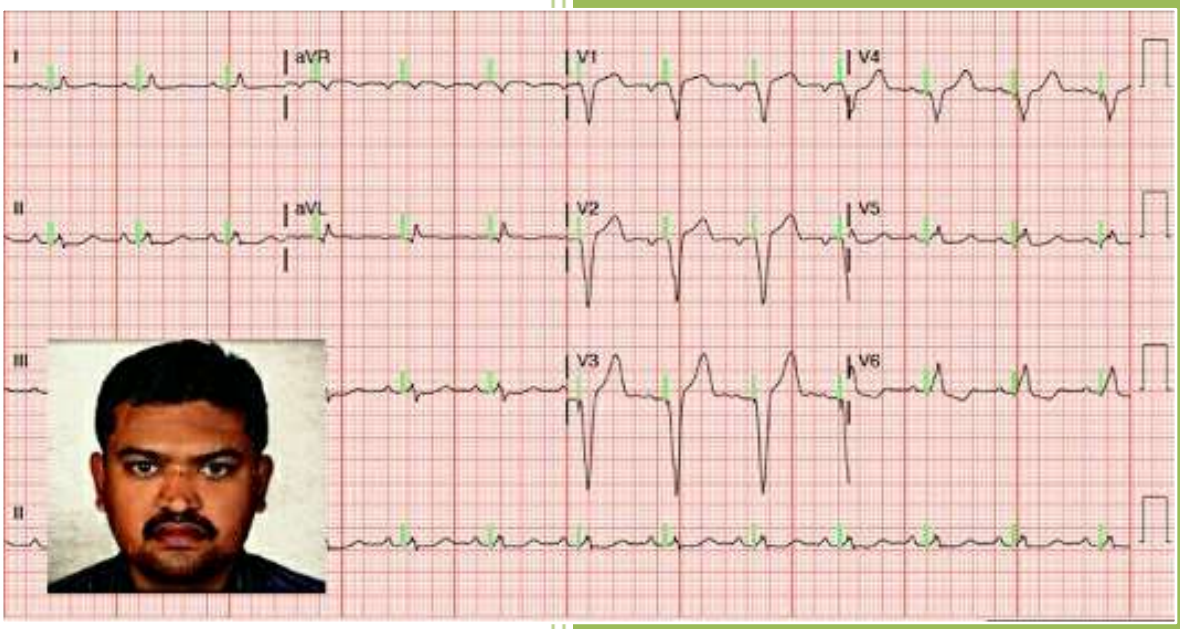
2016

MEDICAL MECHANICS-I



Compiled by

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With great respect to the Hands of Dr.Rama subramanyam,

Dedicated to

Justice Rajiv Sahai Endlaw

Best wishes to The Dynamic Government of Telangana

(and to Dr.C.Laxma Reddy B.H.M.S. *, honourable Health Minister of Telangana)*

We are sailing in the winds of Thomas Hobbes society, bellum omnium contra omnes. Whatever the cause maybe, the government or economic policies, 20% of people will always suffer.If it goes beyond that , to include 40% or 60% or 80% of people,we have to recheck the policies and their implementation.

What happens, if one of our family members becomes bankrupt, and was forced to enter into a debt trap, a situation which is nothing less than a suicide, just because of a sudden spurt in economy and inflation, which he cannot cope with.

What happens, if one of our family members, who, a breadwinner of the family suffers a sudden illness, and dies helplessly infront of our eyes?

There is a need for everyone to be familiar with the changes in economy and management of health to lead a secure life.

A sudden and arbitrary rise in the "value" of some of the goods and services will lead to evolve a marbled economy with regions of boom separated from regions of slump.The policies which are aimed at "Trickle down Economics" will hamper the economy by exploiting the circulation of currency system and denying the principle of "to each according to their contribution".

The barter system has given way to currency system with the objective of easy rotation of currency with all walks of life. A sudden rise in the value of some goods and services will hinder the circulation of currency by avoiding some routes of circulation, while overflowing others.

The blocked money which was deliberately kept away from circulation, as black money will affect the common man depending on the quantity of seclusion, and will effect the government depending on the quantity of tax evasion.

Thanks to the BIG MAN and his bold move. It is worthy to be praised, if it is successful, because it hits the target. It is more worthy to be praised, if it is a failure, because it will surface the real problems and the need for rectification – a trial which many countries cannot afford, as it is a global phenomenon.

This notes is a compilation, useful for the average students like me, to understand some of the concepts of observation of patient suffering with terminal illness, before going to read the standard books.

Declaration of death:

1.Death and the Brain

Clinical Tests : loss of consciousness # absence of spontaneous movements (excluding spinal reflexes) # absence of motor responses in cranial distribution # loss of brainstem reflexes → absent pupillary light reflex-pupils mid-position or greater ('fixed dilated pupils') → corneal → gag/pharyngeal → cough/tracheal → vestibulo-ocular ('cold caloric') → oculo-cephalic ('dolls eye') → loss of capacity to breathe

Laboratory Tests : isoelectric EEG # absent brain blood flow # absence of brain perfusion # absence of cerebral metabolic activity # absent brainstem evoked potentials after wave 1 # evidence of tonsillar herniation by neuro-imaging

(Spinal Reflexes : in brain death***** spinal-mediated reflexes include- plantar flexion and triple flexion responses, muscle stretch reflexes, abdominal contractions, sitting up posturing and respiratory-like movements .Brain death requires the use of a supplementary or confirmatory test. The most commonly recommended supplemental tests are EEG, 4 vessel cerebral angiography or radionuclide testing.*****Newer tests – inconsistently recommended – include CT angiography, CT perfusion, MR angiography and transcranial Doppler**)** (Function should be distinguished from activities. Brain function such as the capacity for consciousness or ability for unassisted breathing is distinguished by examples of brain activity such as posterior pituitary antidiuretic hormone release or residual nests of neuronal electrical function)(performance of **apnea testing** should be reserved as the last test of brainstem function)

