MOH Pocket Manual in Critical Care

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Intracranial hemorrhage

Overview

- The pathological accumulation of blood within the cranial vault) may occur within brain parenchyma or the surrounding meningeal spaces. Intracerebral hemorrhage accounts for 8-13% of all strokes and results from a wide spectrum of disorders. Intracerebral hemorrhage is more likely to result in death or major disability than ischemic stroke or subarachnoid hemorrhage. Intracerebral hemorrhage and accompanying edema may disrupt or compress adjacent brain tissue, leading to neurological dysfunction. Substantial displacement of brain parenchyma may cause elevation of intracranial pressure (ICP) and potentially fatal herniation syndromes.

- **Causes of Intracranial hemorrhage :**

  Possible causes are as follows:

  - Hypertension
  - Arterio-Venous malformation
  - Aneurysmal rupture
  - Intracranial neoplasm
  - Coagulopathy
  - Hemorrhagic transformation of an ischemic infarct
  - Cerebral venous thrombosis

- Sympathomimetic drug abuse
- Sickle cell disease
- Infection
- Vasculitis
- Trauma

Clinical Presentation

- **History:**Onset of symptoms of intracerebral hemorrhage is usually during daytime activity, with progressive (i.e, minutes to hours) development of the following:

  - Alteration in level of consciousness (approximately 50%)
  - Nausea and vomiting (approximately 40-50%)
  - Headache (approximately 40%)
  - Seizures(approximately 6-7%)
  - Focal neurological deficits

- **Physical:** Clinical manifestations of intracerebral hemorrhage are determined by the size and location of hemorrhage, but may include the following:

  - Hypertension, fever, or cardiac arrhythmias
  - Nuchal rigidity
  - Retinal hemorrhages
  - Altered level of consciousness
  - Focal neurological deficits

- ***Putamen*** Contralateral hemiparesis, contralateral sensory loss, contralateral conjugate gaze paresis, homonymous hemianopia, aphasia, or apraxia.

- ***Thalamus*** Contralateral sensory loss, contralateral hemiparesis, gaze paresis, homonymous hemianopia, miosis, aphasia, or confusion

- ***Lobar*** Contralateral hemiparesis or sensory loss, contralateral conjugate gaze paresis, homonymous hemianopia, abulia, aphasia, neglect, or apraxia

- ***Caudate nucleus*** Contralateral hemiparesis, contralateral conjugate gaze paresis, or confusion

- ***Brain stem*** Quadriparesis, facial weakness, decreased level of consciousness, gaze paresis, ocular bobbing, miosis, or autonomic instability

- ***Cerebellum*** Ataxia, usually beginning in the trunk, ipsilateral facial weakness, ipsilateral sensory loss, gaze paresis, skew deviation, miosis, or decreased level of consciousness

Work Up

- ***Laboratory Studies***

  - Complete blood count (CBC) with platelets: Monitor for infection and assess hematocrit and platelet count to

identify hemorrhagic risk and complications.

- Prothrombin time (PT)/activated partial thromboplastin time (aPTT): Identify a coagulopathy.

- Serum chemistries including electrolytes and osmolarity: Assess for metabolic derangements, such as hyponatremia, and monitor osmolarity for guidance of osmotic diuresis.

- Toxicology screen and serum alcohol level if illicit drug use or excessive alcohol intake is suspected: Identify exogenous toxins that can cause intracerebral hemorrhage.

- Screening for hematologic, infectious, and vasculitic etiologies in select patients: Selective testing for more uncommon causes of intracerebral hemorrhage.

- ***Parenchymal imaging***

  - **CT scan**: readily demonstrates acute hemorrhage as hyperdense signal intensity. Multifocal hemorrhages at the frontal, temporal, or occipital poles suggest a traumatic etiology.

  - **MRI:** appearance of hemorrhage on conventional T1 and T2 sequences evolves over time because of chemical and physical changes within and around the hematoma

- ***Vessel imaging***

  - **CT angiography** permits screening of large and medium-sized vessels for AVMs, vasculitis, and other arteriopathies.

  - **MR angiography** permits screening of large and medium-sized vessels for AVMs, vasculitis, and other arteriopathies.

  - **Conventional catheter angiography** definitively assesses large, medium-sized, and sizable small vessels for AVMs, vasculitis, and other arteriopathies. Consider catheter angiography for young patients, patients with lobar hemorrhage, patients without a history of hypertension, and patients without a clear cause of hemorrhage who are surgical candidates. Angiography may be deferred for older patients with suspected hypertensive intracerebral hemorrhage and patients who do not have any structural abnormalities on CT scan or MRI. Timing of angiography depends on clinical status and neurosurgical considerations.

- **Procedures**

  - **Ventriculostomy** allows for external ventricular drainage in patients with intraventricular extension of blood products. Intraventricular administration of thrombolytics may assist clot removal.

Management

- **Medical Care:**

  Medical therapy of intracranial hemorrhage is principally focused on adjunctive measures to minimize injury and to stabilize individuals in the perioperative phase.

  - Perform endotracheal intubation for patients with decreased level of consciousness and poor airway protection.

  - Cautiously lower blood pressure to a mean arterial pressure (MAP) less than 130 mm Hg, but avoid excessive hypotension. Early treatment in patients presenting with spontaneous intracerebral hemorrhage is important as it may decrease hematoma enlargement and lead to better neurologic outcome.

  - Rapidly stabilize vital signs, and simultaneously acquire emergent CT scan.

  - Intubate and hyperventilate if intracranial pressure is increased; initiate administration of mannitol for further control.

  - Maintain euvolemia, using normotonic rather than hypotonic fluids, to maintain brain perfusion with-

out exacerbating brain edema.

- Avoid hyperthermia.
- Correct any identifiable coagulopathy with fresh frozen plasma, vitamin K, protamine, or platelet transfusions.
- Initiate fosphenytoin or other anticonvulsant definitely for seizure activity or lobar hemorrhage, and optionally in other patients.
- Facilitate transfer to the operating room or ICU.

- **Medications Summary** :

Antihypertensive agents reduce blood pressure to prevent exacerbation of intracerebral hemorrhage. **Osmotic diuretics**, such as mannitol, may be used to decrease intracranial pressure. As hyperthermia may exacerbate neurological injury, **paracetamol** may be given to reduce fever and to relieve headache. **Anticonvulsantse.gphentoyn** are used routinely to avoid seizures that may be induced by cortical damage. **Vitamin K and protamine** may be used to restore normal coagulation parameters. **Antacids** are used to prevent gastric ulcers associated with intracerebral hemorrhage.

- **Surgical Care :**

  - Consider nonsurgical management for patients with minimal neurological deficits or with intracerebral hemorrhage volumes less than 10 mL.

  - Consider surgery for patients with cerebellar hemorrhage greater than 2.5 cm, for patients with intracerebral hemorrhage associated with a structural vascular lesion, and for young patients with lobar hemorrhage.

  - Other surgical considerations include the following:

    - Clinical course and timing
    - Elevation of ICP from hydrocephalus
    - Patient's age and comorbid conditions
    - Etiology
    - Location of the hematoma
    - Mass effect and drainage patterns

  - Surgical approaches include the following:

    - Craniotomy and clot evacuation under direct visual guidance
    - Stereotactic aspiration with thrombolytic agents
    - Endoscopic evacuation

Ischemic Stroke

Overview

- Ischemic stroke is characterized by the sudden loss of blood circulation to an area of the brain, resulting in a corresponding loss of neurologic function. Acute ischemic stroke is caused by thrombotic or embolic occlusion of a cerebral artery and is more common than hemorrhagic stroke.

Clinical Presentation

- Consider stroke in any patient presenting with acute neurologic deficit or any alteration in level of consciousness. Common stroke signs and symptoms include the following:

  - Abrupt onset of hemiparesis, monoparesis, or (rarely) quadriparesis
  - Hemisensory deficits
  - Monocular or binocular visual lossor Visual field deficit or Diplopia
  - Facial droop
  - Ataxia or Vertigo (rarely in isolation) or Nystagmus
  - Aphasia or Dysarthria
  - Sudden decrease in level of consciousness

Work Up

- Emergent brain imaging is essential for confirming the diagnosis of ischemic stroke. Noncontrast computed tomography (CT) scanning is the most commonly used form of neuroimaging in the acute evaluation of patients with apparent acute stroke. The following neuroimaging techniques are also used:

  - CT angiography and CT perfusion scanning
  - Magnetic resonance imaging (MRI)
  - Carotid duplex scanning
  - Digital subtraction angiography

Laboratory studies

Laboratory tests performed in the diagnosis and evaluation of ischemic stroke include the following:

- Complete blood count (CBC): A baseline study that may reveal a cause for the stroke (eg, polycythemia, thrombocytosis, thrombocytopenia, leukemia) or provide evidence of concurrent illness (eg, anemia)

- Basic chemistry panel: A baseline study that may reveal a stroke mimic (eg, hypoglycemia, hyponatremia) or provide evidence of concurrent illness (eg, diabetes, renal insufficiency)

- Coagulation studies: May reveal a coagulopathy and are useful when fibrinolytics or anticoagulants are to be used

- Cardiac biomarkers: Important because of the association of cerebral vascular disease and coronary artery disease

- Toxicology screening: May assist in identifying intoxicated patients with symptoms/behavior mimicking stroke syndromes

- Arterial blood gas analysis: In selected patients with suspected hypoxemia, arterial blood gas defines the severity of hypoxemia and may be used to detect acid-base disturbances

Management

- The goal for the emergent management of stroke is to complete the following within 60 minutes of patient arrival:

  - Assess airway, breathing, and circulation (ABCs) and stabilize the patient as necessary

  - Complete the initial evaluation and assessment, including imaging and laboratory studies

  - Initiate reperfusion therapy, if appropriate

- Critical treatment decisions focus on the following:

- The need for airway management
- Optimal blood pressure control (less than 180/110)
- Identifying potential reperfusion therapies (eg, intravenous fibrinolysis with rt-PA or intra-arterial approaches)

- Ischemic stroke therapies include the following:
  - Fibrinolytic therapy
  - Antiplatelet agents
  - Statins
  - ACEI & ARBS
  - Mechanical thrombectomy
- Treatment of comorbid conditions may include the following:
  - Reduce fever
  - Correct hypotension/significant hypertension
  - Correct hypoxia
  - Correct hypoglycemia
  - Manage cardiac arrhythmias
  - Manage myocardial ischemia

Traumatic Brain Injury

Overview

- Often referred to as TBI, is most often an acute event similar to other injuries. Brain injuries do not heal like other injuries. Recovery is a functional recovery

- **Pathophysiology:**

A. Primary brain Injury — Primary brain injury occurs at the time of trauma. Common mechanisms include direct impact, rapid acceleration/deceleration, penetrating injury, and blast waves. Although these mechanisms are heterogeneous, they all result from external mechanical forces transferred to intracranial contents. The damage that results includes a combination of focal contusions and hematomas, as well as shearing of white matter tracts (diffuse axonal injury) along with cerebral edema and swelling.

- Shearing mechanisms lead to diffuse axonal injury (DAI), which is visualized pathologically and on neuroimaging studies as multiple small lesions seen within white matter tracts

- Focal cerebral contusions are the most frequently encountered lesions.

- Extra-axial hematomas are generally encountered when forces are distributed to the cranial vault and the most

superficial cerebral layers. These include epidural, subdural, and subarachnoid hemorrhage.

- Intraventricular hemorrhage is believed to result from tearing of subependymal veins, or by extension from adjacent intraparenchymal or subarachnoid hemorrhage.

B. Secondary brain Injury — Secondary brain injury in TBI is usually considered as a cascade of molecular injury mechanisms that are initiated at the time of initial trauma and continue for hours or days. These mechanisms include :

- Neurotransmitter-mediated excitotoxicity cause free-radical injury to cell membranes
- Electrolyte imbalances
- Mitochondrial dysfunction
- Inflammatory responses
- Apoptosis
- Secondary ischemia from vasospasm, focal microvascular occlusion, vascular injury.

- These lead in turn to neuronal cell death as well as to cerebral edema and increased intracranial pressure that can further exacerbate the brain injury.

CLASSIFICATION:

- **Clinical severity scores** — TBI has traditionally been classified using injury severity scores; the most commonly used is the Glasgow Coma Scale (GCS). A GCS score of 13 to 15 is considered mild injury, 9 to 12 is considered moderate injury, and 8 or less as severe traumatic brain injury. However, it is limited by confounding factors such as medical sedation and paralysis, endotracheal intubation, and intoxication.

- An alternative scoring system, the Full Outline of UnResponsiveness (FOUR) Score, has been developed in order to attempt to obviate these issues, primarily by including a brainstem examination. However, this lacks the long track record of the GCS in predicting prognosis and is somewhat more complicated to perform, which may be a barrier for nonneurologists.

- **Neuroimaging scales** — Traumatic brain injury can lead to several pathologic injuries, most of which can be identified on neuroimaging:

- Skull fracture
- Epidural hematoma
- Subdural hematoma
- Subarachnoid hemorrhage
- Intraparenchymal hemorrhage
- Cerebral contusion

- Intraventricular hemorrhage
- Focal and diffuse patterns of axonal injury with cerebral edema
- Two currently used CT-based grading scales are the Marshall scale and the Rotterdam scale.

Management

- **INTENSIVE CARE MANAGEMENT**

A. General medical care —

- Maintenance of BP (systolic >90 mmHg) and oxygenation (PaO2 >60 mmHg) remain priorities in the management of TBI patients in the ICU. These should be continuously monitored. Isotonic fluids (normal saline) should be used to maintain euvolemia.

- The prevention of deep venous thrombosis (DVT) is a difficult management issue in TBI. Patients with TBI are at increased risk of DVT which can be reduced by the use of mechanical thromboprophylaxis using intermittent pneumatic compression stockings. While DVT risk can be further reduced with antithrombotic therapy, this has to be weighed against the potential risk of hemorrhage expansion, which is greatest in the first 24 to 48 hours.

- Nutritional support should not be neglected in TBI.

Under-nutrition is associated with higher mortality. Patients should be fed to full caloric replacement by day seven.

- TBI patients are at risk for other complications (eg, infection, gastrointestinal stress ulceration), which can be reduced by appropriate interventions.

B. Intracranial pressure control—

- Elevated intracranial pressure is associated with increased mortality and worsened outcome.
- **Initial treatment and ICP monitoring** — several approaches are used in the intensive care setting to prevent and treat elevated ICP. Simple techniques should be instituted as soon as possible:
  - Head of bed elevation to 30 degrees.
  - Optimization of venous drainage: keeping the neck in neutral position, loosening neck braces if too tight.
  - Monitoring central venous pressure and avoiding excessive hypervolemia.

- Indications for ICP monitoring in TBI are a GCS score ≤8 and an abnormal CT scan showing evidence of mass

effect from lesions such as hematomas, contusions, or swelling .

- ICP monitoring in severe TBI patients with a normal CT scan may be indicated if two of the following features are present: age >40 years; motor posturing; systolic BP <90 mmHg. A ventricular catheter connected to a strain gauge transducer is the most accurate and cost-effective method of ICP monitoring and has the therapeutic advantage of allowing for CSF drainage to treat rises in ICP.

- Most guidelines and clinical protocols recommend that treatment for elevated ICP should be initiated when ICP rises above 20 mmHg. Ventricular drainage is generally attempted first. CSF should be removed at a rate of approximately 1 to 2 mL/minute, for two to three minutes at a time, with intervals of two to three minutes in between until a satisfactory ICP has been achieved (ICP <20 mmHg) or until CSF is no longer easily obtained. Slow removal can also be accomplished by passive gravitational drainage through the ventriculostomy.

- If ICP remains elevated, other targeted interventions include osmotic therapy, hyperventilation, and sedation. In refractory cases, barbiturate coma, induced hypothermia, and decompressivecraniectomy may be considered.

- **Osmotic therapy** — The intravascular injection of hyperosmolar agents (mannitol, hypertonic saline) creates an osmolar gradient, drawing water across the blood-brain barrier This leads to a decrease in interstitial volume and a decrease in ICP.

- **Hyperventilation** — Most patients with severe TBI are sedated and artificially ventilated during the first several days. Regarding ICP management, control of ventilation helps prevent increases in intrathoracic pressure that may elevate central venous pressures and impair cerebral venous drainage. (Keeping the PaCO2 between 35-40).

- **Sedation** — Sedative medications and pharmacological paralysis are often used in patients with severe head injury and elevated ICP. The rationale is that appropriate sedation may lower ICP by reducing metabolic demand. Sedation may also ameliorate ventilator asynchrony and blunt sympathetic responses of hypertension and tachycardia. These possible beneficial effects are counterbalanced by the potential for these drugs to cause hypotension and cerebral vasodilation that in turn may aggravate cerebral hypoperfusion and elevate ICP.

- **Cerebral perfusion pressure** —While optimization of CBF is a foundation of TBI treatment, bedside measurement of CBF is not easily obtained. Cerebral perfusion pressure (CPP), the difference between the mean arterial pressure (MAP) and the intracranial pressure: CPP = MAP - ICP, is a surrogate measure. Episodes of

hypotension (low MAP), raised ICP, and/or low CPP are associated with secondary brain injury and worse clinical outcomes.

- An early approach to induce hypertension to target CPP >70 mmHg using volume expansion and vasopressor agents appeared to reduce mortality and morbidity. While patients with more severely impaired autoregulation in particular may be more likely to respond to efforts to lower ICP than to hypertensive-focused CPP therapy.

- **Antiepileptic drugs** — The incidence of early post-traumatic seizures (within the first week or two) is about 6 to 10 percent but may be as high as 30 percent in patients with severe TBI. The use of antiepileptic drugs (AEDs) in the acute management of TBI has been shown to reduce the incidence of early seizures, but does not prevent the later development of epilepsy. We use the following approach to seizure management in patients with severe TBI:

  - Use a seven-day course of prophylactic phenytoin or valproic acid
  - Do not use AED prophylaxis long-term
  - Consider EEG and/or EEG monitoring in patients with coma
  - Treat both clinical and electrographic-only sei-

zures with AEDs

- **Temperature management** — Fever worsens outcome after stroke and probably severe head injury, presumably by aggravating secondary brain injury. Current approaches emphasize maintaining normothermia through the use of antipyretic medications, surface cooling devices, or even endovascular temperature management catheters.

- **Glucose management** — Both hyper- and hypoglycemia are associated with worsened outcome in a variety of neurologic conditions including severe TBI.

- **Hemostatic therapy** —The systemic release of tissue factor and brain phospholipids into the circulation leading to inappropriate intravascular coagulation & a consumptive coagulopathy. Coagulation parameters should be measured in the emergency department in all patients with severe TBI and efforts to correct any identified coagulopathy should begin immediately.

- **ADVANCED NEUROMONITORING** — In order to supplement ICP monitoring, several technologies have recently been developed for the treatment of severe TBI. These techniques allow for the measurement of cerebral physiologic and metabolic parameters related to oxygen delivery, cerebral blood flow, and metabolism with the goal of improving the detection and management of secondary brain injury.

CNS infection

Overview

- An infection of the central nervous system may primarily affect its coverings, which is called meningitis. It may affect the brain parenchyma, called encephalitis, or affect the spinal cord, called myelitis. The nervous system may also suffer from localized pockets of infection. Within the brain or spinal cord there may be an abscess .

	Common bacterial pathogens	**Antimicrobial therapy**
2-50 years	*N. meningitidis*, *S. pneumoniae*	Vancomycin plus a third-generation cephalosporin
>50 years	*S. pneumoniae*, *N. meningitidis*, *L. monocytogenes*, aerobic gram-negative bacilli	Vancomycin plus ampicillin plus a third-generation cephalosporin
Head trauma		
Base skull fracture	*S. pneumoniae*, *H. influenzae*, group A beta-hemolytic strept.	Vancomycin plus a third-generation cephalosporin

Penetrating trauma	*Staphylococcus aureus*, coagulase-negative staphylococci (especially *Staphylococcus epidermidis*), aerobic G –vebacilli	Vancomycin plus cefepime; OR vancomycin plus ceftazidime; OR vancomycin plus meropenem
Post-neurosurgery	Aerobic gram-negative bacilli (including *P. aeruginosa*), *S. aureus*, coagulase-negative staphylococci (especially *S. epidermidis*)	Vancomycin plus cefepime; OR vancomycin plus ceftazidime; OR vancomycin plus meropenem
Immunocompromised state	*S. pneumoniae*, *N. meningitidis*, *L. monocytogenes*, aerobic gram-negative bacilli (including *P. aeruginosa*)	Vancomycin plus ampicillin plus cefepime; OR vancomycin plus ampicillin plus meropenem

Bacterial (septic) meningitis

- **Clinical Presentation**

- Early in the course of the illness, the patient with a purely meningeal infection will be awake, and painfully aware of his symptoms, so you may simply ask him about them. Later in the illness, if untreated, the meningeal inflammation will have led to diffuse brain dysfunction, ischemia or infarction, and the patient will be stuporous.

- The classic signs of meningeal infection are fever, stiff neck (meningismus), and headache. Although characteristic of meningitis, headache and meningismus may occur in other infections, such as pneumonia. Photophobia, nausea, vomiting, malaise and lethargy are common. The latter are also common in "functional" headaches like migraine, and may confuse the unwary physician.

- **Meningeal signs**The stiff neck that occurs in meningitis is often striking--it is really stiff, almost boardlike, but not so painful as it is stiff. It is greatest with flexion, less with extension or rotation. Associated with the stiff neck are two other classic "meningeal signs", the signs of Kernig and Brudzinski. Brudzinski's sign is involuntary flexion of the hip and knee when the examiner flexes the patient's neck. Kernig's sign is limitation of straightening of the leg with the hip flexed. Meninge-

al signs occur not only in infectious meningitis, but in subarachnoid hemorrage and chemical meningitis. Unfortunately, meningismus occurs only in about 50% of cases of bacterial meningits, so the sign is neither highly specific nor highly sensitive.

Work Up

Suspicious clinical symptoms and signs.

- CT of head to rule out abscess or other space-occupying lesion
- Blood cultures.
- Lumbar puncture for CSF analysis

Glucose (mg/dl)		Protein (mg/dl)		Total WBC (cell/microL)		
<10	10-45	>250	50-250	>1000	100-1000	5-100
Bacterial	Bacterial	Bacterial	Viral CNS-lyme Disease	bacterial	Bacterial Viral T.B.	Early Bacterial Viral
T.B Fungal	Neurosyphilis Some viral infection	T.B.	–	Some cases of mumps	Encephalitis	Encephalitis

Management

- **Empiric antimicrobial therapy for purulent meningitis**
- **Dosages for adults with bacterial meningitis with normal renal and hepatic function**

Antimicrobial agent	Dose (adult)
Ampicillin	2 g every 4 hours
Cefepime	2 g every 8 hours
Cefotaxime	2 g every 4 to 6 hours
Ceftazidime	2 g every 8 hours
Ceftriaxone	2 g every 12 hours
Meropenem	2 g every 8 hours
Penicillin G potassium	4 million units every 4 hours
Vancomycin	15 to 20 mg/kg every 8 to 12 hours‡

Status Epilepticus

Overview

- Status epilepticus is defined usually as a condition in which epileptic activity persists for 30 min or more. The seizures can take the form of prolonged seizures or repetitive attacks without recovery in between.

- The physiological changes in status can be divided into two phases, the transition from phase 1 to 2 occurring after about 30–60 minutes of continuous seizures. In phase 1, compensatory mechanisms prevent cerebral damage. In phase 2, however, these mechanisms break down, and there is an increasing risk of cerebral damage as the status progresses. The cerebral damage in status is caused by systemic and metabolic disturbance (for example, hypoxia, hypoglycaemia, raised intracranial pressure) and also by the direct excitotoxic effect of seizure discharges (which result in calcium influx into neurons and a cascade of events resulting in necrosis and apoptosis).

- ***Epidemiology***

- Acute insults to the brain, including meningitis, encephalitis, head trauma, hypoxia,

  hypoglycemia, drug intoxication or withdrawal, tumor

- Chronic epilepsy or febrile convulsions.

- New-onset epilepsy.

Work Up

- **Emergency investigations**
  - Emergency investigations should include assessment of the following: blood gases, glucose, renal and hepatic function, calcium, magnesium, full blood count, clotting screen, and anticonvulsant concentrations. Serum should be saved for toxicology or virology or other future analyses. An electrocardiogram (ECG) should be performed.

  - Frequent or even continuous EEG monitoring until seizures activities subside .

Management

- **Cardiorespiratory function**

  - In all patients presenting in status, the protection of cardiorespiratory function takes first priority.

Hypoxia is usually much worse than appreciated, and oxygen should always be administered.

- **Initial emergency treatment**
  - emergency intravenous antiepileptic drug treatment
  - maintenance antiepileptic drugs orally or via a nasogastric tube
  - intravenous thiamine and glucose if there is the possibility of alcoholism
  - glucose if hypoglycaemia is present
  - the correction of metabolic abnormalities if present
  - the control of hyperthermia
  - pressor therapy for hypotension if present
  - the correction of respiratory or cardiac failure.
  - If the status is caused by drug withdrawal, the withdrawn drug should be immediately replaced, by parenteral administration if possible. Treatment may also be needed for cardiac dysrhythmia, lactic acidosis (if severe), rhabdomyolysis, or cerebral oedema (in late status).

- **Protocol of Treatment of Status Epilepticus :**

Red Flag

- All infusion rates should be adjusted to individual pa-

tients; maximum doses are not always required.

- Cardiac monitoring required.
- Phenytoin or fosphenytoin may be ineffective for toxin-induced seizures and may intensify seizures
- caused by cocaine and other local anesthetics, theophylline, or lindane. Patients with toxin-induced .seizures should receive phenobarbital, midazolam, or propofol infusion as second line therapy.

Guillain-Barré syndrome

Overview

- GBS isan acute monophasic paralyzing illness provoked by a preceding infection.

Clinical features

- The cardinal clinical features are progressive, fairly symmetric muscle weakness accompanied by absent or depressed deep tendon reflexes. Patients usually present a few days to a week after onset of symptoms. The weakness can vary from mild difficulty with walking to nearly complete paralysis of all extremity, facial, respiratory, and bulbar muscles. GBS usually progresses over a period of about two weeks. By four weeks after the initial symptoms, 90% of GBS patients have reached the nadir of the disease. Disease progression for more than eight weeks is consistent with the diagnosis of chronic inflammatory demyelinating polyradiculoneuropathy (CIDP).

