac output.

• One MET is the energy expenditure of sitting quietly at rest and is equal to O₂ consumption of 3.5 ml/kg/min. In stage I of standard Bruce protocol energy expenditure is 5 MET. The metabolic response to treadmill is relatively independent of body mass, but metabolic response of ergometric exercise is inversely related to body mass.

• False negative exercise test commonly occurs in single vessel disease (usually left circumflex) that supplies electrically silent area of myocardium.

• The mechanism of action of heparin depends on its simultaneous binding to antithrombin III to coagulation enzymes.

• Converting enzyme inhibitors (peptidyl dipeptide hydrolase inhibitors) block production of vasoactive octapeptide angiotensin II from decapeptide angiotensin I. ACE inhibitors also inhibit aldosterone secretion and promote diuresis. They increase circulating levels of bradykinin by inhibiting its degradation and hence have vasodilator property. They are agents of first choice in mild to moderate hypertension and in congestive heart failure. A dry cough is troublesome in nearly 10% of patients taking enalapril.

• Digoxin binds to Na⁺ ATPase thus directly causing increased calcium influx. Digoxin is unstable in highly acidic solutions and may be inactivated by hydrolysis if gastric emptying is unduly delayed. About 10% of patients demonstrate extensive intestinal metabolism of digoxin which causes high digoxin requirement.

• Amrinone is a phosphodiesterase inhibitor and thus leads to increased intracellular cyclic AMP and consequent positive inotropic effect. It has also vasodilator properties. It improves cardiac output and diminishes LV filling pressure in patients of

heart failure without causing tachycardia and change in blood pressure.

- Urokinase is more clot selective whereas streptokinase is a nonspecific lytic agent. Allergic reactions are more common with streptokinase. Patients of anterior myocardial infarction seem to benefit more from thrombolysis and early reperfusion.
- The present treatment of choice for digoxin overdose is digoxin specific Fab fragment antibody which rapidly removes digoxin from cell membrane. Fab fragments have low molecular weight and hence rapid renal clearance. Immunodeficiency is a problem if multiple doses are required.
- Dopamine in small doses is renal vasodilator and hence promotes sodium excretion. In a setting of myocardial infarction and hypotension dopamine or norepinephrine infusion is preferred over dobutamine as latter causes vasodilation, tachycardia and decreased LV filling pressure.
- Most thiazide diuretics are ineffective when glomerular filtration rate falls to below 20 ml/min and therefore, are not useful in renal failure. However, metolazone is an exception.
- Gemfibrozil and clofibrate are fibric acid derivatives that (1) stimulate lipoprotein lipase activity, (2) partially inhibit synthesis of VLDL-triglycerides, (3) increase activity of LDL receptors, (4) decrease conversion of cholesterol and, (5) increase bile secretion of cholesterol. Thus, they reduce LDL and increase HDL.
- The value of endomyocardial biopsy is well established in cardiac transplant rejection, amyloidosis, haemochromatosis, sarcoidosis, carcinoid heart disease, endocardial fibroelastosis.
- Internal mammary artery is an excellent alternative to saphenous vein as a conduit since it is relatively free of atherosclerosis with 95% long-term patency rate. Its use as a free graft does not reduce its effectiveness or long-term patency. ;
- The major determinants of pump function are preload, afterload, heart rate and contractility. The determinants of cardiac output are arteriolar vascular resistance, contractility, preload, and heart rate.
- Pulsus alternans is the most specific indication of LV failure. Cardiomegaly, MR, S3, LV enlargement on ECG may all exist in absence of heart failure.

ENDOCRINOLOGY AND METABOLISM

- Osteogenesis imperfecta is a series of at least 6 disorders that can be inherited as autosomal dominant or auto-somal recessive. Some but not all of these syndromes have blue sclera.
- Fabry's disease is inherited as an x-linked trait and is caused by deficiency of alpha-galactosidase which causes intra-lysosomal deposition of glycosphingo lipids. Aminocentesis and cell culture for enzyme study is essential.
- Phenyl ketonuria is autosomal recessive and is due to deficiency of phenylalanine hydroxylase. A liver biopsy is necessary to demonstrate deficiency of the enzyme since hyperphenylalaninemia can be seen in other conditions. Gene therapy for the disorder is a distinct possibility.
- Hereditary angioedema is due to complement C₁ inhibitor deficiency manifesting with intermittent edema of skin, respiratory tract and GI tract, (causes abdominal pain).
- Patients of LCAT deficiency show hyperuricemia and a tendency for self mutilation (Lesch-Nyhan syndrome). Many are mentally retarded, have seizures and ataxia.
- Hereditary haemochromatosis is autosomal recessive and is due to increased intestinal absorption of iron. Most of these patients have hypogonadism due to failure to secrete gonadotropins. Those who develop cirrhosis carry a risk of developing hepatocellular carcinoma in 30%. Arthropathy is common but not renal involvement.
- Hypophosphatasia is a familial disease characterised by a failure to deposit bone mineral. Patients have low level of bone and serum alkaline phosphatase. Presentation is similar to rickets often with multiple fractures.
- Refsum disease is an autosomal recessive disorder with accumulation of phytanic acid, manifesting as peripheral neuropathy and night blindness (retinitis pigmentosa).
- Neurofibromatosis is one of the most pleiotropic of all genetic disorder that can virtually affect any organ system with variable severity and expressivity.
- The gene coding for human G6PD is X-linked. There are more than 80 defined variants of the enzyme. Only older RBCs are the victims of oxidant stress in G6PD deficiency as neocytes have sufficient level of enzyme to avoid drug induced haemolysis.
- Orotic aciduria is characterised by megaloblastic anaemia, leukopenia and growth retardation. Deficiency of phosphoribosyl transferase and ornithine carbamoyl transferase can produce this disorder but not carbamoyl synthetase deficiency.
- Laurence-Moon-Biedl syndrome is associated with obesity, retinitis pigmentosa, hypogonadism and polydactyly.
- Turner's syndrome can be caused by a variety of chromosomal anomalies-45 XO in 50%, isochromosome X in 20%, mosaicism in 20%.
- Defective activity of the enzyme ferrochelatase results in erythropoietic protoporphyria manifesting as pruritic erythema on sun exposure. Acute intermittent porphyria is autosomal dominant and is due to diminished prothobilinogen deaminase activity. Though 90% are asymptomatic, symptomatic patients have abdominal pain, ileus, vomiting etc. Neurological disturbances include proximal motor weakness, mental disturbances. Porphyria cutanea tarda is the most common form of porphyria with deficiency in hepatic uroporphyrinogen decarboxylase. Patients develop bullous eruptions on exposure to sun.
- Xeroderma pigmentosa is an autosomal recessive disorder of DNA synthesis manifesting in children with photo-sensitivity, freckles, zerosis, hypopigmentation etc. These patients have propensity for developing melanoma, basal/squamous cell carcinoma.
- Testicular feminization manifests with underdeveloped female genitalia in a genotypic male. Androgen receptors are defective and inheritance is X-linked.
- Palmar xanthomas are characteristic of familial dysbetalipoproteinemia a disorder resulting from abnormalities in the structure of apoprotein E.
- Tendon xanthomas are seen in patients of familial hypercholesterolemia who fail to clear LDL from plasma but have normal triglyceride level.
- Panacinar emphysema is common to those patients of alpha 1 antitrypsin deficiency who are homozygous for Z allele of the gene.
- C1 esterase inhibitor deficiency causes hereditary angioedema with abdominal pain. Androgen supplement prevents the edema as well as reverses the biochemical defect.

1346 • The major cause of early death in trisomy 21 is cardiovascular malformation. Nonan's syndrome is often termed 'male Turner's syndrome.

- Both adenosine deaminase deficiency and nucleoside phosphorylase deficiency are inherited as autosomal recessive traits. The former leads to severe combined, immune deficiency but the latter leads to T cell deficiency with intact B cell function.
- Hunter's syndrome is X-linked recessive but Hurler's syndrome is autosomal recessive. Both have mental retardation and coarse facies. Cloudy cornea is characteristic of Hurler's syndrome but cornea is normal in Hunter's syndrome.
- Hypothalamic failure results in high prolactin level due to loss of hypothalamic dopamine secretion which is prolactin inhibitory factor. Secretion of all other pituitary hormones is decreased.
- Malignant otitis externa is common to diabetics over the age of 35 and the infecting organism is *P. auroginosa*.
- Lymphocytic thyroiditis is characterised by clinical hyperthyroidism with low radioiodine uptake. Gradual recovery over period of time is usual.
- The occurrence of diabetes insipidus following pituitary surgery is common and is triphasic. Initially polyuria occurs because of inhibition of ADH release. Next there is period of oliguria and high urine osmolality and finally there is polyuria.
- Paget's disease is a relatively common bone disease in patients over age of 70. Mithramycin, prednisone, diphosphonates and calcitonin are all helpful.
- Abrupt weight loss, anorexia, low BP, small heart and pigmentation imply Addison's disease, infection may precipitate addisonian crisis.
- The initial work up in suspected Cushing's syndrome is dexamethasone overnight suppression test or 24 hour urinary free cortisol measurement. Metyrapone test, CT scans of adrenal and pituitary are done subsequently.
- In a patient of elevated FSH despite normal testis, normal testosterone and LH levels suggests diagnosis of Sertoli cell only tumor. There is azoospermia and patients are infertile. Testicular biopsy is of limited help and infertility is irreversible.
- Chronic alcoholics may develop stigmata resembling Cushing's syndrome and biochemical studies may reveal hypercortisolemia. Hence such patients should be reevaluated after abstinence from alcohol.
- In a patient of moderately severe ketoacidosis normokalemia implies severe total body potassium depletion which is likely to be aggravated with fluid replacement. Thus potassium infusion is mandatory.
- In a diabetic with moderate hyperkalemia, metabolic acidosis, and mild depression in renal function have usually hyporeninemic hypoaldosteronism.
- Acute nonthyroidal disease can cause decrease serum T_3 and increased reverse T_3 concentration as T_4 is preferentially converted to reverse T_3 .
- Klinefelter's syndrome should be suspected in patients of hypogonadism with small firm testis, gynecomastia, low testosterone levels and increased plasma FSH and LH. Chromosomal analysis is a must for such patients (XXY pattern).
- The sense of smell must be tested in all patients with delayed puberty or eunuchoid features to exclude Kallmann's syndrome due to reduced pituitary GnRH release.

- Diabetic amyotrophy usually involves proximal muscles i.e., muscles of pelvic girdle and thigh with weakness, atrophy and severe pain but no sensory loss. Spontaneous gradual recovery is usual.
- Gastroparesis diabeticorum refers to reduced gastric emptying and gastrointestinal motility secondary to diabetic neuropathy manifesting with bloating, distension, hiccups etc. Metoclopramide improves symptoms.
- Amiodarone is approximately 40% iodide. It hence induces hypothyroidism. More over it suppresses peripheral conversion of T_4 to T_3 .
- Carcinoids are almost always metastatic at the time of diagnosis. Hence diarrhoea of carcinoid syndrome is treated with cyproheptadine, methysergide or pochlorophenylalanine.
- Patients of isosexual precocious pseudpuberty have usually congenital adrenal hyperplasia. If there is hypertension in the child 11 hydroxylase deficiency is certain.
- Genetics in the most important determinant of obesity. The Ob gene produces leptin? a protein secreted by fat cells in response to fat storage. Leptin acts upon brain to decrease appetite and increase body's metabolic rate. Obese individuals secrete more leptin but their brain is insensitive to it.
- Octreotide in the first line drug for gigantism where transphenoidal surgery is unavailable. When combined with bromocriptine it has additive value.
- Bromocriptine 2.5-20 mg/d and pergolide 0.25-2 mg/d are equally effective in treating hyperprolactinemia. Ladies can have transvaginal bromocriptine.
- Elevated antithyroglobulin and antithyroperoxidase antibodies indicate Hashimoto's thyroiditis while elevated antimicrosomal and TSH receptor antibodies indicate Grave's disease.
- Cyproterone acetate, spironolactone and finasteride are all effective in hirsutism so also flutamide.
- Serum fructosamine level monitoring in diabetes indicates glycemic control over past 2 weeks.
- Blood insulin level of 8ng/ml or more in presence of blood sugar below 40 mg/dL is suggestive of insulinoma. Patients of insulinoma have raised proinsulin representing 30-90% of total immunoreactive insulin.
- Unresectable or partially resectable insulinoma need treatment with diazoxide, verapamil or somatostatin.
- Vit. C, E and A are antioxidants and may retard atherosclerosis. Oxidized LDL is particularly atherogenic. Antibodies to oxidized LDL may promote atherosclerosis.
- Marine fish contain n-3 or omega-3 fatty acid which retard platelet aggregation; fatty acids with transisomer have been associated with increased risk of coronary artery disease.
- Statins reduce LDL more than triglyceride; the opposite is true of gemfibrozil. However over all CHD risk is reduced only by simvastatin and gemfibrozil.
- Obesity is genetically determined Mutation in gene for 83 receptor in adipose tissue involved in lipolysis and thermogenesis, markedly increase the risk of obesity.
- Acute attacks of abdominal pain that are often precipitated by diet or drug (barbiturate, anticonvulsants sulphonamides, alcohol) may be due to acute intermittent porphyria.
- Hormone binding is specific for a single type of receptor but cortisol and estrogens can bind to an array of receptors.