2.Death and Circulation

Clinical Tests : absence of palpable pulse ***** absence of heart sounds ***** absent breath sounds by auscultation ***** pulseless electrical activity (non-perfusing rhythm) ***** isoelectric EKG ***** absence of breathing ***** pupils fixed and dilated ***** no response to pain ***** loss of pulsatile arterial blood pressure (non-invasive)

Laboratory Tests : absent pulse by audible Doppler ***** loss of pulsatile arterial blood pressure (invasive intra-arterial line) ***** echocardiographic absence of aortic valve opening or anterograde circulation ***** absent pulse oximetry (no oxygen saturation and/or no plethysmography tracing) (The clinical criteria and conditions listed here may not be applicable to neonatal patients (term> 36 weeks, age< 30 days)). (Examples of heart function such as effective contractions of the myocardium leading to anterograde flow of blood through the aorta and arterial system should be distinguished from examples of heart activity such as atrial natriuretic hormone release or residual pulseless electrical activity)

(brain death: irreversible loss of all function of the brain, including the brain stem.***** three essential findings in brain death are coma, absence of brain stem reflexes, and apnea.)

- Requirements → Pulse oximeter,.....
- i3 approach in observation of patient → i) imbalance, ii) ischemia, & iii) infection
- Imbalance→ A basic metabolic panel measures sodium, potassium, chloride, bicarbonate, blood urea nitrogen (BUN), magnesium, creatinine, glucose, and sometimes calcium. Some tests, such as those that measure glucose or a lipid profile, require fasting (or no food consumption) eight to twelve hours prior to the drawing of the blood sample. For the majority of tests, blood is usually obtained from the patient's vein. Other specialized tests, such as the arterial blood gas test, require blood extracted from an artery. Blood gas analysis of arterial blood is primarily used to monitor carbon dioxide and oxygen levels related to pulmonary function, but is also used to measure blood pH and bicarbonate levels for certain metabolic conditions.
- Ischemia → Angiography or arteriography is a medical imaging technique used to visualize the inside,or lumen,of blood vessels and organs of the body,with particular interest in the arteries,veins,and the heart chambers.This is traditionally done by injecting a radio-opaque contrast agent into the blood vessel and imaging using x-ray based techniques such as fluoroscopy.The word describes both arteriogram and a venogram.The term angiography is strictly defined as based on projectional radiography, however the term has been applied to newer vascular imaging techniques such as CT angiography and MR angiography.
- Infection → MIC (minimum inhibitory concentration) is the lowest concentration of an antimicrobial (like an antifungal, antibiotic or bacteriostatic) drug that will inhibit the visible growth of a microorganism after overnight incubation.
- Clockwise Observation of patient :

  1'o clock: Imbalance

  2'o clock: Heart and circulation

  3'o clock: Lungs

  4'o clock: Kidney

  5'o clock: Nervous system

  6'o clock: Abdomen

  7'o clock: Endocrine

  8'o clock: Infection

  9'o clock: Orthopaedic

  10'o clock: Pregnancy

  11'o clock: Oncology

  12'o clock: Psychiatric & Anaesthesia

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1'o clock: Imbalance

- Water ≈50-60% of body weight.(TBW=total body water)
- Water= 2/3rd s intracellular + 1/3rd extracellular
- Water extracellular=intra vascular + interstitial
- Water moves from low solute concentration → high solute concentration
- Hypovolemia = decreased intra vascular volume
- Hypervolemia = increased extracellular volume
- Hypovolemia(decreased intra vascular volume) ĉ decreased extracellular volume
  Conditions are – increased fluid losses (GI,polyuria,sweating,burns,haemorrhage), decreased intake of sodium and water, renal sodium wasting, adrenal insufficiency, osmotic diuresis(hyperglycemia),diuretics.
- Hypovolemia(decreased intra vascular volume) ĉ increased or normal extracellular volume conditions are – ascites ,protein loss ,congestive heart failure, increased vascular permeability(sepsis,shock,trauma,burns)
- intra vascular volume=effective arterial volume
- Reduced intra vascular volume stimulates → increased renal sodium reabsorption → increase in total extracellular volume
- intra vascular volume depletion →decreased venous return to the heart →lower stroke volume → sinus tachycardia to maintain cardiac output.
  →increased ADH → retention of water
  →Hypotension(hypotension & shock →inadequate systemic perfusion ,vasoconstriction(cold skin & extremities)cardiac ischemia, liver & kidney failure)
  →diminished urine volume

- Evidence of decreased intra vascular volume: Hypotension, low central venous pressure or pulmonary capillary wedge pressure, tachycardia, oliguria, end- organ dysfunction, peripheral vasoconstriction.
- Hypovolemia requires fluid replacement of, estimated amount of volume depletion over 12-24 hours,in the range of 50-150 ml/hr(200-300ml/hr- if severe volume depletion & organ dysfunction).
- Types of replacement fluids: 1.crystalloid-made of water and small solutes, 2.colloid solutions-consisting of water,electrolytes,and high molecular weight proteins or polymers
- 1.crystalloid≈0.9%NaCl(normal saline), 5% dextrose in 0.9%NaCl, ringers lactate, 5% dextrose in water, 0.45%NaCl, 5% dextrose in 0.45%NaCl
  2.colloids≈albumin5%, albumin 25%, 6% hetastarch in 0.9%NaCl
- Replacement of fluid losses from GI tract ≈ 5%dextrose in 0.45%NaCl+kcl (20meq/l) + NaHCO3(45meq/l)