Differential Diagnosis

- **Cerebral** (Bilateral strokes & Psychogenic symptoms)
- **Cerebellar** (Acute cerebellar ataxia syndromes &

Posterior fossa structural lesion)

- **Spinal** (Compressive myelopathy, Transverse myelitis, Anterior spinal artery
- syndrome, Poliomyelitis & Other infectious causes of acute myelitis)
- **Peripheral nervous system** (Toxic neuropathy, Critical care neuropathy, Diphtheria, Tick
- paralysis, Porphyria, Lyme disease &Vasculitis)
- **Neuromuscular junction** (Botulism, Myasthenia gravis & Neuromuscular blocking agents)
- **Muscle disease** (Acute viral myositis, Acute inflammatory myopathies, Metabolic
- myopathiese.g. HypoKalemia or HperKalemia and periodic paralysis)

Work Up

- ***Laboratory Studies*** The typical finding with lumbar puncture in patients with GBS is an elevated cerebrospinal fluid (CSF) protein with a normal white blood cell count. This finding is called albuminocytologic dissociation, and is present in up to 66 percent of patients with GBS at one week after onset of symptoms.
- ***Clinical neurophysiology studies*** (electromyography and nerve conduction studies) show evidence of

an acute polyneuropathy with predominantly demyelinating features in acute inflammatory demyelinating polyradiculoneuropathy, while the features are predominantly axonal in acute motor axonal neuropathy and acute sensorimotor axonal neuropathy.

- ***Diagnostic criteria*** These criteria are based on expert consensus, required features include:

  - *Progressive weakness* of more than one limb, ranging from minimal weakness of the legs to total paralysis of all four limbs, the trunk, bulbar and facial muscles, and external ophthalmoplegia

  - *Areflexia.* While universal areflexia is typical, distal areflexia with hyporeflexia at the knees and biceps will suffice if other features are consistent.

Management

- **SUPPORTIVE CARE** is extremely important since up to 30 percent of patients develop neuromuscular respiratory failure requiring mechanical ventilation. In addition, autonomic dysfunction may be severe enough to require ICUmonitoring. Thus, many patients with GBS are initially admitted to the ICU for close monitoring of respiratory, cardiac, and hemodynamic function. Less severely affected patients can be managed in intermediate care units, and mildly affected patients can be

managed on the general ward with telemetry, along with monitoring of blood pressure and vital capacity every four hours.Prophylaxis for deep vein thrombosis, bladder and bowel care, physical and occupational therapy, and psychological support are essential. Adequate pain control is necessary.

- **DISEASE MODIFYING TREATMENT** The main modalities of therapy include plasma exchange (**plasmapheresis**) &administration of intravenous immune globulin (**IVIG**).Plasmapheresis is thought to remove circulating antibodies, complement, and soluble biological response modifiers.The precise mechanism of action for intravenous immune globulin (IVIG) in GBS is unknown.

- **Plasma exchange**

  - Plasma exchange was most effective when started within seven days of symptom onset.

  - **Intravenous immune globulin**

  - Intravenous immune globulin (IVIG) either three or six days of IVIG 0.4 g/kg,is as effective as plasma exchange for the treatment of GBS. Patients with more severe clinical disease may benefit from longer duration of IVIG treatment. However, six days of treatment significantly improved the rate of recovery for the subgroup of patients who re-

quired mechanical ventilation.

- Choice of therapy Disease-modifying therapy with plasma exchange or IVIG is recommended for nonambulatory patients with GBS who present within four weeks of neuropathic symptom onset. Therapy with plasma exchange or IVIG is suggested for ambulatory patients with GBS who present within the same time frame, except for those who are mildly affected and already recovering. Patients recover sooner and better when treated early.The choice between plasma exchange and IVIG is dependent on local availability and on patient-related risk factors, contraindications, and preference. Because of its ease of administration and wide availability, IVIG is frequently the preferred treatment.

Myasthenia Gravis

Overview

- This acquired condition is characterized by weakness and fatigability of proximal limb, ocular and bulbar muscles. The heart is not affected. The prevalence is about 4 in 100 000. It is twice as common in women as in men, with a peak age incidence around 30.

- ***Cause***sThe cause is unknown. IgG antibodies to acetylcholine receptor protein are found. Immune complexes (IgG and complement) are deposited at the postsynaptic membranes, causing interference with and later destruction of the acetylcholine receptor.

- Thymic hyperplasia is found in 70% of myasthenic patients below the age of 40. In 10% a thymictumour is found, the incidence increasing with age; antibodies to striated muscle can be demonstrated in these patients. Young patients without a thymoma have an increased association with HLA-B8, and DR3.

Clinical Presentation

- Fatiguability is seen in many muscles. Proximal limb muscles, extraocular muscles, and muscles of mastication, speech and facial expression are those commonly affected in the early stages. Respiratory difficulties may occur.

- Complex extraocular palsies, ptosis and fluctuating proximal weakness are found. The reflexes are initially preserved but may be fatiguable, i.e. disappear. Muscle wasting is sometimes seen after many years.

Work Up

The clinical picture of fluctuating, fatigability and weakness is often diagnostic.

- **Serum acetylcholine receptor antibodies**

- These disease-specific IgG antibodies are present in 90% of cases of generalized myasthenia gravis. The antibodies are found in no other condition. In pure ocular myasthenia they are detectable in < 50% of cases.

- **Nerve stimulation**

- There is a characteristic decrement in the evoked muscle action potential following repetitive motor nerve stimulation. The anticholinesterase edrophonium (10 mg) is injected i.v. as a bolus after a 1-2 mg test dose. Improvement in weakness occurs within seconds and lasts for 2-3 minutes when the test is positive. To be certain, it is wise to have an observer present and to perform a control using saline. Occasionally edrophonium causes bronchial constriction and syncope. The test must not be done without resuscitationfacilities.

Other tests A thymoma on chest X-ray is confirmed by mediastinal MRI. All patients should have a chest CT - even if the chest X-ray is normal. Routine peripheral blood studies are normal - the ESR is not raised, and CPK normal. Autoantibodies to striated muscle (suggests a thymoma), intrinsic factor or thyroid may be found. Rheumatoid factor and antinuclear antibody tests may be positive. Muscle biopsy is usually not performed, though ultrastructural abnormalities can be seen.

Management

- Myasthenia gravis fluctuates in severity; most cases have a protracted, lifelong course. Respiratory impairment, dysphagia and nasal regurgitation occur; emergency assisted ventilation may be required. Simple monitoring tests, such as the duration the arm can be held outstretched, and the vital capacity, are useful.

- Exacerbations (myasthenic crises) are usually unpredictable and unprovoked but may be brought on by infections, by aminoglycosides or other drugs. Enemas (magnesium sulphate) may provoke severe weakness.

- **Treatment**

A. Oral anticholinesterases

- Pyridostigmine (60 mg tablet) is the drug most widely used. Its duration of action is 3-4 hours. The dose (usually 4-16 tablets daily) is determined by the response. Pyridostigmine prolongs acetylcholine action by inhibiting cholinesterase. Overdose of anticholinesterases cause severe weakness (cholinergic crisis). Muscarinic side-effects, e.g. colic and diarrhoea, can be caused by anticholinesterases. Oral atropine 0.5 mg with each dose helps reduce this. Anticholinesterases help weakness but don't alter the natural history of myasthenia.

B. *Thymectomy*

- Thymectomy improves prognosis, particularly in women below 40 years with positive receptor antibodies and a history of myasthenia of more than 7 years. Some 60% of non-thymoma cases improve. The precise reason is unclear. If a thymoma is present, surgery is necessary to remove a potentially malignant tumour; it is less usual for myasthenia to improve.

C. *Immunosuppressant drugs*

- Corticosteroids are often used. There is improvement in 70% of cases, although this may be preceded by an initial relapse. Azathioprine is often used in addition to steroids.

- ***Plasmapheresis and intravenous immunoglobulin therapy***

- During exacerbations these interventions are of value.

Red Flg

- **myasthenic crises** Occurs when the muscles that control breathing weaken to the point that ventilation is inadequate, creating a medical emergency and requiring a respirator for assisted ventilation. In individuals whose respiratory muscles are weak, crises—which generally call for immediate medical attention—may be triggered by infection, fever, or an adverse reaction to medication.

HYPERTENSIVE CRISIS

OVERVIEW

- **DEFINITIONS**

  - Hypertensive crisis is defined as a severe elevation in the blood pressure (BP)

    - Hypertensive emergencies and/or may occurs with chronic hypertension urgencies are categories of hypertensive crisis that are potentially life threatening, secondary forms of hypertension.

    - Usually associated with systolic BP's > 180mm Hg and diastolic BP's >120mm Hg /orMAP>95mm Hg.

  - Differentiated by the presence or absence of acute and progressive target organ damage (TOD)

    - In hypertensive emergencies, BP elevation is associated with ongoing central nervous system (e.g. encephalopathy or hemorrhage), myocardial (e.g. ischemia, pulmonary edema), or renal (e.g. acute renal failure) TOD

    - In hypertensive urgencies, the potential for TOD damage is great and likely if BP is not soon controlled. These may be associated with symptoms such as headache, shortness of breath, or anxiety.

- **CAUSES OF HYPERTENSIVE CRISIS**

Generalized	Cardiovascular	Neurologic	renal
Microangiopathic hemolytic anemia Eclampsia Catecholamine excess (drug,Phenochromocytoma) Vasculitis	Acute left ventricular failure Unstable angina Pectosis Myocardial infarction Aortic dissection	Hypertensive encephalopathy Subarachnoid hemorrhage Intracerebral hemorrhage Cerebrovascular accident	Acute renal failure Acute glomerulonephritis.

CLINICAL PRESENTATION

- Immediate identification of both hypertension and potential TOD is critical to properly triage patients. Patients with hypertensive emergencies should be admitted to an intensive care unit (ICU) setting for continuous monitoring and treatment.

- In ICU, therapy must often begin before a comprehensive patient evaluation is completed.

- A brief history and physical examination should be initiated to assess the degree of TOD and rule out obvious secondary causes of hypertension.

A. History

- History of hypertension or other significant medical disease
- Medication use and compliance
- Drugs
- Symptoms attributable to TOD:
  - Neurologic (headache, nausea, & Vomiting, visual changes seizures, focal deficits, mental status changes)
  - Cardiac (chest pain, shortness of breath)
  - Renal (hematuria, decreased urine output)

B. Physical Examination

- BP readings in both arms
- Signs of neurologic ischemia, such as altered mental status or focal neurologic deficits
- Direct ophthalmologic examination
- Auscultation of lung and heart
- Evaluation of the abdomen and peripheral pulses for bruit.

WORK-UP

- Laboratory evaluation
  - Electrolytes, blood urea nitrogen and creatinine, cardiac enzymes, liver function test complete blood count with differential, coagulation studies urinalysis, VMA

- Electrocardiogram
- Chest radiography
- ECHO
- CT Head
- Doppler Renal arteries

TREATMENT

- Goal of initial therapy is to terminate ongoing TOD, not to return BP to normal levels

- Goal is approximately 25% lower than the initial mean arterial pressure with the first minutes to hour after initiation of treatment

- After initial stabilization, the goal should be to reduce BP to 160/100 – 110mm Hg over the next several hours.

  - Intervention such as intubation, control of seizures, treating withdrawal, hemodynamic monitoring, and maintenance of urine output can be as important as prompt control of BP.

  - Care should be given to avoid aggressive BP reduction because it may lead to ischemia of the kidneys, brain, or myocardium because of arterial autoregulation. Also, patients with ischemic strokes are often manage with higher BP range.

- After 24 hours of maintaining BP in the 160/100mm Hg

range, further BP therapy can be initiated to achieve the final goal BP

- Parenteral therapy with close hemodynamic monitoring is prefered as it is the most rapid and reliable method to reduce the BP.

SPECIAL SCENARIOS OF HYPERTENSIVE EMERGENCIES

- New onset of server hypertension in patients without prior history

- Secondary causes, such as pain, anxiety, new onset of angina, hypercarbia or hypoxia, hypothermia, rigors, excessive arousal after sedation, withdrawal, or fluid mobilization with volume overload, can all lead to short-term evaluation in BP.

- Perioperative hypertension

- Perioperative. BP > 160/100 mm Hg or an increase of > 30mm Hg (systolic or diastolic) above preoperative are worrisome and require evaluation

- PHARMACOLOGIC AGENTS

A. Direct vasodilator

- Sodium nitroprusside. The most predictable and effective agent for the treatment of severe hypertension. It dilates both arterioles and the venules

(reducing both afterload and preload) and lowers myocardial oxygen demands.

- Nitroglycerine. Predominantly dilates the venous system. Useful in patient with cardiac ischemia or congestive heart failure.

- Hydralazine. A direct parenteral arterial vasodilator that will increase cardiac output, but may cause a reflect increase in heart rate drug choice in pregnancy.

B. B-Adrenergic receptor blockers

- Labetalol, which has both β- and a-blockingproperties, is particularly useful for hypertension emergencies.

- Esmolol is a short-acting β_1 selective agent that needs to be given as a continuous infusion.

C. Calcium channel antagonist

Dihydropyridines, principally direct vasodilatory effects.

- Nimodipine: recommended only for patients with subarachnoid hemorrhage

Non-dehydropyridines:

- Verapamil: an arterial vasodilator that delays atrioventricular conduction and has negative inotropic effect. Avoid in patients with left ventricular dysfunction.

- Diltiazem: effective arterial vasodilator, slows electrical conduction but with less negative chronoscopic effects compared to verapamil

D. Angiotension-converting enzymes inhibitors

- Captopril: rapid onset of effect after oral administration (30 minutes) with little changes in cardiac output or reflex tachycardia

E. Others Agents

- Clonidine – oral centrally acting α_2 adrenergic receptors agonists that decrease peripheral vascular resistance peripheral vascular resistance, takes severe days t achievea steady state,

ACUTE CORONARY SYNDROMES

UNSTABLE ANGINA AND NON-ST-ELEVATION MYOCARDIAL INFARCTION

OVERVIEW

- Accounts for 80% of ACS
- On the basis of new or accelerating symptoms of coronary ischemia, with or without ECG changes.
- Elevation of cardiac troponin distinguishes NSTEMI from UA.
- ECG changes in UA/NSTMI may include:
  - ST-segment depressions
  - Transient ST segment elevations
  - New T-wave inversions

CLINICAL PRESENTATION / WORK-UP

- Physical examination is directed toward assessment of:
  - Possible precipitants of UA-NSTEMI, such as hypertension, thyroid disease, or anemia
  - Hemodynamic effects of UA/NSTEMI, such as congestive heart failure and arrhythmia
- A 12-lead ECG

- If initial ECG is not diagnostic of ACS, follow-up ECG should be performed every 30 minutes with pain to evaluate for evolving ST elevations or depressions.

- Cardiac biomarkers, preferably, cardiac- specific troponin, should be measured.

    - For patients present < 6hours from symptoms onset.

    - Repeat troponin levels in 6 to 8 hour, or as guided by timing of symptoms onset.

- On the basis of clinical history, ECG and initial laboratory and imaging tests, patients are assigned the probability of having ACS.

A. Patient with possible UA/NSTEMI who has a nondiagnostic ECG and normal initial cardiac biomarkers are observed for at least 6 to 12 hours from symptoms onset.

    - If recurrent ischemia pain is present or follow-up studies are positive, treatment for definite ACS is initiated.

    - If there is further pain and ECG/biomarkers remain within the range of normal, stress testing should be considered.

- If stress test slowly provokable ischemia or new regional left ventricular (LV) dysfunction, therapy for ACS is started.

- If stress test is negative, a diagnosis of noncardiac chest pain is likely and arrangements should be made for outpatient follow-up.

B. Patients with probable/definite UA/NSTEMI are admitted to a coronary care unit for continuous cardiac monitoring, risk stratification antithrombotic and antianginal therapy, and consideration of revascularization.

DIFFERENTIAL DIAGNOSIS

- Acute aortic dissection
- Pulmonary embolism
- Esophageal rupture
- Tension pneumothorax
- Acute pericarditis
- Gastroesophageal reflux disease
- Costochondritis
- Esophageal spasm
- Pleurisy

MANAGEMENT OF UA/NSTEMI

- General aspects of care

  A. Goals

     - Immediate relief of myocardial ischemia
     - Prevention of adverse outcomes, specifically: (re) infarction, death and future heart failure, due to factors that increase myocardial oxygen consumption requirement.

  B. The general plan of management of patients.

     - Established basic care and monitoring: oxygen, continuous ECG monitoring, resuscitation equipment.
     - Administer analgesic and anti-ischemic therapy β-blockers nitrates and morphine.
     - Administer antithrombotic therapy
        - Antiplatelet therapy: aspirin, clopidogrel.
        - Anticoagulant therapy: unfractionated heparin (UFH), LMWH

- Anti-ischemic, analgesic, and other initial therapy

- Nitrate therapy is recommended initially, with the use of sublingual or intravenous nitrates for ongoing ischemic pain. Nitrates can be safely discontinued upon successful revascularization.

- B-Blockade administered to patients, targeted to heart rate of 50 to 60 bpm, in the absence of the following contraindications:

    - Signs of decompensated heart failure or low-output state “shock stat”

    - Second-or third-degree heart block pulse < 60bpm

    - Active asthma

    - SBP < 90 mmHg

        - Morphine sulfate is effective in treating angina discomfort and also modesty reduces heart rate and blood pressure.

        - Angiotensin converting enzymes inhibitors (ACEi) are indicate within the first 24 hour in patients with pulmonary congestion or LV ejection fraction <40% Angiotensin receptor blockers (ARBs) may be used in place of ACEi in patients with known intolerant.

    - Antiplatelet therapy

Aspirin and clopidogrel

- Aspirin – is effective across a broad range of risk profiles, should be started immediately in all patients and continued indefinitely. Initial recommended dose of aspirin is 160 to 325 mg

- Clopidogrel blocks the adenosine diphospate pathway and decreases platelet activation and aggregation.

- Anticoagulant therapy

  - It is recommended that all patient with non-ST-segment elevation acute coronary syndromes received an anticoagulant

    - Unfractionated heparin (UFH):

      - Typically titrated to an activated partial thromboplastin (aPTT) time of 50 to 70 seconds.

      - LMWH enoxaparin

      - Factor Xa inhibitor fondaparinux is administered once daily subcutaneously.

- Revascularization

- Most beneficial when preformed in high Risk patient early in the Hospital course.
- Technique
  - PCI
  - CABG

- Statins
  - For plaque stabilization
  - A target LDL should be < 70mg /dl
  - HDL should be > 40 mg/dl

ST-SEGMENT ELEVATION MYOCARDIAL INFACTION

OVERVIEW

- Rapid perfusion of the infarct-related artery (IRA), with either primary percutaneous coronary intervention (PCI) or fibrinolytic therapy is the cornerstone of management for patient with ST-segment elevation myocardial infarction. (STMI).

- Adjunctive therapy with aspirin(ASA), clopidogrel, β-blocker (BB), angiotensin-converting enzymes inhibitors (ACEi) and statins further prevents deaths and major cardiovascular events after reperfusion.

CLINICAL PRESENTATION

- History

  - Angina is classically described as severe, pressure-type pain in midsternum, often with radiation to left neck, arm, or jaw.

  - Associated symptoms: dyspnea, nausea, vomiting, diaphoresis, weakness.

  - Silent infarction in 25% of cases, especially in elderly and diabetic patients.

- Physical examination
  - Not helpful in confirming the diagnosis of STEMI
  - Examination should focus on eliminating other potential diagnosis and assessing for complications of STEMI.

WORK-UP

- ECG
  - ST elevations are found in regional distributions with concurrent ST depression in reciprocal leads.
  - Consider pericarditis with global ST elevations and PR depressions.
  - New left bundle branch block (LBBB) represents large anterior infarction, indication for reperfusion therapy
- Cardiac Biomakers
  - Rise of troponin above upper reference limit within the expected time for elevation 2 – 6 hours

MANAGEMENT

Performance therapy

- Goal of reperfusion therapyis rapid and complete restoration of coronary artery blood flow:

- Reperfusion method depends on availability of PCI within 90 minutes of medical contact.

- Resolution of ST-segment elevation is the best indicator of successful reperfusion.

  - Reperfusion therapy in non-PCI centers

    - Administer fibrinolytics within 12 hours of onset of symptoms.

- **CONTRAINDICATION TO FIBRINOLYTIC THERAPY**

Absolute contraindications	Relative contraindications
Active internal bleeding Any history of CNS hemorrhage Ischemic stroke within 3 mo Significant head trauma within 3 mo Known cerebrovascular lesion (e.g. AVM) CNS neoplasm Suspected aortic dissection	Prolonged CPR(.10min) Pregnancy Major surgery or trauma within 3 wk. Active peptic ulcer Anticoagulation use SBP > 180 mmHg Non-compressible vascular puncture

- **AGENTS**

Alteplase (tPA)	Tenecteplase (TNK-tPA)	Steptokinase	Reteplase
15mg bolus over 2 mins Then 0.75 mg/kg over 30 min; then 0.5mg/kg over 60 min	0.53 mg/kg as a single bolus	1.5 million units over 30-60min.	10 µ over 2 min. Then after 30 min 10 µ over 2 min

- No indication for fibrolytic therapy if symptoms >24 hours or non-STEMI.
- Primary PCI preferred if symptoms onset >3hours or patient is in cardiogenic shock.

- **ADJUNCTIVE ANTITHROMBOTIC THERAPY**

- ASA reduces mortality, reocclusion, and reinfarction.
- Clopidogrel is indicated in all STEMI patients for 1 year regardless of reperfusion methods.
- Unfractionated heparin (UFH), low molecular weight heparin (LMWH) fondaparinux.
    - Adjunctive therapy for all intravenous fibrinolytics.

- **ANTIISCHEMIC THERAPY**

  - B-blocker (BB)

  - Limit size of infarction decrease recurrent MI, improve survival and prevent arrhythmias and cardiac rupture

  - Administer BB orally on days 0-1 only if no signs of heart failure, low output state (systolic blood pressure (SBP), <90 mm Hg, heart rate (HR) >110 or <60), second-or third-degree heart block, or active ashma.

  - Angiotension-converting enzymes inhibitors (ACEi)

    - Prevent congestive heart failure (CHF) and death by halting adverse remodeling of LV chamber.

    - Decrease recurrent ischemic events through direct vascular effects.

  - Nitrates

    - Decrease myocardial demands by decreasing preload and afterload

    - Increase oxygen supply by dilating coronary resistance vessels

- Sublingual or intravenous nitrates beneficial for

angina, CHF, hypertension

- Contraindicated in right ventricular infarction.

- Calcium channel blockers (CCB)
  - Diltiazem and verapamil may be effective in patients with BB contraindications, but theyshould be avoided in patients with CHF.

- Aldosterone antagonist
  - Mortality benefits in STEMI complicated by heart failure or LV dysfunction
  - Avoid with renal insufficiency and heperkalemia.

- Statins
  - As NSTMI

VENTICULAR TACHYCARDIA

OVERVIEW

A. Definitions

- Ventricular tachycardia (VT)
  - ≥3beats at arate ≥100bpm
  - QRS width .0.12 seconds
  - Originated from the ventricles
- Nonsustained ventricular tachycardia (NSVT)
  - Terminates spontaneously within 30 seconds without causing severe symptoms

B. Classification

- Monomorphic VT Same configuration from beat to beat
  - Usually due to a circuit through a region of old myocardial infarction (MI) scar
  - Idiopathic VT (less common)
- Polymorphic VT

- Etiologies
    - Active cardiac ischemia (most common)
    - Electrolyte disturbance
    - Drug toxicity
- Torsade de pointes
    - Unique form of polymorphic VT
    - Waxing and waning QRS amplitude during tachycardia associated with prolonged QT interval
    - Secondary to QT-prolonging drugs, electrolyte abnormalities.
        - Sinusoidal VT Sinusoidal appearance often associated with severe electrolyte disturbance (e.g. hyperkalemia)
        - Accelerated idioventricular rhythm.
- Wide complex, ventricular rhythm at 40 to 100 beats/minute
- Usually hemodynamically stable
- Can occur in the first 12 hours after reperfusion of an acute MI or during periods of elevated sympathic tone

- Usually resolves without specific therapy

DIFFERENTIAL DIAGNOSIS

- Differentiating VT from suspraventricular tachycardia (SVT) in a patient with a wide complex tachycardia (WCT)
- Differential diagnosis of WCT:
  - VT “80% of cases of wct”
  - SVT with aberrancy (bundle branch block)
  - SVT conducting of an accessory pathway
- WCT with a history of MI can be assumed to be VT
- ECG criteria that favor VT over SVT
  - AV dissociation, with atrial rate < ventricular rate
  - QRS concordance absence of an rS or Rs complex in any precordial lead ($V_1 V_6$)

MANAGEMENT

- Treatment First Priority – Determine Whether The Patient Is Hemodynamically Stable.

A. Management ofhemodynamically unstable VT (Pulse less VT)

- Rapid defibrillation (up to 3 shock) is the most important measure to improve survival

- If VT/VF persists after defibrillation, epinephrine (1mg IV every 3 minutes) should be given. Vasopressin (40 units IV, single bolus) is an acceptable alternative to epinephrine.

    - Used when cardioversion fails or VT/VF recurs

    - Amiodarone (often used as first-line therapy) Procainamide (alternative to amiodarone), lidocaine (most appropriate during suspected acute myocardial ischemia).

B. Management of hemodynamically stable WCT

- Amiodarone

- Procainamide

- Lidocaine

C. Management of polymorphic VT/sinusoidal VT

- Correct reversible cause

- Cardiac ischemia
- Metabolic abnormalities
- Drug toxicity including QT-prolonging drugs
- Lidocaine and amiodarone can be considered for recurrent episodes
- Treatment of torsade depointes (polymorphic VT due to QT prolongation):
    - Intravenous magnesium sulfate (1 to 2g) (Often can be repeated).

- Correct electrolyte abnormalities (hypocaleamia, hypomagnesemia, hypocalcemia).
- Discontinue QT prolonging medications.
- Increasing heart rate with transvenous temporary ventricular pacing is most reliable (target rate of 110 to 120 bpm).

D. Management of NSVT/ventricular ectopy:

- NSVT/premature ventricular constructions (PVCs) are common in the intensive care unit (ICU).
- Treatment:

- Evaluate for possible aggravating factors (e.g., ischemia, electrolytes disturbance, hypoxia, and hypoventilation).

- β-blocking agents (if not contraindicated).