- Membrane receptors for hormones are of 4 major groups (a) GPCR (for LH, FSH, ACTH, PTH etc) (2) tyrosine kinase receptors (insulin) (3) Cytokine receptors (GH) and (4) serine kinase (TGF β) Nuclear receptors (T_3, T_4 , cortisol) number around 100, many of which are orphan because their ligands are unidentified.
- Carney syndrome is characterised by skin pigmentation, myoxmas and endocrine tumors of testis, adrenal, and pituitary-a chromosome 2 disorder.
- Cabergoline is a long acting dopamine (D2) agonist, suppressing PRL for over 2 weeks with a single dose 0.5-1 mg twice weekly shrinks 80% microadenomas and is effective in those resistant to bromocriptine. Other D₂ receptor agonist are pergolide, lisuride and quinagolide.
- Dose of octreotide for growth hormone secreting adenoma is 50 μ g tid increased upto 1500 μ g/day. Modest regression of tumor occurs in 40% but effect is reversed when treatment is stopped.
- Lanreotide is a depot preparation of somatostatin whose effect lasts for 10-14 days after 30 μ g IM.
- Inferior petrosal venous sampling before and after CRH administration is best to differentiate between pituitary ACTH secreting tumor from ectopic ACTH secreting tumor.
- The main mechanism of thyroid tissue destruction in idiopathic hypothyroidism is activation of T₄ and T₈ cells with increased apoptosis of thyroid follicles by upregulation of Fas. Antibodies present to thyroid tissue have minimal role (Tg, TP0). TPO antibodies fix complement but not Tg anti bodies. These antibodies only amplify the ongoing autoimmune response.
- TSH-R blocking antibodies are present in 20% of Asian patients with hypothyroidism and cause thyroid atrophy
- Thyroid associated ophthalmopathy is due to cytokine induced synthesis of glycosaminoglycans that trap water. Orbital fibroblasts are uniquely sensitive to cytokines.
- Hashimoto's encephalopathy of hypothyroidism is associated with myoclonus and progresses to confusion and coma but is corticosteroid responsive.
- Conversion of angiotensin I to angiotensin II is mainly in pulmonary vasculature, and latter is converted to angiotensin III in liver. Angiotensin II and III act through AT-1 receptor, role of AT-2 receptor is unidentified.
- In normal women 90% urinary ketosteroids (DHEA metabolism) is of adrenal origin and in men 60-70% is of adrenal origin .
- Statins can reduce progression of diabetic retinopathy, so also strict blood pressure control but not strict glycemic Le. control. Once advanced retinopathy is present, strict glycemic control is of less benefit.
- Insulin lispro and aspara are short and quick acting soluble insulins. In the former lysine and proline in 28th and 29th position of betachain are reversed by rDNA technology.
- Insulin glargine is a long acting biosynthetic insulin which has later onset of action and longer duration of action ies without pronounced peak, hence may replace nocturnal NPH.
- Insulin sensitizers rosiglitazone and pioglitazone reduce insulin resistance and improve glucose utilization in ted peripheral tissues and skeletal muscle. They may induce ovulation in PCOD.
- Osteoblast is of mesenchymal origin whereas osteoclast has haematopoietic origin. PTH, Vit D help in formation of active osteoblast that secretes collagen I, osteopontin, osteocalcin and alkaline phosphatase. Osteoclast formation is influenced

by IL-1, IL-6, M-CSF and active osteoclasts secrete 13 integrin, TRAF, cathepsin and carbonic anhydrase. The RANK signalling pathway links osteoblasts with osteoclasts.

- Jansen's disease is AD with mutations in PTH/PTHrP receptor. There is short limbed dwarfism with multiple cystic areas in bone, undetectable PTH, hypercalcemia and hypophosphatemia.
- Zoledronate is third generation biphosphonate, upto 800 times more potent than pamidronate and normalizes raised serum calcium more quickly.
- Raloxifene is selective estrogen receptor modulator, approved for use in postmenopausal osteoporosis. It is antiestrogenic for breast cancer whose risk is reduced by 70%. Unlike tamoxifen it does not increase risk of uterine mer cancer.

GASTROENTEROLOGY

- In liver failure, there is failure of conversion of all amino acids (except for branched chain ones like leucine, isoleucine, valine) taken up from portal circulation to urea. Hence ammonia level rises to cause CNS dysfunction.
- Other mechanism for hyperammonemia in liver failure include-bacteria deamination of amino acids in gut following bleeding, portal hypertension allowing gut ammonia to bypass the hepatic detoxification and alkalosis which favors NH_4^+ , NH_3 equilibrium in favour of ammonia.
- Carcinoma colon is the most common cause of mechanical obstruction of colon and is followed in frequency by sigmoid diverticulitis and volvulus. Adhesions and hernias cause 75% of small intestinal obstruction.
- Gut sterilization with neomycin leads to defective absorption of vit K and this can compound hypoprothrombinemia.
- Interferon-alfa is the only promise for chronic active hepatitis of HBV and HCV. Prednisolone is effective when CAH is of nonviral etiology. 4 month course of interferon achieves 40% seroconversion from HBeAg positivity to detectable levels of anti HBe.
- The risk of subsequent complications or symptoms in a patient of silent GB stone is less than 1% per year. Hence diabetics with silent gallstone need not have cholecystectomy as long as there is no cholesterosis, porcelain gallbladder or adenomyomatosis.
- The clinical constellation of tender hepatomegaly, a bruit in right upper abdomen, bloody ascites and very high alkaline phosphatase in a stable patient of cirrhosis indicate hepatoma. There is high level of alfa fetoprotein.
- Vit B12 malabsorption occurs in chronic pancreatitis and is due to excessive binding of vitamin by non-intrinsic factor binding proteins which are normally destroyed by pancreatic proteases.
- The combination of weight loss, anaemia and a bullous akin eruption in a patient with hepatic metastasis and evidence of pancreatic lesion is highly suggestive of glucagonoma.
- Presence of HBeAg is linked to infectiousness and the antigen is present during viremic period of HBV. Although HBeAg correlate% well with viral replication, its detection in serum does not predict development of chronic active hepatitis. Disappearance of HBeAg from serum indicates resolution of infection. HBeAg negative persons should be considered infectious till antibody to HBsAg is no longer detected in serum.
- Most gastrinomas are found in the pancreas and usually multiple. About two thirds of gastrinomas are malignant. It should be suspected when multiple, fulminant, poorly responding peptic ulcers are present at unusual sites.

Two areas in CNS control the act of vomiting. The vomiting centre in the lateral reticular formation in medulla receives input from GI tract and controls outflow to phrenic, vagus and spinal nerves which innervate muscles involved in retching. The CTZ in floor of 4th ventricle is stimulated by drugs and metabolic toxins and abnormalities. CTZ is connected to vomiting center by distinct pathway. Antivomiting drugs, i.e. dopaminergic inhibitors or serotonin antagonists act on CTZ.

- Risk factors for development of colon cancer in patients of ulcerative colitis include presence of disease for more than 10 years, pancollitis and family history of colon cancer. Neither steroids nor megadblon and pseudopolyps increase risk of colon cancer.
- Acute haemorrhage from colonic diverticula is the most common cause lower GI bleed among elderly. Bleeding usually arises from ascending colon even though diverticular disease is common on the left.
- Adenomatous polyps of the colon are very common in general population and the incidence increases with age. An increasing size and flatness correlate with increased risk of malignancy.
- Chronic liver disease of any etiology is associated with increased risk of hepatic cancer. Aflatoxin, alcoholic liver disease, hepatitis B, alfa antitrypsin deficiency are main villains.
- All dyspeptic patients should undergo test for *H. pylori* (breath test, IgG serology) because *H. pylori* eradication will cure dyspepsia. 18. The haematocrit is a poor indicator of severity of acute bleeding because it takes 24-72 hours to equilibrate with extravascular fluid.
- Somatostatin 250 pg IV bolus followed by 250 pg every hour controls variceal bleed. Continuous IV infusion of octreotide 50-100 pg/hour also reduces portal pressure and splanchnic blood flow. Combination of vasopressin and nitroglycerine is another alternative.
- In lower GI bleed embolisation is promising but is associated with infarction in 15% cases.
- The serum ascites albumin gradient (SAAG) is the best single test for classifying ascites; the gradient correlates directly with portal pressure. SAAG < 1.1 indicates ascites due to non-portal hypertension.
- Transjugular intrahepatic portosystemic shunt can control variceal bleed in 90% cases. Several trials indicate band ligation or sclerotherapy can control acute variceal bleed better than medical management though do not decrease overall mortality.
- Chronic *H. pylori* infection is attributed to causing chronic gastritis, duodenal and gastric ulcer, gastric lymphoma and gastric carcinoma. *H. pylori* is eradicated with MOC regime (metronidazole 500 mg bid, omeprazole 20 mg bid and clarithromycin 500 mg twice daily) or AOC regime (amoxicillin 1 gm twice daily, omeprazole and clarithromycin as above). Amoxicillin can replace clarithromycin in MOC regime. These regimes achieve cure rate of 85-90% in 1-2 weeks of therapy.
- Omeprazole 20mg/d and lansoprazole 15 mg/d achieve 90% duodenal ulcer healing in 4 weeks. Omeprazole 40 mg/d and lansoprazole 30-60 mg/d heal 90% gastric ulcer after 8 weeks. Patients on long-term proton pump inhibitors should have serum gastrin estimation after 6 months of therapy and if its level is above 500 pg/ml, the dose should be reduced or stopped.
- Sucralfate is more effective in duodenal than gastric ulcer. Bismuth promotes ulcer healing through stimulation of mucosal bicarbonate and prostaglandin production. It has antibacterial action against *H. pylori* similar to proton pump inhibitors.
- About 10% of gastric lymphomas arise from mucosa associated lymphoid tissue and tend to be lowgrade indolent tumors

without dissemination to lymph nodes and hence carry excellent prognosis.