- Hypervolemia(increased extracellular volume) ĉ decreased intra vascular volume conditions- ascites ,protein loss ,congestive heart failure, portal hypertension, excess sodium intake
- Hypervolemia(increased extracellular volume) ĉ increased intra vascular volume conditions-increased sodium retention(renal insufficiency, hyperaldosteronism, hypercortisolism, increased rennin and angiostensin, drugs
- Hypervolemia ĉ decreased intra vascular volume requires diuretic treatment but should be delayed until intra vascular fluid deficit is corrected.
- Hypervolemia ĉ increased intra vascular volume requires diuretics(may also require vasodilators, mechanical ventilator/non invasive positive pressure ventilation).Failure to induce appropriate diuresis may require hemodialysis or ultrafiltration.
- Hypervolemia without change in intra vascular volume requires-1.sodium retention 2.diuretics 3.elimination of extracellular volume(paracentesis, continuous venovenous hemofiltration)
- Water moves from hypotonic (lower osmolality) solution to hypertonic (higher osmolality) solution(osmolality is the concentration of solute in a solution.Ex: plasma osmolality is the sum of concentrations of cations & anions)(urea contributes to osmolality but not tonicity)
- Since sodium is the most abundant extracellular cation,the sum of cation and anion concentrations is approximately 2×(Na+).Hypernatremia always denotes hypertonicity,but hyponatremia may be seen with hypotonicity,normotonicity,or hypertonicity.
- The amount of water that can be excreted in 24 hrs depends on renal concentrating and diluting ability and the quantity of solute excreted per day.
- Urine concentration depends on the amount of ADH(AVP-arginine vasopressin) and renal tubular function.ADH is secreted by posterior pituitary in response to plasma osmolality(↑P.O.→↑ADH, ↓P.O.→↓ADH).(Decreased extracellular volume also stimulates ADH release).Maximum urine concentration(to conserve water excretion) may be limited , if there is renal insufficiency,nephrogenic diabetes insipidus(inadequate response to ADH), & central diabetes incipidus (absence of ADH)
- Failure to dilute urine maximally may result from renal insufficiency,inappropriate secretion of ADH,& adrenal insufficiency(increased permeability of collecting ducts to water)(excess water in the body should be countered by increased volume of maximally diluted urine)
- Normal urine solute excretion≈800 mosm/d, including sodium, potassium, anions, ammonium & urea (urea,breakdown product of amino acids ,makes up about 50% of solute excreted.). Decrease in urine solute excretion(Ex: severely limited protein intake)limits maximum water excretion even if urine is maximally diluted.
- Hyponatremia=plasma sodium<135meq/l, indicates excess total body water for the amount of solute(dilutional hypo natremia)(compensatory mechanism →rapid excretion of water in normal subjects to correct imbalance)
- Hyponatremia ĉ decreased extracellular volume: Normally urinary sodium excretion is low. Increased water intake(thirst) and retention(↑ADH) leads to ↑TBW relative to the reduced amount of solute. conditions in which ↑sodium and water loss in urine : adrenal insufficiency (lack of cortisol causes collecting ducts excessively permeable to water

reabsorption and ADH fails to be suppressed by low P.O.),diuretic use, and salt losing nephropathies.

- Hyponatremia ĉ increased extracellular volume: congestive heart failure ,nephritic syndrome,cirrhosis,protein losing enteropathy,& pregnancy.(oedema, ascites, pulmonary oedema)
- Hyponatremia ĉ Normal extracellular volume: SIADH(syndrome of inappropriate secretion of ADH≈ release of ADH in response to disorders of lung & CNS),decreased solute intake,psychogenic water ingestion.
- Hyponatremia=plasma sodium<135meq/l →altered mental status,(confusion ,lethargy)& seizures . plasma sodium<115meq/l → Hyponatremic encephalopathy (dangerous in patients with acute neurologic disorders-head injury,stroke,haemorrhage).severe Hyponatremia or rapid correction of Hyponatremia leads to osmotic demyelination syndrome(central pontine & extrapontine myelinolysis) →corticospinal and corticobulbar signs,including weakness,spastic quadriparesis,dysphonia, dysphagia & impaired leval of consciousness.
- Low plasma osmolality (<280mosm/kg) confirms hyponatremia owing to increased water relative to solute.(plasma electrolytes,glucose,creatinine,urea nitrogen,urine osmolality,urine sodium,urine creatinine should be measured)
- Diagnosis of SIADH: inappropriately high urine osmolality (300-500mosm/kg)in the presence of low plasma osmolality,and the absence of low urinary sodium concentration.
- Correction of hyponatremia requires administration of normal saline to correct hypovolemia & to increase water excretion. Restriction of water intake(1000-1500ml/day) for asymptomatic Normovolemic hyponatremia .hypertonic saline(3%NaCl) and diuretics for symptomatic or severe hyponatremia.
- Hypernatremia=plasma sodium>145meq/l, always associated with hypertonicity,serum osmolality >300mosm/kg ,indicates a deficit of TBW relative to total body solute. conditions: 1.addition of solute(exogenous-hypertonic saline,sodium bicarbonate, glucose,mannitol etc, endogenous-hyperglycemia by gluconeogenesis,glucogenolysis)((↑P.O.→↑ADH→minimize water excretion)2.inadequate water intake≈failure to take mandatory intake of 600-700ml/day.3.excessive water loss≈impaired urine concentrating ability.(diuresis, diabetes insipidus) →altered mental status,polyurea
- Water diuresis and solute diuresis can be distinguished by the ratio of urine osmolality to plasma osmolality. solute diuresis=Uosm/Posm>0.9(=osmotic diuresis ĉ isosthenuria) Water diuresis=Uosm/Posm<0.9(ĉ excretion of dilute urine)
- Hypernatremia correction requires1. diuretics and administration of water or 5% dextrose in water –for increased solute.(in renal insufficiency→hemodialysis or ultra filtration with replacement of water,hyperglycemia→intravenous insulin).2.- 5% dextrose in water or 0.45%NaCl –for diminished extracellular volume.3. administration of water orally or 5% dextrose in water I.V-for diabetes insipidus.(central diabetes insipidus→synthetic ADH compounds≈desmopressin)
- Hypokalemia=plasma K^+ <3.5meq/l conditions:1.total body potassium is low≈decreased intake(<30-40meq/day),non- renal losses(diarrhoea,sweating),increased renal secretion(increased mineralocorticoids,increased aldosteron,primary hyper aldosteronism),solute diuresis,hypomagnesemia 2.abnormal distribution of potassium between extracellular and intracellular spaces≈drugs and acid-base disturbances,insulin