OVERVIEW OF DRUGS COMMONLY USED FOR MANGEMENT OF VT/VF IN THE ICU

- β-blocking
  - Indications
    - Symptomatic ventricular ectopy.
    - Recurrent sustained ventricular tachyarrhythmias.
  - Short-acting agents (e.g., metoprolol) are preferable in the ICU setting
    - Metoprolol can be given orally or as a 5-mg is low intravenous push and repeated every 5 to 10 minutes up to a total of 20 mg. IV. Can repeat intravenous boluses every 4 to 6 hours.
    - Esmolol (useful when there is concern that a β-blocking poorly tolerated 500µg/kg IV bolus over 1 minute followed by maintenance dose of 50µg/kg/minute titrated for effect up to 300 µg/kg/minute

- Adverse effects β-blocking
    - Negative inotropy (avoid with decompensated heart failure)
    - Bradycardia
    - Aggravation of bronchospasm

- Amiodarone
    - Indications
        - First-line AAD in advanced cardiac life support (ACLS) VF/pulseless VT algorithm
            - Hemodynamically stable VT that recurs after cardioversion or fails IV procainamide
    - Dosing
        - A 150 to 300 mg IV bolus over 10 minutes, followed by an infusion at 1mg/minute for 6 hours, then 0.5 mg/minute.
    - Adverse effects
        - Causes QT prolongation
        - Hypotension

- Bradycardia
- Exacerbation of congestive heart failure (negative inotropic effect)
- Phlebitis (when administered through a peripheral intravenous line). Continuous infusion should be administered through a central venous catheter.

- Procainamide
  - First-line agent for WCT (along with amiodarone) for treatment of hemodynamically stable WCT and WCT due to WPW syndrome.
  - Alternative agent for hemodynamically unstable WCT and VF
  - Dosing loading dose up to a total initial dose of 17 mg/kg followed be a maintenance infusion of 1 to 4 mg/minute
  - Adverse effects
    - Vasodilation and negative inotropy
      - Avoid with depressed ventricular function (ejection fraction <40%) in favor of amiodarone

- N-acetyl-procainamide (NAPA), a metabolite of the drug, can increase QTc and cause torsade de pointes.
    - QTc interval and QRS complex width should be monitored.
    - Discontinued if the QRS widens by >50% from baseline.
- Avoid in patients with significant renal dysfunction.

- Lidocaine (IB)
    - Indication
        - Acute management life-threatening ventricular arrhythmias, especially when associated with myocardial ischemia.
    - Dosing: 1to 1.5 mg/kg IV bolus. Can repeat to maximum bolus of 3mg /kg, followed by an infusion of 1 to 4mg /minute.
    - Adverse effects:
        - Neurologic toxicity (seizures, tremors)

SUPRAVENTRICULAR TACHYCARDIA

OVERVIEW

- **MECHANISMS**

  - Abnormal automaticity: inappropriate sinus tachycardia, ectopic atrial tachycardia

  - Abnormal repolarization/triggered activity: atrial premature contraction, multifocal atrial tachycardia (MAT)

  - Reentry: atrioventricular reentrant tachycardia (AVRT) atrioventricular nodal reentrant tachycardia (AVRT) atrial flutter.

- **RECOGNATION AND DIAGNOSIS**

  - QRS duration <120milliseconds in all surface leads: likely supraventricular SVT may result in a wide complex tachycardia when there is a bundle branch block or intraventicular conduction delay.

  - Irregularly irregular QRS complexes most commonly signify atrial fibrillation.

  - Rapid irregularly irregular wide QRS tachycardia may represent atrial fibrillation with Preexcitation over an accessory pathway (AP) (Wolf-Parkinson/white syndrome).

- Organize continuous atrial activity faster than 240 beats per minute is classified as atrial flutter.

- **GENERAL MANAGEMENT OF SVTs**

  - Asses patient stability

  - Identify sinus tachycardia and MAT: threat the underlying causes and control heart rate.

  - Prompt direct current (DC) cardiovertion

    - Electrical cardiovertionshould be synchronized. atrial Flatter and other SVTs are usually terminable with a single 50 to 100-J countershock. atrial fibrillation often requires 200 to 360J

  - Stable patients

    - Vagal maneuvers:-carotid sinus massage or a valsalva maneuver.

    - Adenosine 6-12 mg IV push.

    - IV verapamil, diltiazem β-blockers maybe used.

    - Atrial flutter and atrial fibrillation are unlikely to terminate with these measures.

    - Type III antriarrhytmic agent maybe used for conversation alone or in combination with DC cardioversion

- **SPECIFIC ARRYTHMIAS AND THERPIES**

A. Atrial Fibrillation

- Atrial fibrillation is the most common.
- Acute treatment
  - Unstable: Synchronized DC cardioversion is the treatment of choic.
  - Stable pharmacologic rate control
    - β_1-Selective adrenergic receptor antagonists in nonashmatic patients.
    - Nondihydropyridine calcium channel blockers (e.g., verapamil, diltiazem) may be used in absence of ventricular dysfunction.
    - Digitalis may be used with relative safety in patients with poor ventricular function but provides only modest control of ventricular rate.
    - Amiodarone effectively controls ventricular rate response during atrial fibrillation when administered IV and is safe for use in patients.

      - Treat underlying causes

- Stop offending drugs

- Correct electrolyte abnormalities.

- Attend to other cardiac, endocrine (particularly thyroids), and pulmonary disease.

- Correct/treat severe metabolic stress, severe non-cardiac disease, and other hyperadrenergic states.

- Rate versus rhythm control

- Rate control and anticoagulation are a reasonable approach in stable patients with limited: symptoms.

- Patients in atrial fibrillation <48 hours or who have been anticoagulated (INR) >2 for at least 3 weeks. Are candidates for early cardioversion.

- Pharmacologic cardioversion: -amiodarone.

- Unanticoagulated patients in atrial fibrillation for >48 hours (or for an uncertain duration) are at elevated risk of thromboembolism. These patients require anticoagulation before conversion from atrial fibrillation an alternative approach is to exclude left atrial thrombus with transesophagealechocardiograpy, initiate IV anticoagulation, and proceed to DC cardioversion, followed by oral anticoagulation for at least 4 weeks.

- Patient with recurrent atrial fibrillation should be considered for anticoagulation

B. Atrial Flutter

- The clinical presentations and management of atrial flutter are very similar to those of atrial fibrillation. However, rate control can be more difficult to achieve.

- Rare control, especially before attempting chemical cardioversion.

- The risk of thromboembolism from atrial flutter is significant. Atrial flutter warrants anticoagulation in the same manner as for atrial firbillation.

C. AV Nodal reentry tachycardia

- AVNRT is the most common cause of rapid regular, SVT

- Paroxysmal rapid regular narrow complex tachycardia with heart rate often 150 to 250 beats per minute and P waves either buried within the QRS

comples or visible at its termination.

- Symptoms; palpitation, pounding in the neck, lightheadedness, shortness of breath, chest pressure, weakness, and fatigue.

- Presents in third to fifth decade, with a 70% female preponderance.

- Acute treatment:- See section III

D. Atrioventricularreently tachycardia

- AVRT is common form of regular SVT, accounting for up to 30% of patients

- During tachycardia, the QRS usually appears normal, and waves is visible, will be seen at the end of the QRS complex, within the ST segment or within the T wave.

- Acute treatment: - See section III

E. Wolf-Parkinson/white syndrome

- The Wolf-Parkinson/white syndrome (WPW) consists of a short interval and ventricular preexcitation (delta wave) due to an AP, with symptoms of palpitations.

- The most common arrhythmia associated with WPW is AVRT.

- The accessory tract may also participate in arrhytmogenesis by allowing rapid ventricular rates during atrial fibrillation. The AP may permit very rapid ventricular fibrillation.

- Patients with WPW may be at risk for sudden cardiac death, although the overall risk is rather low, on the order of 0.15% per patient-year.

- Fast preexcited ventricular response to atrial fibrillation (irregular rhythm with varying QRS complexes) should undergo electrical cardioversion.

- Stable preexcited atrial fibrillation may be treated with class 1a, 1c, or IIIdrugs or procainamide (10 to 15mg/kg) may be effective.

- During rapid preexcited atrial fibrillation, AV nodal blocking drugs are contraindicated (digoxin, adenosine, calcium channel blockers, and B-blockers) due to the potential for more rapid ventricular rates.

F. Ectopic atrial tachycardia

- Narrow complex tachycardia with an RP interval that is usually, but not always longer than the PR interval.
- The P wave morphology may or may not be visibly different from sinus.
- Ectopic atrial tachycardia may occur in short runs, may be sustained.
- May be associated with underlying disease (coronary artery disease, myocardial infarction, ethanol ingestion, hypoxia, theophylline toxicity, digitalis toxicity, or electrolyte abnormalities).
- Acute treatment
    - B-Blockade
    - Calcium channel blockade
    - Amiodarone.

G. MAT

- It is recognized by a rapid atrial rhythm with at least three P wave morphologies and variable ventricular response.
- B-Blockade

- Calcium channel blockers may be effective and are the treatment of choice in patients with known reactive airways disease.

BRADYARRHYTHMIAS

CAUSES

- Hypovolaemia, hyperkalaemia, hypotension, acute myocardial infarction, digoxin toxicity, B-blocker toxicity, hypothyroidism, hypopituiatarism, and raised intracranial pressure.

DIAGNOSIS

- **SINUS BRADYCARDIA**

  - Slow ventricular rate with normal P waves, normal PR interval and 1:1 AV conduction.

- **HEART BLOCK**

  - Normal P waves, a prolonged PR interval and 1:1 AV conduction suggest 1º heart block.

  - In 2 º heart block, regular P waves and an increasing PR interval until ventricular depolarization fails (Mobitz I or Wenkebach) normal PR interval with regular failed ventricular depolarization (Mobitz II). In the latter case, the AV conduction ratio may be 2:1 or more.

  - In 3º heart block, there is complete AV dissociation with a slow, idioventricular rate.

TREATMENT

- Hypoxaemia must be corrected in all symptomatic bradycardias. First line drug treatment is usually atropine 0.3mg. If the arrhythmia fails to respond, 0.6mg followed by 1.0mg atropine may be given. Failure to respond to drugs requires temporary pacing. This may be accomplished rapidly with an external system. If there is haemodynamic compromise or by transvenous placement.

- Indications For Temporary Pacing

- Persistent symptomatic bradycardia.
- Blackouts associated with:
  - 3º heart block
  - 2º heart block
  - RBBB and left posterior hemiblock
- Cardiovascular collapse.
- Inferior myocardial infarction with symptomatic 3º heart block
- Anterior myocardial infarction with:
  - 3º heart block
  - RBBB and left posterior hemiblock
  - Alternating RBBB and LBBB

HEART FAILURE

OVERVIEW

- Impaired ability of the heart to supply adequate oxygen and meet the demands of the body's metabolizing tissues.

- Type: Systolic

  Diastolic

MAJOR CAUSES:

- Myocardial infarction/ ichaemia
- Drugs, e.g. B-blockers, cytotoxics
- Tachyarrhythmia's or bradyrrhythmias
- Valve dysfunction
- Sepsis
- Cardiomyopathy
- Pericardial tamponade.

CLINICAL PRESENTATION

- Decrease forward flow leading to poor tissue perfusion

  - Muscles fatigue
  - Confusion, agitation, drowsiness
  - Oliguria
  - Increasing metabolic acidosis, arterial hypoxeimia.

- Increased venous congestion secondary to right heart failure
  - Peripheral oedema
  - Hepatic congestion

- Increased pulmonary hydrostatic pressure from left heart
  - Pulmonary oedema&dyspnoea
  - Hypoxaemia

NEW YORK HEART ASSOCIATION NYHA (CLASSIFICATION)

- Class I: No limitation, Normal physical examination does not cause fatigue, dyspnea & palpitation.
- Class II: Mild limitation, comfortable at rest but normal activity produces fatigue, dyspnea palpitations.
- Class III: Marked limitation comfortable at rest but gentle activity procedures marked symptoms of heart failure
- Class IV: Symptoms of heart failure occurs at rest and or extubated by physical activity.

WORK-UP

Test	Diagnosis
ECG	Myocardial ischaemia/ infarction, arrhythmias, LVH
Chest X-ray	With left heart failure pulmonary oedema, structural abnormality
Blood test	Low SaO_2, variable $PaCO_2$,hyperlactataemia, low venous O_2 raised cardiac enzymes troponin, BNP
Echocardiogram	Poor myocardial contractibility ventricular akinesiahypokinesia or dyskinesia, pericardial effusion, stenosis or incompetence.

TREATMENT AND MANAGEMENT

- **BASIC MEASURES**
  - Determine likely causes and treat as appropriate
  - Oxygen – to maintain $SaO_2 \geq 98\%$
  - GTN spray SL, then commence IV nitrate infusion titrated rapidly until good clinical effect.
  - If patient agitated or in pain, give morphine IV

- Consider early BiPAP and/or CMV to reduce work of breathing and provide good oxygenination.

- Furosemide

  - If Fluid overload is causative. Initial symptomatic relief is provided by its prompt vasodilating action, however, subsequent diuoresis may result in marked hypovolaemia leading to compensatory vasoconstriction increased cardiac work, and worsening myocardial function. Diuretics may be indicated for acute –on-chronic failure especially if the patients is long-term diuretic therapy, but should not be used if hypovolaemic.

- **DIRECTED MANAGEMENT**

  - With Hypovolaemia fluid challenge if necessary or ultrafiltration with fluid overload.

  - If vasoconstriction persist (high BP, low cardiac output) titrate nitrate infusion to optimize stroke volume. Within 24 hours of nitrate infusion, commence ACE inhibition, initially at low dose but rapidly increased to appropriate long-term doses.

  - Inotropes are needed if tissue hypoperfusion, hypotension, or vasoconstriction persists despite optimal fluid loading and nitrate dosing dobutamine, or milrinon. May excessively vasodilate.

- Intra-aortic balloon counter pulsation augments cardiac output, reduces cardiac work, and improves coronary artery perfusion.

- Angioplasty or surgical revascularisation is beneficial if performed early after myocardial infarct.

- **TREATMENT ENDPOINTS.**

  - BP and cardiac output adequate to maintain organ perfusion (e.g. no oliguria, confusion, dyspnea metabolic acidosis).

  - Venous oxygen saturation $\geq$ 60%.

  - Symptomatic relief.

SHOCK

OVERVIEW

- Definition

  - Shock is a multifactorial syndrome leading to systemic and localized tissue hypoperfusion resulting in cellular hypoxia and multiple organ dysfunctions.

- Description

  - Perfusion may be decreased systemically with obvious signs such as hypotension.

  - Perfusion may be decreased because of maldistribution as in septic shock where systemic perfusion may appear elevated.

  - Prognosis is determined by degree of shock, number of organs affected, and possibly some general predisposition.

CLASSIFICATION AND PRESENTATION OF SHOCK

- Hypovolemic shock

  - Loss of circulating intravascular volume and decrease in cardiac preload

  - May be from hemorrhage such (as with trauma, gastrointestinal bleeding, nontraumatic internal

bleeding such as aneurysm, ectopic rupture), or vaginal bleeding.

- May be nonhemorrhagic fluid loss from the gastrointestinal tract (vomiting, diarrhea, fistula) urinary losses (hyperglycemia with glucosuria), evaporative loss (fever, hyperthermia), and internal fluid shifts (third spacing as with a bowel obstruction).

- Symptoms include tachycardia, hypotension, decreased urine output, mental status changes, and tachypnea.

- Treatment is with volume resuscitation with crystalloid solution, and, in addition, blood if from hemorrhage.

- Obstructive shock

  - Caused by a mechanical obstruction to normal cardiac output (CO) with a decrease in systemic perfusion.

  - Consider cardiac tamponade and tension pneumothorax.

  - Other causes are massive pulmonary embolism and air embolism.

  - Treatment is maximizing preload and relief of the obstruction.

- Cardiogenic shock
    - Caused by myocardial (pump) failure.
    - Most common cause is extensive myocardial infarction.
    - Other causes are reduced contractility (cardiomyopathy, sepsis induced), aortic stenosis, mitral stenosis, atrial myxoma, acute valvular failure, and cardiac dysrhythmias.
    - Treatment is optimizepreload, cardiac performance and reducing afterload.
- Distributive shock
    - Caused by systemic vasodilatation from an inciting cause (infection, anaphylaxis) resulting in systemic hypotension, and increased or decreased CO.
- **RESUSCITATION ENDPOINTS**
    - Lactic acid production
        - Cells with inadequate oxygen will switch to anaerobic metabolism.
        - Lactic acid is a byproduct of anaerobic metabolism.

- Elevation of serum lactate is a measure of the severity of shock. Elevated lactate is a global measure of hypoperfusion. Lactate may be elevated in liver or kidney failure

- Base deficit

  - Base deficit is the amount of base required to titrate whole blood to a normal pH.

  - The presence of an elevated base deficit correlates with the severity of shock.

TREATMENT

Rapid recognition and restoration of perfusion is the key to preventing multiple organ dysfunction and death with shock. In all forms of shock, rapid restoration of preload with infusion of fluids is the first treatment. Crystalloid is first infused and then blood if shock is secondary to hemorrhage. Shock must be treated while identifying its cause.

- **HYPOVOLEMIC SHOCK**

  - Rapid infusion of multiple liters of crystalloid is the treatment of hypovolemic shock. Large-bore venous access is needed, and central access may be necessary.

  - If the cause is hemorrhage, then after 2 to 3 L of crystalloid, blood is transfused. Coagulopathy will persist until the source of bleeding is controlled.

- Resuscitation is not complete until the base excess or serum lactate has decreased to an acceptable level.

- **OBSTRUCTVE SHOCK**

  - The cause of the obstruction must be identified and relieved early.

    - Pericardiocentesis or pericardiotomy for a cardiac tamponade.

    - Needle decompression and tube thoracostomy for tension pneumothorax.

    - Ventilator and cardiac support, heparin for pulmonary embolism.

- **CARDIOGENIC SHOCK**

  - Optimize preload with infusion of fluids.

  - Optimize contractility with inotropes as needed

  - Adjust afterload. This may involve as using a vasoconstrictor if a patient is hypotensive. Patients with cardiogenic shock may need vasodilatation to decrease. Resistance to flow from a weak heart. Consider nitroprusside or nitroglycerin.

  - The underlying cardiac cause needs to be treated if possible.

- **DISTRIBUTIVE SHOCK**

  - Treatment is with aggressive fluid resuscitation, pressors can be used to augment BP.
    - Dopamine is frequently used because of its splanchnic vasodilatation
    - Norepinephrine is a good vasoconstrictor and is the recommended pressure in septic shock once adequate volume is achieved.
    - Vasopressin has been used effectively in profound septic shock, especially when norepinephrine is not working.
    - Low-dose steroids can be considered in patients with adrenal insufficiency.
  - Treatment of the underlying cause of SIRS is essential.

ACUTE EXACERBATION OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE

OVERVIEW

- History of well established diagnosis of COPD or first time presentation.
- acute exacerbation includes an acute increase in one or more of the following symptoms:
    - Cough increases in frequency and severity
    - Sputum production increases in volume and/or changes character
    - Dyspnea increases

PRESENTATION

- Include worsening dyspnea, progressive exercise intolerance, and alteration in mental status.presence of wheeze indicates acute bronchospasm.
- Acute worsening of dyspnea should be evaluated for potential alternative diagnoses, such as heart failure, pulmonary thromboembolism, and pneumonia.

DIFFERENTIAL DIAGNOSIS

- acute asthma

- pneumonia
- PE
- heart failure
- pneumothorax

WORKUP

- (ABG) analysis helps to give a clue to the severity of the respiratory acidosis.
- Consider any pH below 7.3 a sign of acute respiratory compromise.
- CBC – Polycythemia, leukocytosis in the presence of infection.
- Pro BNP by measuring the pro BNP level, it might differentiate between CHF and COPD exacerbation.
- Chest xray to evaluate for the presence of pneumonia, pulmonary edema and pneumothorax.
- Computed cut scan more sensitive in evaluation lung paryncyhma and the extent of the emphysematous change.
- CT angio helps to rule out pulmonary embolism.

TREATMENT GOALS

- Successful management of acute exacerbations of COPD requires attention to a number of issues:

  - Identifying and ameliorating the cause of the acute exacerbation, if possible

  - Optimizing lung function by administering bronchodilators and other pharmacologic agents

  - Assuring adequate oxygenation and secretion clearance

  - Avoiding the need for intubation, if possible

  - Preventing complications of immobility, such as thromboemboli and deconditioning

  - ensure nutritional needs

- **Oxygen Therapy**

- Supplemental oxygen is a critical component of acute therapy. It should target an arterial oxygen tension (PaO2) of 60 to 70 mmHg, with an oxyhemoglobin saturation of 90 to 94 percent.

- There are numerous devices available to deliver supplemental oxygen during an acute exacerbation of COPD:

  - Venturi masks are the preferred means of oxygen

delivery because they permit a precise delivered fraction of inspired oxygen (FiO2). Venturi masks can deliver a FiO2 of 24, 28, 32, 34, 40, or 60 percent.

- Nasal cannulae can provide flow rates up to 6 L per minute with an associated FiO2 of approximately 40 percent. They are more comfortable and convenient for the patient, especially during oral feedings.

- When higher inspired concentrations of oxygen are needed, simple facemasks can provide an FiO2 up to 55 percent using flow rates of 6 to 10 L per minute. However, variations in minute ventilation and inconsistent entrainment of room air affect the FiO2 when simple facemasks (or nasal cannulae) are used.

- Non-rebreathing masks with a reservoir, one-way valves, and a tight face seal can deliver an inspired oxygen concentration up to 85 percent.

- Inhaled medications :

- The administration of inhaled medications to mechanically ventilated patients is problematic because the medications accumulate in the ventilator tubing and the endotracheal tube.

- A metered dose inhaler (MDI) can be used.

The following has been proposed for using MDIs in mechanically ventilated patients:

- Shake the MDI.
- Place the canister in the actuator of a cylindrical spacer, situated in the inspiratory limb of the ventilator circuit.
- Synchronize the MDI with the onset of inspiration by the ventilator.
- Repeat the puff every 20 to 30 seconds until the total dose is delivered.

A. Beta adrenergic agonists :

- Typical doses of salbutamol for this indication are 2.5 mg diluted to a total of 3 mL by nebulizer every one to four hours as needed, or four to eight puffs (90 mcg per puff) by MDI with a spacer every one to four hours as needed.

B. Anticholinergic agents:

- Typical doses of ipratropium for this indication are 500 mcg by nebulizer every four hours as needed. Alternatively, two puffs (18 mcg per puff) by MDI with a spacer every four hours as needed.

C. Glucocorticoids Dose :

- Methylprednisolone 60 to 125 mg, 3 times daily, then taper the dose.

- Duration 2 weeks duration to minimize lung function decline.

- Antibiotic Therapy

- Common organism H.influenza, strep pneumonia, moraxilla catarrhalis, pseudomonas.

- Indications: severe exacerbation requiring mechanical ventilation (noninvasive or invasive) or an exacerbation with increased sputum purulence plus either increased dyspnea or increased sputum volume

- **Pseudomonas risk factors:**

- Frequent administration of antibiotics

- Recent hospitalization (2 or more days' duration in the past 90 days)

- Isolation of Pseudomonas during a previous hospitalization

- Severe underlying COPD (FEV1 <50 percent predicted)

- For Critically ill patients with risk factors for Pseudomonas, antibiotic choices include levofloxa-

cin, cefepime, ceftazidime, and piperacillin-tazobactam. Hospitalized patients without risk factors for Pseudomonas can be treated with a respiratory fluoroquinolone (levofloxacin, moxifloxacin) or a third-generation cephalosporin (ceftriaxone or cefotaxime).

- Antiviral Therapy

  - Patients whose COPD exacerbation was triggered by influenza virus should be treated with antiviral therapy such as oral oseltamivir.

- Mechanical Ventilation

A. Noninvasive ventilation

  - It is the preferred method of ventilatory support in most ofthe patients with an acute exacerbation of COPD.

B. Invasive ventilation

  - Invasive mechanical ventilation should be administered when patients fail NPPV, do not tolerate NPPV, or have contraindications to NPPV.

STATUS ASTHMATICUS

OVERVIEW

- Status Asthmaticus is a life threatening form of asthma defined as “a condition in which a progressively worsening attack is unresponsive to the usual appropriate therapy with adrenergic drugs and that leads to pulmonary insufficiency.

PRESENTATION

- History:
  - Previous history of wheezing, known asthmatic, non Compliant Previous hospitalizations or intubations history.
- Physical Examination Vital signs
  - Temperature: fever may indicate URI, pneumonia, other source of infection
  - Pulse: Usually tachycardic, bradycardia is an ominous sign
  - Respiratory rate: tachypneic > 30 breaths/min.
  - Blood pressure: Pulsus paradoxus
- Presence of hypoxia, bilateral wheeze or silent chest and mental confusion with impending collapse.
- Peak flow a peak flow rate below 200 L/min indicates severe obstruction for all but unusually small adults.

DIFFERENTIAL DIAGNOSIS

- Upper airway obstruction
- Vocal cord dysfunction
- Laryngeal edema

WORKEUP

- CBC : elevation in WBc may indicate infection specially bacterial ,signs of viral infection such as leucopenia and thrombocytopenia
- ABG might help in the presence of normal or elevated CO2 that indicate severe presentation.
- Chest x-ray to exclude reversible pathology such as pneumothorax.

MANAGEMENT

- If the patient does not respond to appropriate therapy in the emergency department, if the frequency of required aerosol treatments is greater than can be administered on the ward (usually q1 hour), or if the patient is deteriorating significantly despite appropriate therapy, he/she should be transferred/admitted to the ICU.
- *Oxygen therapy should* be started immediately to correct hypoxemia.

- *Inhaled beta agonists* The standard regimen for initial care in the emergency department has become albuterol or salbutamol 5 mg by continuous flow nebulization every 20 minutes for three doses, every one to four hours as needed . Continuous nebulization can be administered 10 to 15 mg over one hour.

- *Inhaled anticholinergics* the dosing of ipratropium for nebulization is 500 mcg every 20 minutes for three doses, then every 6hours, 4to8 puffs by MDI with spacer.

- *Systemic glucocorticoids* methylprednisolone 60 to 80 mg every 6 to 8 hours is often chosen for patients who in status asthmaticus.

- *Magnesium sulfate* Intravenous magnesium sulfate 2 gm infused over 20 min has bronchodilator activity in acute asthma, possibly due to inhibition of calcium influx into airway smooth muscle cells.