- Whipple's disease is a multisystem disease caused by *Tropheryma Whippeli bacillus* producing intestinal malabsorption arthritis and myocardial involvement. Treatment is with trimethoprim-sulfamethoxazole for 1 year.
- Octreotide represents a major advance in the treatment of severe carcinoid syndrome and diarrhoea. Carcinoid syndrome is seen only in those with hepatic metastasis. Virtually all patients with carcinoid syndrome have obvious signs of cancer with liver metastasis on imaging.
- HCV is responsible for over 90% cases of post-transfusion hepatitis. HCV may be a pathogenic factor in cryoglobulinemia, glomerulonephritis, and sporadic porphyria cutanea tarda.
- Recombinant human interferon alfa 2b, 3 million units 3 times a week for 24 weeks achieves biochemical and histologic improvement in 50% cases of hepatitis C. In addition to interferon lamivudine 100 mg daily is useful in treatment of HBV. Ribavirin plus interferon yields better result in HCV but this combination therapy is disappointing in interferon non responders.
- HBV vaccine in a dose of 10-20 µg, 3 doses provides protection for upto 10 years and is recommended for all children and high risk groups.
- Hepatopulmonary syndrome is the triad of liver disease, increased alveolar-arterial gradient and right to left intrapulmonary shunt. Patients have platypnea.
- Alfa antitrypsin deficiency frequently presents in the neonatal period with cholestasis and then often progresses to cirrhosis.
- In addition to abdominal cramps and diarrhoea patients of whipple disease may have a variety of extra-intestinal symptoms like arthritis, lymphadenopathy and fever. Small bowel obstruction is of course a feature.
- Granuloma inguinale is a papulo-vesicular and ulcerating infection of skin, perianal area and anus. Unlike LGV it never causes proctitis.
- Pericholangitis associated with ulcerative colitis is usually a benign process consisting of portal tract inflammation and occasionally periductular fibrosis but jaundice is rare.
- Celiac sprue typically involves only the mucosa where as eosinophilic gastroenteritis involves deeper layers in addition.
- When a patient has melanin deposit on lips, buccal mucosa, palms, soles and perianal skin, GI bleed and history of intestinal obstruction the possible diagnosis is Peutz-Jeghers syndrome, an autosomal dominant disorder with benign intestinal polyposis. Since these polyps are benign hamartomas, not adenomas, malignancy potential is only 3% where as polyps of Gardner's syndrome (familial polyposis) have a 95% risk of adenocarcinoma.
- Chronic diverticulitis can present with pneumaturia, left lower abdominal pain, fever, lower GI bleed. Such colon-vesicular fistula can also occur in Crohn's disease and carcinoma of colon.
- Excessive flatus production results from lactase deficiency because the breakdown of undigested lactose in the colon yields hydrogen and carbon dioxide. The hydrogen breath test is more specific and more sensitive than the traditional lactose tolerance test. 'Gas pain' of otherwise normal individual is due to disorder of intestinal motility.
- There is no need to treat an asymptomatic patient of chronic active hepatitis with prednisolone and azathioprine since they do not prolong survival. As long as patient remains

asymptomatic and his biomedical studies do not change, there is no need of repeat liver biopsy.

- While prescribing a liquid antacid for peptic ulcer, the principal factor to be taken into consideration is the acid neutralizing capacity not the mere volume of antacid. A bedtime dose is essential to neutralise nocturnal acid production.
- Milk has a weak acid neutralizing capacity but its high calcium content is a potent stimulator of gastric acid production. Antacid tablets have only a limited place in treatment of acid peptic disease.
- Aspirin and other NSAID which block production of prostaglandin E_2 and I_2 are ulcerogenic because they hamper with prostaglandin mediated cytoprotection.
- Ulcer on the posterior duodenal bulb juxtaposed to the gastroduodenal artery is far more likely to cause massive GI bleed.
- Wilson's disease can manifest with chronic active hepatitis and fulminant hepatic failure with normal ceruloplasmin. Kayser-Fleischer ring may be absent in very young children with Wilson's disease and it may be present in any patient with severe and prolonged cholestasis.
- Though *A. lumbricoides*, *F. hepatica* and *C. sinensis* can all infest the biliary tree and cause obstruction and infection, only *C. sinensis* can live in human host for decades to cause cholangiocarcinoma
- Adults of *S. mansoni* live primarily in rectal submucosal venous channels, deposit eggs that find their way into inferior mesenteric venous plexus to land up in portal venules but not in bile ducts.
- Half of the right colonic haemorrhages are due to vascular ectasia. Radionuclide scans are helpful but distal small bowel lesion is difficult to exclude
- Pancreatic pseudocysts can compress the gastric outlet or common bile duct. Chronic leakage of cyst contents can result in ascites which is high in digestive enzyme content. Cystadenocarcinomas of pancreas never arise from pseudocysts
- Persisting elevation in serum amylase after recovery from acute pancreatitis indicates pseudocyst formation. Amylase elevation occurs in 20% cases of pancreatic cancer but it can also be elevated in acute cholecystitis.
- Asymptomatic cholelithiasis is a relatively benign condition and less than 25% of these patients subsequently develop serious complications. The risk of gallbladder cancer in a patient of asymptomatic cholelithiasis is exceedingly small and does not call for prophylactic cholecystectomy.
- Colchicine affects intestinal epithelial cell function and can result in mild steatorrhoea and an abnormal D xylose test.
- Individuals who are HBSAg +ve are 200 times more prone to develop hepatocellular carcinoma than those who are HBSAg -ve, making hepatitis B virus infection perhaps the strongest known risk factor for any human cancer.
- Up to 80% of patients of duodenal ulcer suffer a relapse within one year of treatment and many recurrent ulcers are asymptomatic.
- Midcolon transverse diameter more than 7 cm with loss of haustral details in a patient of ulcerative colitis indicates toxic megacolon. Toxic megacolon can occur in Crohn's disease, amoebic colitis and shigella infection as well.
- Unlike renal insufficiency, there are no practical nomograms for calculating drug dosage in liver disease. Liver disease offers no protection for drug-drug interaction.
- Haemochromatosis, a chromosome 6 disorder can only definitely diagnosed form quantitation of hepatic iron from liver biopsy. Presence of stainable iron in more than 75% of hepatocytes only correlates roughly with quantitative measurement. Chronic alcoholics also have increased hepatic iron.
- No biochemical values like serum levels of (1) GABA mercaptan and ammonia (2) CSF levels of glutamine and (3) ratio of aromatic to branched chain amino acids accurately stage hepatic encephalopathy. Hence EEG is the only dependable tool.
- Valproic acid has been associated with acute and sometimes fatal hepatic failure, the histological picture resembling acute fatty liver of pregnancy or tetracycline toxicity.
- Vit A when taken in amounts exceeding 40,000 IU 8 day for years leads to hepatic damage as well as systemic symptoms of hairloss, fever, pruritus and bone pain.
- Androgenic anabolic steroids like oxymethelone can cause peliosis hepatis, hepatic rupture and haemorrhage as well as hepatocellular carcinoma.
- Cimetidine which has an imidazole ring has anti-androgenic effect but ranitidine which has the furan ring is devoid of antiandrogenic effect.
- Any mother who is HBEAg +ve is most likely to transmit the infection to her baby. 72. Only side to side portocaval shunt besides reducing portal pressure improves ascites.
- Villous adenomas of descending colon, sigmoid colon and rectum can be associated with secretory diarrhoea, and hypokalemia. They carry a more chance of malignancy than a similar sized adenomatous polyp.
- Endoscopic US plays an important role in evaluating depth of invasion of upper GI malignancy.
- Dieulafoy's lesion refers to a large caliber arteriole that runs immediately beneath the gastrointestinal mucosa, usually in the proximal lesser curvature that causes occult GI haemorrhage.
- Magnetic resonance cholangiopancreatography and helical CT can diagnose bile duct malignant without need for ERC P.
- Charcot's triad of abdominal pain, fever and jaundice is present only in 70% of patients with ascending cholangitis and biliary sepsis.
- All patients with history of heart burn for over 10 years need frequent endoscopic surveillance for Barret's esophagus, dysplasia and early malignancy.
- Barret's esophagus can also lead to chronic peptic ulcer of esophagus with high and long strictures. Endoscopic mucosal resection or photodynamic laser ablation may be curative.
- The cause of duodenal ulceration in *H.pylori* infection is uncertain. There is gastric metaplasia in duodenum, less of duodenal bicarbonate production or increased gastric acid secretion from *H.pylori* induced gastrin release.
- A BAO:MAO ratio >0.6 is highly suggestive of ZES; an increase in gastrin >200 pg/ml within 15 minutes of secretin infusion is also $>90\%$ specific for ZES.
- Medium chain triglycerides (8-10 carbon atoms) are abundant in coconut oil and are absorbed directly to portal blood without a micellar phase independent of pancreatic lipase.
- In celiac disease IgA antigliadin and antiendomysial antibodies are present but the relation of these antibodies to disease is not

certain. Patients of celiac sprue are at higher risk of developing intestinal lymphoma, GI and non GI neoplasms.

- Single dose of IV infliximab 5 mg/kg can bring remission in resistant Crohn's disease upto 3 months and repeated injection can maintain remission. However IL-10 that decreases TH₁ response, has only modest effect in CD.
- An AST: ALT ratio > 2:1 is suggestive of alcoholic liver disease. The AST rarely exceeds 300 IU/L but ALT is often low due to alcohol induced pyridoxine deficiency.
- GGT is rarely elevated in conditions other than liver disease. 92. HBV mutants exist (precore mutants and escape mutants) and may complicate vaccination strategies and serologic diagnosis. Precore mutants that are unable to secrete HBeAg tend to have severe and resistant liver diseases rapidly progressing to cirrhosis.
- HGV and TT virus are also transmitted by transfusion but do not cause hepatitis.
- Interferon therapy in chronic HBV is not advisable if patient has immunosuppression, acquisition of infection in childhood (Asian), decompensated liver disease, or precore mutant. However lamivudine can be safely given in all above situations.
- A distinguishing feature of chronic HDV is presence of anti LKM₃ (anti LKM₁ is present in autoimmune hepatitis and subset of HCV). HDV clearance needs 9 million units of IFN α . Thrice weekly for 12 months with clinical improvement in 50%.
- Hepatitis C can be associated with lichen planus, myxed cryoglobulinemia and porphyria cutanea tarda and interferon therapy may cause their regression.
- Transjugular intrahepatic portosystemic shunt (TIPS) is good to reduce portal pressure for control of variceal bleed. It is also promising in refractory ascites but no way prolongs survival.

INFECTIONS

- Nucleic acid probe technology is used to identify difficult to grow or noncultivable bacterial pathogens like Mycobacteria, Legionella, Ehrlichia, Rickettsia, Babesia, Borrelia and Trepheryma whippeli.
- Third generation vaccines use DNA/RNA to induce immunity. A DNA plasmid containing the gene sequence for the immunogenic protein is assembled. A single immunization with plasmid results in DNA uptake into cells where the gene is expressed and the product stimulates the immune response.
- HIV infected individuals should receive pneumococcal and other nonlive attenuated vaccines; but measles vaccine is not contraindicated.
- Septic shock is due to exaggerated response to cytokines like TNF, IL-1 β , INF γ and IL-8 and nitric oxide, and phospholipid derived mediators (leukotrienes) promoted by lipid A. However, no antilipid A agent is yet available.
- TTE is 65% sensitive to detect vegetation in endocarditis but TEE is 90% sensitive.
- In infective endocarditis moderate to severe refractory heart failure caused by valve dysfunction is the major indication for surgical intervention because 60-90% of them die within 6 months without surgery.
- Fluoroquinolone resistance among mycobacteria is a major concern. Hence random use of them in tuberculosis be discouraged.