- Hypokalemia →muscle weakness. Severe Hypokalemia→skeletal muscle paralysis,respiratory muscle weakness,arrhythmias,postural hypotension
- Hypokalemia correction requires oral or I.V.-potassium chloride , potassium phosphate.
- Hyperkalemia= plasma K^+ >5meq/l conditions:1. addition of K^+ to extra cellular space≈impaired insulin release,rapid K^+ administration,rhabdomyolysis,tumor lysis syndrome, 2.impaired disposal of K^+ ≈metabolic acidosis,insulin deficiency,beta-blockers use,aldosterone deficiency. Pseudo Hyperkalemia can be seen in extreme thrombocytosis or leukocytosis
- Severe Hyperkalemia →may develop heart block,VF
- Hyperkalemia correction requires-1.intravenous calcium chloride or calcium gluconate(for cardiac conduction system changes)2.insulin+glucose,sodium bicarbonate I.V(for Metabolic acidosis)3.CVVHD
- Hypophosphatemia=plasma phosphorus <2.5mg/dL, severe <1.0 mg/dL. hypophosphatemia always results from a problem of maldistribution of total body phosphorus. Decreased plasma phosphorous and extracellular phosphorus → large quantity of phosphorus in the intracellular space. Should be anticipated in- postoperative patients; in patients with chronic or acute alcoholism, diabetic ketoacidosis, or head trauma; and in patients receiving total parenteral nutrition or mechanical ventilation.Causes-1. Redistribution of Phosphorus ≈ administration of insulin and glucose or acute hyperventilation(treatment of diabetic ketoacidosis and in the refeeding syndrome- as glucose and phosphate move into cells.) Respiratory alkalosis also causes a shift of extracellular phosphorus into cells.2- Decreased intake of phosphorus≈ preexisting diseases leading to decreased dietary intake of calcium, phosphorus, and vitamin D. Binding of phosphorus in the gastrointestinal tract by antacids and specific phosphate-binding compounds prevents absorption.3- increased renal tubular excretion of phosphate≈ subclinical hyperparathyroidism. Clinical consequences of hypophosphatemia are due to decreased production of ATP and erythrocyte 2,3-DPG → Impaired function of skeletal muscles, including respiratory muscles, and myocardium
- Hypophosphatemia correction requires→ Intravenous phosphate is given as sodium or potassium phosphate. Rapid phosphate shifts during treatment, may resolve or worsen the problem. Therefore, close monitoring of plasma phosphorus and other electrolytes is necessary during repletion. . Adult patients receiving parenteral hyperalimentation generally require about 1 g phosphorus daily. Routine repletion of phosphorus in patients with diabetic ketoacidosis has been recommended.
- Hyperphosphatemia= Plasma phosphorus >5 mg/dL. acute elevation can have consequences owing to precipitation of calcium phosphate salts in the heart, kidneys, and lungs, rarely, acute cardiac conduction disturbances. Calcium phosphate precipitation results in acute hypocalcemia. Severe hyperphosphatemia is seen when there is massive tissue breakdown.Causes-1. Impaired Phosphate Excretion- chronic renal insufficiency, hypoparathyroidism(Normal cell turnover releases a steady quantity of phosphorus into the extracellular space that is taken back up into the cells or bone or excreted by the kidney).2- Redistribution of Phosphorus≈ massive tissue breakdown- rhabdomyolysis from trauma or other muscle injury from infection, drugs, seizures, or metabolic problems. Tumor lysis syndrome is seen after chemo or radiotherapy of highly responsive tumors (eg, lymphoma).3- Excessive replacement of phosphorus

- Hyperphosphatemia correction requires→ normal saline infusion in patients who can tolerate this treatment will enhance phosphate excretion, Orally administered phosphate binders. Dietary phosphorus can be minimized by prescribing a low-protein diet and avoiding dairy products that contain both calcium and phosphorus
- Hypomagnesemia= plasma magnesium concentration of less than 1.7 mg/dL, but about 25% of plasma magnesium is bound to albumin. While the plasma level reflects both bound and unbound magnesium, the clinical effects of magnesium, like those of calcium, are due to the unbound ion.Causes-1. Decreased intake, intestinal causes of malnutrition interfere with its absorption.2. Increased losses of magnesium≈ renal magnesium wasting. Hypomagnesemia is also found in association with diabetes mellitus, phosphate depletion, hyperparathyroidism, and thyrotoxicosis. Hypomagnesemia occurring with acute myocardial infarction → ventricular arrhythmias. Cardiac arrhythmias are the most important complications of hypomagnesemia. Hypocalcemia is strongly associated with hypomagnesemia. Tetany, positive Chvostek and Trousseau signs, seizures, weakness, and altered mental status may be seen. Disorder should be anticipated in certain high-risk groups, that is, patients with hypocalcemia, acute myocardial infarction, congestive heart failure, alcoholism, acute pancreatitis, mal-nutrition, diarrhea, or seizures and those receiving diuretics, amphotericin B, or aminoglycosides. . Hypomagnesemia is seen in a large percentage of those with hypokalemia. Refractory potassium deficiency results because administered potassium is unable to enter cells readily and therefore is excreted in the urine. Hypomagnesemia also stimulates renin release and thereby increases aldosterone, further enhancing potassium excretion. Hypomagnesemia is also strongly linked with hypocalcemia and inappropriately low levels of parathyroid hormone.
- Hypomagnesemia correction requires→ Intravenous magnesium sulfate ($MgSO_4$) can be given as 50% solution added to D_5W or normal saline.
- Hypermagnesemia≈ Plasma [Mg^{2+}] >2.7 mg/dL: usually asymptomatic, Plasma [Mg^{2+}] >7 mg/dL: weakness, loss of deep tendon reflexes, and paralysis, Plasma [Mg^{2+}] >10 mg/dL: hypotension and cardiac arrhythmias.-Causes-1. Increased intake(Magnesium-containing antacids and laxatives)2. impaired renal magnesium excretion
- Hypermagnesemia correction requires →Intravenous calcium gluconate or calcium chloride
- Majority (98%) of calcium is in the form of hydroxyapatite in the bone, and only a very small amount is in the extracellular fluid. Plasma calcium is regulated by a complex system of hormones, vitamins, and organ function and is closely tied to phosphorus and magnesium regulation.
- Hypocalcemia= Plasma [Ca^{2+}] <8.5 mg/dL, → Nervous system irritability, including altered mental status, focal and grand mal seizures, paresthesias, tetany, hyperreflexia, muscle weakness, Prolonged QT interval, cardiac arrhythmias.Causes-1. loss of plasma calcium by deposition of calcium salts in tissues→ may be seen in acute pancreatitis, and rhabdomyolysis. Most other patients with hypocalcemia from calcium deposition have hyperphosphatemia. In these patients, when the product of calcium × phosphorus is greater than 60, calcium phosphate tends to deposit in soft tissues→ the tumor lysis syndrome.2. Decreased PTH or PTH Effect ≈ Hypomagnesemia decreases the action of PTH on bone.