MECHANICAL VENTILATION

- INDICATIONS: should be based on clinical judgment that considers the entire clinical situation but acute respiratory failure is a strong indication. Delayed intubation should not occur .

    - Poor response to therapy

    - Worsening hypoxia and hypercapnia

- Mental status worsening
- Signs of muscle fatigue

- Dynamic hyperinflation creates intrinsic PEEP and elevates the plateau pressure (Pplat), which can lead to cardiovascular collapse and barotrauma, as well as increase the work of breathing. Adjustments of the ventilator settings should try to minimize the risk of these events, preferably maintaining an inspiratory Pplat less than 30 cm H2O and an intrinsic PEEP less than 10 to 15 cm H2O. The following adjustments may help achieve these goals by decreasing air trapping (2):

    - Increasing the inspiratory flow will shorten the inspiratory time, increase the expiratory time, and allow the patient more time to exhale.
    - Decreasing the tidal volume causes less lung inflation and gives the patient a smaller volume to exhale before the next breath.
    - Decreasing the respiratory rate increases the expiratory time and allows the patient more time to exhale.

- *General anesthesia* Induction of general anesthesia, either by intravenous infusion (ketamine) or inhalation (sevoflurane), can reduce bronchospasm .

- *Antibiotic* no role for empiric antibiotic therapy for the treatment of an asthma exacerbation, because most respiratory infections that trigger an exacerbation of asthma are viral rather than bacterial.

ACUTE RESPIRATORY DISTRESS SYNDROME

OVERVIEW

- ARDS is an acute condition characterized by bilateral pulmonary infiltrates and severe hypoxemia in the absence of evidence for cardiogenic pulmonary edema.
- ARDS is associated with diffuse alveolar damage (DAD) and lung capillary endothelial injury.
- ARDS require the four criteria :
  - Acute onset
  - Bilateral infiltrates (radiographically similar to pulmonary edema)
  - No evidence of elevated left atrial pressure (the pulmonary capillary wedge pressure is ≤18 mmHg if measured)
  - A ratio of arterial oxygen tension to fraction of inspired oxygen (PaO2/FiO2) <200 mmHg. (1)
  - Major Risk Factors Of Ards
  - Sepsis
  - Trauma, with or without pulmonary contusion
  - Fractures, particularly multiple fractures and long bone fractures
  - Burns
  - Massive transfusion
  - Transfusion related acute lung injury (TRALI)
  - Pneumonia
  - Aspiration

- Drug overdos
- Postperfusion injury after cardiopulmonary bypass
- Pancreatitis
- Fat embolism

PRESENTATION

- **History**

  - Acute presentation of dyspnea, tachypnea, anxiety, agitation ,cough tachypnea, tachycardia, and a high (FIO_2) to maintain oxygen saturation, Cyanosis and symptoms of causing risk factor .

- **Examination**

  - Reveal severe hypoxia and the lungs reveal bilateral rales and Mechanical ventilation is almost required.

DIFFERENTIAL DIAGNOSIS:

- Acute pulmonary edema
- Acute eosinophilic pneumonia
- Acute interstitial pneumonia
- Acute pneumocystic pneumonia in HIV
- Diffuse alveolar hemorrhage.

WORKUP

- In septic patients, leukopenia or leukocytosis. Thrombocytopenia may be observed in septic patients in the presence of (DIC). Von Willebrand factor (VWF) may be elevated in patients at risk for ARDS and may be a marker of endothelial injury. Acute tubular necrosis (ATN) as a course of ARDS, probably from ischemia to the kidneys.
- A BNP level of less than 100 pg/mL in a patient with bilateral infiltrates and hypoxemia favors the diagnosis of ARDS/ acute lung injury (ALI) rather than cardiogenic pulmonary edema.
- X Ray
  - Might show bilateral pulmonary infiltrates. The infiltrates may be diffuse and symmetric or asymmetric.
- Echocardiography
  - To exclude cardiac causes of pulmonary edema.
- Bronchoscopy
  - can be done if FIO2 not high and early of the disease course
  - Bronchoscopy to evaluate the possibility of infection, alveolar hemorrhage, or acute eosinophilic pneumonia bronchoalveolar lavage (BAL) can be optained. The fluid is analyzed for cell differential, cytology, silver stain, and Gram stain and is quantitatively cultured. the finding of a high percentage of eosinophils (>20%) in the BAL fluid is consistent with the diagnosis of acute

eosinophilic pneumonia. Silver stain may be helpful in diagnosing an infection, such as *Pneumocystic pneumonia.* Increased number of lymphocytes observed in acute hypersensitivity pneumonitis, sarcoidosis, or cryptogenic organizing pneumonia (COP). Hemosiderin-laden macrophages observed in alveolar hemorrhage.

- 1-a An exudative phase occurs in the first several days and is characterized by interstitial edema, alveolar hemorrhage and edema, pulmonary capillary congestion, and hyaline membrane formation.
- 2-a Proliferative phase of ARDS, characterized by the growth of type 2 pneumocytes in the alveolar walls and the appearance of fibroblasts, myofibroblasts, and collagen deposition in the interstitium.
- 3-a Fibrotic phase Alveolar walls are thickened by connective tissue.

TREATMENT

- Supportive Care
  - Patients with ARDS require meticulous supportive care, including proper use of sedatives and neuromuscular blockade, hemodynamic management, nutritional support, control of blood glucose levels, evaluation and treatment of nosocomial pneumonia, and prophylaxis of deep venous thrombosis (DVT) and gastrointestinal (GI) bleeding.

- Fluid management:
  - Pulmonary edema is more likely to develop in ARDS than in normals for any given pulmonary capillary hydrostatic pressure.
  - A strategy of conservative fluid management may help patients by reducing edema formation.
- Corticosteroids
  - Systemic corticosteroids of less than 72 hours
  - Methylprednisolone 1mg/kg followed by 1mg/kg/day for 14 days.
  - Followed by methylprednisolone 0.5mg/kg/day for 4days then 0.25mg/kg/day for 4 days then 0125mg/kg/day for 3 days.
- Prone Positioning
  - Prone positioning improves oxygenation in the majority of patients with ALI and ARDS..
- Increase Oxygen Delivery
  - Blood transfusion to keep hemoglobin concentration between 7 and 9 g/dL to maintain the oxygen delivery.
- Mechanical Ventilation

- LOW TIDAL VOLUME VENTILATION (LTVV) is a lung protective ventilation.the smaller tidal volumes are less likely to generate alveolar overdistension, one of the causes of ventilator-associated lung injury(VALI). The initial tidal volume is set to 6 mL/kg PBW and the initial respiratory rate is set to meet the patient's minute ventilation requirements. The respiratory rate is increased (up to a maximum of 35 breaths per minute) . The tidal volume adjustments are made on the basis of the plateau airway pressure. The plateau airway pressure is checked at least every four hours and after each change in PEEP or tidal volume. The goal plateau airway pressure is ≤30 cm H2O.

- OPEN LUNG VENTILATION Open lung ventilation is a strategy that combines low tidal volume ventilation (LTVV) and PEEP to maximize alveolar recruitment. The LTVV aims to decrease alveolar overdistension, while the applied PEEP seeks to minimize cyclic atelectasis.

- RECRUITMENT MANEUVERS A recruitment maneuver is the brief application of a high level of continuous positive airway pressure, such as 35 to 40 cm H2O for 40 seconds. The purpose is to open alveoli that have collapsed. (PaO2) generally increases after a recruitment maneuver.

- HIGH-FREQUENCY VENTILATION is a protective technique that uses high levels of positive end-expiratory pressure (PEEP) and low tidal volumes. it may decrease ventilator-induced lung injury and reduce barotrauma in patients with ARDS. HFV provides

tidal volumes below that of the anatomic dead space at frequencies greater than 60 breaths per minute. Benefits of HFV include reduced barotrauma, improved V/Q matching, and less risk of hemodynamic compromise. Complications of the technique include inspissation of mucus, airway damage due to high gas velocities, air trapping.

- **Trachestomy**

- Allows the establishment of a more stable airway, which may allow for mobilization of the patient and may facilitate weaning from mechanical ventilation.

PNEUMONIA

OVERVIEW

- **Definitions**

  - Pneumonia is an inflammation of the lung parenchyma, in which consolidation of the affected part and a filling of the alveolar air spaces with exudate, inflammatory cells, and fibrin.

  - Community-acquired Pneumonia (CAP) is defined as pneumonia that develops in the outpatient setting or within 48 hours of admission to a hospital.

  - Health care associated Pneumonia (HCAP) is defined as pneumonia that develops within 48 hours of admission to a hospital in patients with increased risk of exposure to MDR bacteria as a cause of infection. Risk factors for exposure

  - To MDR bacteria in HCAP include the following:

    - Hospitalization for 2 or more days in an acute care facility within 90 days of current illness

    - Exposure to antibiotics, chemotherapy, or wound care within 30 days of current illness

    - Residence in a nursing home or long-term care facility

- Hemodialysis at a hospital or clinic
- Home nursing care (infusion therapy, wound care)
- Contact with a family member or other close person with infection due to MDR bacteria

- Hospital-acquired Pneumonia (HAP)

- is defined as pneumonia that develops at least 48 hours after admission to a hospital and, as in HCAP, is characterized by increased risk of exposure to MDR organisms as well as gram-negative organisms.

- Ventilator-associated Pneumonia (VAP)

- is defined as pneumonia that develops more than 48 hours after endotracheal intubation or within 48 hours of extubation.

- Aspiration Pneumonia

  - Develops after the inhalation of oropharyngeal secretions and colonized organisms.

- *Causative organisms:*

  - *Bacterial* (S. pneumonia, H. influenza, Mycoplasma pneumoniae , Chlamydia pneumonia, Legionella , Gram-negative bacilli especially K. pneumoniae, Escherichia coli, Enterobacter spp, Serratia spp, Proteus spp, Pseudomonas aerugino-

sa, and Acinetobacter spp).

- *Viruses* include(Influenza ,Ryspiratory Syncityal Virus, parainfluenza viruses, adenovirus , novel H1N1 , middle east respiratory syndrome MERS corona virus)

PRESENTATION

- Symptoms

  - Chest pain, dyspnea, hemoptysis, decreased exercise tolerance,chest pain,fever, rigors or shaking chills, and malaise are common.

- *Physical Examination*
  - Signs of bacterial pneumonia may include the following: Hyperthermia (fever, typically >38°C) [or hypothermia (< 35°C) ,Tachypnea ,Use of accessory respiratory muscles, Tachycardia ,Central cyanosis, Altered mental status
  - Physical findings may include the following: Adventitious breath sounds, such as rales/crackles, signs of consolidation, Pleural friction rub.
- Examination findings that may indicate a specific etiology for consideration are as follows:
  - Bradycardia may indicate a *Legionella*.
  - Bad oral hygiene may suggest an anaerobic and/or polymicrobial infection.

- Bullous myringitis may indicate *Mycoplasma pneumoniae* infection.

- Physical evidence of risk for aspiration may include a decreased gag reflex, bedridden and history o stroke.

• Severity index

- CURB-65 is a scoring system developed from a multivariate analysis of 1068 patients that identified various factors that appeared to play a role in patient mortality. One point is given for the presence of each of the following:

  - **C** onfusion – Altered mental status
  - **U** remia – Blood urea nitrogen (BUN) level greater than 20 mg/dL
  - **R** espiratory rate –30 breaths or more per minute
  - **B** lood pressure – Systolic pressure less than 90 mm Hg or diastolic pressure less than 60 mm Hg
  - Age older than **65** years
    - Score of 0-1 – Outpatient treatment
    - Score of 2 – Admission to medical ward
    - Score of 3 or higher – Admission to intensive care unit (ICU)

- The acute physiology and chronic health evaluation (APACHE II) score can be used to estimate the risk of mortality.

DIFFERENTIAL DIAGNOSIS:

- Non bacterial pneumonia (COP, hypersensitivy pneumonitis ,TB pneumonia , vasculitis)
- Malignancy (lymphoma ,broncholaveolar cancer)
- Heart failure
- Pulmonary embolism

WORK-UP

CBC count with differential Leukocytosis with a left shift observed in any bacterial infection; however, their absences, particularly in patients who are elderlywill not exclude it. Leukopenia may be an ominous clinical sign of sepsis. An elevated (INR) indicates severe illness.

- Blood cultures
- Blood cultures should be obtained before administering antibiotic therapy. When the findings are positive, they correlate well with the causative organism blood cultures show poor sensitivity in pneumonia; even in pneumococcal pneumonia, the results are often negative.

- Sputum Gram stain and culture a good-quality containins < 10 squamous epithelial cells per low-power field can be obtained. The white blood cell (WBC) count should be more than 25 per low-power field.

- Bronchoscopy can be done to obtain a good sample of broncho-alveolar lavage and protected brush for stain and culture.

- Chest xray can be done to detect the findings of consolidation, the lobes involved and complications such as pleural effusion. CT chest has more sensitivity than chest X-ray.

TREATMENT

- Direct admission to an intensive care unit (ICU) is mandated for any patient in septic shock with a requirement for vasopressors or with acute respiratory failure requiring intubation and mechanical ventilation.

- Empirical antibiotic For ICU patients, choose one option below:
  - IV beta-lactam plus IV macrolide
  - IV beta-lactam plus IV antipneumococcal quinolone

- For patients at increased risk of infection with *Pseudomonas* , choose one option below:

- IV antipseudomonal beta-lactam plus IV antipseudomonal quinolone

- IV antipseudomonal beta-lactam plus IV aminoglycoside plus one of the following: (1) IV macrolide; (2) IV quinolone

- For antibiotics for HAP and VAP, The prevalence and resistance patterns of MDR pathogens vary between institutions and even between ICUs within the same hospital. So embirical coverage depends on the resistance. Taking a considerations of MDR gram negative (consider colistin, tigecycline and carbapenem) and MRSA (vancomycin or lienozolid)

- *Aspiration pneumonia* empirical antibiotic: the causative organisms in aspiration pneumonia similar to those of CAP or HCAP, patients with severe periodontal disease, putrid sputum, or a history of alcoholism with suspected aspiration pneumonia may be at greater risk of anaerobic infection. One of the following antibiotic regimens is suggested for such patients:

- Piperacillin-tazobactam

- Imipenem

- Clindamycin or metronidazole plus a respiratory fluoroquinolone plus ceftriaxone.

- MERS corona virus needs supportive treatment and coverage for secondary bacterial infection.

PULMONARY EMBOLISM

OVERVIEW

- PE is an obstruction of the pulmonary artery or one of its branches by (thrombus, tumor, air, or fat) that originated elsewhere in the body.

- Massive PE causes hypotension, defined as a systolic blood pressure <90 mmHg .

- Three risk factors lead to thrombus formation (Virchow triad), which consists of the following :
    - Endothelial injury
    - Stasis of blood flow
    - Blood hypercoagulability

PRESENTATION

- Dyspnea , Pleuritic chest pain ,Cough , Hemoptysis, Tachypnea ,Rales ,Accentuated second heart sound ,Tachycardia ,Fever ,S_3 or S_4 gallop, Clinical signs and symptoms suggesting of DVT and thrombophlebitis ,Lower extremity edema and Cardiac murmur .

- Massive PE
    - Patients are in shock. They have systemic hypotension, poor perfusion of the extremities, tachycardia, and tachypnea. In addition, patients appear

weak, pale, sweaty, and oliguric and develop impaired mentation. Signs of pulmonary hypertension, such as palpable impulse over the second left intercostal space, loud P_2, right ventricular S_3 gallop, and a systolic murmur louder on inspiration at left sternal border.

WORK-UP

- ABGs usually reveal hypoxemia, hypocapnia, and respiratory alkalosis. Wide A-a gradient.
- D-dimer with a level >500 ng/mL is usually considered abnormal. D-dimer level <500 ng/mL by quantitative ELISA or semi-quantitative latex agglutination is sufficient to exclude PE in patients with a low or moderate pretest probability of PE.
- BNP, NT-proBNP and Troponin may have a prognostic role in PE .
- Electrocardiographic abnormalities considered to be suggestive of PE (S1Q3T3 pattern, right ventricular strain, new incomplete right bundle branch block , tachycardia and atrial fibrillation .

- **Chest Xray**
  - Common radiographic abnormalities include atelectasis, pleural effusion, parenchymal opacities, and elevation of a hemidiaphragm. The classic radiographic find-

ings of pulmonary infarction include a wedge-shaped, pleura-based triangular opacity with an apex pointing toward the hilus (Hampton hump) or decreased vascularity (Westermark sign). A prominent central pulmonary artery (knuckle sign), cardiomegaly (especially on the right side of the heart). A normal-appearing chest radiograph in a patient with severe dyspnea and hypoxemia, but without evidence of bronchospasm or a cardiac shunt, is strongly suggestive of pulmonary embolism.

- **Echocardiography (Echo)**
  - May allow diagnosis of other conditions that may be confused with pulmonary embolism, such as pericardial effusion and left ventricular failure . ECHO allows visualization of the right ventricle and assessment of the pulmonary artery pressure. ECHO has a prognostic value . the presence of right ventricular dysfunction can be used to support the clinical suspicion of pulmonary embolism.

- **COMPUTED TOMOGRAPHY ANGIOGRAPHY (CTA)**
  - Is the initial imaging modality of choice for stable patients with suspected pulmonary embolism. Visualizing a filling defect in the pulmonary arteries confirm the diagnosis. Sensitivity is lower with subsegmental branches of the pulmonary artery.

- **V/Q SCAN:**

  - Diagnostic accuracy was greatest when the V/Q scan was combined with clinical probability, which was determined by the clinician prior to the V/Q scan :

  - Patients with high clinical probability of PE and a high-probability V/Q scan had a 95 percent likelihood of having PE

  - Patients with low clinical probability of PE and a low-probability V/Q scan had only a 4 percent likelihood of having PE

  - A normal V/Q scan virtually excluded PE

- **ANGIOGRAPHY**

- Pulmonary angiography is the definitive diagnostic technique or "gold standard" in the diagnosis of acute PE.

TREATMENT

- Anticoagulation

  - Immediate therapeutic anticoagulation is initiated for patients with suspected DVT or pulmonary embolism.(1)_Start the patient on unfractionated heparin (UFH), low–molecular weight heparin (LMWH), or fondaparinux in addition to an oral anticoagulant (warfarin) at the time of diagnosis,

and to discontinue UFH, LMWH, or fondaparinux only after the international normalized ratio (INR) is 2.0 for at least 24 hours,and continue the bridging for at least 5 days.

- oral rivaroxaban (oral factor Xa inhibitor) can be given with initial dose of 15 mg BID for 21 days then 20 mg singal daily dose and no need for bridging with heparin

- Thrombolysis

  - Thrombolytic therapy accelerates the lysis of acute PE and improves important physiologic parameters, such as RV function and pulmonary perfusion. Uptodate no clinical trial has been large enough to conclusively demonstrate a mortality benefit. Thrombolytic therapy is associated with an increased risk of major hemorrhage, defined as intracranial hemorrhage, retroperitoneal hemorrhage, or bleeding leading directly to death, hospitalization, or transfusion.

  - Persistent shock is the most accepted indication for thrombolytic therapy .

  - The Decision for thrombolysis should be individualized.

  - TPA can be given in a dose of 100mg intravenous for one hour duration.

- <u>Inferior vena caval (IVC) filters</u>

- *Indications* — Insertion of an inferior vena cava (IVC) filter is indicated for acute PE in the following settings and should be case by case

- Absolute contraindication to anticoagulation (eg, active bleeding)

- Recurrent PE despite adequate anticoagulant therapy

- Complication of anticoagulation (eg, severe bleeding)

- Hemodynamic or respiratory compromise that is severe enough that another PE may be fat

CHEST TRAUMA

OVERVIEW

- Immediate death usually involves disruption of the heart or great vesseles.Early death(those occurring within 30 minutes to 3 hours) are due to cardiac tamponade,tension pneumo-thorax,airway obstruction,aspiration. Pulmonary sepsis and missed injury account for late cause of death.

- Approximately 85% of all thoracic trauma can be managed nonoperatively(conservatively). Only 10%-15% of victims of blunt or penetrating injuries will require thoracotomy or sternotomy.

- Patients who have injury below nipple(4th intercostal space) anteriorly or inferior to tip of scapula posteriorly should suspected to have abdominal injury in addition to thoracic trauma.

  - Major thoracic trauma can be remembered as the(DEADLY DOZEN).THe **"LETHAL SIX"** and the **"HIDDEN SIX"**.

  - "THE LETHAL SIX" is immediately life-threatening injuries and should be sought in primary survey.

  - The"HIDDEN SIX" are potentially life-threatening injuries and should be detected during the secondary survey.

THE LETHAL SIX

A. AIRWAY OBSTRUCTION

- Early preventable deaths are often due to lack of or delay in airway control. Remember to protect the cervical spine as the airway being managed. However, do not delay definitive airway management because of concern about possibility of cervical spine injury.

- Causes

- The most common cause in an unconscious patient is the tongue fallen backward.

- Dentures, avulsed teeth, tissues, secretions, and blood can contribute to airway obstruction in trauma.

- Bilateral mandibular fracture involving anterior attachment of the tongue.

- Expanding neck hematoma.

- Direct laryngeotracheal trauma.

- Physical Findings

    - Anxiety, stridor, hoarseness of voice, active accessory muscles,cyanosis,or apnea.

- **Treatment**

  - INTUBATION SHOULD BE EARLY, ESPECIALLY IN CASES OF NECK HEMATOMAS OR POSSIBLE AIRWAY OEDEMA AND MIGHT NEED SURGICAL AIRWAY.

  - MOST EARLY PREVENTABLE TRAUMA DEATH ARE DUE TO AIRWAY OBSTRUCTION.

B. TENSION PNEUMOTHORAX

- Occurs when air enters the pleural space from lung injury or through the chest wall without a means of exit. The affected lung collapses completely with sub sequent mediastinal shift, kinking of superior and inferior vena cava,decreased cardiac output. Ventilation of the contralateral lung is also decreased by the mediastinal shift.

- Causes

  - Penetrating injury to the chest.

  - Blunt trauma with parenchymal lung injury that did not spontaneously close.

  - Mechanical ventilation with PEEP

- Work-Up

- IT SHOULD BE NOTED THAT DIAGNOSIS OF TENSION PNEUMOTHORAX IS A CLINICAL DI-

AGNOSIS NOT A RADIOLOGICAL DIAGNOSIS:

- Severe respiratory distress.
- Severe hypotension (obstructive shock).
- Hyperresonance to percussion over affected hemi-thorax.
- Unilateral absence of breath sound.
- Neck vein distension (absent in hypovolemia).
- Cyanosis (preterminal).
- Tracheal shift to the other side.

MANAGEMENT

- Immediately decompress by inserting a 12-14G catheter into second intercostal space in the midclavicular line or fifth intercostal space in the anterior axillary line.
- Follow immediately with chest tube insertion.
- Again, avoid using chest-X ray to confirm diagnosis.

C. PERICARDIAL TAMPONADE

- Commonly result from penetrating injury,but it can also seen in blunt injury.The pericardial sac does not acutely distend ;100-150 ml of blood can produce tamponade.

- Work-Up

- In awake patient,the patient is extremely anxious,and will state that he sense"impending doom" and may "appear deathlike".

- One should suspect tamponade in any trauma patient with persistent hypotension, acidosis, and base deficit despite adequate blood and fluid resuscitation, especially the risk of ongoing blood loss is minimal or ruled out.

- "BECK'S TRIAD": JVD, HYPOTENSION, MUFFLED HEART SOUND.This triad only present 33% of confirmed cases.JVD absent in state of hypovolemia.

- Pulsus paradoxicus: decrease systolic Bp more than 10mmHg during inspiration.

- KAUSSMAUL'S sign: which is jugular venous distention during spontaneous respiration.it is good sign for tamponde.

- ECHOCARDIOGRAPHY FINDING: diastolic collape of right side of the heart"pathognomonic sign".

- Pulmonary artery catheter monitoring will show equalization of right and left filling pressure of the heart.

- Treatment

- It is emergent state, pericradiocentesis should be performed if surgeon not available.But in presence of surgeon the patient should be taken to OR for thora-

cotomy(pericardial window) and further management according to patient condition.

D. **OPEN PNEUMOTHORAX:**

- Large open defect in chest wall (>3cm) with equilibration between intrathoracic and atmospheric pressure.If the opening is greater than two third of the diameter of trachea, then air follows the least resistance through the chest wall with each inspiration,leading to profound hypoxia and hypoventilation.

- Treatment :

- Early intubation and mechanical ventilation plus surgical closure of the defect.

E. **MASSIVE HEMOTHORAX**

- Commonly due to penetrating injury with hilar or systemic vessels disruption. Intercostal internal mammary vessels are most commonly affected.Thoracic cavity can accommodate up to 3 liters of blood.

- Work-UP

- Hemorrhagic shock.

- Unilateral absence of breath sound.

- Dullness to percussion.

- Chest Xray will show diffuse opacity with contralateral

shift of the mediastinum.

- Treatment:

- **Airway- shock is compelling indication for intubation.**

- Management of hemorrhagic shock.

- Place a single chest tube (28F-32F) in fifth intercostal space to decompress chest wall cavity.

- Thoracotomy is indicated in:

  - -Hemodynamic instability despite aggressive volume resuscitation.

  - -1500 mL blood evacuated initially.

  - -Ongoing bleeding of >200 mL/hr for 4 hours.

  - -Failure to evacuate hemothorax by at least two functioning and appropriately positioned chest tubes.

  - -Failure of the lung to expand or persistence air leak.

F. FLAIL CHEST

- Usually results from direct impact. The flail segment classically involves anterior (sternal separation) or lateral rib fractures. Posterior rib fractures usually do not

produce flail segment due to heavy musculature provides stability. Flail segment usually occurs when two or more ribs in two or more separate locations with resultant paradoxical motion of chest wall segment. Usually associated with underlying lung contusion or hemo/pneumothorax.

- Work-Up

- Is clinically based,not radiological. chest wall must be observed for several respiratory cycles and during

- Coughing to check paradoxical movement of chest wall.

- **Treatment:**

- Pain Control

  - Epidural controlled analgesia with local anesthetic and/or opioids.

  - Intercostal nerve block or intrepleural analgesia through intercostal tube.

  - Systemic NSAID may be used in mild cases. do not over sedate these patients.