- WHO recommended regimen for leprosy is questioned since 20-40% relapse in LL and demonstrable activity in 50% cases of tuberculoid leprosy. So present recommendation is that TT patients be given dapsone 100 mg daily for 5 years; LL patients dapsone 100 mg daily for life plus rifampicin 600 mg daily for 3 years.
- Nontuberculous mycobacteria are ubiquitous in the environment. Their isolation from sputum or urine does not constitute proof of disease.
- Live attenuated varicella vaccine is available and is given in 2 doses 4-8 weeks apart to persons of 12 years or older. Duration of immunity in about 10 years.
- Influenza vaccination is recommended yearly. It is a chick embryo vaccine like measles, mumps and yellow fever vaccines.
- Pneumococcal vaccine, single dose confers life long immunity and is recommended for patients of asplenia, nephrotic syndrome, transplant recipients.
- Absolute CD4₊ lymphocyte count is used as predictor of HIV progression. Risk of progression is high with CD4₊ count below 200/pl. p2 microglobulin is a cell surface protein indicative of macrophage monocyte stimulation; levels
- Cervical cancer and vulval cancer are related to HPV infection
- In clostridial myonecrosis, the efficacy of polyvalent gas gangrene antitoxin is questionable so also that of hyperbaric oxygen.
- Ehrlichiosis is a tick borne rickettsial disease causing myalgia, fever, headache, severe infection; can cause meningoencephalitis, toxic septic shock and ARDS, bleeding and neutropenia/thrombocytopenia. Tetracycline is the drug of choice.
- Fomivirsen is antisense oligonucleotide active against CMV- which is otherwise resistant to gancyclovir, foscarnet, cidofovir.
- IFN α 2a, 2b and alfacon have similar efficacy in HCV but treatment of HDV requires higher doses for 12 months with 50% response rate, only to relapse after stoppage of therapy.
- Neuraminidase inhibitors like zanamivir and oseltamivir are effective against both influenza A & B; both in treatment and prophylaxis. HTLV-1 causes tropical spastic paraparesis as well as neoplasms, i.e. adult T cell leukemia/lymphoma (ATL) due to proviral integration of T4 cells. Treatment is a combination of antiretroviral drugs plus chemotherapy as for lymphoma but success rate is poor. HTLV II is a virus "searching for a disease".
- Severe measles in small children can be ameliorated by high dose vit A-1-2 lakh units on two consecutive days; ribavirin may be considered for immunocompromised.
- Hantavirus pulmonary syndrome is a fatal condition that needs aggressive treatment for hypoxemia, but has a fatality of 30-50%.
- Quinine-clindamycin combination is effective for babesiosis; resistant cases may be tried with azithromycin, atovaquone.
- Formalin inactivated hepatitis A vaccine is available to be given 1 ml (adult) and 0.5 ml 2 doses for children followed by booster after 6-12 months.

IMMUNOLOGY AND RHEUMATOLOGY

- Antacids increase urine pH thereby increasing renal excretion of salicylates and hence lower serum salicylate level.

- The risk of developing non Hodgkin's lymphoma in Sjogren's syndrome is very high. Sjogren's syndrome hence is not only keratoconjunctivitis sicca with seropositive rheumatoid arthritis but with renal and pulmonary involvement and vasculitis.
- A walking stick or cane should be held on the side opposite the arthritic knee. The most common deformity of knee in osteoarthritis is bowleg not knock knee; in rheumatoid arthritis opposite is true.
- In older patients renal prostaglandin synthesis maintains renal perfusion. Use of NSAIDs in them can cause oliguric renal failure.
- Most patients of Still's disease do not have positive rheumatoid factor. Leukocytosis and quotidian fever are characteristic.
- Oral ulcers of Reiter's syndrome are painless while those of Behcet's syndrome are painful.
- Gottron's patches are erythematous, scaling lesions overlying the proximal and distal interphalangeal joints, the characteristic of dermatomyositis.
- Sausage digits are seen primarily in the seronegative spondyloarthropathies.
- Sacroilitis of longstanding ankylosing spondylitis is invariably bilateral and symmetric.
- Annulus fibrosus calcification is characteristic and also contributes to radiographic appearance of "bamboo spine".
- Pregnancy, particularly in the first trimester and puerperium is associated with increased risk of lupus flareups. Prednisone has little effect on fetus, probably because it is broken down by placental hydroxylase but dexamethasone can cross placenta and hence is contraindicated.
- Ear inflammation i.e., destruction of cartilage of pinna sparing the ear lobule is a feature of relapsing polycondritis.
- Visual loss in atherosclerosis of carotid artery is due to involvement retinal vessels and may be reversible but that in giant cell arteritis it is irreversible as there is ischaemic necrosis of ophthalmic nerve.
- Back pain worsening with rest and improving with moderate activity is distinct feature of ankylosing spondylitis.
- Chondromalacia patellae is a common cause of pain beneath the patella.
- Avascular necrosis is a complication of SLE. Bilateral involvement is common.
- Urticaria pigmentosa or systemic mastocytosis results from infiltration of skin by mast cells. The involved areas have freckle-like lesion that produce wheal and flare when stroked (Darier's sign).
- The presence of wrist involvement in a patient thought to have osteoarthritis should prompt for other diagnostic considerations like rheumatoid disease, infection etc.
- Eicosanoids refers to all metabolites of cyclooxygenase and lipooxygenase pathways of arachidonic acid metabolism. Salicylates and NSAIDs inhibit cyclooxygenase pathway with reduced formation of endoperoxides like prostaglandins and thromboxane. Lipooxygenase pathway is for formation of leukotrienes.
- Complement activity plays an important role in inflammatory response. C_1 binds to immune complex with activation mediated by $C1q$. Activated C_1 then activates C_4 and C_2 . Activated $C1$ is destroyed by C_1 esterase inhibitor. Latter also regulates factor XIII and kallikrin. C_1 esterase inhibitor deficiency causes angioedema.
- Null cells (large granular lymphocytes) constitute 5-10% of peripheral blood lymphocytes. They have receptors for Fc portion of IgE and proliferate in response to IL_8 . A subset of NK cells mediate antibody mediated cytotoxicity and natural killer cell activity. These cells have antitumor activity and play some role in transplant rejection.
- Macrophages secrete $IL_{1\alpha}$ and $IL_{6,8}$ to clonally amplify the specific T cell and also secrete IL_8 and gamma interferon to recruit additional T cells.
- Isolated IgA deficiency is the most common immunodeficiency disorder. Both serum and secretory IgA are reduced. Recurrent sinopulmonary infection is most common. Some patients have antibodies against IgA. Immunoglobulin therapy does not restore IgA level.
- Combination of sinusitis, pulmonary disease and glomerulonephritis should arouse suspicion of Wegener's granulomatosis. Biopsy shows granulomatous necrotising vasculitis. Steroid and cyclophosphamide are mainstay of treatment.
- Dendritic cells are key initiators both of innate immune responses via cytokine production and of adaptive immune responses via presentation of antigen to T lymphocytes.
- NK cells kill target cells that do not express HLA class I molecule i.e. malignant cells and virus infected cells.
- Ligand for CD28 is CD80, CD86 and for CD 40 is CD 154.
- Monocytes macrophages express CD14, CD16, CD32 and CD64 and CD35 (activated complement component). Dendritic/ Langerhans cells are bone marrow derived APCs, derived both from myeloid and lymphoid lineage and lack standard T, B, NK cell and monocyte markers.
- LPS of gram-negative bacteria binds to CD14 and TLR_4 protein on macrophage initiating an intracellular signalling cascade that leads to expression of immunomodulatory genes, including cytokines and costimulatory molecules. High levels of immune system activation by bacterial LPS may lead to septic shock.
- Eosinophils express CD32 and are cytotoxic effector cells for parasites. Basophils and mast cells are reservoirs for $IL-4$ that produces TH2 response.
- T_4 helper cells can be subdivided on basis of cytokine production. TH_1 cells secrete $IL-2$, IFN γ , $IL-3$, TNF α , TNF- β and GM-CSF while activated TH_2 helper T cells secretes $IL-3, 4, 5, 6, 10$ and 13 essential for humoral immunity and isotype switching. Excess of TH1 response is linked to Crohn's disease, rheumatoid arthritis but is basically meant to induce cytotoxic T cells (TNF α) macrophage activation (GM-CSF) and antibody production (TNF β).
- Lymphocyte endothelial cell interactions have 4 stages:
 - Stage I—attachment and rolling mediated by L-selection
 - Stage II—adhesion triggering by $IL-8, PAF, LTB_4, C_5a$
 - Stage III—Sticking and arrest mediated by integrin and their ligand ICAM-1 and ICAM-2 "
 - Stage IV—Transendothelial migration mediated by CD44 Lps.
 - In the immune system apoptosis is a mechanism induced to remove autoreactive T cells in thymus and to remove but autoreactive T and B cells from peripheral lymphoid organs (lymph node and spleen)
- Bcl2 and Bel XL are two proteins that inhibit apoptosis.

- 1352** • Wide variety of stimuli trigger TNF receptor family on cell surface or cytoplasmic receptors that activate FLICE or caspase-8. Caspase activation leads to formation of DEDD that inhibits DNA transcription in nucleolus with fragmentation of DNA. Caspase-8 is inhibited by Bcl2 and Bel XL.
- Soluble TNF- α and IL-1 α inhibit TNF- α and IL-1 and are useful in RA. IL-12 which induces IFN γ and CTLs can be of value in tuberculosis and cancer. IL-2 has been used in treatment of renal cell carcinoma and when used in HIV disease increases T₄ cells.
 - HLA class I-peptide complex is preferentially recognised by CD8 T cells and class II peptide complex by CD4 T cells. The CD8 recognition site is on $\alpha 3$ domain of MHC class I molecule while CD4 recognition site is on β_2 132 domain of class II molecule.
 - A polymorphism in the promoter region of TNF α gene in the HLA class III region is linked to cerebral malaria, LL leprosy, HBV chronicity and fatal meningococcal meningitis.
 - HIV-C subtype is the most common form worldwide and also in India, while subtype B is prevalent in USA and subtype E in South East Asia.
 - SDF-1 is the lateral ligand for CXCR-4, where as RAN-TES, MIP a and 13 are natural ligands for CCR5.
 - HIV envelop glycoprotein gp 120 and gp 160 have high affinity for CD4.
 - Western blot is only to be taken as positive if antibodies are present to atleast 2 of the 3 major gene products i.e. p24, gp-41 and gp 120/160 (gag, pol, and env). Absence of pD 31 band may be indicator of false positivity Faint bands in Western blot with negative PCR, may represent cross reactivity and demands DNA PCR, RNA PCR or (b) DNA assay.
 - ELISA for P-24 antigen is only positive in 50% of patients and detects only when p24 level is > 15 pg/ml.
 - Treatment should be started when CD4 count is < 500/cmm or viral load is >20,000 copies of HIV RNA/ml. End point of treatment is to achieve viral load to < 50 copies/ml.
 - Altered androgens are effective in angioedema of CI INH deficiency, else alpha aminocaproic acid may be used.
 - A number of additional antibodies may be found in RA including antibodies to filaggrin, citrulin, calpastatin and RA33. Some of them appear even before RA is positive and may indicate aggressive disease.
 - Infliximab and etanercept are the two TNF α neutralizing agents which can bring remission the RA who have otherwise failed to DMARD.

NEPHROLOGY

- Prerenal azotemia is certain when serum BUN to creatinine is > 20:1, urine osmolality is above 500 and fractional excretion of sodium is less than 1.
- Large kidneys in US with renal failure implies amyloidosis, obstructive uropathy, diabetes mellitus, PKD or multiple myeloma.
- Hypertension is a complication of erythropoietin therapy. Dose of erythropoietin in CRF is 30-150 units 3 times a week SC.
- Platelet dysfunction in uraemia can be tackled with desmopressin 0.03 mg/kg and conjugated estrogen.
- Components of renal osteodystrophy are osteomalacia and osteitis fibrosa, mostly caused by hyperphosphatemia with

decreased serum calcium and increased PTH production. Diseased kidney cannot form active vit. D₃.