- Hypocalcemia correction requires →Treatment with intravenous calcium gluconate or calcium chloride. Hypoparathyroidism is treated with calcium supplementation and vitamin D.
- Hypercalcemia= Plasma [Ca2+] >10.5 mg/dL, → Altered mental status with confusion, lethargy, psychosis, and coma, Hyporeflexia and muscle weakness, Constipation, shortening of QT interval, and pancreatitis. Chronic hypercalcemia → bone changes, band keratopathy & features of underlying disease(hyperparathyroidism, malignancy, sarcoidosis, vitamin A toxicity). Severe hypercalcemia is almost always due to malignancy, including solid tumors, lymphoma, and multiple myeloma. Hypercalcemia is the result of failure of the regulatory mechanisms for calcium, including inability to suppress PTH normally, or excessive mobilization of calcium by an abnormally produced PTH-like compound or vitamin D. PTH activates or stimulates osteoclasts that mobilize calcium from bone. Vitamin D primarily increases calcium absorption from the gastrointestinal tract.Causes-1. Hypercalcemia in primary hyperparathyroidism is caused by unregulated PTH secretion from parathyroid adenoma or hyperplasia.2. *parathyroid hormone–related peptide* (PTHrP) release by the tumor. The effects of PTHrP are similar to those of PTH. 3. Excessive administration or ingestion of vitamin D, Toxic doses of vitamin A also may cause hypercalcemia
- Hypercalcemia correction requires → expansion of extracellular volume, furosemide, calcitonin, and pamidronate.
- Decreased arterial pH is called *acidemia,* and increased arterial pH is called *alkalemia.* The disturbances responsible for these changes are *acidosis* and *alkalosis,* respectively, and these changes are defined as "metabolic" (owing to primary increase or decrease in HCO_3^-) or "respiratory" (owing to primary increase or decrease in CO_2).
- pH=6.1+log ... [HCO3-] / 0.03 × PaCO2. the pH of the arterial blood is between 7.35 and 7.43. For $PaCO_2$, the limits are 37 and 45 mm Hg. Bicarbonate concentration normally varies between 22 and 26 meq/L.
- The bicarbonate–carbon dioxide buffering system is the major extracellular buffer. (CO2 is the respiratory acid & metabolic acids include all of the body's acid except CO2) The main intracellular buffer systems include hemoglobin, protein, dibasic phosphate, and carbonate in bone. For usual buffers, the addition or removal of hydrogen ion, for example, is countered by corresponding opposite effects of the buffer components. Metabolic acidosis can be countered by decreased arterial $PaCO_2$, whereas a respiratory acidosis is countered by increased plasma bicarbonate.
- Metabolic acidosis results from a primary reduction in plasma bicarbonate concentration, usually accompanied by a compensatory decrease in $PaCO_2$. The normal compensatory response is -to maximize renal reabsorption of bicarbonate. Classification for metabolic acidosis- uses the *anion gap.* The anion gap is calculated as

  Anion gap=(Na+)-[(HCO3-)]+[(Cl-)]

  The normal value for the anion gap is 12 ± 4 meq/L. The anion gap is equal to the difference between "unmeasured" anions and "unmeasured" cations. In normal subjects, unmeasured anions include albumin (2 meq/L), phosphate (2 meq/L), sulfate (1 meq/L), lactate (1–2 meq/L), and the anions of weak acids (3–4 meq/L). The predominant unmeasured cations include calcium (5 meq/L), magnesium (2 meq/L), and certain cationic immunoglobulins. The anion gap widens most commonly because of increased

unmeasured anions, but occasionally widening is due to decreased unmeasured cations. In metabolic acidosis, an increased anion gap indicates that a strong acid is present that dissociates into hydrogen ion and an "unmeasured" anion. On the other hand, failure of the kidneys to generate sufficient bicarbonate results in metabolic acidosis in which chloride, a "measured" anion, is the predominant anion. Therefore, the anion gap does not widen. This classification divides metabolic acidosis, into those with an increased anion gap and those without an increase in the anion gap. The latter are often called *hyperchloremic metabolic acidosis.* Failure of normal urinary acidification increases bicarbonate losses. This condition, called *renal tubular acidosis,* leads to metabolic acidosis because the kidneys are unable to compensate for normal acid production or fail to reabsorb normal amounts of filtered bicarbonate. Hyperchloremic metabolic acidosis can be caused by acetazolamide, a carbonic anhydrase inhibitor and diuretic. Acetazolamide inhibits proximal tubular bicarbonate reabsorption; the result is metabolic acidosis with inappropriate loss of renal tubular bicarbonate, a drug-induced renal tubular acidosis.