- Mechanical Ventilation; indicated in:

  - Significant respiratory distress,such as increased work of breathing,tachypnea(RR>35/min,persistent hypoxia inspite oxygen supplementation more than 40%,

- Associated hemodynamic instability or the need for surgical intervention for other surgical problems.

- Associated co-existing severe lung contusion (ALI).

- Pre-existing lung diseases, cardiac diseases or advanced ages.

- N.B, duration of mechanical ventilation should be ranged between 7-10 days. Avoid the use of muscle relaxant and steroids because of no benefits from their use with possible risk of myo-neuropathy.

THE HIDDEN SIX

A. THORACIC AORTIC DISRUPTION

- The mechanism of injury is rapid deceleration injuries. 85% of these individuals die at the scene. (If undiagnosed, 50% of the survivors will suffer a ruptured aneurysm within first 24 hours,Only 2% will live long enough to form a chronic pseudoaneurysm. Diruption usually in 85% occurs near ligamentum arteriosum, but occasionally occurs at ascending aorta,at the diaphragm,or in mid-descending aorta.

- Survivors usually are initially hypotensive, and respond to volume resuscitation. Persistent or recurrent hypotension is due to another bleeding source. Because free rupture of transected aorta is rapidly fatal.

- Work-Up

  - Clinical signs: asymmetry in upper extremity blood pressures, widened pulse pulse pressure, chest wall contusion. 50% of patients has absent signs of external trauma.

  - X-ray finding: widened mediastinum>8cm (the most consistent finding),fracture of the first three ribs,scapula, or sternum;obliteration of aortic knob (most reliable sign);deviation of trachea to right. Supine X-ray may be misleading, erect X-ray gives better information.

- Transoesophageal echocardiography: sensitivity 63%, specificity 84%. It is the procedure of choice for unstable patients.

- Aortography is gold standard.but CT with contrast can be done initially.

- **Treatment:**

  - Establish airway.

  - Control and prevent hypertension (keep syst Bp 100mmHg)

  - Further surgical management for cardiac surgeon assessment according to site of disruption, patient stability, and facilities available.

B. TRACHEOBRONCHIAL INJURIES

- Most patients with major airway injuries die at the scene as the result of asphyxia.

- An incomplete injury may lead to granuloma formation with late stenosis,persistent atelectasis,and recurring pneumonia.

- **Location**

- Cervical Tracheal injuries:

  - Usually present with upper airway obstruction and cyanosis not relieved with oxygen.

- Symptoms include local pain, dysphagia, cough, and hemoptysis.

- Subcutaneous emphysema.

- Blunt transection uncommon; tends to occur at cricotracheal junction.

- Thoracic tracheal or bronchial injuries:

  - 80% of major bronchial injuries occur within 2cm of carina.

  - Intrapleural laceration; The patient develops persistent dyspnea,massive air leak via chest tubes,and massive pneumothorax that does not re-expand with chest tube drainage.

  - Extrapleural rupture into mediastinum. The patients will have pneumomediastinum and subcutaneous emphysema.

  - Intraparenchymal injuries will usually seals spontaneously if the lung is adequately expanded.

- Radiographic signs on chest X-ray:

  a. 95% will have abnormal admission chest X-ray;finding include pneumothorax,pleural effusion,subcutaneous emphysema.

  b. Specific finding:

- Peribonchial air.
- Deep cervical emphysema; radiolucent line along prevertebral fascia(early and reliable sign).
- Dropped lung; seen with complete intrapleural bronchial transection;the apex of the the lung sits at the level of the pulmonary hilum.

Treatment:

- Airway management.
  - Endotracheal intubation with double lumen tube to isolate affected lung
- Immediate bronchoscopy if patient condition is stable.
  - CT scan chest with contrast
  - Surgical repair according to site of injury.

C. **BLUNT MYOCARDIAL INJURY**

- Contusion usually involve anterior surface of right ventricle. Suspect blunt myocardial in any patients with significant blunt trauma who develops a dysrhythmia in ECG.
- Risk factors for cardiac contusion include :
  - Marked precordium tenderness,ecchymosis or contusion.

- Previous history of cardiac disease.
- Fracture sternum.
- Deformation of steering wheel.
- Thoracic spine or multiple ribs fractures.
- Age > 50 years.

- If ECG is positive for cardiac dysrhythmia; echocardiography is indicated.

- Echocardiography may be the most sensitive test for diagnosis of blunt myocardial injury. Myocardial enzymes elevations are not diagnostic in blunt myocardial injury.These enzymes can be elevated multiple trauma, crush injury,gas gangrene...etc.

  - With echo-finding proven contusion; patient should be admitted to intensive care for further monitoring and management.

D. **DIAPHRAGMATIC TEARS**

- Blunt Trauma

- Tears are classically large and radial and located posterlaterally.Left hemidiaphragm is mostly affected(65%-85%). The mechanism usually rapid deceleration injury

- Or direct trauma to upper abdomen.

- Penetrating Trauma

- Defect tend to be smaller.left-sided tears still predominate. Although the tear is small but it tend to enlarge over time.

Work-Up

- Chest X-ray:
  - Stomach, colon, or small bowel in chest, blurred diaphragmatic contour and left pleural effusion.
  - Nasogastric tube in left hemithorax.
  - Hemidiaphragm elevation or lower lobe atelectasis.
- C.T may miss diaphragmatic injury.
- Laparoscopy or thoracoscpy is more useful in diagnosis.

Treatment

- Diaphragmatic tears will not heal spontaneously. Surgical repair should be done once diagnosed.

E. ESOPHAGEAL INJURY

- Most injuries result from penetrating trauma. Blunt injury is rare.

- In thoracic esophageal injury; subcutaneous emphysema, mediastinal emphysema, pleural effusion, and unexplained fever within 24 hours.

Work-Up

- Esophagoscope is reliable in 60% of injuries.

- Esophagoscope plus esophagogram detect 90% of esophageal tears.

- **Treatment:**

- Injuries< 6 hours-> primarily closure of tears.

- Injury > 6 hours------>diverting proximal esophagostomy+oversewing distal oesophagus(with signs of mediastinitis)+big sized ICD+gastrostomy.

- Injury from 6-12hours------> controversial, but if there is shock with multiple injuries------>divert.

F. **PULMONARY CONTUSION:**

- Caused by hemorrhage into lung parenchyma. Usually beneath a flail segment or fractured ribs. This the most common potentially lethal chest injury. The natural progression of pulmonary contusion is worsening hypoxemia for the first 24-48 hours which may complicate into ALI/ARDS

Work-Up

- Chest X-ray finding are typically delayed,if abnormalities seen on admission X-ray,the pulmonary contusion is severe.

- High Resolution CT (HRCT) ; can detect early contusion phase and assess degree of contusion severity.

- **Treatment:**

- Mild contusion-----> oxygen administration+monitor saturation+aggressive pulmonary toilet.

- Moderate to severe contusion----->intubate+mechanical ventilation.

- Contusion induced ALI/ARDS------>follow ventilatory management protocol of ALI/ARDS.

MECHANICAL VENTILATION

Indications for initiation of mechanical ventilarory support

- Oxygenation abnormalities (Type I respiratory failure)
  - Refractory hypoxemia
  - Need for positive end-expiratory pressure (PEEP)
  - Excessive work of breathing
- Ventilation abnormalities(Type II respiratory failure)
- Respiratory muscle dysfunction
- Respiratory muscle fatigue
- Chest wall abnormalities
- Neuromuscular disease
- Decreased ventilarory drive
- Increased airway resistance and / or obstruction
- General considerations
- To permit heavy sedation and / or neuromuscular blockade
- To decease systemic or myocardial oxygen consumption
- To protect the airway in patients with decrease level of consciousness
- Need for mild hyperventilation as in increase ICP.

INTIAL VENTILATOR SETTINGS

- Mode of Ventilation

  - Use any familiar mode (e.g volume cycled mode)

  - Start preferably **by IPPV (intermittent positive pressure ventilation)**

  - **or AC (assist controlled ventilation)** to reduce work of

    - Breathing but watch for hypotension and hyperventilation.

    - All breaths are assisted.

    - During the control and assisted breaths, the tidal volume

      (Vt) and inspiratory flow and characteristics are exactly

      the same with each breath

  - Use **SIMV** (synchronized intermittent mandatory ventilation)

with **pressure support** (PS) of (5-10) to encourage synchronization

and reduce disuse muscle atrophy.

- If no breaths are initiated within a period of time, a mandatory

Breath will be delivered. If the machine senses that the patient has

taken a spontaneous breath just before the mandatory breath,

the machine will recycle and then wait for the next spontaneous breath and

Assist it.

- Fio2:

- When initiating ventilarory support in adults, an Fio2 level of 1.0 is

used so that maximal amounts of oxygen are available during the

patient's adjustment to the ventilator and during the initial attempts to stabilize the patient's condition .the Fio2 thereafter can be titrated

Downward to maintain the Spo2 at 92% - 94%.

- Tidal Volume
    - The usual recommendations for (Vt) levels are 8 to 10 ml/kg, in most patients, a VT level of 6-8 ml/kg may be used to avoid high inspiratory airway pressures and lung injury.
- Respiratory Rate
    - Choose a respiratory rate and minute ventilation appropriate for the particular clinical requirements. usually 10 – 12 breaths /min
- Peep
    - 5 cm of H2O in most patients to start with.
    - Use PEEP in diffuse lung injury to support oxygenation and reduce the Fio2 (PEEP levels >15 cm H2O are rarely necessary , if needed consider sedation and/or muscle paralysis)
        - Inspiratory flow
            - Use appropriate flow rates or a respiratory rate to avoid stacking breaths and auto-PEEP (40-80 L/mim)

- When there are difficulties with oxygenation, ventilation or excessive high inspiratory pressure which are not corrected by other interventions to achieve coordination between patient and ventilator, consider the use of deep sedation and/or muscle relaxant.

USE OF POSITIVE END – EXPIRATORY PRESSURE (PEEP)

- Initiation of PEEP:
- Initiate PEEP at 5 cmH2O and titrate up in increments of 2-3 cm H2O
- The full effect may not be apparent for several hours.
- Monitor the blood pressure, heart rate, and Pao2 during PEEP titration.
- Adverse effects of PEEP :
- Barotraumas/ volutrauma.
- Hypotension and decreased cardiac output
- Increase in Paco2
- Worsening oxygenation

MONITORING DURING MECHANICAL VENTILATION

- Inspiratory pressure (peak inspiratory and plateau pressure):
  - Potential adverse effects from high inspiratory pressure include barotraumas and reduced cardiac output
  - The inspiratory plateau pressure should ideally be maintained at <30- 35 cm H2O
  - Increase in peak inspiratory pressure (>40-45) indicates an increase in either airway resistance or decrease compliance of the lungs and chest wall, or both.
- When pressure increase reduce TV to reduce pressure.
  - if the peak pressure is increased but the plateau pressure is unchanged, the problem is an increase in
  - airway resistance, obstruction of the tracheal tube, airway secretions or acute bronchospasm
  - if the peak and plateau pressures are both increased the problem may by decrease complience: pneumothorax, lo-

bar atelectasis, acute pulmonary edema, worsening

- Pneumonia or ARDS.

- if the peak is decreased the problem may be an air leak in the system (e.g. tubing disconnection, cuff leak)

- Inspiratory time : expiratory time relationship (I:E ratio):

  - During spontaneous breathing, the normal I:E ratio is 1:2 ,

    in chronic lung diseases the exhalation time becomes

    prolonged the I:E ratio changes, e.g., 1:2.5 , 1:3 etc.

  - If the expiratory time is too short breath stacking may occur

    and this process may result in auto PEEP.

- To reduce the auto PEEP :

  - Shorten the inspiratory time

- Increasing the flow rate
- Decreasing VT
- Reduce respiratory rate

- Fio2
  - Inspired oxygen may be harmful to the lung parenchyma after prolonged exposure therefore, it is desirable to reduce the Fio2 to <0.5 (50 %) as soon as possible within 48hs.

- Minute ventilation:
  - The primary determinant of CO2 exchange during mechanical ventilation is alveolar minute ventilation calculated as VE = (VT – VD) X rate
  - Patients with chronic hypercapnia should receive sufficient minute ventilation during mechanical ventilation to maintain the PaCO2 at the patient's usual level
  - if acute respiratory deterioration with no change in peak inspiratory pressure, the problem may be : pulmonary embolus or extra thoracic process

- lung compliance : static lung compliance = Vt / Ppl- PEEP
    - Normal value is 50 to 80 ml/cm H2O; it will be low in patients with stiff lungs.
    - PEEP should be subtracted from the plateau pressure for the compliance determination
- Peep :
    - Decrease in venous O2 saturation after PEEP can be used as evidence for a PEEP induced decrease in cardiac output.
    - the best PEEP is the PEEP which will not increase the peak airway pressure
- Important monitoring during mechanical ventilation includes:
    - primary ventilator alarm functions (high pressure, low volume and apnea alarm
    - continuous pulse oximetry
    - physical assessment of the patient
    - intermittent arterial blood gases

- Chest radiographs as needed

COMMON PROBLEMS:

- Decrease oxygenation:
  - Increase FiO2.
  - Increase PEEP.
  - Change mode to pressure control.
  - Increase I:E ratio
  - Increase sedation.
  - Prone position
  - High frequency ventilation
  - Consider Muscle relaxant.
    - Increase PO2:
    - Decrease FiO2
    - Decrease I:E ratio
    - Decrease PEEP

- High PCo2:
  - Increase TV.
  - Increase rate.
    - Decrease Dead space>
    - Increase sedation.
  - Low PCo2:
  - Decrease TV.
  - Decrease Rate.

WEANING FROM MECHANICAL VENTILATION

- It is a daily practice to provide standardized protocol for weaning patients from mechanical

  Ventilation in the ICU.

DEFINITIONS

- PEEP : positive end expiratory pressure
- SIMV : Synchronized intermittent
- PSV : Pressure support ventilation.
- CPAP : Continuous positive airway pressure

- SB : Spontaneous breathing.

WEANING CRITERIA AND GUIDELINES

- Discontinuation from MV can be started when:
- The underlying reason for MV has been stabilized and the patient is
- improving and has good Cough.
- The patient is hemodynamically stable (HR< 140) on no or minimal
- pressors.
- Oxygenation is adequate (e.g.PO2 > 60, Po2/Fio2 > 200,
- PEEP < 5-10 cmH2O , Fio2 <0.4)
- The patient is able to initiate spontaneous inspiratory effort.
- Minute ventilation (L/min) < 15
- Tidal volume (ml/kg) > 4
- Respiratory frequency (breath/min) < 38
- **Frequency to tidal volume ratio (shallow**

breathing index) < 105

- Of all the indices rapid shallow breathing index had the highest positive and negative predictive values.
- Dynamic compliance (ml/cmH2O) > 22
- Static compliance (ml/cmH2O) >33
- Adequate mentation (GCS >13, Arousable, no continuous sedation)
- Afebrile (less than 38),
- No clinical significant respiratory acidosis and stable metabolic status
- (acceptable electrolytes)
- Being unable to generate a maximum inspiratory pressure of
- (- 15 cm H2O) had a negative predictive value of 100 %.
- Cuff leak should be tested prior extubation (> 20% of inhaled TV)

MODES OF DISCONTINUING MECHANICAL VENTILATION

- SIMV with gradual rate and pressure support reduction till reach 5 cm of H2O
- PSV with gradual reduction till 5 cm of H2o.
- SB "T- piece" for 30-120 mints most of the time tried daily till liberation of MV.
- Reventilate if the patient:
  - Exhausted, agitated or clammy
  - Tachypnoeic >35/min
  - Tachycardic >110/min
  - Respiratory acidosis, pH <7.2
  - Hypoxemic with Spo2 < 90%.

MANAGEMENT OF WEANING FAILURE

- If weaning failed, do not try weaning again for 24 hours.
- When the patient met the criteria for weaning but failed, this failure is predominantly due to inspiratory muscle fatigue.
- If patient extubated and failed, NPPV might be considered.

- Ways to increase respiratory muscle strength and decrease muscle demand

  - Increase muscle strength by :

    - Improve cardiovascular function

    - Discontinue sedative drugs

    - Reverse malnutrition and metabolic deficiencies:(hypokalemia, hypomagnesemia ,Hypocalcemia, hypophosphatemia, hypothyroidism)

    - Revert to SIMV mode.

    - Decrease muscle demand :

      - Maximize treatment of systemic disease (e.g., infection) to decrease metabolic requirement

      - Use diuretics to keep patients with lung edema on dry side to make lung less stiff

- If endotracheal tube size is small (<7 mm), consider changing to a larger size to avoid increased work of breathing.

GASTROINTESTINAL BLEEDING

OVERVIEW

- Acute gastrointestinal (GI) bleeding is common clinical emergency. Early recognition of clinical and endoscopic prognostic signs helps in the triage to the intensive care unit of patients at risk of rebleeding.

- Prognosis: The mortality rate from upper GI bleeding remains approximately 6% to 12%, while that from lower GI bleeding typically is <5%.

ETIOLOGY

Upper GI bleeding

A. Common causes:

- Duodenal and gastric ulcers and erosions
- Esophageal and gastric varices
- Esophagitis
- Mallory – Weiss tears

B. Uncommon causes

- Angiodysplasia

- Cancer
- Portal Gastropathy
- Aortoenteric fistula

Lower GI bleeding

A. Common causes

- Diverticulosis
- Angiodysplasia
- Cancer and polyps
- Colitis, including inflammatory bowel disease, infectious colitis, ischemic colitis.
- Hemorrhoids

B. Uncommon causes

- Anal fissure, rectal ulcers
- Vasculitis
- Meckel's diverticulum
- Colonic varices.

CLINICAL PRESENTATION

- Hematemesis indicates an upper GI bleed.
- Passage of red or dark red blood in the stool usually indicate lower intestinal bleeding
- Repeated passage of liquid bloody stool indicates ongoing or recurrent bleeding because fresh blood has laxative properties.
- Passage of black, sticky, tarry stool (melena) usually indicates upper GI bleeding.
- Melena can persist for several days, and the stool may remain positive for occult blood for up to 2 weeks after GI bleeding has ceased.
- Bright or dark red blood in the stool is infrequently seen with an upper GI bleeding source, but, when it occurs, indicates rapid bleeding; it is usually associated with hemodynamic compromise.

WORK-UP

- Nasogastric aspiration
  - Passage of a nasogastric tube may help to detect upper GI bleeding in patients with an obscure bleeding site.

- Further use of nasogastric tube for lavage. Help removes clots from the stomach in preparation for endoscopy and provide an indication of the acuity and rapidity of bleeding.

- Endoscopy

  - Endoscopy is performed when the patient is hemodynamically stable but resuscitation usually is ongoing at the time of the procedure.

  - When a bleeding site proximal to the jejunum is suspected, esophagogastroduodenoscopy (EGD) is the diagnostic procedure of choice.

  - When a lower GI bleeding source is suspected colonoscopy, after bowel preparation, may be helpful. Help to detect and treat colonocopic bleeding sources or to localize fresh blood to a segment of colon and to direct other therapeutic measures.

  - Push enteroscopy evaluates the proximal small bowel when a bleeding site is not found in the upper GI tract or colon on conventional endoscopy.

  - While EGD is frequently performed with therapeutic intent in the course of bleeding, other endoscopic procedures typically are performed after the bleeding has ceased or in patients with subacute bleeding.

- Imaging studies

  - A 99m Technetium(99m Tc) labeled red blood cell scan can detect bleeding rates as low as 0.1 ml/ minutes and is reasonable initial imaging test in the patient with signs of active bleeding distal to the upper GI tract..

  - If active bleeding is found, angiography often is indicated for confirmation of the site and administration of intra-arterial vasopressin or embolization of the bleeding artery for bleeding control.

MANAGEMENT

- Initial approach

  - Rapid evaluation – All haemodynamically unstable patients should be admitted to ICU

    - Mental confusion, agitation, diaphoresis, mottled skin (livedoreticolaris), and cold extremities accompany hypotension with hemorrhagic shock.

    - A quantitative estimate of the amount of bleeding is helpful because the initial blood count may not reflect the degree of blood loss.

- Initial blood testing should be performed urgently to obtain baseline hemoglobin/hematocrit values, measures platelet count and coagulations parameters, and type and cross-match blood for transfusion.

- Resuscitation

  - Recognizing and aggressively treating intravascular volume depletion is of the highest priority and should proceed concurrently with the initial diagnostic evaluation.

  - Intravenous access with large-bore peripheral catheters or central venous catheter is needed for aggressing administration of fluids or blood product.

  - Massive hematemesis may require endotracheal intubation for airway protection before endoscopy.

- Acid suppression

  - Early treatment with oral or intravenous proton-pump inhibitors is standards in acute upper GI bleeding.

- Octreotide

  - Octreotide (usually administered as 25 – 100 µg IV bolus followed by a continuous infusion at 25

-50 µg/hour for 48 to 120 hours) should be initiated if a variceal bleed is suspected.

- Endoscopy

  - Endoscopic therapy, using thermal device (heater probe, electrocoagulation, lasser), hemoclips, injection therapy) sclerosing solutions, hypertonic saline, epinephrine), or banding devices, offers a convenient and expedient methods of treating upper GI bleeding from many causes.

  - Recurrent bleeding occurs in up up to 30% of patients with bleeding ulcers despite successful endoscopic therapy, and continued observation for up to 72 hours is recommended.

  - Endoscopic therapy is of use for some colonic bleeding sites, such as angiodysplasia.

- Angiographic Therapy

  - Intra-arterial vasopressin has been used for angiographic management of upper and lower GI bleeding.

  - Vasopressin use is attended by risk of cardiovascular complications.

- Gelfoam or metal coil embolization of the bleeding artery is an alternate approach which causes localized thrombosis and vessels occlusion, tissue ischemia and perforation are potential complications.

- Surgery

  - Surgical consultation should be obtained early in patients with clinical and endoscopic risk factors for high morbidity and mortality.
  - Patients with massive ongoing hemorrhage that overwhelms the resuscitative effort need urgent surgical assessment.
  - Patients failing to respond to endoscopic or angiographic management also need surgical assessment.
  - Arterial embolization and transjugular intrahepatic portosystemic shunts for variceal bleeding are alternatives in high-rick surgical candidates.

PROPHYLAXIS

- Small-bore feeding tubes
- Nasogastric enteral nutrition
- Adequate tissue perfusion (flow and pressure)
- Prophylactic drugs therapy (proton pump inhibitor, H_2 antagonist)

VARICEAL BLEEDING

OVERVIEW

- Variceal bleeding is the most common lethal complication of cirrhosis.
- The mortality of an acute bleeding episode is 20% at 6 weeks.
- Varices are present in 50% of patients with cirrhosis.
- Spontaneous bleeding occurs at rate of 5% to 15% per year.
- Mortality is often related to liver decompensation, aspiration, hepatic encephalopathy, hepatorenal syndrome, and septicemia.

CLINICAL PRESENTATION

- Variceal bleeding typically is brisk, presenting as hematemesis, melena or bright red blood per rectum, and varying degree of hemodynamic instability.
- Acute bleeding is self-limited in 50% to 60% of case; there is a high rate of bleeding without appropriate therapy.
- Approximately a third of the patients with stigma of chronic liver disease who present with acute upper gastrointestinal bleeding have nonvariceal sources of hemorrhage, and endoscopic verification is required.

WORK-UP

- Variceal bleeding is diagnosed by upper endoscopy

- Findings suggestive of a variceal bleed include a fresh fibrin clot protruding from a varix, a nipple-like protrusion from a varix, red signs, or varices with no other potential bleeding source.

MANAGEMENT

- Initial resuscitation

  - Approximate resuscitative efforts should be initiated without delay and before endoscopic evaluation. Hemodynamic stability and hemoglobin of approximately 8g/dl are the goals.

  - Packed red blood cell transfusion, fresh frozen plasma, and platelet infusion may be necessary before endoscopy, depending on initial laboratory results.

  - Nasogastric aspiration may be necessary when the diagnosis of an upper gastrointestinal hemorrhage is in doubt. Nasogastric aspiration not only aids in diagnosis but can guide resuscitation efforts based on degree of hemorrhage and clear the stomach and esophagus of blood before upper endoscopy.

  - Airway protection with endotracheal intubation is

manadatory in the massively bleeding or obtunded patient.

- Pharmacotherapeutic agents

  - Octreotide is the pharmacotherapeutc agent of choice in acute variceal bleeding

    - A bolus of 50µg is followed by a continuous infusion of 50µg hours 48 to 72 hours

    - Octreotide is effective in stopping active bleeding from varices and is an important role in the prevention of early recurrent bleeding the initial hematemesis.

  - Vasopressin, when infused intravenously, is a potent vasoconstrictor the reduces splanchnic blood flow and portal pressure.

    - Adverse cardiac effects (myocardial ischemia, hypertension)

    - The starting dose is typically a 0.4 U bolus and 0.4 U/minute, titrated to a maximum of 0.8 – 1 U/minute if required for bleeding control.

    - Concurrent intravenous nitroglycerin infusion, starting at 10 µg/minute and titrated to maintain a systolic blood pressure (SBP) of

100 mm Hg, has been shown to reduce the systemic side effects of vasopressin.

- Used only when octreotide is not available.

- Nonselective β-blocker should not be used in acute variceal bleeding as they can contribute to hypotension and block the physiologic increase in heart rate. These medication are indicated for primary and secondary prevention of variceal bleeding, but are initiated electively and not in the acute bleed setting.

- Endoscopic therapy

  - Band ligation is the technique of choice for endoscopic control of bleeding varices

    - Active bleeding is controlled in 80% to 90% of patient after one or two treatment

    - Band ligation has a lower incidence of esophageal ulceration, stricture formation, perforation, bacteremia, and respiratory failure compared to sclerotherapy

    - Serial scheduled endoscopic treatment sessions at weekly to monthly intervals ensure obliteration of the varices.

- Sclerotherapy

  - A sclerosant solution is injected into the variceal lumen or into the adjacent submucosa.

  - This technique is reserved for massive bleeding, wherein visualization of the variceal columns to perform band ligation is impossible, and for gastric variceal bleeding.

- Antibiotics prophylaxis is recommended to prevent infection and bleeding in all cirrhosis patients with variceal bleeding. Ciprofloxacin 400mg BID & Ceftriaxone 1g/day.

- Balloon tamponade

  - Gastric and esophageal balloon devices for direct tamponade of the bleeding varices (Sengstaken-Blakemore) may be required for patients with severe or persistent bleeding.

  - Initial success approaches 90%, but rates of recurrent bleeding are high.