- IgA nephropathy is the most common form of acute glomerulonephritis in Asia. It presents with haematuria associated with upper respiratory infection. In comparison to poststreptococcal GMN-hypertension and edema are uncommon.
- In IgA nephropathy serum IgA is increased in half the patient, serum complement level is normal and dermal capillaries have IgA deposit. In kidney there is diffuse deposit of IgA in mesangium.
- Recent evidence suggests that daily dose of 12 gm of fish oil (N₃-fatty acid) retard rate of loss of renal function in IgA nephropathy.
- A diagnosis of Goodpasture's syndrome is confirmed by finding anti-GBM antibodies in an individual with pulmonary haemorrhage or alveolar infiltrates and glomerulonephritis but over 50% of these patients do not have pulmonary haemorrhage or extrarenal manifestation.
- Accumulative analgesic intake of 3 kg or 1 gm daily for 3 years strongly supports the diagnosis of analgesic nephropathy.
- 80% renal carcinoma are hypervascular, 15% hypovascular and 5% are avascular.
- A renal cyst in US can be malignant if has thick walls, calcifications, solid component and mixed echogenicity.
- APKD is aptosomal dominant, the defective gene located in short arm of chromosome 16. Patients have aneurysm in circle of Willis aortic aneurysm and abnormalities of mitral valve.
- The earlier changes in kidneys in diabetes mellitus is increased in kidney size and rise in GFR by 20-50%.
- Lupus nephritis can take any of the 5 forms. A patient can progress from one type to another. Serologic evidence of activity includes increased level of antinuclear antibodies, antibodies to double stranded DNA, reduced C₃, C₄, CHSO.
- Most prostatic cancers are hypoechoic. Transrectal ultrasound helps in staging prostate cancer and helps in guiding biopsy.
- Abnormal PSA (>4 ng/ml) has a sensitivity of 67% and specificity of 97% in diagnosis of prostate cancer. A rate of change of PSA. greater than 0.75 ng/ml per year is associated with increased likelihood of cancer detection.
- All patients of prostate cancer with PSA level greater than 10 ng/ml should under go radionuclide bone scan.
- 90% bladder cancer are transitional cell carcinomas.
- Renal cell carcinoma originates from proximal tubule cells. Various cell types (acinar, papillary solid) are observed but cell type and histologic pattern do not affect treatment.
- No effective chemotherapy is available for metastatic renal cell carcinoma. Vinblastine in single most effective agent with short-term partial response rate of 15%.
- Cryptorchidism is more common on right side and paripassu testicular malignancy is more common on right side.
- Orchiectomy does not alter the malignant potential of cryptorchid testis but facilitates examination and tumor detection.
- In a patient of multiple myeloma, a negative urine dipstick test but positive sulfosalicylic acid reaction indicates Bence Jones proteinuria.

- Renal involvement occurs in 50% cases of multiple myeloma. Acute renal failure may result from hypercalcemia, dehydration or tubular dysfunction. When a patient of carcinoma of lung without apparent brain metastasis presents with confusion, hyponatremia and high urine osmolality, the diagnosis is SIADH. Oatcell carcinoma of lung is known to produce ADH.
- Alport's syndrome is an autosomal dominant renal disorder characterized by microscopic haematuria, mild proteinuria, nerve deafness, and progression to endstage renal failure by 3rd to 4th decade. Renal histology shows diffuse glomerular and interstitial changes.
- The diagnosis of antiglomerular basement membrane disease is warranted only when anti GBM antibodies are present in serum and glomeruli where a characteristic linear immunofluorescent pattern is seen.
- IgA nephropathy is characterized by IgA deposits in mesangium. Gross haematuria may occur but the course is usually benign. Only 25% of adults progress to renal failure gradually.
- The EM examination of renal biopsy specimens in membranous glomerulonephritis reveals granular electron dense deposits but complement levels are always normal.
- Mild anaemia, enlarged kidney and chronic renal failure indicate polycystic kidney disease.
- In medullary sponge kidney there is ectasia and calcification of medullary collecting tubules. Most patients are asymptomatic and renal failure is uncommon but urinary tract infections and renal calculi formation are frequent.
- Distal (type 1) renal tubular acidosis is characterised by constant low grade bicarbonate loss and persistently high urinary pH. In children it may be familial or sporadic but in adult it is due to drugs (amphotericin, gentamicin, vit. D intoxication), toxins, cirrhosis, SLE, sickle cell disease etc.
- Proximal (type II) renal tubular acidosis is a result of impaired bicarbonate reabsorption in proximal tubule. It can be associated with cystinosis, Wilson's disease, myeloma, lead poisoning etc. When associated with aminoaciduria, glycosuria and phosphaturia it is called Fanconi syndrome.
- The key to diagnosis of urinary tract obstruction is the demonstration of a dilated urinary collecting system. The nephrogram will be delayed but quite dense in acute obstruction.
- Nephrogenic diabetes insipidus unresponsive to vasopressin and causing polyuria and pure water loss may be a side effect of drugs like lithium, demeclocycline, and vinblastine.
- As long as liver function and muscle mass remain constant, plasma urea and creatinine are inversely related to GFR.
- Only 20% of filtered IC^+ is excreted in urine. A K^+ secretory process operates in distal tubule, dependent upon sodium absorption. Hence daily K^+ intake is balanced by equal amount of excretion in urine minus the loss in sweat and stool.
- Most ARF is due to renal hypoperfusion with intact renal parenchyma. Most ARF is hence reversible, the kidney being unique among major organs in its ability to recover from almost complete loss of function.
- Angiotensin II preserves GFR by selective constriction of efferent arterioles. ACE inhibitors blunt this response and precipitate ARF.
- Renal biopsy is indicated only when pre- and postrenal failure are excluded and cause of intrinsic renal failure is unclear.
- Progression of CRD to ESRD has individual variability irrespective of underlying etiology and is probably influenced by inheritable factors like insertion/deletion of ACE gene.
- Low turnover uremic osteodystrophy is not only due to lack of active vit D_3 but due to lack of PTH (PTH is usually \dot{I} in ESRD). This PTH lack is accounted for by supraphysiologic Ca^{++} and vit D_3 given to these patients. Aluminium deposition in bone due to its presence in dialysate or given orally to bind phosphates also lowers bone turnover causing osteomalacia.
- Secondary hyperparathyroidism and osteitis fibrosa cystica are best prevented by phosphate restricted diet and CaCO_3 and CaSO_4 used as binding agents. Suppression of PTH to <120 pg/ml should not be attempted.
- Dietary protein restriction and effective control of intraglomerular hypertension and/or glomerular hypertrophy can retard progression of CRD.
- Polysulfone, polymethylmethacrylate and polyacrylonitrile membranes are more biocompatible and do not activate complement. They are reusable too.
- In renal histology for GM, lesions are classified as focal when they involve $<50\%$ glomeruli and diffuse if they involve $>50\%$ glomeruli. The clinical term RPGN and pathologic term crescentic GM are used interchangeably.
- "Starry sky" appearance in immunofluorescence microscopy is feature of poststreptococcal GM. Garland pattern bears worse prognosis.
- Fibrillary immunotactoid glomerulopathy presents with nephrotic syndrome and progresses to ESRD in 1-10 years. No treatment is available except for transplantation.
- Essential mixed cryoglobulinemia is complicated by in 50% cases with nephrotic syndrome, and haematuria. C_3 , C_4 , CHSO are low and HCV RNA may be present. Hence alfa interferon therapy is warranted.

NEUROLOGY

- The pontine gaze centre controls ipsilateral horizontal gaze. The rostral interstitial nucleus of MLF controls vertical gaze, MLF connects the gaze centres and oculomotor nuclei.
- A lesion of dominant parietal lobe causes Gerstman syndrome. Affected individual is unable to calculate, write and differentiate right from left.
- Unilateral occlusion of vertebral artery typically causes lateral medullary syndrome with damage to 9th and 10th cranial nerves, inferior cerebellar peduncle, lower vestibular complex, sympathetic tract ipsilaterally and the spino thalamic fibers subserving pain and temperature on opposite side.
- Cranial nerves III, IV and VI pass through cavernous sinus, so that complete ophthalmoplegia may occur in cavernous sinus thrombosis. Since mandibular are division of trigeminal does not pass through it, the brow and cheek may be numb but not the chin.
- Bilateral lateral rectus palsies that develop acutely in alcoholics imply Wernicke's encephalopathy.
- Acute mononeuropathy involving oculomotor or peroneal calls for exclusion of diabetes. Neuropathy that is primarily sensory, distal and progressive is most characteristic of diabetes but may occur with occult neoplasm. Relapsing neuropathy is more typical of idiopathic polyneuritis.

1354 • The essential or familial tremor is faster (8 Hz) and responds to alcohol and propranolol. Rest tremor is associated with Parkinsonism but is suppressed by willful activity.

• Conventional EMG, muscle biopsy and nerve conduction studies are not useful in evaluation of myasthenia gravis because it is not a disease of muscle or nerve. Single fiber EMG showing "jitter" or repetitive stimulation of motor nerves showing decremental response are useful in diagnosis.

• Duchenne's dystrophy is an X-linked recessive disorder. The responsible gene is 2000 kb that codes for 400 kDa protein, the dystrophin. About 60% of patients have an exon deletion or duplication in dystrophin gene.

• The findings of total hemianaesthesia and loss of all sensory modalities in the face, arm and leg are characteristic of thalamic infarction.

• More than 75% of myasthenia have circulating antibodies to components of postsynaptic membrane including acetylcholine receptors. Antibody action leads to unfolding or simplification of the membrane. As a result existing acetylcholine in the synapse is less effective.

• A pure motor hemiparesis on one side without aphasia or cortical sensory loss suggest lesion at internal capsule. either lacunar infarct or hypertensive bleed.

• Meralgia paresthetica is due to entrapment of lateral cutaneous nerve beneath the inguinal ligament near anterior superior iliac spine causing pain and blunting of sensation in lateral thigh in the obese.

• Neurofibromatosis type I is an autosomal dominant carried on long arm of chromosome 17. It is characterized by peripheral neurofibromas and cafe-au lait spots. There is mutation in gene encoding protein neurofibromin. These patients may have optic glioma, glioblastoma and meningioma.

• In neurofibromatosis II bilateral acoustic neuromas are seen in addition to peripheral neurofibroma. There is mutation in gene encoding for protein fibrillin.

• In syringomyelia pain is lost but touch is preserved. Tissue loss in central gray matter of spinal cord where pain fibers cross to contralateral spinothalamic tract are destroyed. Thoracic scoliosis and atrophy of small muscles of hand are usual.

• Trigeminal neuralgia is not synonymous with trigeminal neuropathy. Aneurysms, neurofibromas and meningiomas impinging on 5th cranial nerve at any point along its course cause trigeminal neuropathy, with weakness of jaw and sensory loss which are not seen in trigeminal neuralgia.

• Antipsychotics in schizophrenia are more useful against positive symptoms like hallucination and agitation but less active against negative symptom like social withdrawal.

• The most common tumor of CNS is metastatic in nature; cancer of lung in men and breast cancer in women. Malignant melanoma has predilection for spread to CNS.

• Meningioma are most common benign brain tumors and may grow to very large size before detection. They are common in women in 5th or 6th decade. Common sites are around the midline in cerebral hemisphere, olfactory groove, sphenoidal ridge, foramen magnum and tentorium of cerebellum.

• Diseases that cause rapid dementia within weeks include metabolic encephalopathy, encephalitis, poisoning, white matter infarction and CZ disease.

• There are 4 major hypertensive haemorrhage syndromes. The most common site of bleeding is internal capsule adjacent to

basal ganglia which generally produce contralateral hemiplegia with eye deviation away from side of paralysis.

• Transient ischaemic attacks are caused either by low flow in large vessels, embolism from arterial or cardiac sources or penetrating vessel atherosclerosis.

• Radiosensitivity is a well known feature of most primary CNS lymphomas, which are almost always of B cell origin. Its complete disappearance with steroids may mimic multiple sclerosis.

• To differentiate between syncope and seizure syncope rarely occurs during recumbency and patient recovers fully once BP returns to normal without any headache, confusion or drowsiness postictally.

• Patients of Wernicke's aphasia have damage in posterior temporoparietal regions, supplied by lower division of middle cerebral artery. Speech is effortless and well woven but spoken, written communication, auditory and visual understanding is affected.

• In peripheral nerve, small fibers mediate sensations of pain, and temperature, large fibers are involved in touch, joint position and vibration.