- The major causes of metabolic acidosis with elevated anion gap are-
  1.Lactic acidosis occurs in a number of situations ≈ shock, diabetes, renal failure, liver disease, sepsis, drug intoxication, severe volume depletion, and hereditary metabolic abnormalities. Transient lactic acidosis is a feature of grand mal seizures. Patients with liver disease have difficulty removing lactate.2. Ketoacidosis is most commonly due to poorly controlled diabetes mellitus, occasionally in those with heavy ethanol consumption in the absence of food intake (alcoholic ketoacidosis), and during starvation.3.Uremia,4. Ingestion of ethylene glycol (radiator antifreeze), methanol, and excessive salicylic acid may give rise to anion gap metabolic acidosis. May present with peripheral vasodilation, depressed cardiac contractility in severe acidosis, fatigue, weakness, stupor, and coma.
- As acidosis worsens, increased respiratory rate and tidal volume (Kussmaul respiration) provide partial respiratory compensation. Peripheral vasodilation occurs and produces palpable cutaneous warmth. Paradoxical venoconstriction increases central pooling and may result in pulmonary edema. Cardiac contractility may decrease below a pH of 7.10 and may result in reduced blood pressure or shock. CNS depression produces fatigue, weakness, lethargy, and ultimately stupor and coma, but CNS disturbances are much more common with respiratory acidosis at similar pH
- If treatment is indicated for severe metabolic acidosis, intravenous sodium bicarbonate is the preferred agent.
- Metabolic alkalosis consists of the triad of increased [HCO_3^-], increased pH, and decreased plasma chloride concentration. principal mechanisms leading to metabolic alkalosis include (1) addition of bicarbonate to the plasma, (2) loss of hydrogen ion,(vomiting) (3) volume depletion, (4) chronic use of chloruretic diuretics, and (5) potassium depletion. A decrease in minute ventilation is usually noted in moderate cases of metabolic alkalosis. If preexisting pulmonary disease is present, CO_2 retention may result in severe hypercapnia. As alkalemia progresses, the ionized calcium concentration decreases and produces neuromuscular findings similar to those of hypocalcemia. Initial lethargy and confusion give way to obtundation and seizures as the alkalemia worsens. Patients may complain of

paresthesias and muscle cramps. The Chvostek and Trousseau signs may be present. In severe cases, respiratory muscle paralysis may develop.

- A useful distinction can be made by separating metabolic alkaloses into those that are chloride-sensitive (sometimes called *volume-* or *saline-responsive*) and those that are non-chloride-sensitive. Chloride- or volume-sensitive patients are volume-depleted, hypokalemic, and will respond to chloride or volume administration (see above). The latter group is usually volume overloaded and will worsen or fail to improve with chloride-containing solutions or volume repletion. These groups can be distinguished by measurement of urine chloride. Lethargy and confusion→ progressing to seizures in severe cases, Ventricular and supraventricular arrhythmias, Impaired oxygen delivery because of increased hemoglobin affinity for oxygen
- Once a high plasma bicarbonate is identified, the most important distinction must be made between metabolic alkalosis and chronic respiratory acidosis with renal compensation. Mild alkalemia (pH 7.40–7.50) is well tolerated and does not require treatment unless preexisting cardiac or pulmonary disease complicates the situation. If the alkalemia worsens (pH >7.60), treatment is indicated. The key to therapy is restoration of normal circulating blood volume and repair of the associated hypokalemia
- Elevated $PaCO_2$ (hypercapnia) with resulting acidemia is termed *respiratory acidosis*. In cases of marked respiratory acidosis→ fatigue, weakness, and confusion are present. In milder cases, patients may complain of headache. Physical findings are nonspecific and include tremor, asterixis, weakness, incoordination, cranial nerve signs, papilledema, retinal hemorrhages, and pyramidal tract findings. The syndrome of pseudotumor cerebri (increased CSF pressure and papilledema) may be simulated by respiratory acidosis. Coma begins at levels of CO_2 that vary from 70–100 mm Hg depending on arterial pH (pH <7.25) and the rate of increase of $PaCO_2$. The key to management of respiratory acidosis is correction of its primary cause. For some patients, this will require endotracheal intubation and mechanical ventilation or noninvasive positive-pressure ventilation
- A primary decrease in arterial PCO_2 (hypocapnia) indicates respiratory alkalosis. By definition, alveolar hyperventilation is synonymous with hypocapnia. The most common causes of hyperventilation include hypoxemia, CNS disorders, pulmonary disease, and excessive mechanical ventilation.→ Anxiety, irritability, vertigo, and syncope, Flattened ST segments or T waves, Tetany in severe cases.
- An infectious process will attract monocytes that will be transformed into macrophages at the site of infection. These macrophages will secrete proteins known as cytokines and other peptides that attract other white blood cells and initiate the inflammatory response common to many types of injury. These cytokines include tumor necrosis factor-α (TNF-α) and interleukins 1–32. TNF-α and other cytokines circulate to the liver, where they inhibit albumin synthesis and stimulate the synthesis of acute phase proteins, including (1) C-reactive protein, which promotes phagocytosis and modulates the cellular immune response, (2) α_1-antichymotrypsin, which minimizes tissue damage from phagocytosis and reduces intravascular coagulation, and (3) α_2-macroglobulin, which forms complexes with proteases and removes them from circulation, maintains antibody production, and promotes granulopoiesis. TNF-α and some of the interleukins also circulate to the brain, where they are responsible for induction of fever and initial stimulation of adrenocorticotropic hormone release with a subsequent rise in serum cortisol.