  - Complication occurs in 15% to 30% of patients.

  - Endotracheal intubation should precede balloon placement for airway protection.

- Transjugular intrahepatic portosystemic stent (TIPS) shunt

  - TIPS are an iatrogenic fistula between radicals of the hepatic and portal veins, created by interventional radiologist using ultrasonographic and fluoroscopic guidance. An expandable metal stent is left in the place, and the portosystemic pressure gradient is reduced to <12 mmcof Hg. Cross-sectional imaging of the liver is necessary before TIPS placement to evaluate the patency of the portal vessels as well as to rule out liver masses.

  - TIPSis recommended if bleeding continuous despite combined pharmacologic and endoscopic therapy. If bleeding recurs after two endoscopic attempts at prevention, or if bleeding has occurred from gastric varices or portal hypertensive gastropathy.

  - The technical success rate in constructing a TIPS is >90%

  - Insufficiency is seen in 15% to 60% of patients within 6 months.

  - Twenty percent to 30 % of patients develop transient deterioration of liver function after elective shunt placement, and up to one fourth of patients may experience new or worsened hepatic encephalopathy.

ACUTE LIVER FAILURE ALF

OVERVIEW

- Acute liver failure (ALF), also known as fulminant hepatic failure, is an uncommon condition.
- ALF is defined as the development of encephalopathy within 24 weeks of the onset of jaundice in individuals without pre-existing liver disease.
- ALF can be subdivided into three catergories based on the time from jaundice to encephalopathy:
  - Hyperacute liver failure (7 days)
  - ALF (8 to 28 days)
  - Subacute liver failure (>29 days)
- **Etiology**

  The causes of ALF are many.

  A. **Acute viral hepatitis**

  - Hepatitis A
    Cytomegalovirus
  - Hepatitis B
    Varicella zoster virus

- Hepatitis C
  Adenovirus
- Delta Agent
  Ebsteinbarr virus
- Hepatitis E
  Herpes virus

B. Metabolic disorders

- Acute fatty liver pregnancy
- HELLP syndrome
- Wilson's disease

C. Cardiovascular disorders

- Budd Chiari syndrome
- Cardiovascular shock
- Hyperthermia

D. Drug and Toxins

- Acetaminophen
- Sodium valproate

- Isoniazid
- Halothane
- Indentification of the cause of ALF is important for several reasons:
  - Specific treatments are available for drug and toxin overdoses.
  - Prognosis varies with cause
- A specific cause for ALF may be unidentifiable in as many as 20% of adult cases

CLINICAL PRESENTATION

- Encephalopathy and cerebral edema
  - All patients with ALF have encephalopathy, with symptoms ranging from subclinical confusion (grade 1) to coma (grade 4).
  - Cerebral edema occurs up to 80% of patients with ALF and grade 4 encephalopathy and can result in death from brain herniation.
- Coagulopathy
  - Prolongation of international normalized ratio (INR) and activated partial thromboplastin

time occurs as a consequence of reduced hepatic synthesis of vitamin K-dependent coagulation factors.

- The combination of severe coagulopathy and platelet dysfunction can result in bleeding even in minor mucosal lesions.

- Cardiorespiratory complications

  - Typical hemodynamic changes in ALF mimic distributive shock: increase cardiac output, decreased peripheral oxygen extraction, and low systemic vascular resistance.

  - The development of arterial hypertension may herald the development of cerebral edema

  - Hypoxemia can result from cardiogenic shock, noncardiogenic pulmonary edema, pneumonia, or arveolarhemorrhage.

- Renal Failure

  - Renal failure in ALF can result from acute tubular necrosis, prerenal azotemia, or the hepatorenal syndrome (HRS).

- Metabolic disorder

  - Lactic acidosis develops as the combined conse-

quence of tissue hypoxia with increased lactate production and impaired hepatic metabolism of lactate, renal dysfunction also may contribute.

- Hypoglycemia as a consequence of the loss of hepatic gluconeogenesis and glycogenlysis and signifies sever hepatocellular injury.

- Infection

  - Patients with ALF are at risk for bacterial and fungal sepsis

  - The most common organisms isolated include Staphylococcus, Streptococcus, gram-negative enteric organisms, and Candida spp.

  - Fungal infections occur late in the course of illness and are associated with high mortality.

WORK-UP

- CBC
- LFT's
- Renal profile
- Coagulation profile
- ABG

- Hepatitis screen
- Drug screen

TREATMENT AND MANAGEMENT

- General measures
  - Early identification of the cause of ALF is critical
  - Laboratory assestment of hepatic synthetic function, renal function, and acid-base status provides useful prognostic information.
  - Invasive hemodynamic monitoring is useful in the management of hemodynamic changes associated with ALF.
- Sepsis
  - Surveillance cultures of blood, sputum, and urine should be collected with a low threshold for the use of empiric antibacterial and/or antifungal therapy.
  - Coagulopathy: the correction of the coagulopathy with fresh frozen plasma (FFP) or platelet transfusion should be reserved for active bleeding or prevention of bleeding during invasive procedures, as excessive blood product transfusion may worsen cerebral and pulmonary edema

- Administration of vitamin K is safe but often ineffective.

- Parenteral Administration of recombinant factor VIIa may reverse the coagulopathy.

- Encephalopathy and cerebral edema

  - Frequent neurological examination, including assessment of level of alertness, papillary response to light and motor reflexes.

  - Nursing with head of bed at >30 degree elevation may improve cerebral venous drainage.

  - Treatment options for increased ICP include hyperventilation to maintain an arterial carbon dioxide partial pressure 30 to 33 mm Hg, intravenous (IV) mannitol (0.5 to 1g/kg), and hypothermia to a core body temperature of 32 ºC

- Metabolic disorders

  - Volume resuscitation with colloid is preferable for the treatment of prerenal azotemia.

  - Hemodialysis may be required.

  - Prevention of hypoglycemia is essential for preservation of neurologic function; frequent glucose monitoring and infusions of 10% to 50% dextrose

solutions may be required.

- Acetaminophen toxicity. The administration of N-acetylcysteine (NAC) is an effective, life-saving antidote to acetaminophen toxicity.

  - NAC is most effective when given within the first 24 hours after ingestion; NAC may still be usful even when treatment is delayed >24 hours or when signs and symptoms of ALF have developed.

  - NAC can be given as a continuous IV infusion 150mg.kg IV given over 15 minutes followed by 50mg/kg IV given over 4 hours then 100mg/kg IV given over 20hours

- Liver Transplant: Patients with ALF without contraindications to LT should be managed at LT center.

  - The King's College criteria can be useful to identify poor prognostic fators that identify individuals who require LT for survival.

KING'S COLLEGE CRITERIA FOR LIVER TRANSPLANTATION FOR ACUTE LIVER FAILURE (ALF)

1. Nonacetaminophen causes of ALF

INR > 7.7 (irrespective of grade of encephalopathy) or any three

of the following

Age < 10 or > 40

Unfavorable cause

Non-A, Non-B hepatitis

Drug reaction

Wilson's disease

Period of jaundice to encephalopathy >7 days

INR > 3.85

Serum bilirubin >17 mg/dl

2. Acetaminophen-related ALF

PH < 7.3 (irrespective of grade of encephalopathy) or all three of the following

Grade III-IV encephalopathy

INR > 7.7

Serum creatinine> 3.4mg/dl

INR, international normalized ratio

HEPATIC ENCEPHALOPATHY

GRADING

- Confused, altered mood.
- Inappropriate, drowsy.
- Stuporose buy rousable, very confused, agitated.
- Coma, unresponsive to painful stimuli.
- The risk of cerebral oedema is far higher at grades 3 and 4, suggestive signs include systemic hypertension, progressive bradycardia, and increasing muscle rigidity at ICP >30mmHg.

MANAGEMENT

- Correct/avoid potential aggravating factors, e.g. gut haemorrage, oversedation, hypoxia, hypoglycaemia, infection, electrolyte imbalance.
- Consider (ICP) monitoring.
- Maintain patient in slight head-up position (20-30 º)
- Regular lactulose, e.g. 20-30mL qds PO, to achieve 2-3 bowel motions/day.
- Give mannitol (0.5-1mg/kg over 20-30min) if serum osmolality <320mOsm/kg and either a raised ICP or clinical signs of cerebral oedema persist. If severe renal

dysfunction is present, use renal replacement therapy in conjunction with mannitol. Consider maintaining NA^+ 145-155mmol/L.

- Sodium benzoate (2g tds PO) may be considered if the patient is severely hyperammonaemic.

- If still no response, consider possibility of liver transplantation.

IDENTIFICATION OF PATIENTS UNLIKELY TO SURVIVE WITHOUT TRANSPLANTATION

- Prothrombin time >100s
- Or any three of the following:
  - Age <10 ro>40 years.
  - Aetiology is seronegative hepatitis. Wilson's disease , halothane or other drug reaction.
  - Duration of jaundice pre-encephalopathy >7days.
  - Prothrombin time >50 seconds.
  - Serum bilirubin >300umol/L.
- If paracetamol-included:
  - PH<7.3 or prothrombin time >100s and creatinine>200umol/L plus grade 3 or 4 encephalopathy.

ACUTE PANCREATITIS

OVERVIEW

- Definitions
  - Clinically acute pancreatitis: process of rapid onset associated with pain and alterations in exocrine function.
  - Morphologically acute pancreatitis: occurs in a gland that was and will be functionally normal before and after the attack.
  - Pathologically acute pancreatitis:
    - Mild: associated with interstitial edema, intrapancreatic, or peripancreatic acute necrosis
    - Severe: associated with focal or diffuse acinar cell necrosis, thrombosis of intrapancreatic vessels, intraparenchymal hemorrhage, and abscess formation
- Etiology
  - Biliary tract stone disease
  - Ethanol abuse
  - Drugs:
    - Most commonly seen in patients with acquired

immunodeficiency syndrome (AIDS) receiving dideoxyinosine and pentamidine or transplant or inflammatory bowel disease (IBD) patients receiving azathioprine.

- Diuretics: thiazides, ethacrynic acid, and furosemide have high association with pancreatitis.

- Pancreatic duct obstruction
    - Tumors: duodenal, ampullary, biliary tract, or pancreatic
    - Inflammatory lesions, peptic ulcer, duodenal.
    - Pancreatic cysts
    - Ductal strictures
    - Parasites: Ascaris

- Miscellaneous causes of acute pancreatitis
    - Traumatic
    - Postoperative: duct exploration, sphincteroplasty, (ERCP)

- Idiopathic pancreatitis
    - Affects 5% to 10% population

CLINICAL PRESENTATION

- Symptoms: epigastric abdominal pain of rapid onset, nausea, vomiting
- Physical examination
  - Tachycardia, tachypnea, diaphoresis, hyperthermia, restlessness, and jaundice (20% incidence)
  - Abdominal tenderness with voluntary and involuntary guarding, rebound, distension, and diminished or absent bowel sounds.
  - Flank ecchymoses (Grey Turner sign) or other evidence of retroperitoneal bleeding (Cullen sign) ecchymoses around umbilicus
  - Chest examination may reveal evidence of atelectasis and left pleural effusion.

DIFFERENTIAL DIAGNOSIS

- Perforated hollow viscus
- Cholecystitis/cholangitis
- Bowel obstruction
- Mesenteric ischemia/infarction

WORK-UP

- Routine blood tests
    - Increased hemoglobin, hematocrit (HCT), blood urea nitrogen (BUN), creatinine, bilirubin, white blood cells (WBCs), glucose, and trighycerides
    - Decreased calcium, albumin
- Amylase
    - Level increase 2 to 12 hours after attack onset; normalize after 3 to 6 days.
    - Usually elevated to levels >1,000 IU/L.
- Serum lipase remains elevated for days after the attack.
- Routine radiography
- Chest radiograph: left pleural effusion, basal atelectasis
- Ultrasonography: detection of gallbladder stones or bile duct dilatation, or both
- Computed tomography (CT):
    - Mild pancreatitis – normal or slightly swollen pancreas with streaking of retroperitoneal or transverse mesocolic fat

- Severe pancreatitis – peripancreatic or intrapancreatic fluid collections

- Dynamic CT – areas of pancreatic necrosis that fail to enhance with contrast administration

TREATMENT AND MANAGEMENT

- TREATMENT OF ACUTE PANCREATITIS

  - Treatment of pain. Pethidine is the drug of choice; it relaxes the sphincter of Oddi.

  - Fluid and electrolyte replacement

    - Initially – hypochloremic alkalosis due to vomiting

    - Later – metabolic acidosis due to hypovolemia and poor tissue perfusion

    - Hemodynamics in severe attacks resemble shock: increased heart rate, cardiac output, cardiac index (CI), arterial-venous oxygen difference; decreased pulmonary vascular resistance (PVR); hypoxemia

    - Intravenous imipenem or meropenem for 14 days may be of benefit in patients with infected pancreatitis by reducing mortality and morbidity.

- Fluconazole decreases the emergence of resistant fungi.

- Use of early enteral nutrition (initiated within 36 hours of symptom onset) has shown benefit over parenteral nutrition in terms of duration of hospital stay, infectious morbidity, and need for surgery.

- Antibiotic propyhlaxis does not reduce the risk of infectious complications and is associated with an increased risk of mortality.

- Severe gallstone pancreatitis – early surgical or endoscopic intervention

- TREATMENT OF SYSTEMIC COMPLICATIONS

  - Aggressive fluid and electrolyte therapy may be the most effective method of preventing pulmonary and renal failure.

  - Pulmonary toilet and monitoring of pulmonary function with arterial blood gas measurements.

  - Prophylaxis with either antacids or H_2-blockers may prevent stress-induced bleeding of gastroduodenal lesions,

PROGNOSIS

- Approximately 5% to 10% will have severe attack associated with 40% morbidity and mortality
- Ranson's prognostic signs
  - On admission: age older than 55 years; WBC > 16,000/mm^3; glucose > 200mg/dL; lactate dehydrogenase (LHD) >350 IU/L; glutamicoxaloacetic transaminase (GOT) >250 U/dL
  - After 48hours: HCT decrease >10%; BUN rise >5mg/dL; serum calcium <8mg/dL; Pao_2<60mm Hg; base deficit >4 mEq/L; fluid sequestration >6L
  - Less than three criteria: mild pancreatitis – 1% mortality
  - Seven or eight criteria: severe pancreatitis – 90% mortality
  - Admission to ICU of >Ranson's≥ 3
- APACHE-2 another useful system to evaluate severity of an attack if >8
- Peripancreatic fluid collections on CT scan

- Two or more fluid collection – 61% incidence of late pancreatic abscess

- One fluid collection – 12% to 17% incidence of pancreatic abscess

- Pancreatic enlargement only – zero incidence of pancreatic abscess

ACUTE MESENTERIC ISCHEMIA (BOWEL ISCHEMIA)

OVERVIEW

- Defined as compromise of intestinal mesenteric arterial or venous flow, which may occur acutely or over the course of several weeks

- Intestine is deprived of blood and oxygen leading ischemia, acidosis, leukocytosis, and the development of sepsis and multiple organ failure.

- Risk factors include advanced age, atrial arrhythmias, history of congestive heart failure or recent myocardial infarct, and valvular heart disease.

- **Etiology**

- Approximately 50% of cases of acute mesenteric ischemia are due to arterial embolic event, 25% of cases are the result of arterial thrombosis, 20% to 30% of cases are due to nonocclusive mesenteric ischemia (NOMI), and fewer than 10% of cases are the result of mesenteric venous thrombosis (MVT).

- Mesenteric arterial embolism and thrombosis involve the superior mesenteric artery (SMA) almost exclusive.

- Emboli from a cardiac source typically lodge at the first branch point of the SMA. Arterioarterial emboli tend

to be smaller and lodge in the more distal concurrent atherosclerotic stenosis

- Thrombosis usually develops at or near the origin of vessels or areas of concurrent atherosclerotic stenosis

- NOMI is caused by primary splanchnic vasoconstriction resulting in a low flow state to the mesenteric vascular bed.

- MVT is a rare disorder resulting on hypercoagulable states.

CLINICAL PRESENTATION

- Hallmark of acute mesenteric ischemia is pain out of proportion to the physical examination

- Onset of pain may be accompanied by gut emptying-vomiting, bowel movement, or diarrhea.

- Physical examination may reveal abdominal tenderness, which is not well localized and hypoactive to absent of bowel sounds, with progression of disease to bowel infarction and perforation, the patient will develop peritoneal findings.

- High index of suspicion in patients with preexisting cardiac disease and critically ill patients with a shock state from trauma, burns, and sepsis.

WORK-UP

- Laboratory
  - CBC
  - Renal Hepatic coagulation profiles
  - Amylase
  - ABG Serum lactate
    - Elevation of serum amylase concentration
    - Elevation of serum lactate, often implies severe ischemia or bowel infarction
    - Most common laboratory abnormality is a persistent and profound leukocytosis.
    - Electrolyte derangement from dehydration and acidosis seen in the advanced stage of intestinal infarction.
- Imaging
  - Plain radiographs. Late findings include distended bowel loops with air fluid levels, bowel wall thickening, gas within the mesenteric venous circulation and free air.
  - Computed tomography (CT) using an intravenous(IV) contrast agent
  - Angiography remains the “gold standard” for imaging of mesenteric occlusion.
- Others
  - ECG, ECHO

TREATMENT

- SMA embolism

- Arteriotomy with embolectomy

- Perform bowel resection after revascularization unless faced with an area of Franck necrosis or perforation and peritoneal soilage, second look laparotomy within 48hours.

- SMA thrombosis

- SMA bypass. In patients with obviously infarcted bowel or bowel perforation, autogenous vein is the preferred conduit.

- NOMI

    - Expedient management of cardiac events and shock state are essential. Systemic vasoconstriction should be avoided and replaced by vasodilators that diminish cardia preload and afterload.

    - Pharmacologic treatment may involve selective intra-arterial infusion of papaverine into SMA.

    - If peritoneal signs develop or abdominal pain persists despite papaverine infusion, emergent exploratory laparotomy indicated.

- Mesenteric venous thrombosis

  - Bowel rest and anticoagulation.

  - Surgery reserved for complications (e.g. intestinal infarction) Management involved bowel resection and venous thrombectomy.

INTESTINAL PERFORATION/OBSTRUCTION

OVERVIEW

- Upper bowel perforation can be described as either free or contained. Free perforation occurs when bowel contents spill freely into the abdominal cavity, causing diffuse peritonitis (e.g, duodenal or gastric perforation). Contained perforation occurs when a full-thickness hole is created by an ulcer, but free spillage is prevented because contiguous organs wall off the area. Lower bowel perforation results in free intraperitoneal contamination.

- Frequency

  - Duodenal ulcer perforations are 2-3 times more common than are gastric ulcer perforations. About a third of gastric perforations are due to gastric carcinoma.

  - Approximately 10-15% of patients with acute diverticulitis develop free perforation. Although most episodes perforated diverticulum are confined to the peridiverticular region or pelvis.

- Etiology

  - Penetrating injury to the lower chest or abdomen (e.g, knife injuries). The small bowel is the most commonly injured intra-abdominal viscus.

  - Blunt abdominal trauma to the stomach include motor

vehicle-related trauma

- Ingestion of aspirin, nonsteroidal anti-inflammatory drugs (NSAIDs) and steroids, particularly observed in elderly patients.
- Presence of a predisposing condition, peptic ulcer disease, acute appendicitis, acute diverticulitis.
- Bowel injuries associated with endoscopy – injuries can occur with ERCP and colonoscopy.
- Endoscopic biliary stent
- Intestinal puncture as a complication of laparoscopy
- Inflammatory bowel disease
- Perforation secondary to intestinal ischemia
- Bowel perforation by intra-abdominal malignancy, lymphoma , or metastatic renal carcinoma
- Radiotherapy of cervical carcinoma and other intra-abdominal malignancies
- Ingestion of caustic substances
- Foreign bodies (e.g. Toothpicks)

CLINICAL PRESENTATION

- History

A careful medical history often suggests the source of the problem

- Penetrating injury or blunt trauma to the lower chest or abdomen
- Aspirin, NSAIDs, or steroid intake
- Treatment for peptic ulcer disease or ulcerative colitis
- Abdominal pain
- Vomiting
- History of travel to or of residing in tropical areas, with symptoms suggestive of typhoid fever (e.g. Fever, abdominal pain, abdominal distension, constipation, bilious vomiting)
- History of endoscopic procedures
- History of chronic disease, such as ulcerative colitis

- Physical

- Take vital signs and assess for any hemodynamic

changes.

- Abdominal examination:

  - Examine the abdomen for any external signs of injury, abrasion, and/or ecchymosis. Observe patients' breathing patterns and abdominal movements and breathing, and note any abdominal distension or discoloration.

  - Carefully palpate the entire abdomen, noting any masses or tenderness. Tachycardia, fever, and generalized abdominal tenderness may suggest peritonitis.

  - Bowel sounds are usually absent in generalized peritonitis.

  - Rectal and bimanual vaginal and pelvic examination

DIFFERENTIAL DIAGNOSIS

- Peptic ulcer disease
- Gastritis
- Acute pancreatitis
- Cholecystitis, biliary colic

- Acute gastroenteritis
- Ovarian torsion
- Pelvic inflammatory disease

WORK-UP

- CBC
- Hepatic profile
- Renal profile
- Coagulation profile
- Chest X-ray may show free as under diagram
- X-rays supine and either erect or lateral abdominal X-ray may reveal either free gas in the peritoneum (perforation) or dilated bowel loops with multiple fluid levels (obstruction).
- CT may identify the site of perforation or obstruction.

MANAGEMENT

Patient with bowel perforation or obstruction may be admitted to the ICU Before surgery, for preoperative resuscitation, and cardiorespiratory optimisation, or for concervative management or after surgery for haemodynamically monitoring.

- Correct fluid and electrolyte abnormalities. Resuscitation should be prompt and aggressive. Inotropes or vasopressors may be required to restore an adequate circulation, particularly following perforation.

- Prompt surgical exploration should be encouraged if the patient shows signs of systemic toxicity.

- Both conservative and post-operative management of perforation and obstruction usually require continuous nasogastric drainage to decompress the stomach, nil by mouth, and parenteral nutrition.

- Pain relief should not be withheld

- Broad-spectrum antibiotic therapy should be started for bowel perforation after approximate specimens have been taken for laboratory.

- Post-operative management of bowel perforation may involve repeated laparotomies to exclude collections of pus and bowel ischaemia/infacrtion.

CONTRAINDICATIONS

- Surgery is contraindicated if the patient refuses the operation and no evidence of generalized peritonitis exists.

- Surgery is contraindicated if a contrast meal confirms spontaneous sealing of the perforation and the patient prefers a nonsurgical approach.

COMPARTMENT SYNDROMES

COMPARTMENT SYNDROMES OF THE EXTREMITIES

OVERVIEW

- Compartment syndromes are typically described in two areas: extremities, abdomen.
- Anatomically, extremity compartments are formed by fascial layers surrounding muscle groups.
- As compartment pressure increases, nerves, followed by muscles, and loss of function.
- Extremity compartment syndrome can occur in the calf, thigh, buttock, forearm, arm, hand, or foot. The most frequent area affected is the anterior compartment of the calf.
- **Etiology**
  - Extremity compartment syndrome: Crush ischemia, arterial injury, vascular ligation, fracture, direct blunt trauma (with hematoma or edema), prolonged external pressure, and electrical injury.
  - Secondary extremity compartment syndrome: hypotension and/or massive volume resuscitation lead to whole body tissue edema, including the muscles of the various compartments.

CLINICAL PRESENTATION

- High index of suspicion is the key.
- Clinical examination:
  - Tense or tight compartments to touch
  - Pain disproportionate to associated injury
  - Increased pain with passive muscle stretch (classically for anterior calf compartment: dorsiflexion of the great toe).
  - Hypesthesia and/or muscle weakness.
  - Distal pulses remain intact

WORK-UP

- Measurement of compartment pressure by 18-GA needle and arterial line setup
- Commercial device with direct readout
- Less than 20 mm Hg is usually not problematic, > 30 is clearly abnormal and requires fasciotomy.
- Between 20-30 mmHg managed individually with other clinical suspicion.

TREATMENT

- First step is always to remove constricting wraps or dressings, any cast.
- Fasciotomy
  - Prophylactic, if high enough index of suspicion or with prolonged ischemia or ligated major vein, especially in the face of a proximal arterial injury.
  - Mandatory for high compartment pressure
  - Skin left open

RED FLAG

- Watch For Complications
  - Rhabdomyolysis
  - Ischemic neourapthy
  - Myonecrosis and fibrosis
  - Renal failure from myoglobinemia
  - Reperfusion syndrome

ABDOMINAL COMPARTMENT SYNDROME (ACS)

OVERVIEW

- Abnormally high pressure in the abdomen = intra-abdominal hypertension that causes physiological consequences.
- Renal function, ventilator dynamics, and cardiovascular performance may all suffer.
- May be divided into primary ACS and secondary ACS based on etiology.
- Etiology

A. Primary ACS

- Abdominal injury or disease
- Postoperative abdominal surgery
- Ascites in critically ill cirrhotic patients

B. Secondary ACS

- Massive volume resuscitation, typically after trauma or burns
- Medical problems, such as sepsis and multiple organ failure

- Space-occupying fluid in the abdomen (blood, ascites)
- Edematous tissue in the abdomen (bowel, retroperitoneum)
- Space-occupying hematomas in the retroperitoneum (including the associated with pelvic fractures)

- Pathophysiology

A. Decreased venous return

- Causes renal dysfunction
- May cause elevation in intracranial pressure (ICP)

B. Abdominal contents exert pressure through the diaphragm

- Respiratory dysfunction
- Cardiovascular dysfunction
- GIT and Liver dysfunction

CLINICAL PRESENTATION

- Hallmarks are tensely distended abdomen
- May also have decreased cardiac output, decreased pulmonary function, and/or increased ICP.

WORK-UP

- Intra-abdominal pressure measurement is helpful
- Methods of measurement
- Bladder pressure
    - Method: clamp Foley; instill 50 to 100 mL normal saline (NS), measure pressure at level of symphysis.
    - Results: > 12mm Hg is abnormal, 25 to 35 mm Hg is the range for operative decompression in the operating room (OR).