• Polymyalgia rheumatica typically occurs in elderly with pain, weakness and stiffness of proximal muscles. ESR is high and there may be associated inflammatory arthritis and temporal arteritis.

• Lesions in basal ganglia produce a host of movement disorders like akinesia, bradykinesia, lead pipe rigidity, chorea, dystonia, myoclonus, asterixis, hemiballismus, tics. There is no weakness of muscles

• Testing of evoked potentials is of greater utility in detecting subclinical spinal cord or optic nerve lesions. Upto two-third of persons who have multiple sclerosis have neurologic deficits in evoked potential testing but not clinical examination.

• Isolated lesions of third nerve with pupillary sparing are usually due to microinfarction of third nerve in association with diabetes or hypertension.

• The abrupt onset of isolated peripheral facial palsy which may include ipsilateral hyperacusis, and loss of test in anterior two-thirds of tongue is most often idiopathic—Bell's palsy.

• Although pathophysiology of migraine is unclear, electrical stimulation of midline dorsal raphe nuclei of brainstem leads to characteristic pain. Sumatriptan and dihydroergotamine provide relief by blocking 5 HT receptor (type I-D subtype).

• An anomalous artery or vein impinging upon trigeminal nerve root produces trigeminal neuralgia despite normal GT, MRI and angiogram. Decompression by posterior fossa exploration provides lasting relief.

• Gabapentin, felbamate and lamotrigine are approved as adjunctive therapy to partial and secondarily generalized seizure. Felbamate causes fatal bone marrow depression.

• Antiphospholipid antibodies (lupus anticoagulants, and anticardiolipin antibodies) promote thrombosis and may cause stroke.

• Cerebral infarction following thromboembolic stroke has better prognosis than that after cerebral or subarachnoid haemorrhage.

• In subarachnoid haemorrhage ECG may show ischaemia or arrhythmia due to excess sympathetic activity. Leukocytosis and glycosuria are common.

- In subarachnoid haemorrhage vasospasm can be reduced by nimodipine 60 mg every 4 hours for 21 days without serious side effects.
- Cerebral venous thrombosis produces diffuse haemorrhagic superficial cortical infarction with headache meningeal irritation, raised ICP, confusion, convulsion and focal deficits. CT, MRI, MR venography provide the diagnosis.
- Infarction of spinal cord only involves anterior two-third because of supply from anterior spinal artery which is fed by a limited number of feeders. The paired posterior spinal arteries by contrast are supplied by numerous arteries at different levels of cord.
- Meningioma originates from dura or arachnoid, compresses rather than invades adjacent structures, is highly vascular but completely removable.
- Tumors of frontal lobe cause intellectual decline, personality changes, and contralateral grasp reflexes.
- Temporal lobe lesions produce seizures with olfactory-gustatory hallucinations, impairment of internal awareness without loss of consciousness, depersonalization, emotional changes, behavioral changes, sensations of déjà vu or jamais vu, micropsia-macropsia and visual field defects (Crossed upper quadrantanopia).
- Parietal lobe lesions cause sensory seizures, sensory loss or inattention. Tactile discrimination and postural sense is lost. Right sided lesions cause constructional and dressing apraxia. Anosognosia, Gerstmann syndrome, ideational, apraxia, homonymous field defects can occur.
- Tumors of occipital lobe produce crossed homonymous hemianopia. With left sided or bilateral lesions, there may be visual agnosia for objects and colours. Prosopagnosia, simultagnosia, Anton's syndrome, Balint's syndrome and visual hallucination may occur.
- False localizing signs in brain tumors include third and sixth cranial nerve palsy and extensor plantar response bilaterally produced by herniation syndromes or compression of opposite cerebral peduncle against tentorium causing ipsilateral extensor plantar.
- Cryptococcal meningitis is an opportunistic infection in AIDS patients. Clinically it resembles cerebral toxoplasmosis or lymphoma but cranial CT is usually normal. CSF India ink preparation is positive in 75% and cryptococcal antigen test in 95%.
- Only 10% of spinal tumors are intramedullary and ependymoma is the most common. Carcinomatous metastasis, lymphomatous and leukemic deposits are usually extradural. Treatment of epidural metastasis is always irradiation irrespective of cell type.
- Pseudotumor cerebri consists of headache, diplopia, due to papilledema and sixth nerve dysfunction CT does not show space occupying lesion and CSF is normal except for intracranial hypertension. Oral contraceptives, vit. A toxicity, tetracycline, cerebral venous thrombosis, COPD, Addison's disease need exclusion.
- Tuberous sclerosis presents with seizure and progressive psychomotor retardation. It is autosomal dominant the responsible gene located on long arm of chromosome 9. Associated anomalies include retinal lesions and tumors bone cyst, lung cyst, cardiac rhabdomyoma and visceral benign neoplasms.
- Sturge-Weber syndrome is sporadic with capillary haemangioma of upper face, leptomeningeal angiomatosis and choroidal angioma. Tramline intracranial calcification is characteristic. Focal or generalised seizure are common manifestation.
- Carbidopa inhibits dopa decarboxylase responsible for breakdown of levodopa to dopamine but it does not cross blood-brain barrier. Hence, more levodopa is available in brain for conversion to dopamine and daily requirement of levodopa is reduced with less incidence of nausea, hypotension and cardiac irregularities
- Selegiline is MAO-B inhibitor and is an adjunct to levodopa. It inhibits break down of dopamine. Dose is 5 mg twice daily.
- Huntington's disease is autosomal dominant. It causes chorea and dementia. The responsible gene is in short arm of chromosome-4.
- Botulinum toxin finds application in focal torsion dystonia like blepharospasm, writer's cramp, spasmodic torticollis.
- Intensive immunosuppressive therapy with azathioprine or cyclophosphamide may arrest course of chronic progressive multiple sclerosis. Beta interferon reduces exacerbation and copolymer I (simulates myelin basic protein) may be helpful.
- Vitamin E deficiency may produce a neurologic disorder similar to Friedreich's ataxia with spinocerebellar degeneration.
- Pupils are pinpoint but responsive with opiates, small but reactive in pontine lesion. Ipsilateral pupillary dilatation with absence of direct and consensual light reflex implies third cranial nerve compression as in uncus herniation.
- Conjugate deviation of eyes to the side suggests the presence of an ipsilateral hemispheric lesion or a contralateral pontine lesion. A mesencephalic lesion causes downward conjugate deviation.
- In spinal trauma early treatment with high dose corticosteroid (methyl prednisolone 30 mg/kg IV bolus-then 5.4 mg/kg/hr for 23 hours) improves neurologic recovery. Treatment with GM, ganglioside for 4 weeks is also beneficial.
- Riluzole, which reduces presynaptic release of glutamate, may slow progress of amyotrophic lateral sclerosis. Patients with gammopathy may improve with plasma pheresis and immunosuppression.
- Peripheral neuropathy may occur during acute attacks of ALP and variegate porphyria. Motor symptoms occur first and weakness is most marked proximally and in the upper limbs than lower limbs. IV glucose/levulose and hematin 4 mg/kg IV once or twice daily control the symptoms.
- Sensory polyneuropathy is the most common manifestation of diabetes neuropathies but is the most subtle one with no more than depressed tendon reflexes or impaired vibration.
- Diabetic amyotrophy is characterised by asymmetric weakness and wasting involving predominantly the proximal muscles of leg. In patients with autonomic neuropathy postural hypotension, postgustatory hyperhydrosis, diarrhoea, impotence, urinary retention and incontinence may occur.
- Autonomic disturbances are common in Guillain-Barre syndrome. They include tachycardia, cardiac irregularities, hypotension or hypertension, facial flushing, pulmonary dysfunction and impaired sphincter control.
- Treatment of Guillain-Barre syndrome with prednisolone is ineffective and may actually affect the outcome adversely by prolonging recovery time. Plasma pheresis and IV immunoglobulin (400 mg/kg/d for 5 days) are helpful.
- A centrally prolapsed lumbar disc causes bilateral limb disturbances and sphincter involvement. An L5 radiculopathy

causes weakness of dorsiflexion of foot and toes. With S1 root lesion there is weakness of eversion, plantar flexion and a depressed ankle jerk.

- In cervical spondylosis, the C5, C6 nerve roots are most commonly involved with weakness of deltoid, supra and infraspinatus, biceps and brachioradialis; pain or sensory loss about the shoulder and outer border of arm and forearm.
- In myasthenia gravis thymectomy usually leads to symptomatic benefit or remission and should be considered in all patients younger than 60 years, unless weakness is only restricted to extra ocular muscles.
- In botulism, anticholine esterase drugs are of no value but guanidine hydrochloride 20-50 mg/kg/d in divided doses is often helpful by facilitating release of acetylcholine from nerve endings.
- There is no specific treatment for muscular dystrophies. In Duchenne type rapid progression with death with 15 years of onset is usual. Becker's type has slow progression and may have normal life span.
- Myotonia can be treated with quinine, procainamide phenytoin, tocainide or mexilentine but in myotonic Ors dystrophy phenytoin is preferred since other drugs affect cardiac conduction adversely.
- Basilar skull fractures can manifest with bilateral periorbital ecchymosis (anterior fossa fracture), CSF rhinorrhoea, haemoptysis and subcutaneous blood over mastoid bone (Battle sign). There can be intracranial air. Cranial nerve palsies involving 2,3,4,7,8 are common but 6th palsy is uncommon.
- Despite presence of multiple and major neurological deficits prognosis of intracranial venous sinus thrombosis is good. Headache and papilledema are prominent and CSF is haemorrhagic, convulsion is present in 1/2 the cases. 80. Phanel's sign is the reproduction of painful numbness in the hand on extreme flexion in carpal tunnel syndrome.
- The "locked in state" describes patients who are awake and retain mental content but cannot express because of paralysis of both motor pathways affecting speech and limb movements. The site of lesion is in motor pathways in the pons and mid-brain, sparing the reticular formation.
- Apraxia is the inability to perform a learned act in response to an appropriate stimulus which cannot be accounted for by muscle weakness, incoordination, sensory loss, etc. Lesions of corpus callosum, of Broca's and of odic left parietal operculum frequently produce apraxia. In all forms of apraxia axial movements remain normal. Apraxia is most marked in response to verbal command.
- EEG is of limited benefit in following patients of epilepsy because EEG abnormalities may persist even when lasic seizure is controlled and 25% of patients with epilepsy have normal EEG interictally.
- Normal pressure hydrocephalus in adults manifests with dementia, gait ataxia and urinary incontinence. Half of ellar the patients have a history of past SAH, head injury, meningitis or craniovertebral anomalies.
- In evaluating a patient of dizziness, a careful neurologic examination differentiates central from peripheral causes. Mary In the Nylen-Barany maneuver a delay before onset of vertigo and nystagmus indicates peripheral vestibular mal dysfunction.
- Posterior hypothalamic lesions can produce gastrointestinal ulceration, lethargy, hypersomnolence, memory teral disturbances. Anterior hypothalamic lesions produce hyperthermia and diabetes insipidus.
- The vegetative state implies cerebral dysfunction with intact brainstem function; usually follows traumatic or a 5.4 hypoxic damage.
- Narcotic overdose produces small pupils, shallowed respiration, hypotension, hypothermia and coma. Lesions of splenium of corpus callosum produce alexia without agraphia.) ccur 90. Huntington's chorea is autosomal dominant, Alzheimer's dementia is frequently accompanied by seizures with an abundance of neurofibrillary tangles and senile plaques.
- Essential or familial tremor is usually bilateral, occurs with volitional movements and is suppressed by alcohol one Parkinsonian tremor is present at rest, usually abates with activity, and is almost always distal.
- Asterixis is an abrupt flapping movement of outstretched arms or legs characteristic of metabolic encephalopathy, dmal i.e. of hepatic and renal failure.
- Visual acuity is normal in papilledema but is reduced in optic neuritis.
- Amaurosis fugax (transient monocular blindness) is due to ophthalmic artery embolism from carotid ities, atheromatous plaques, as ophthalmic artery is first branch of internal carotid.
- Opsoclonus is pathognomonic of nonmetastatic effect of malignancy, commonly neuroblastoma.
- Phenytoin intoxication produces gaze evoked nystagmus. Lower basilar lesions produce a down beat nystagmus.)
- Reflex sympathetic dystrophy is a syndrome characterised by (1) pain and tenderness in an extremity (2) diffuse n L5 swelling of soft tissues (3) diminished motor function (4) trophic skin changes (5) vasomotor instability and (6) sion, patchy osteoporosis.
- The clinical picture of encephalopathy with brisk oculocephalic responses, hyperreflexia and no focal neurological I and signs suggest metabolic encephalopathy.
- Persistent signs of severe brainstem dysfunction in patients who remain unconscious for upto 48 hours generally imply poor chanties of survival.
- The clinical picture of internuclear ophthalmoplegia and spastic paraparesis with distal posterior coloumn sensory impairment in a young woman strongly suggests multiple sclerosis.
- Lithium carbonate is the drug of choice for prevention of recurrent cluster headaches.
- Auditory hallucinations are common to schizophrenics but visual hallucinations are common in acute toxic th 15 delirium due to drugs and alcohol.
- Fasciculation, hyperreflexia and muscle atrophy with normal motor conduction implies amyotrophic lateral sclerosis. There is degeneration of motor nerve cell arising from layers 3 and 5 of the precentral cortex, cranial motor nerve nuclei and spinal nerve nuclei.
- In a patient of subarachnoid bleed, initial lateralizing sign like hemiplegia suggests associated intracranial haematoma or subdural haematoma. Localising signs of cerebral vasospasm in subarachnoid bleed appear late.
- Worsening coma and diffuse sensory motor dysfunction in a patient of subarachnoid bleed indicates intracranial vasospasm or recurrence of bleeding.
- Excessive outpouring of catecholamines in SAH causes myonecrosis of the myocardium in ECG resembling myocardial infarction.