- As a result of severe injury, many patients develop the syndrome of insulin resistance with hyperglycemia even though they had no history of diabetes prior to the injury
- Both the injury response and the septic states are associated with a decrease in whole body glucose oxidation and an increase in the fasting hepatic glucose production rate. Recently, it has been demonstrated that the elevated blood glucose in sepsis and injury is due to an overproduction of glucose by the liver
- The rise in serum cortisol is one of the many factors responsible for the development of insulin resistance. In addition to cortisol, elevations in catecholamines, glucagon, and growth hormone in the injured patient also contribute to the development of insulin resistance. All these hormones increase the rate of hepatic glucose production
- Increased catecholamine levels are a direct response to the injury via secretion of these hormones by the adrenal gland and sympathetic ganglia throughout the body. Glucagon and growth hormone levels increase in response to the injury. Both hormones are known to increase hepatic glucose production
- As a normal response to injury, the body's ability to convert the stored form of thyroid hormone, thyroxine (T_4), into the active form, triiodothyronine (T_3), becomes impaired. There is increased conversion of T_4 to an inactive thyroid hormone known as *reverse* T_3 (rT_3) rather than T_3. This may have evolved as an energy-saving response during severe injury or illness to reduce the known contribution of T_3 to increased resting energy expenditure. Thus the syndrome of low T_3 (sick euthyroid syndrome) seen in acute illness is an adaptive strategy that reduces the normal effects of T_3 on resting energy expenditure
- As part of the injury response resulting in protein breakdown, critically ill adult patients may lose about 16–20 g of nitrogen (in the form of urea) in the urine per day— compared with about 10–12 g/day in normal individuals. In some septic patients, losses have been noted to be as high as 24 g of urinary urea nitrogen per day. The loss of 1 g of urinary urea nitrogen is equal to the nitrogen contained in 6.25 g protein. This amount of protein is equal to approximately 1 oz of lean body mass
- Specific areas of loss of lean body mass loss may result in functional impairment of the respiratory muscles (including the diaphragm), heart muscle, and gastrointestinal mucosa, thus contributing to the development of respiratory failure, heart failure, and diarrhea. Rapid development of malnutrition can occur in the critically ill patient as a result of these large daily losses of lean body mass
- Body weight needs to be correlated with loss in lean body mass (estimated from urinary creatinine) to confirm that any weight changes are not just due to changes in fluid volume
- The injury response is associated with an increase in both protein synthesis and protein degradation, as determined by either stable or radioactive amino acid tracer infusion studies. In contrast to increased whole body protein synthesis, skeletal muscle protein synthesis is usually reduced, so the increased whole body protein synthesis may be due to production of acute phase proteins, leukocytes, complement, and immunoglobulins. Leukocytes have a 4–6 hour half-life during infection, so adequate nutritional support is important for their replacement and function. It has been estimated that the average adult can break down and resynthesize up to 400 g protein per day

- The 24-hour urine urea nitrogen measurement is the single best determination of the severity of the injury response, but it cannot be used in those who have oliguric renal failure
- Protein requirements for critically ill patients can be estimated by the use of the 24-hour urinary urea loss. Add 4 g to the quantity of urinary urea (in grams) to get an estimate of total nitrogen losses (in grams). For example, if the urine urea nitrogen is 12 g per day, add 4 g to equal 16 g of nitrogen loss per day. Multiply this amount by 6.25 to determine the protein requirement per day (16 g nitrogen × 6.25 g protein/g of nitrogen = 100 g of protein per day).
- The serum albumin level is one of the best predictors of malnutrition. Albumin is a 584-aminoacid protein with a net negative charge of 19, permitting transport of many compounds. Large portions of the plasma's calcium, magnesium, zinc, bilirubin, many drugs (eg, anticoagulants, antibiotics, etc.), and free fatty acids are transported bound to albumin. Approximately 40% of whole body albumin reserves (4–5 g/kg) are intravascular, and albumin is responsible for about 76% of the colloid oncotic pressure of the plasma
- Hypoalbuminemia results from an increase in plasma volume; an increase in skin, urine, or stool losses of albumin; an increase in albumin degradation; loss into ascites; or a reduction in albumin synthesisBecause the skin stores approximately 20% of the total albumin mass, excessive losses of albumin occur with burns and subsequent exudative losses. Massive losses of protein can occur in the nephrotic syndrome, in which 60% to as much as 90% of the protein lost in the urine is albumin. Gastrointestinal losses of protein can vary markedly, and the amount of albumin normally degraded and lost in the stool is not known. Large amounts can be lost into ascites fluid. A third factor contributing to the development of hypoalbuminemia is impaired albumin synthesis in the liver. The rate of albumin synthesis (normally 150 mg/kg per day) is stimulated by (1) reduction in colloid oncotic pressure, (2) antibiotic treatment, (3) glucocorticoid therapy in cirrhosis, and (4) amino acid administration.
- Marasmic malnutrition is starvation with-out injury; protein malnutrition always accompanies injury (eg, trauma, sepsis, inflammation, or cancer).
- Body weight can be divided into three compartments: extracellular mass, lean body mass, and fat mass.
- Lean body mass is the sum of skeletal muscle, plasma proteins, skin, skeleton, and visceral organs, with the skin and skeleton accounting for 50% of the total. Urinary creatinine is related to the size of the skeletal muscle mass.
- Reduced levels of vitamin C, vitamin A, copper, manganese, and zinc are associated with poor wound healing.
- The best marker of catabolism is the determination of urine urea nitrogen loss. Approximately 80% of the total urine nitrogen appears as urinary urea nitrogen(urine urea nitrogen loss over a 24-hour period). Urinary loss of less than 6 g urea nitrogen is normal; loss of 6–12 g/day is mild, 12–18 g/day is moderate, and more than 18 g/day is severe catabolism
- In severely catabolic patients, losses as much as 24 g urea nitrogen per day (28 g total) requires approximately 175 g of protein intake per day (2.5 g/kg per day) to maintain "nitrogen balance." Nitrogen losses can be even higher in thermal injury