TREATMENT

- Elevated intra-abdominal pressure alone is not an indication for operative decompression. The patient must also demonstrate evidence of organ dysfunction.
- Laparotomy to decompress in OR – beware of reperfusion syndrome

- Temporary abdominal closure
    - Intravenous (IV) bag sewn to skin
    - Vacuum pack
    - Close abdomen
    - Primarily after a few days delay, if possible

RED FLAG

- Watch for Complications
- Multiple organ dysfunction/failure
- Renal failure
- Pulmonary failure
- Cardiovascular failure

ACUTE RENAL FAILURE

OVERVIEW

- Acute renal failure (ARF) remains a major diagnostic and therapeutic challenge for the critical care physician. Today, acute kidney injury (AKI) is considered the correct nomenclature for the clinical disorder formerly termed 'acute renal failure' (ARF).

- The Syndrome is characterized by abrupt—that is, hours to days—decline in the kidney's ability to eliminate waste products. Such loss of function is marked by the accumulation of end products of nitrogen metabolism such as urea and creatinine.

- ARF has been reported in 5% to 25% of critically ill patients.

- Etiology

  - **Prerenal:** renal blood flow (RBF) is diminished by decreased cardiac output, hypotension, or raised intra-abdominal pressure. A pressure of greater than 25 to 30 mm Hg above the pubis should prompt consideration of decompression. Treatment of the cause while promptly resuscitating the patient by using invasive hemodynamic monitoring to guide therapy.

  - **Parenchymal Renal Failure:** the principal source of damage is within the kidney and where typical structural changes can be seen on microscopy. **Causes of**

Parenchymal ARF are, Glomerulonephritis, Vasculitis, Renovascular, Interstitial nephritis, Nephrotoxins, Tubular deposition/obstruction, renal allograft rejection& Trauma and surgeries.

- **Drugs That May Cause Acute Renal Failure in the Intensive Care Unit:**

  - Radiocontrast media, Aminoglycosides, Amphotericin, Nonsteroidal anti-inflammatory drugs, β-

  - Lactam antibiotics (interstitial nephropathy), Sulphonamides, Acyclovir, Methotrexate, Cisplatin &

  - Cyclosporin A.

  - **Post-renal Failure:** Obstruction to urine outflow is the most common cause of functional renal impairment in the community but is uncommon in the ICU.

    - Common causes are bladder neck obstruction from an enlarged prostate, ureteric obstruction from

    - Pelvic tumors or retroperitoneal fibrosis, papillary necrosis, or large calculi. Finally, the sudden and

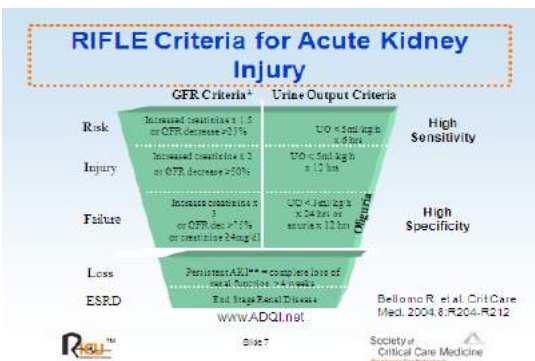
    - unexpected development of anuria in an ICU patient should always suggest obstruction of the urinary

- Catheter. Appropriate flushing or changing of the catheter should be implemented in this setting.

- **Comorbid conditions:** Hypertension, CRF, Diabetis, Multiple myeloma, Chronic infection & Multiple proliferative, connective tissues and autoimmune disorders.

CLINICAL PRESENTATION

- This definition, which goes by the acronym of RIFLE, divides renal dysfunction into the categories of injury, and failure (Fig. 1)



- Oliguria is defined as a urine output that less than 0.5 mL/kg/h for six consecutive hours in adults.

    - In critically ill patients, oliguria is often a sign of acute kidney injury that precedes serum creatinine

    - increases and requires immediate attention. Anuria is defined in the adult population as a passage of

    - less than 50 mL of urine per day.

- Acute kidney injury does not invariably present with oliguria: nonoliguric AKI occurs in 28- 45% of the general ICU population It is therefore important to identify non-oliguric AKI patients who might require early dialytic therapy and not to delay this important intervention.

- If oliguria or anuria is suspected, urinary output should be monitored hourly. In patients with urinary catheters in situ, an initial assessment of the urinary catheter's position and patency should be performed

- This can be achieved if indicated by 'flushing' the urinary catheter and examining the abdomen for a palpable bladder. Once the clinician has established there is no mechanical reason for the oliguria/anuria, further evaluation and diagnosis should proceed.

- A full clinical history and physical examination can frequently identify events and/or disease processes that underlie AKI and suggest an underlying diagnosis.

WORK-UP

- Urine analysis: blood, protein, WBC, esinophils, cast .. ext.
- Biochemical assessment

(Not applicable if furosemide has been given previously)

Pre-renal cause		Renal cause
Urine osmolality (mOsm/kg)	>500	<400
Urine Na (mmol/L)	<20	>40
Urine : plasma creatinine	>40	<20
Fractional Na excretion*	<1	>2

urine: plasma Na/U:P creatinineX 100

- Blood chemistry: hyponatremia, hyperkalemia

- Blood gases: metabolic acidosis
- CBC: anemia, thrombocytopenia.
- Radiolgy studies:
    - Renal ultrasound: to assess renal parenchyma and collecting system to rule out obstructive uropathy.
    - Renal scan
    - Renal MRI

MANAGEMENT

- Identify and correct reversible causes.
- Attend to fluid management and nutritional support carefully.
- Keep CVP 10-12 cm of H2O and MAP 60-65 mmHg.
- Early use of renal replacement techniques allow normal fluid and nutritional intake and may improve outcome.
- Urinary tract obstruction
    - Decompress lower urinary tract obstruction with a urinary catheter (suprapubic if there is urethral disruption).

- Decompress ureteric obstruction by nephrostomy or stent.

- Haemodynamic management

  - The circulating volume must be corrected first. Prompt restoration of circulating volume, and any necessary inotrope or vasopressor support may reverse pre-renal failure.

  - Diuretics (furosemide, mannitol) may establish diuresis if oliguria persists after pre-renal factors have been corrected. (80-120 mg Frusemide IV may continue 5-60 mg/ h. to keep urine output)

- Metabolic management

  - Urgent treatment of hyperkalaemia

  - Hypocalcaemia is best treated with renal replacement and calcium supplementation.

  - Hyponatraemia is usually due to water excess although salt-losing nephropathies may require sodium chloride supplements.

  - Hyperphosphataemia may be treated with renal replacement or aluminium hydroxide PO.

  - Metabolic acidosis (not due to tissue hypoperfusion) may be corrected with dialysis, filtration, or a

1.26% sodium bicarbonate infusion.

- Nephrotoxins and crystal nephropathies
    - Nephrotoxic agents should be withheld if possible. Drug dosage should be modified according to GFR. In some cases, urinary excretion of nephrotoxins and crystals may be encouraged by urinary alkalinisation.
- Renal replacement therapy
    - Continuous haemofi ltration forms the mainstay of replacement therapy in critically ill patients who may not tolerate haemodialysis.
- Glomerular disease
    - Immunosuppressive therapy may be useful. Dialysis is often required for the more severe forms despite steroid responsiveness.
- Dialysis for:
    - Fluid overload
    - Hyperkalemia
    - Persistent Metabolic Acidosis.
    - Uremia rising >30 mmol/l

- Rising creatinine >100 mmol/l/day

Red Flag

- Acute renal failure developing in hospital is usually due to hypotension, sepsis or nephrotoxic drugs (including contrast media).

RHABDOMYOLYSIS

OVERVIEW

- Myoglobin, which is released by the injured muscle and is capable of damaging the renal tubular epithelial cells after it is filtered through the glomerulus.
- Acute renal failure develops in about one-third of patients with diffuse muscle injury (Rhabdomyolysis)
- Causes
  - Trauma, Burn and Crush injuries, Vascular occlusion, infection, immobility (in alcoholics), drugs (e.g., lipid lowering agents), Hyperpyrexia, and electrolytes Abnormalities (e.g. hypophosphatemia)

WORK-UP

- High creatinine more than urea.
- CPK > 2000 IU/L
- The best predictor of acute renal failure are the combination of:
  - Serum creatinine >1.5,

- Creatine kinase (CPK) >5,000 IU/L,
- Myoglobin in the urine.
- The principal conditions that predispose to renal injury are hypovolemia and acidosis.

- Myoglobin in Urine:
  - Detected in urine with the orthotoluidine dipstick reaction (Hemastix) that is used to detect occult blood in urine.
  - If the test is positive, the urine should be centrifuged (to separate erythrocytes) and the supernatant should be passed through a micropore filter (to remove hemoglobin). A persistently positive test after these measures is evidence of myoglobin in urine.

MANAGEMENT

- The plasma levels of potassium and phosphate must be monitored carefully
- Aggressive volume resuscitation to prevent hypovolemia and maintain renal blood flow is one of the most effective measures for preventing or limiting the renal injury in rhabdomyolysis.
- To keep urine output > 2 ml/kg/h

- Alkalinizing the urine can also help to limit the renal injury, by using NaHco3 infusion to keep urine PH> 8.

- About 30% of patients who develop myoglobinuric renal failure will require dialysis

DISSEMINATED INTRAVASCULAR COAGULATION (DIC)

OVERVIEW

- DIC is a syndrome that occurs in response to a number of predisposing conditions or diseases, most of which are associated with widespread inflammation

- Causes
    - Severe infections, particularly septicemia.
    - Malignancy as metastatic carcinoma and leukemia
    - Fulminant liver disease
    - Severe trauma, extensive burns and heat stroke
    - Obstetric complications such as abruptio placentae and amniotic fluid embolism
    - Vascular abnormalities.
    - Hemolytic transfusion reactions
    - Toxic insults (snake venom, drugs)

- Pathophysiology
    - Diffuse activation of the coagulation system, frequently accompanied by activation of fibrinolysis.

CLINICAL PRESENTATION

- Diffuse bleeding due to consumption of coagulation factors and platelets is frequently
- Paradoxically, thrombosis may also occur, sometimes in conjunction with bleeding.
- A more common presentation is multiple organ failure, due to microthrombi-induced ischemia, diffuse fibrin deposition, and hemorrhagic tissue necrosis.

WORK-UP

- Clinical suspicion, predicated by the presence of an appropriate underlying disease and abnormal laboratory studies.
- No single assay can reliably diagnose DIC.
- Screening tests for DIC include the PT, PTT, platelet count, fibrinogen, and D-dimers.
- The PT is a more sensitive assay for DIC than the PTT.
- The least sensitive indicators of DIC are fibrinogen levels which may be reduced due to consumption.
- Increase in D-dimer which is a more sensitive assay for DIC than fibrin degradation products; however, increased levels of fibrin degradation products or D-dimers are not specific for DIC and may be elevated in the presence of

large fibrin clots.

- Moreover, because fibrin degradation products are metabolized by the liver and excreted by the kidney, their levels must be interpreted in light of hepatic and renal function

- A microangiopathic hemolytic anemia, characterized by

  - Thrombocytopenia and the Presence of schistocytes on the peripheral blood film may be present in more severe cases of DIC and is useful in distinguishing DIC from other causes of coagulopathy.

MANAGEMENT

- Treatment of the cause such as antibiotics for sepsis.

- Transfusion of coagulation factors and platelets could perpetuate ongoing microthrombosis in DIC.

- Reserve fresh-frozen plasma (FFP) and platelet transfusion for only

  - Those patients with severe coagulation abnormalities or clinical evidence of bleeding, or for those patients who require invasive procedures.

  - In these patients, therapy should begin with FFP transfusion to replace depleted coagulation factors.

  - In general, fibrinogen should be replaced using cryopre-

cipitate if the plasma fibrinogen level is less than 100 g per dL;

- If fibrinogen replacement does not correct the prolonged PT, then additional therapy with FFP could be provided to replenish deficient coagulation factors.

- Thrombocytopenia can be managed using platelet transfusions. No specific platelet count has been designated as safe in patients with severe DIC.

- Anticoagulant drugs could effectively interrupt the cycle of coagulation. In fact, that low-dose heparin (5-10 u/kg with no bolus) may be effective in controlling DIC. This may be especially true in patients with thromboembolic complications, such as digital ischemia or acral cyanosis.

SICKLE CELL CRISIS

OVERVIEW

- A hereditary disease most common to the black population, where the gene for Hb S is inherited from each parent. The red blood cells lack Hb A; when deprived of oxygen, these cells assume sickle shapes, resulting in erythrostasis, occlusion of blood vessels, thrombosis, and tissue infarction. After stasis, cells are more fragile and prone to haemolysis. Occasionally, there may be bone marrow failure.

CLINICAL PRESENTATION

- chronic hemolytic anemia, episodes of painful sickle crises, chronic and acute lung disease

- Chronic features

  - Patients with sickle cell disease are chronically anaemic (7–8g/dL) with a hyperdynamic circulation.

- Sickle Cell Crises

  - Crises are precipitated by various triggers, e.g. hypoxaemia, infection, cold, dehydration, and emotional stress.

  - Thrombotic crisis (or Vaso-occlusive):This occurs most frequently in the bones or joints, but also affect chest and abdomen, giving rise to severe pain. Occasionally,

neurological symptoms (e.g. seizures, focal signs), haematuria, or priapism may be present.

- Aplastic crisis: Related to parvovirus infection, it is suggested by worsening anaemia and a reduction in the normally elevated reticulocyte count (10–20%).

- Haemolytic crisis: Intravascular haemolysis with haemoglobinuria, jaundice, and renal failure sometimes occurs.

- Sequestration crisis: rapid live and splenic enlargment-due to red cells trapping with severe anemia.

- Pulmonary crisis (acute chest syndrome): is common; secondary chest infection or ARDS may supervene, worsening hypoxaemia, and further exacerbating the crisis.

WORK-UP

- Blood smear showing sickle cells, hemoglobin electrophoresis showing presence of hemoglobin S.

-

MANAGEMENT

- Prophylaxis against crisis includes avoidance of hypoxaemia, other known precipitating factors, prophylactic penicillin, and pneumococcal vaccine.

- Painful crises usually require prompt opiate infusions, analgesia should not be withheld (pethidine is drug of choice)

  - Give oxygen to maintain SaO2 at 97–99%.
  - Rehydrate with intravenous fluids.
  - If infection is suspected, antibiotics should be given as indicated.
  - Transfuse blood for severe anemia
  - Lower proportion of sickle cells to <30% by exchange transfusion.
  - Mechanical ventilation may be necessary for chest crisis
  - For Chronic episode: hydroxyurea for patients with more than three painful crisis/year

COMPLICATIONS

- Chest crisis—acute respiratory disease/failure with severe hypoxemia; therapy is red cell exchange.
- Aplastic crisis—acute infection with parvovirus B19 leads to suppression cytopoiesis; therapy is transfusion.
- Megaloblastic crisis—due to folate deficiency; therapy is administration of folate.

SEPTIC SHOCK

OVERVIEW

- Systemic inflammatory response syndrome (SIRS) describes the clinical manifestations that result from the systemic response to infection. Criteria for SIRS are considered to be met if at least 2 of the following 4 clinical findings are present:
    - Temperature greater than 38°C or less than 36°C
    - Heart rate (HR) greater than 90 beats per minute (bpm)
    - Respiratory rate (RR) greater than 20 breaths per minute or arterial carbon dioxide tension ($PaCO_2$) lower
    - than 32 mm Hg
    - White blood cell (WBC) count higher than 12,000/μL or lower than 4000/μL, or 10% immature (band) forms
- Sepsis
    - Is defined as the presence (probable or documented) of infection in association with SIRS.
        - With sepsis, at least 1 of the following manifestations of inadequate organ function/perfusion is

typically included:

- Alteration in mental state
- Hypoxemia (arterial oxygen tension [PaO_2] < 72 mm Hg at fraction of inspired oxygen [FiO_2] 0.21; overt
- pulmonary disease not the direct cause of hypoxemia)
- Elevated plasma lactate level
- Oliguria (urine output < 30 mL or 0.5 mL/kg for at least 1 h)

- Bacteremia
  - is defined as the presence of bacteria in the blood.
- Septic shock
  - is defined as a state of acute circulatory failure characterized by persistent arterial hypotension despite adequate fluid resuscitation or by tissue hypoperfusion.
- Multiple organ dysfunction syndrome (MODS)
  - is defined as the presence of altered organ function in a patient who is acutely ill and in whom homeostasis cannot be maintained without intervention.

- Etiology

  - Respiratory tract infection and urinary tract infection are the most frequent causes of sepsis, followed by abdominal and soft tissue infections.

PRESENTATION

- Fever , Chills , Mild disorientation or confusion,coma , Hyperventilation and localized symptoms (cough, abdominal pain, diarrhea ,flank pain , dysuria ,bone pain, skin redness)

- Tachycardia, tachypnea, Petechiae can be associated with (DIC) depressed mental status .

DIAGNOSIS

- White blood cell (WBC) more than 10,000/µL, band count of greater than 1500/µL

- Platelets, an acute-phase reactant, usually increase. However, the platelet count will fall with persistent sepsis, and (DIC).

- Serum electrolytes, including magnesium, calcium, phosphate, and glucose. Sodium and chloride levels are abnormal in severe dehydration.low Bicarbonate indicates acute metabolic acidosis.

- Elevation in Serum lactate is the serum marker for tissue hypoperfusion

- The PT and the aPTT are elevated in DIC. Fibrinogen levels are decreased and fibrin split products increased in the setting of DIC.

- Blood cultures are positive in less than 50% of cases of sepsis. Gram stain and culture from the sites of potential infection (urine, sputum, soft tissue, CSF, fluid collection, ascetic tap).

- Chest image for pneumonia, early, ARDS, central line and endotrachial tube position.

- Abdominal ultrasound and CT for abdominal collection and possible source of infection.

- Bone xray for possible osteomylitis MRI is much more sensitive.

MANAGEMENT

A. General

- Respiratory support_an initial assessment of airway and breathing is very important in a patient with septic shock. Supplemental oxygen should be administered to all patients with suspected sepsis. Early intubation and mechanical ventilation should be considered for patients with an oxygen requirement, dyspnea or increased respiratory rate,

persistent hypotension, or those with evidence of poor peripheral perfusion.

- Circulatory support

- Patients with suspected septic shock require an initial crystalloid fluid challenge of 20-30 mL/kg (1-2 L) over 30-60 minutes, with additional fluid challenges at rates of up to 1 L over 30 minutes.

- Crystalloid administration is titrated to a central venous pressure (CVP) goal between 8 and 12 mm Hg or signs of volume overload. Patients with septic shock often require a total 4-6 L or more of fluid.

- Urine output (UOP) should be monitored as a measure of dehydration. UOP lower than 30-50 mL/h should indicate further fluid resuscitation.

- Volume resuscitation can be achieved with either crystalloids or colloid solutions. The crystalloids are 0.9% sodium chloride and lactated Ringer solution; the colloids are albumin, dextrans. No fluid superior as the resuscitation fluid of choice in septic shock. Crystalloids take a longer time to achieve the same end points, whereas the colloid solutions are much more expensive. hydroxyethyl starches

- HES) for fluid resuscitation of severe sepsis and septic shock showed increased mortality (2).

- If the patient does not respond to several liters of volume infusion with isotonic crystalloid solution (usually 4 L or more) or evidence of volume overload is present, the blood pressure can be elevated by vasopressors, such as dopamine, norepinephrine, epinephrine, phenylephrine, and vasopressin.
- Vasopressor administration is required for persistent hypotension once adequate intravascular volume expansion has been achieved. Persistent hypotension is typically defined as systolic blood pressure lower than 90 mm Hg or MAP lower than < 65 mm Hg with altered tissue perfusion.
- In early goal directed therapy EGDT, vasopressors are recommended once a CVP of 8-12 mm Hg is achieved in the setting of persistent hypotension, and the goal is to titrate the dose to a MAP greater than 65 mm Hg. Vasopressors should be started early, regardless of fluid resuscitation, if frank shock is apparent (systolic blood pressure < 70 mm Hg or signs of tissue hypoperfusion).
- The recommended first-line agent for septic shock is either norepinephrine or dopamine. Norepinephrine has predominant alpha-receptor agonist effects and results in potent peripheral arterial vasoconstriction without significantly increasing heart rate or cardiac output.
- Second-line vasopressors for patients with persistent hypotension despite maximal doses of norepinephrine or dopamine are epinephrine, phen-

ylephrine, and vasopressin. Epinephrine has been shown to increase MAP in patients unresponsive to other vasopressors, because of its potent inotropic effects on the heart. Its adverse effects include tachyarrhythmias, myocardial and splanchnic ischemia, and increased systemic lactate concentrations.

B. Antimicrobial Therapy

- Antibiotic choice must be broad spectrum, covering gram-positive, gram-negative, and anaerobic bacteria when the source is unknown.

- Coverage of methicillin-resistant S aureus (MRSA) with an agent such as vancomycin or linezolid.

- Antianaerobic coverage is indicated in patients with intra-abdominal or perineal infections. Antipseudomonal coverage (ceftazidime, cefepime, piperacillin, imipenem, meropenem) should be considered in patients who are immunocompromised, especially those with neutropenia or hospital acquired infection.

- Combination empirical therapy for neutropenic patients with severe sepsis and for patients with difficult-to-treat multidrug-

- Resistant bacterial pathogens such as Acineto-

bacter and Pseudomonas spp. For patients with severe infections

- associated with respiratory failure and septic shock, combination therapy with an extended spectrum beta-lactam and either an

- Aminoglycoside or a fluoroquinolone is for P. aeruginosa bacteremia . A combination of beta-lactam and macrolide for patients with septic shock from bacteremic Streptococcus pneumoniae infection.

-

C. Blood sugar control An approach to blood glucose management in ICU patients with severe sepsis commencing insulin dosing when 2 consecutive blood glucose levels are >180 mg/dL

- This protocolized approach should target an upper blood glucose <180mg/dL

D. VTE prophylaxis daily pharmacoprophylaxis against venous thromboembolism (VTE) with low-molecular weight heparin (LMWH).

E. Stress ulcer prophylaxis using H2 blocker or proton pump inhibitor to be given to patients with severe sepsis/septic shock who have bleeding risk factor.

F. Red Blood Cell Transfusions In early goal directed therapy During the first 6 hrs of resuscitation, if ScvO2 less than 70% or SvO2 equivalent of less than 65% persists with what is judged to be adequate intravascular volume repletion in the presence of persisting tissue hypoperfusion, then dobutamine infusion (to a maximum of 20 µg/kg/min) or transfusion of packed red blood cells to achieve a hematocrit of greater than or equal to 30% in attempts to achieve the ScvO2 or SvO2 goal are options.

- It is recommended restricting red blood cell transfusion in adults with severe sepsis/septic shock until hemoglobin falls below 7.0 g/dL, and not transfusing above 9.0 g/dL, if ischemic heart disease, severe hypoxemia, or active bleeding are not present.

- Transfusing platelets prophylactically only when platelets fall to 10,000 / mm^3, assuming no bleeding is present. In patients considered at significant risk for bleeding, a threshold of 20,000 / mm^3 is suggested, and for those with active bleeding or who are undergoing surgery or invasive procedures, transfusing platelets to 50,000 mm^3 is suggested.

G. Intravenous corticosteroid therapy to patients with septic shock for whom fluid resuscitation and vasopressors

can restore an adequate blood pressure should not be given . For those with vasopressor-refractory septic shock, it is recommended to give IV hydrocortisone in a continuous infusion totaling 200 mg/24 hrs.

ANAPHYLAXIS

OVERVIEW

- Anaphylaxis is an acute, potentially lethal, multisystem syndrome resulting from the sudden release of mast cell- and basophil-derived mediators into the circulation as a result of immunologic reaction.

- Mechanisms:
  - IgE-mediated
  - Immune complex/complement mediated
  - Other proposed mechanisms.
  - Nonimmunologic anaphylaxis.

- Chemical Mediators of Anaphylaxis:
  - Histamine—
  - Tryptase—
  - Platelet activating factor—
  - Nitric oxide(NO)—
  - Arachidonic acid metabolites—

- Organ Systems in Anaphylaxis

- Cardiovascular system Fluid shifts — Occurs during anaphylaxis due to increased vascular permeability

- Heart rate— Tachycardia is the most common arrhythmia

- Exacerbation of underlying cardiac disease — e.g. acute coronary events

- Respiratory system—

- Anaphylaxis causes upper airway symptoms as well as lower airway manifestations leading to respiratory failure, or respiratory arrest.

- Anaerobic Metabolism— Due to decreased blood flow to the periphery and impaired oxygen consumption by the skeletal muscles

RECOGNITION

- History of acute onset of an illness involving:
  - Skin, mucosal tissue, or both
  - Respiratory compromise
  - Reduced BP or symptoms of end-organ dysfunction

- Persistent gastrointestinal symptoms and signs

PRESENTATION

- Skin symptoms and signs, occur in up to 90 percent of episodes.
- Respiratory symptoms and signs, occur in up to 70 percent of episodes.
- Gastrointestinal symptoms and signs, in up to 45 percent of episodes.
- Cardiovascular symptoms and signs, in up to 45 percent of episodes.

RISK FACTORS

- Asthma, cardiovascular disease and concurrent administration of certain medications: beta- blockers, ACE inhibitors, and alpha- blockers.

DIFFERENTIAL DIAGNOSIS

- acute generalized urticaria and/or angioedema
- acute asthma exacerbations
- syncope/faint, and
- anxiety/panic attacks.

WORK-UP

- Serum or plasma total tryptase - **(normal range 1 to 11.4 ng/mL).**
- Plasma histamine - **Typically peak within 5 to 15 minutes**

MANAGEMENT

- Immediate Management — Prompt assessment and treatment are critical in anaphylaxis because of the possibility of respiratory or cardiac arrest
  - Removal of the inciting antigen, if possible
  - Call for help (summon a resuscitation team)
  - Intramuscular injection of epinephrine
  - Supine position with the lower extremities elevated
  - Supplemental oxygen
  - Volume resuscitation with intravenous fluids
- Initial assessment — Interventions to be instituted concomitantly
  - ABC's, Examination of the skin.
  - Epinephrine injection IM. Intravenous infusion if

symptoms are severe.

- Recumbent position with the lower extremities elevated
- Supplemental oxygenup to 100 percent, should be administered.
- Two large-bore cannulae for administration of fluids and medications.
- Isotonic (0.9 percent) saline at a rate of 125 mL per hour.
- Continuous monitoring: BP, HR, RR, SpO2

- Airway management — Rapid assessment of the patient›s airway:

O2 by face mask, Intubation, Cricothyroidotomy may be required.