- The prognosis for ruptured aneurysm is worse than ruptured AV malformation.
- A delirious patient is disoriented and confused but never forgets his personal identity.
- Pain referred to the contralateral back or leg when the nonpainful leg is raised (Crossed straight leg raising implies root compression within the spinal canal and is the most accurate sign of herniated intervertebral disk)
- In traumatic brachial plexopathy, motor weakness is more proximal with intense pain but little sensory loss.
- During REM sleep, muscle tone decreases but heart rate, BP rise with dreams and penile tumescence.
- Distal limb weakness usually indicates a neuropathic disorder while proximal weakness is more likely myopathic origin. Nerve conduction velocity is slow in demyelinating neuropathy but normal in true axonal neuropathy.
- Brown-Sequard syndrome or hemisection of spinal cord is contralateral pain and temperature loss and ipsilateral corticospinal tract signs with loss of proprioception and vibration.
- Syrinx in the central region of cervical cord typically produces pharyngeal and vocal cord paralysis with atrophy of tongue. It is associated with Arnold-Chiari malformation and intramedullary tumors. Syrinx in cervical cord do not extend posteriorly to impair vibratory and position sense.
- Clinical picture of coma, bilateral corticospinal tract dysfunction and bilateral inter-nuclear ophthalmoplegia strongly suggests intrinsic disease of mid-brain.
- Reye syndrome is an acute encephalopathy of childhood manifesting with cerebral edema and hepatic failure. Delirium, convulsions and coma are common.
- Corticospinal and posterior columns are frequently involved early in cord compression. Lateral spinothalamic tracts are initially spared.
- Charcot-Marie-Tooth disease is a polyneuropathy producing predominant peroneal muscular atrophy with hypertrophic nerves. Sensory changes are frequent.
- Myotonic dystrophy is autosomal dominant and in contrast to other dystrophies principally affects the distal musculature of hands and feet. The weakness in muscular dystrophies affects the skeletal and cardiac muscles but sparing the smooth muscles.
- Peri-orbital edema, chemosis, haziness of cornea, photophobia, eye pain with external ophthalmoplegia and fever in clear consciousness indicate cavernous sinus thrombosis.
- Channelopathies account for many neurological disorders. Calcium channelopathy accounts for spino cerebellar ataxia, familial hemiplegic migraine, and hypokalemic periodic palsy. Na⁺ channelopathy for paramyotonia congenita, hyperkalemic periodic palsy; chloride channel for myotonia congenita and K⁺ channel for JL Nielsen syndrome.
- Peptide neurotransmitters are synthesized in the cell body (not presynaptic region). Substance P, neurotensin, enkephalins, 13 endorphine, histamine, VIP, CCK, somatostatin, neuropeptide Y are few neuropeptides having role in neurotransmission. NO and CO may signal in retrograde fashion in CNS.
- A single oligodendrocyte usually ensheaths multiple axons in CNS whereas a Schwann cell typically myelinates single axon in PNS.
- NMDA receptors are excitotoxic and bring about neuronal death in ischaemic injury except for cerebellar Purkinje cells that lack NMDA receptors but still are vulnerable to ischaemia. Hence, NMDA antagonist may prevent focal ischaemia. In global cerebral ischaemia non-NMDA receptors are activated and their antagonists are protective.
- Immune privilege of CNS is due to blood-brain barrier, lack of MHC expression in neurone, non-existence of lymphatic system and expression of fas ligand that induces apoptosis of immune cells entering CNS. The BBB is also impermeable to antibodies unless inflamed.
- P3 component of ERP is delayed in dementia but not in pseudodementia. Motor evoked potential is employed for knowing subclinical involvement in MND and MS.
- MR angiography provides vascular flow map rather than anatomic map given by conventional angiography. In commonly used TOF MR angiography either venous or arterial tree can be highlighted. However, MRA has lower resolution than conventional angiography and cannot detect small vessel details, e.g. vasculitis.
- Echoplanar perfusion and diffusion MR imaging are useful in early detection of ischaemic injury and the tissue at risk. MR functional imaging can be as useful as ERP. 134. FDG PET scanning is presently used to differentiate areas of gliosis/radiation necrosis from tumor, in localising areas of temporal lobe foci in epilepsy.
- Disorders associated with trinucleotide repeats are Friedreich's ataxia, myotonic dystrophy, fragile X, Huntington's disease and various forms of spinocerebellar ataxias. 136. Among the newer antiepileptics only lamotrigine is used as first line drug for partial or generalised tonic-clonic seizure; topiramate and felbamate are alternatives in tonic-clonic; gabapentine, tiagabine and topiramate are alternatives in partial; lamotrigine, felbamate and topiramate are alternatives in atopic, myoclonic and atypical absence seizure. 137. Valproic acid is the most versatile since it can be used as first-line therapy for all forms of seizures in a dose range of 750-2000 mg/day (20-60 mg/kg) to achieve plasma therapeutic concentration of 50-150 µg/ml.
- APP gene mutation in chromosome 21 is linked to Alzheimer disease. Elevated plasma Aβ peptide may be a risk factor for developing AD. Similarly APOE4 on chromosome 19 and α2 macroglobulin on chromosome 12 are also involved.
- Selective COMT inhibitors tolcapone and entacapone when given with sinemet reduce dose of later and on-off phenomena.
- Sporadic CJD accounts for 55% cases of prion disease; familial CJD, GSS, FFI are all dominantly inherited prion diseases caused by mutation in PrP gene. CJD presents with dementia and myoclonus with death within 1 year of diagnosis. Prions are devoid of nucleic acid and cause a α to β transition in prion protein of body which becomes then pathogenic.
- While dealing with raised ICP, all measures be taken to keep ICP < 20 mm Hg and CPP at or above 70 mmHg.
- The dopamine receptors of both class D₁ and D₂ though have opposing action on adenylylase, they reinforce drug seeking behavior.

PULMONARY MEDICINE

- The most useful and predictive tool in evaluating an asthmatic attack is FEV₁.
- In a person standing erect, blood flow per unit volume increases from apex to lung base. Ventilation also increases from apex to base, but the gradient is less than that of blood flow. Hence, the dependent portions are better perfused than ventilated.

1358 • Macrophages produce fibronectin that induces fibroblast proliferation. Macrophages also produce IL1 and IL B4. the chemotaxins that attract neutrophils and eosinophils.

- Cystic fibrosis is autosomal recessive resulting from gene mutation in chromosome. The gene codes for protein called cystic fibrosis transmembrane regulator that function as AMP regulated chloride channel.
- Respiratory infections, particularly those of viral origin are common precipitants of acute asthmatic attacks. Hyperventilation with cold air is a bronchoprovocation test for asthma. Asthma is precipitated by acetyl salicylic acid but sodium salicylate is well tolerated.
- Platypnea is opposite of orthopnea, i.e. dyspnea in upright position relieved by recumbency. It occurs in right to left shunt or pulmonary vascular shunting of venous blood.
- The median survival of sever COPD (FEV_i < IL) is about 4 years. It is better in chronic asthmatic bronchitis than emphysematous form.
- Recombinant human deoxyribonuclease (domase-alfa) given by aerosol 2.5 mg twice daily reduces respiratory infections in cystic fibrosis.
- Bronchoalveolar lavage in idiopathic pulmonary fibrosis shows abundance of alveolar macrophages.
- Asthma is primarily due to immune inflammation, not simple allergy.
- Aspiration is by far the most common cause of lung abscess. The infecting organisms are therefore the anaerobic bacteria found in mouth. Aerobes that cause lung abscess are those that cause necrotizing pneumonia, especially *S. aureus*, *Pneumococcus* and *M. tuberculosis*.
- Pleural tuberculosis may be the first manifestation of primary infection. The effusion is exudative and usually reveals lymphocytosis although neutrophils may predominate initially.
- *Pneumocystis pneumonia* is almost never accompanied by pleural effusion which is usual with other infecting agents.
- Pleural effusion and pleurisy rarely occur with sarcoidosis but hilar symmetrical adenopathy, erythema nodosum, keratoconjunctivitis sicca, parotid enlargement are common.
- Cardiac involvement in sarcoidosis occurs in 25% cases with bundle branch block, arrhythmias, congestive failure and pericarditis.
- With advancement of surgery, and chemoradiotherapy the overall 5-year survival of lung cancer is around 10%.
- Thrombolysis with streptokinase/urokinase speeds up clot lysis and brings haemodynamic improvement much quicker than heparin but should be followed up by heparin and customary anticoagulants for 6-12 weeks in PE.
- Respiratory complications in heroin addicts include pulmonary hypertension, septic emboli (right sided endocarditis), pulmonary edema and aspiration pneumonia.
- Cilia, responsible for motility and mucous clearance functions of many cell types have a double tubular structure. Kartagener's syndrome is best known ciliary dyskinesic syndrome caused by absence of inner or outer dynein arms normally present in functional cilia.
- The working definition of exudative effusion is one that meets one of the following criteria (1) pleural fluid to serum protein > 0.5, (2) pleural fluid to serum LDH > 0.6, (3) pleural fluid LDH > 60% of upper limit of normal serum LDH.