- In acute oliguric renal failure, vitamins A and D should be reduced or eliminated from the enteral or parenteral solutions. Potassium, phosphorus, magnesium, zinc, and selenium should be reduced or eliminated. Iron and chromium are known to accumulate in renal failure and should be removed from parenteral or enteral formulations. Copper and manganese are excreted via the biliary tree, and intake should be reduced or eliminated in patients with cholestatic liver disease to prevent toxicity
- Sepsis owing to microbial translocation or endotoxin translocation from the gut into the portal system is a frequent source of fever in those who do not have an obvious source of infection. Use of the gastrointestinal tract for feeding can reduce the incidence of bacterial translocation.
- The feeding tube should be positioned in the small bowel up to the ligament of Treitz. This is best achieved with the aid of fluoroscopy but also can be achieved by passage of the feeding tube into the small bowel by a "corkscrew" technique after bending the distal tip of the feeding tube to about 30 degrees with the wire stylet in place. On placement in the stomach, the tube is rotated so that the tip can pass via the pylorus into the duodenum. The infusion of enteral products into the small bowel will reduce the incidence of aspiration because the infusion is below the pylorus. Patients with a cuffed endotracheal tube have a smaller risk of aspiration, so placement of a feeding tube into the small bowel is less essential. A large number of enteral feeding products are manufactured including elemental formulas (eg, amino acids, mono- and oligosaccharides, and lipids), specialized products for certain critical care situations (eg, renal failure and liver failure), products containing fiber, and lactose-free nonelemental products containing 1–2 kcal/mL.
- Peripheral parenteral nutrition (ie, given through a peripheral vein) can be used in patients who can tolerate the daily 3-L fluid requirement necessary to obtain adequate calorie administration or in patients in the early phase of enteral alimentation as a supplement. Currently, the permissible concentrations of glucose, amino acids, and other nutrients delivered via peripheral vein alimentation are limited by phlebitis caused by the high osmolality of the alimentation solution. Advances in catheter technology may allow for peripheral administration of solutions of greater than 600 mOsm/L without damage to the vein. A solution of 900 mOsm/L may be well tolerated and could reduce the volume of peripheral alimentation fluid to 2 L/day. Even with this new technology, patients requiring severe fluid restriction should receive central parenteral nutrition (via a central venous catheter) using one of several fluid-restricted formulas
- Patients with a serum albumin level of less than 2.8 g/dL, a 20% weight loss over the preceding 3 months, or an ideal body weight less than 90% for height should be provided nutritional support
- percutaneous endoscopic gastrotomy (PEG) feeding
- TPN should be initiated in the diabetic patient with only 150 g of dextrose over the first 24 hours (eg, as 1 L of 15% dextrose at 40 mL/h). Approximately one-third to one-half the patient's usual total daily subcutaneous insulin dose should be added to the TPN solution. Additional subcutaneous insulin should be administered using a "sliding scale" regimen written as a standing order, with the dose of insulin based on bedside glucose measurements and serum glucose concentrations from venous blood measured every 3–4 hours. After the first 24 hours, approximately half the additional subcutaneous regular insulin administered over the 24-hour period then is added to the TPN solution prior to

increasing the rate of TPN administration or the concentration of dextrose. The use of separate intravenous infusions of insulin and TPN solution has been associated with severe hypoglycemia and death

- Careful monitoring of the serum phosphorus level over the first 48 hours of insulin therapy is important to prevent hypophosphatemia (refeeding syndrome), which has a mortality of up to 33%. Respiratory failure and cardiac dysfunction can be seen at serum phosphorus levels below 2.5 mg/dL. A severely reduced serum phosphate concentration of less than 1 mg/dL is often lethal.
- Growth hormone treatment increased survival in adults with severe burns. However, the use of growth hormone also was associated with an increase in insulin resistance and the need to administer an increased insulin dose. Growth hormone probably improves wound healing by increasing protein synthesis without increasing protein oxidation, so there is a net protein deposition in the body, likely in the liver
- A complex interaction of vascular endothelium, platelets, red blood cells, coagulation factors, naturally occurring anticoagulants, and fibrinolytic enzymes results in formation of blood clot at the site of vascular injury and activation of repair mechanisms to promote healing of the injured blood vessel. Vascular injury results in platelet adhesion and aggregation, activation of coagulation factors ultimately resulting in cleavage of fibrinogen to fibrin, and formation of a stable blood clot consisting of cross-linked fibrin polymers, platelets, and red blood cells. Simultaneously, naturally occurring anticoagulants and fibrinolytic enzymes are activated, a process that limits the amount of clot formed and degrades clot once the vessel is repaired. The latter aspects of hemostasis serve to confine clot formation to the site of vascular injury while permitting continued blood flow through the affected blood vessel.
- Normal hemostasis:1. Endothelium's procoagulant elements→ Release of von Willebrand factor (vWF), factor VIII, tissue factor, plasminogen activator inhibitor, and platelet activating factor in response to injury; maintains tight interendothelial junctions to prevent blood extravasation 2. Endothelium's anticoagulant elements→ Negative charge repels platelets and coagulation factors; produces prostacyclin; releases tissue plasminogen activator in response to vessel injury; provides thrombomodulin for thrombin-mediated activation of protein C; provides heparin-like molecules which interact with antithrombin III and accelerate its inactivation of thrombin and other serine proteases 3. platelets→ Adhere to exposed subendothelium via vWF and aggregate in response to activation (via fibrinogen-glycoprotein IIb/IIIa interaction); secrete agonists which stimulate further platelet aggregation; provide phospholipid for production of thromboxane A2 and for coagulation reactions; provide surface on which coagulation reactions are localized; secrete coagulation factors (V, vWF), which increase local concentration; provide contractile machinery for clot retraction; perhaps maintain interendothelial tight junctions by secretion of metabolically active substances 4. Coagulation factors- Proenzymes (*In response to vascular injury, sequential activation (VII, IX, X, II) results in generation of thrombin and cleavage of fibrinogen to fibrin*) Thrombin(*In addition to cleavage of fibrinogen, activates platelets, factors V, VIII, and XIII, and protein C*) Fibrinogen(Cleaved by thrombin to fibrin, which polymerizes to insoluble fibrin clot) Factor XIII(After activation by thrombin, cross-links fibrin polymers to stabilize clot) Cofactors(Factors V and VIII, both activated by thrombin, act as cofactors for X and IX,