- Reduced serum level of antiprotease α 1 antitrypsin, which is primarily synthesized in liver is associated with inability to control the alveolar damaging effect of neutrophil elastase and clinical emphysema. Gene responsible is on chromosome 14. and the zz genotype is more serious, not ss genotype.
- The volume of air remaining in the lungs at the end of forced expiration is residual volume and is measured by body plethysmography or helium dilution method.
- Inhalation of asbestos fibers for 10 years or more may lead to interstitial fibrosis that typically begins in lower lobes and spreads upwards. Pulmonary function shows a restrictive pattern.
- The acute respiratory distress syndrome is a clinical triad of hypoxemia, diffuse lung infiltrate and reduced lung compliance not attributable to CHF.
- The combination of nonproductive cough, dyspnoea hypoxemia, bibasilar infiltrates in X-ray and restrictive pulmonary function suggest the diagnosis of idiopathic pulmonary fibrosis.
- About 10% of asthmatics have a peculiar triad of bronchospasm, nasal polyp and sensitivity to aspirin but these patients do not react to sodium salicylate.
- Pleural plaques occur in 10-20% of asbestos workers but rarely cause functional impairment and are not associated with greater risk of pulmonary fibrosis or mesothelioma in comparison to similarly exposed workers without the plaques.
- Rheumatoid arthritis may adversely affect the airways and lungs but certainly does not cause or aggravate asthma. It can cause interstitial fibrosis, upper airway obstruction (cricoarytenoid arthritis), rheumatoid nodules.
- Massive unilateral pleural effusion in elderly should arouse suspicion of thoracic duct erosion by metastasis, lymphoma or leaking aortic aneurysm.
- Bronchoalveolar lavage in a healthy person only yields macrophages more than 90% and lymphocytes less than 20%.
- Gram - ve pneumonia, particularly by *Pseudomonas* is a complication of prolonged artificial ventilation.
- Patients of cystic fibrosis are vulnerable for respiratory infection with *Pseudomonas* and *Staph. aureus*.
- In chest X-ray a lesion <6 cm in diameter is a nodule and >6 cm in diameter is a mass.
- Normal PAO₂-PAO₂ is 15 mm Hg but may be as high as 30 mm Hg in elderly.
- Pulse oxymetry calculates oxygen saturation (S_aO₂), not P_aO₂.
- HRCT is best to diagnoses interstitial lung diseases, bronchiectasis, sarcoidosis, lymphangitis carcinomatosa and eosinophilic granuloma.
- Leukotriene modifier (zileuton) and LTD₄ receptor antagonists (Monte leukast, zafirlukast) are only useful in chronic stable asthma in single-bid doses but are not uniformly effective in all patients.
- Bronchocentric granulomatosis is a nonspecific pulmonary reaction to (i) aspergillus or other fungi with asthma like presentation, (ii) systemic diseases like RA, chest X-ray shows unilateral solitary upper lobe lesion with good response to corticosteroids.
- Patients of primary pulmonary hypertension can be given temporary relief pending lung transplantation by nitric oxide inhalation, IV adenosine 50 pg/kg/min infusion or prostacycline 2mg/kg/rain continus infusion through central venous catheter.

- With bilateral diaphragmatic paralysis, both respiratory symptoms and blood gases worsen in supine position due to upward displacement of diaphragm by abdomen. Unilateral palsy is usually asymptomatic.
- Theophylline is metabolized in the liver and both liver disease and congestive heart failure prolong its half-life. Cigarette smokers metabolize theophylline more rapidly than nonsmokers. Theophylline is a stimulant to diaphragm.
- The association of symptoms of systemic disease, peripheral nonsegmental, nonmigratory lung infiltrates and blood eosinophilia in a middle aged/elderly woman is strongly suggestive of chronic eosinophilic pneumonia. Asthmatic symptoms occur in 50% of these patients.
- Tension pneumothorax must be considered in the presence of an asymmetric decrease in breath sounds and sudden appearance of hypotension in a patient on mechanical ventilation.
- Rifabutin 300 mg OD is used as prophylaxis against MAC infection in advanced HIV disease ($CD4 < 100/mm$)
- About 25% cases of bronchogenic carcinoma present as solitary pulmonary nodule and 5-year survival in them is up to 50% as compared to 10-15% for overall lung cancer.
- Aspiration is by far the commonest cause of lung abscess. The infecting organisms are therefore, the anaerobic bacteria found in mouth. Aerobes that cause lung abscess are those causing necrotizing pneumonia, i.e. Staph. aureus, K pneumoniae, Clindamycin, chloramphenicol, and second generation, cephalosporins are active against most anaerobes.
- Irreversible dilatation of proximal and medium size bronchi with destruction of elastic and muscular components of bronchial wall characterise bronchiectasis. Tuberculosis is an important cause in developing countries.
- Simple chronic bronchitis is diagnosed when productive cough is present on most of the days for 3 months a year for 3 years.
- Small cell lung cancer disseminates widely behaving like leukemia. Because local resection is ineffective early combination chemotherapy and radiation therapy are indicated.
- In asthma bronchial obstruction is due to combination of factors like mucosal edema, inspissated mucus and smooth muscle spasm.
- Nitrofurantoin may cause slowly progressive diffuse pulmonary infiltration if taken over long periods. It may produce an acute syndrome of cough, fever, pulmonary infiltrates and eosinophilia. Busulphan also produces diffuse pulmonary infiltrates, cough, fever and dyspnoea. Corticosteroids cause increase in mediastinal fat with its widening in chest X-ray.
- Epidermoid lung carcinoma is common in men and appears as perihilar mass. Adenocarcinoma, the most common among bronchogenic cancer is more common among women and presents as a peripheral nodule. Large cell cancer frequently cavitates with thickwalled cavity. Small cell carcinoma often causes mediastinal widening and spreads haematogenously seeding to bone marrow, liver, brain and adrenals early.
- Asthma is associated with an increase in drive for ventilation, so that arterial PCO_2 is in the low to mid 30 during an acute attack. A normal or increased PCO_2 indicates severe bronchospasm and hence demands aggressive treatment.
- Inhalation of 20% O_2 and 80% helium is likely to be useful in young persons with extrinsic tracheal compression.
- Carbon monoxide diffusion across alveoli is increased in Goodpasture's syndrome, or when there is increase in mean wedge pressure and in asthma. Diffusion is decreased when

there is obstruction to pulmonary vascular bed, filling of alveoli with fluid or exudate or thickening of alveolar wall as in fibrosing alveolitis.

ONCOLOGY

- Marrow stem cells can differentiate into mesenchyma, myosite, endothelial, haemopoietic and neural cells. Engraftment capacity is good in G1 but nil in S, G2 and M phases.
- IL2 is essential for growth of T-lymphocytes, IL-5 for NK cells, eosinophils, IL-7 for plasma cells and IL-3 for mast cells and basophils and IL-6, IL-11 for platelets.
- Stem cells are inhibited by IFN, $MIP1\alpha$, TNF and TGF13, whereas antibody to VLA-4 causes mobilisation of haematopoietic progenitors.
- Serum levels of transferrin receptors protein (TRP) reflects the total erythroid marrow mass. TRP level is t in absolute iron deficiency. Marrow expansion to erythropoietin can be assessed from rise in TRP. Normal value of TRP is 4-9 Ng/L.
- HbA has high affinity for 2-3 BPG but HbF does not bind 2-3 BPG, so it tends to have higher oxygen affinity in vivo.
- Red cells at 6 weeks of conception have embryonic Hb like Hb portland and Hb Gower. At 10 weeks, HbF formation starts which is replaced by HbA at 38 weeks of intrauterine life. Fetal haemoglobin gene can be activated by butyrate.
- Hydroxyurea and BMT are the treatments for HbS disease. Hydroxyurea is indicated if patient has repeated acute chest syndromes or more than 3 crises a year. BMT is indicated if repeated crises occur early in life, Is neutrophil and development of hand-foot syndrome.
- The destruction of parietal cells in pernicious anaemia is by cytotoxic T cells. Pernicious anaemia is unusually common in patients of agammaglobulinemia. 90% of them have antibody against 11+1V-AT Passe and 60% against intrinsic factor.
- Pig A gene mutation in X-chromosome causes PNH, since biosynthesis of GPI anchor is disturbed. 20 proteins have been documented to be missing in RBCs of patients with PNH.
- In childhood ALL hyperploidy has a favorable prognosis. t(4:11) translocation is associated with younger age, L1 morphology and high WBC count; whereas t(8:14) is associated with older age, CNS involvement and L3 morphology. Both are associated with poor prognosis.
- All B cell neoplasms express CD5 but not lymphoplasmacytic lymphoma which is associated with HBC and is a tissue manifestation Waldenstrom's macroglobulinemia.
- Flower cells refer to CD4 positive T cell lymphoma. Null cells are CD30 positive.
- Nonsecretors of A, B blood group antigen are susceptible to infection by Candida, meningococci, pneumococci, haemophilus. The 'P' antigen is expressed on uroepithelial cells and mediates binding of E.coli.
- Umbilical cord blood has high concentration of stem cells and is a good source for transplantation; chances of GVHD is less but marrow repopulation is slow.
- Oral iron chelating agent (L2 desferal) is a respite for patients of beta thalassemia. Allogenic bone marrow transplantation in betathalassemia major achieves long-term survival in more than 80% cases.

Both leukemoid reaction and CML can have similar bone marrow picture. Hence increased LAP score, mild splenomegaly if at all and normal karyotype speak of leukemoid reaction while positive philadelphia chromosome with low LAP score and large spleen are indicators of CML.

- Aspirin does not prolong clotting time. There is no family history of bleeding disorder in upto 30% cases of classic haemophilia. Prenatal bleeding is distinctly uncommon in patients of classic haemophilia.
- The diagnosis of dysfibrinogenemia is usually made by the presence of normal fibrinogen level with a prolonged thrombin time. It can be associated with increased risk of thrombosis as the abnormal fibrin clot is relatively resistant to digestion by plasmin, particularly in congenital variety. Acquired dysfibrinogenemia is common in all forms of chronic liver disease.
- Radiotherapy causes the biologic effects by breaking DNA from superoxide and hydroxyl radical formation of these reactive oxygen metabolites but hyperbaric oxygen enhances radiation effects.
- Radiation is given in doses of 150-250 rads per day to a total of 5000-6000 rads.
- Adjuvant chemotherapy is given after surgical resection of a primary tumor to eradicate micrometastasis. It increase survival in breast tumor, sarcomas and solid tumor of childhood. Heparin acts as an anticoagulant by increasing action of antithrombin III which is the most important inhibitor of activated clottign factor in plasma.
- In granulomatous disease neutrophils cannot generate sufficient amount of hydrogen peroxide to kill micro-organism that contain catalase e.g. Staphylococcus, gram-negative bacteria and Aspergillus.
- Neutropenia may occur with use of chloramphenicol and chlorpromazine but the former drug should be immediately stopped while latter is to be continued despite neutropenia which is mild and dose related. Neutropenia may accompany megaloblastic anaemia which is manifestation of impaired DNA synthesis.

- Hairy cell leukemia may have an indolent course with prolonged survival with or without therapy. Splenectomy has a beneficial effect in these patients. Tartarate resistant acid phosphatase stain helps in distinguishing hairy cell leukemia from lymphoproliferative disorders.
- Vitamin B12 deficiency causes defective DNA synthesis in all proliferative cells including red cells, white cells and platelet precursors. Thus leukopenia and thrombocytopenia frequently accompany anaemia.
- Serum LDH is markedly elevated in vitamin B12 deficiency because of ineffective erythropoiesis, i.e. intramedullary haemolysis consequent to defective maturation of red cell precursors.
- Chronic lymphocytic leukemia is characterized by the accumulation of immunoincompetent lymphocytes. Associated findings include autoimmune disorders, antibodies directed against platelets or red cells and hypogammaglobulinemia.
- Myeloblasts have positive staining reaction with peroxidase and sudan black but not lymphoblasts. Lymphoblasts have coarse cytoplasmic staining with periodic acid schiff. Auer bodies, the highly refractile cytoplasmic rods are present in 1/3 cases of AML but are pathognomonic. TDT is found in high concentration in patients of ALL.
- Pure red cell aplasia appears to be an autoimmune disease often associated with thymoma. Such patients have no chance of transformation to leukemia and recover with thymectomy or steroids.
- Necrolytic migratory erythema and eczematous dermatitis are associated with glucagon secreting pancreatic carcinoma.
- Hypercalcemia is much more commonly associated with epidermoid carcinoma of lung but is unusual with oat cell carcinoma of lung despite its higher incidence of bone marrow metastasis.
- Almost all of what is measured in plasma as factor VIII antigen is von Willebrand factor. Hence factor VIII antigen level is normal in hemophilia but not factor VIII coagulant activity.