- Intravenous fluids — Massive fluid shifts can occur rapidly in anaphylaxis due to increased vascular permeability [7]. Isotonic (0.9 percent) saline

- Pregnant women — During labor and delivery, positioning of the patient on her left side and continuous fetal monitoring are important

- Medications:
  - **Epinephrine** — **IMI** 0.3 to 0.5 mg, may be repeated at 5

to 15 minute intervals.

- **Intravenous infusion** — 2 to 10 mcg per minute, titrated to effect..
- With continuous hemodynamic monitoring.
- Contraindications –There is **NO** absolute contraindication to epinephrine use in anaphylaxis .
- Adjunctive agents — Antihistamines, bronchodilators, and glucocorticoids,.

SEVERE MALARIA

OVERVIEW

- Severe malaria is acute malaria with major signs of organ dysfunction and/or high level of parasitemia.

- Most of these are P. falciparum, but P. vivax, ovale and malaria rarely cause severe presentation.

- Following the bite of an infected female Anopheles mosquito, the inoculated sporozoites go to the liver. Patients are asymptomatic for 12 to 35 days, until the erythrocytic stage of the parasite life cycle. Release of merozoites from infected red cells when they rupture causes fever . The relapsing species P. vivax and P. ovale can present as a new infection weeks or months after the initial illness due to activation of dormant hypnozoites in the liver.

- The incubation period for P. falciparum infection is about 12 to 14 days. The incubation period for P. vivax and P. ovale is about two weeks. The incubation period for P. malariae is about 18 days; low grade asymptomatic infections can persist for years. P. falciparum and malariae have no dormant (hypnozoite) phase, so do not relapse.

PRESENTATION

- History of exposure to area where malaria is endemic . The symptoms include tachycardia, tachypnea, chills, malaise, fatigue, diaphoresis, headache, cough, anorexia, nausea, vomiting, abdominal pain, diarrhea, arthralgias,

and myalgias .

- Physical signs include mild anemia and a palpable spleen . Mild jaundice may also develop in patients with otherwise uncomplicated falciparum malaria.

DIFFERENTIAL DIAGNOSIS

- Brucellosis
- TB
- Dengue fever
- HIV
- Meningio encephalitis

WORK-UP

- Blood film will show parasitemia , anemia, thrombocytopenia, elevated transaminases, mild coagulopathy, and elevated BUN and creatinine.
  - Severe malaria Patients with severe malaria may have parasitemia ≥100,000 parasites/microL of blood (≥5 % of parasitized RBCs).
  - The WHO uses cutoffs of 5 percent (in low transmission areas) and 10 percent (in high transmission areas) to define hyperparasitemia for diagnosis of severe disease diagnosis(1) .

- Many of the clinical findings are the result of the parasitized RBCs adhering to small blood vessels causing small infarcts, capillary leakage, and organ dysfunction; these include the following:

- Altered consciousness with or without seizures (cerebral malaria)
    - Respiratory distress or acute respiratory distress syndrome (ARDS) , cough , heamoptysis
    - Circulatory collapse
    - Metabolic acidosis
        - Renal failure, hemoglobinuria (blackwater fever)
        - liver failure
        - Coagulopathy with disseminated intravascular coagulation
        - Severe anemia or massive intravascular hemolysis
        - Hypoglycemia

MANAGEMENT

- Supportive measures (oxygen, ventilatory support, cardiac monitoring, and pulse oximetry) should be instituted as needed.

- If the coma score decreases after initiation of treatment, investigations should focus on the possibility of seizures, hypoglycemia, or worsening anemia.

- Antimalarial therapy the risk of death due to severe malaria is greatest in the first 24 hours of illness.

- There are two major classes of drugs available for parenteral treatment of severe malaria:

- The cinchona alkaloids (quinine and quinidine) and the artemisinin derivatives (artesunate and artemether).

- Artemisinin derivatives include artesunate, artemether and artemotil. Artesunate is the treatment of choice.

- Administration of intravenous artesunate consists of 2.4 mg/kg as first dose, followed by 2.4 mg/kg at 12 and 24 hours, followed by 2.4 mg/kg once daily . Following four doses of intravenous artesunate, oral antimalarial treatment may be administered if the patient is able to tolerate oral therapy. Intravenous antimalaria for more than three days could be given in very sick patients.

- Artemether can be given as 3.2mg/kg intramuscular then 1.6 mg/kg daily.

- **Quinine-Quinidine**

  - Quinine (or quinidine) should be administered by intravenous infusion beginning with an initial loading dose.

    - Intravenous quinine dihydrochloride 20 mg salt/

kg (in 5 percent dextrose) loading dose over 4 hours, followed by 20 to 30 mg salt/kg divided into two to three equal administrations of 10 mg salt/kg (over 2 hours) at 8 or 12 hour intervals (maximum 1800 mg salt/day) .

- Intravenous quinidine gluconate 10 mg salt/kg loading dose (maximum 600 mg salt) in normal saline over 1 hour, followed by 0.02 mg/kg/minute continuous infusion .

- Infusions should be done with care and the rate should be reduced if the corrected QT interval becomes prolonged by more than 25 percent of the baseline value in cardiac patients.

- the total duration of therapy with quinine/quinidine for severe malaria is 7 days. The total duration of therapy with artemisinin based therapy is 3 days.

- Bacterial infection empiric antibiotic therapy in the setting of severe malaria is considered. Bacterial infection should be suspected in patients with severe anemia together with signs or symptoms of sepsis.

TETANUS

OVERVIEW

- Tetanus occurs when spores of Clostridium tetani, an anaerobe normally present in the gut of mammals and widely found in soil, gains access to damaged human tissue. After inoculation, C. tetani transforms into a vegetative rod-shaped bacterium and produce the tetanus toxins. After reaching the spinal cord and brainstem via axonal transport and binding tightly and irreversibly to receptors at these sites , tetanus toxin blocks neurotransmission by its cleaving action on membrane proteins involved in neuroexocytosis . The net effect is disinhibition of neurons that modulate excitatory impulses from the motor cortex. Disinhibition of anterior horn cells and autonomic neurons results in increased muscle tone, painful spasms, and widespread autonomic instability.

- The predisposing factors :
  - Neonates (due to infection of the umbilical stump)
  - Obstetric patients (after septic abortions)
  - Postsurgical patients (with necrotic infections involving bowel flora)
  - Patients with dental infections
  - Diabetic patients with infected extremity ulcers
  - Patients who inject illicit and/or contaminated

drugs

- Cryptogenic mainly minor unnoticed wound

PRESENTATION

- The presenting symptom in more than half of such patients is trismus (lockjaw). Patients with generalized tetanus typically have symptoms of autonomic overactivity that may manifest in the early phases as irritability, restlessness, sweating and tachycardia. In later phases of illness, profuse sweating, cardiac arrhythmias, labile hypertension or hypotension, and fever are often present.

  - Patients with generalized tetanus characteristically have tonic contraction of their skeletal muscles and intermittent intense muscular spasms. both the tonic contractions and spasms are painful.

  - Tetanic spasms may be triggered by loud noises or other sensory stimuli such as physical contact or light. Tonic and periodic spastic muscular contractions are responsible for most of the clinical findings of tetanus such as:

    - Stiff neck
    - Opisthotonus
    - Risus sardonicus (sardonic smile)
    - A board-like rigid abdomen

- Periods of apnea and/or upper airway obstruction due to vise-like contraction of the thoracic muscles and/or glottal or pharyngeal muscle contraction

- Dysphagia

- Tetanus toxin-induced effects are long-lasting because recovery requires the growth of new axonal nerve terminals. The usual duration of clinical tetanus is 4 to 6 weeks.

MANAGEMENT

- Wound debridement to eradicate spores and necrotic tissue.

- Metronidazole is the preferred treatment for tetanus, but penicillin G is a safe and effective alternative for 7 to 10 days (2). For mixed infection we can use the second or third generation cephalosporins.

- Human tetanus immune globulin (HTIG) with the dose of 3000 to 6000 units intramuscularly should be given as soon as the diagnosis of tetanus is considered to neutralize unbound toxin is associated with improved survival, and it is considered to be standard treatment.

- All patients with tetanus should receive active immunization with a total of three doses of tetanus and diphtheria toxoid spaced at least two weeks apart immediately upon the diagnosis.

  - Control of muscle spasms

    - Benzodiazepines are generally effective in con-

trolling rigidity and spasms. They also provide a sedative effect. The usual starting dose of diazepam is 10 to 30 mg IV, although doses as high as 120 mg/kg per day have been used. Ventilatory assistance is needed at these higher doses . propofol may also control spasms and rigidity.

- Neuromuscular blocking agents are used when sedation alone is inadequate. Atracurium can be given as needed.

RED FLAG

- Prolong excessive sedation might lead to critical illness myopathy.

HYPERNATRAEMIA

OVERVIEW

- Hypernatremia is most often due to water loss, but can be caused by the intake of salt without water or the administration of hypertonic sodium solutions. Hypernatremia due to water loss is called **dehydration**. This is different from **hypovolemia**, in which both salt and water are lost

- Causes

A. Unreplaced water loss

- Central or nephrogenic diabetes insipidus
- Gastrointestinal losses
- Osmotic diuresis
- Hypothalamic lesions impairing thirst or osmoreceptor function

B. Water loss into cells Severe exercise or seizures

C. Sodium overload IncreasedIntake of food rich with Na or administration of hypertonic sodium solutions**.**

CLINICAL PRESENTATIONS

- Thirst, lethargy, coma, seizures, muscular tremor and rigidity, and an increased risk of intracranial haemorrhage. Thirst usually occurs when the plasma sodium rises 3–4 mmol/L above normal. Lack of thirst is associated with central nervous system disease

MANAGEMENT

- Depends upon the cause and whether total body sodium stores are normal, low or elevated and body water is normal **o**r low**.**

- Rate Of Correction

  - **Estimate H2O deficit in Lliters=(** (Wt.x0.5) (Na/140-1)**)**

  - If hyperacute (<12 h), correction can be rapid, Otherwise, aim for gradual correction of plasma sodium levels (over 1–3 days), particularly in chronic cases (>2days' duration), to avoid cerebral oedema through sudden lowering of osmolality. A rate of plasma sodium lowering (0.5-1) mmol/h has been suggested.

- **Hypovolaemia**

  - If hypovolaemia is accompanied by haemodynamic alterations, use colloid initially to restore the circulation. Otherwise, use isotonic saline, Artificial colloid solutions consist of hydroxyethyl starches

(e.g.Hestinal&Voulvent) dissolved in isotonic saline .

A. Normal total body Na (water loss)

- Water replacement either PO (addition to enteral feed) or as 5% glucose IV. Up to 5L/day may be necessary.

- if cranial diabetes insipidus (CDI): restrict salt and give lasix diuretics. Complete CDI will require desmopressin (DDAVP) (10µg BD intra-nasally or 1–2µg BD IV) whereas partial CDI may require

- desmopressin, but often responds to drugs that increase the rate of ADH secretion or end-organ responsiveness to ADH, e.g. chlorpropamide, hydrochlorthiazide

- If nephrogenic DI: manage by a low salt diet and thiazides. High dose desmopressin may be effective.

- Consider removal of causative agents, e.g. lithium, demeclocycline.

B. Low total body Na (Na and water losses)

- Treat hyperosmolar non-ketotic diabetic crisis, uraemia as appropriate

- Otherwise consider 0.9% saline or hypotonic (0.45%) saline. Up to 5 L/day may be needed.

C. **Increased total body Na (Na gain)**

- Water replacement either PO (addition to enteral feed) or as 5% glucose IV. Up to 5L/day

- may be necessary

- In addition, furosemide 10–20 mg IV PRN may be necessary.

Causes of Hypernatraemia

Type	Etiology	Urine
Low total body Na	Na Renal losses: Diuretic excess, Osmotic diuresis (glucose, urea,mannitol)	[Na+] >20 mmol/l iso- or hypotonic
Extra-renal losses: excesssweating		[Na+] <10 mmol/lhypertonic

Normal total bodyNa	Renal losses: Diabetes Insipidus	[Na+] variable hypo-, iso- or hypertonic
Extra-renal losses: Respiratoryand Renal insensible losses		[Na+] variable hypertonic
Increased total body Na	Conn's syndrome. Cushing's syndrome, Excess NaCl, hypertonic NaHCO3	[Na+] >20 mmol/liso- or hypertonic

HYPONATRAEMIA

OVERVIEW

- It is an electrolyte disturbance in which the sodium ion concentration in the plasma is lower than normal. Sodium is the dominant extracellular cation (positive ion). Its homeostasis inside the cell is vital to the normal function of any cell. Normal serum sodium levels are between approximately (135 - 145 mmol/L). Hyponatremia is generally defined as a serum level of less than 135 mEq/L and is considered severe when the serum level is below 125 mEq/L

CLINICAL PRESENTATION

- Nausea, vomiting, headache, fatigue, weakness, muscular twitching, obtundation, psychosis, seizures and coma.
- Symptoms depend on the rate as well as the magnitude of fall in the plasma [Na+]

WORK-UP

- Chemistry, including all electrolytes and blood sugar.
- Liver Function Test
- Cortisol level , ACTH

MANAGEMENT

- Rate and degree of correction

  - Calculate Na-Deficit = Wt. X 0.6 (target Na – current Na)

  - Volume of Hypertonic Saline in c.c. = Na deficit/512 X 1000

  - Infusion Rate (L/h) = Volume of hypertonic saline in cc/ target Na – current Na/desired correction rate

  - In chronic hyponatraemia correction should not exceed 0.5 mmol/L/h in the first 24 h and 0.3

  - mmol/L/h thereafter.

  - In acute hyponatraemia the ideal rate of correction is 1.5 – 2 mEq/h for 4 hours then slow

  - correction 12 mEq/Lover 24 hours.

  - A plasma Na+ of 125–130 mmol/L is a reasonable target for initial correction of both acute

  - and chronic states, Attempts to achieve normo- or hypernatraemia rapidly should be avoided.

  - Neurological complications, e.g. Central Pontine Myelinolysis, are related to the degree of

- correctionand the rate. Premenopausal women are more prone to these complications.

- **Extracellular fluid (ECF) volume excess**

  - If symptomatic (e.g. seizures, agitation), and not oedematous, 100 ml aliquots of hypertonic

  - (1.5%) saline can be given, checking plasma levels every 2–3 h.

  - If symptomatic and oedematous, consider furosemide (10–20 mg IV bolus PRN), mannitol

  - (0.5g/kg IV over 15–20 min), and replacement of urinary sodium losses with aliquots of

  - hypertonic saline. Check plasma levels every 2-3 h. Haemofiltration or dialysis may be

  - necessary if renal failure is established.

  - If not symptomatic, restrict water to 1–1.5 L/day. If hyponatraemia persists, consider

  - inappropriateADH (SIADH) secretion.

  - If SIADH likely, give isotonic saline and consider demeclocycline.

  - If SIADH unlikely, consider furosemide (10–20 mg IV

bolus PRN), mannitol (0.5 g/kg IV over

- 15–20 min), and replacement of urinary sodium losses with aliquots of hypertonic saline.

- Check plasma levels regularly. Haemofiltration or dialysis may be necessary if renal failure is

- Established.

- **Extracellular fluid volume (ECF) depletion**

  - If symptomatic (e.g. seizures, agitation), give isotonic (0.9%) saline. Consider hypertonic

- (1.8%) saline**.**

  - If not symptomatic, give isotonic (0.9%) saline.

- **General points**

  - Equations that calculate excess water are unreliable. It is safer to perform frequent estimations of plasma sodium levels.

  - Hypertonic saline may be dangerous in the elderly and those with impaired cardiac function.

- An alternative is to use furosemide with replacement of urinary sodium (and K+) losses each 2–3 h. Thereafter, simple water restriction is usually sufficient.

- Many patients achieve normonatraemia by spontaneous water diuresis.

- Use isotonic solutions for reconstituting drugs, parenteral nutrition, etc.

- Hyponatraemia may intensify the cardiac effects of hyperkalaemia.-

- A true hyponatraemia may occur with a normal osmolality in the presence of abnormal

- Solutes e.g. ethanol,ethylene glycol, glucose

CAUSES OF HYPONATRAEMIA

Urine (Na+)	Etiology	Type

mmol/l 20 >	Renal losses: diuretic excess, osmotic diuresis (glucose, urea, mannitol), renal tubular acidosis, salt-losing nephritis, mineralocorticoid deficiency.	ECF volume depletion
mmol/l 10 <		Extra-renal losses: vomiting, diarrhea burns, pancreatitis
mmol/l 20 >	Water intoxication , post-operative TURP syndrome, inappropriate ADH secretion, hypothyroidism, drugs (e.g carbamazepine, chlorpropamide), glucocorticoid deficiency, pain, emotion	Modest ECF volume excess (no edema)
mmol/l 20 >		Acute and Chronic renal failure

mmol/l 10 <	Nephrotic syndrome, Cirrhosis, Heart failure	ECF volume excess (oedema)

HYPERKALAEMIA

OVERVIEW

- Plasma potassium depends on the balance between intake, excretion and the distribution of potassium across cell membranes. Excretion is normally controlled by the kidneys.

- Causes

- Reduced renal excretion (e.g. chronic renal failure, adrenal insufficiency, diabetes, potassium sparing diuretics).

- Intracellular potassium release (e.g. acidosis, rapid transfusion of old blood, cell lysis including rhabdomyolysis, haemolysis, and tumourlysis andK+ channel openers.

- Potassium poisoning

CLINICAL PRESENTATION

- Hyperkalaemia may cause dangerous arrhythmias including cardiac arrest. Arrhythmias are more closely related to the rate of rise of potassium than the absolute level. Clinical features such as paraesthesiae and areflexic weakness are not clearly related to the degree of hyperkalaemia but usually occur after ECG changes (tall T-waves, flat P-waves, prolonged PR interval and wide QRS)

WORK-UP

- Chemistry including all electrolytes, blood sugar and CPK
- Arterial Blood Gases.
- ECG.

MANAGEMENT

- Treat reversible causes first e.g. stop medications that increase serum K level as NSAID, ACE-Inhibitors& K-sparing diuretics.
- Add K eliminating drugs through loop diuretics.
- Potassium restriction is needed for all cases and haemodiafiltration or haemodialysis may be needed for resistant cases.
- **Cardiac arrest associated with hyperkalaemia***

- Sodium bicarbonate (8.4%) 50–100 ml should be given in addition to standard CPR and other treatment detailed below.

- **Potassium >7 mmol/L***

  - Calcium chloride (10%) 10 ml should be given urgently in addition to treatment detailed below. Although calcium chloride does not reduce the plasma potassium, it stabilizes the myocardium against arrhythmias.

- **Clinical features of hyperkalaemia or potassium >6**

mmol/L with ECG changes*

- Glucose (50 ml 50%) and soluble insulin (10 iu) should be given I.V. over 20 min. Blood glucose should be monitored every 15 min and more glucose given if necessary. In addition, Calcium Resonium 15 g QDSorally or 30 gBIDrectally can be considered.

HYPOKALAEMIA

OVERVIEW

- Normal plasma potassium levels are between 3.5 to 5.0 mEq/L , about 98% of the body's potassium is found inside cells, with the remainder in the extracellular fluid including the blood. Alternately, the NIH denotes 3.7–5.2 mEq/L as a normal range.

- Plasma potassium depends on the balance between intake, excretion and the distribution of potassium across cell membranes. Excretion is normally controlled by the kidneys.

- Causes

- Inadequate intake

- Gastrointestinal losses (e.g. vomiting, diarrhea, fistula losses)

- Renal losses (e.g. diabetic ketoacidosis, Conn's syndrome, secondary hyperaldosteronism, Cushing's syndrome, renal tubular acidosis, metabolic alkalosis, hypomagnesaemia, drugs including diuretics, steroids, theophylline)

- Haemofiltration losses

- Potassium transfer into cells (e.g. acute alkalosis, glucose infusion, insulin treatment,

familial periodic paralysis)

CLINICAL PRESENTATION

- Arrhythmias (SVT, VT and Torsades de Pointes)
- ECG changes (ST depression, T-wave flattening, U-waves)
- Metabolic alkalosis
- Constipation
- Ileus
- Muscular Weakness

WORK-UP

- Chemistry including all electrolytes and blood sugar.
- Arterial Blood Gases.
- ECG.
- Cortisol level

MANAGEMENT

- Wherever possible, the cause of potassium loss should be treated.

- Potassium replacement should be intravenous (via central line) with ECG monitoring when there is a clinically significant arrhythmia (20 mmol over 30 min, repeated according to levels)

- Slower intravenous replacement (20 mmol over 1 h) should be used where there are clinical featureswithout arrhythmias.

- Oral supplementation (to a total intake of 80–120 mmol/day, including nutritional input) can be given where there are no clinical features.

- Mg++ level as adequate Mg++ is necessary for correction.

HYPERGLYCEMIC HYPEROSMOTIC STATE (HHS)

OVERVIEW

- HHS, also often referred to as the hyperosmolar non ketotic syndrome

- It is most commonly occurs in patients with type 2 DM who have some concomitant illness that leads to reduced fluid intake.

- HHS usually carries a higher mortality than DKA, estimated at approximately 10-20%

- According to the consensus statement published by the American Diabetes Association, diagnostic features of HHS may include the following:

  - Plasma glucose level of 600 mg/dL or greater
  - Effective serum osmolality of 320 mOsm/kg or greater
  - Profound dehydration, up to an average of 9L
  - Serum pH greater than 7.30
  - Bicarbonate concentration greater than 15 mEq/L

CLINICAL PRESENTATION

- HHS presents with a longer history than DKA (typically 7–10 days)
- Presented with polyuria, polydipsia and lethargy
- confusion and even coma in severe cases
- Patients with HHS are profoundly dehydrated. They present with tachycardia, hypotension, cool peripheries, dry mucous membranes and decreased skin turgor.

DIFFERENTIAL DIAGNOSIS

- DKA , Diabetes Insipidus , Lactic Acidosis

WORK-UP

- CBC, renal function test, electrolyte, amylase and lipase level
- Blood sugar , ketones in urine
- serum osmolality. Blood gas ,lactate level

MANAGEMENT

A. General: Airway protection ,breathing and circulation support

B. Specific:

HYPOGLYCEMIA

OVERVIEW

- Hypoglycemia is (blood glucose level <60 mg/dL)
- Severe hypoglycemia was strongly associated with a higher risk for cardiovascular disease .
- Common causes of hypoglycemia in the ICU:
  - Hepatic failure, renal failure
  - Sepsis,
  - Adrenal insufficiency
  - Tumors including hepatoma or pancreatic islet b-cell tumor
  - Drugs such as B-blockers

CLINICAL PRESENTATION

- Nervousness, tremulousness, dizziness,confusion and blurred vision
- Tachycardia,hypertension or hypotension, and dysrhythmias
- Diaphoresis, tachypnea
- Nausea and vomiting, dyspepsia, and abdominal cramping.

- Coma in severe cases

DIFFERENTIAL DIAGNOSIS

- Addison Disease - Adrenal Crisis
- Alcoholism - Anxiety Disorders

WORK-UP

- CBC, renal function test, electrolyte
- Blood sugar
- Blood gas ,lactate level
- Toxicology

MANAGEMENT

- General :Airway protection ,breathing and circulation support
- specific :
  - Dextrose, containing 50 mL of 50% dextrose solution, IV push.
  - Blood glucose should be monitored hourly via finger-stick measurements.
  - Glucagon, hydrocortisone, or octreotide canbe administered if hypoglycemia is profound andrefractory to dextrose .

DKA

OVERVIEW

- DKA occurs most frequently in younger patients with type 1 diabetes mellitus
- It is characterized by a syndrome of hyperglycemia, ketonemia, and an anion gapmetabolic acidosis.
- The most common precipitating factor for hyperglycemia crisis like DKA is infection.
- Other precipitants include:
  - Insulin error (omission or inadequate dosing)
  - acute pancreatitis
  - myocardial infarction,
  - certain drugs (e.g., corticosteroids, thiazide diuretics, beta-adrenergic blockers, chlorpromazine and phenytoin)

CLINICAL PRESENTATION

- Normally DKA has a rapid onset (1–3 days)
- Patients may present with polyuria, polydipsia, weight loss ,weakness. Nausea, vomiting and abdominal pain

- On examination:
  - Patients will exhibit the signs of dehydration(dry mucosa, lax skin turgor, tachycardia and tachypnoea)
  - Progressing to hypotension or even shock can happen if no treatment
  - Kussmaul–Kien respiration(rapid and deep breathing) is classical in DKA
  - Decrease level of consciousness or coma in severe cases

WORK-UP

- CBC, renal function test, electrolyte, amylase and lipase level
- Blood sugar , ketones in blood and urine
- Serum osmolality, Blood gas ,lactate level

MANAGEMENT

- General :Airway protection ,breathing and circulation support
- Specific :Treat any precipitating infection and follow the protocol

THYROTOXIC CRISIS

OVERVIEW

- Difention-It is an acute, life-threatening, hyper-metabolic state induced by excessive release of thyroid hormones (THs) in individuals with thyrotoxicosis.

- Pathophysiology-Thyroid storm is the most extreme state of thyroid hormone–induced, severe

- Hypermetabolism involving multiple systems. The clinical picture relates to severely exaggerated effects of THs due to increased release (with or without increased synthesis) or, rarely, increased intake of TH.

  - Causes

  - Thyroid storm is precipitated by the following factors in individuals with thyrotoxicosis:

  - Sepsis Surgery - Anesthesia Induction - Radioactive iodine therapy - DKA

  - Drugs (anticholinergic and adrenergic drugs such as pseudoephedrine; salicylates;

  - [NSAIDs]; chemotherapy) and iodinated contrast agents

  - Excessive thyroid hormone (TH) ingestion

- Direct trauma to the thyroid gland
- Toxemia of pregnancy and labor in older adolescents; molar pregnancy

CLINICAL PRESENTATION

- History
  - General symptoms (Fever , Profuse sweating , Poor feeding and weight loss)
  - GI symptoms (Nausea & vomiting , Diarrhea and abdominal pain)
  - Neurologic symptoms (Anxiety , Altered behavior , Seizures and Coma)
- Physical
  - Fever (Temperature consistently exceeds 38.5°C and may progress to hyperpyrexia and frequently exceeds 41°C)
  - Excessive sweating
    - Cardiovascular signs
    - Hypertension with wide pulse pressure

- Hypotension in later stages with shock
- Signs of high-output heart failure

- Neurologic signs
  - Agitation and confusion
  - Hyper-reflexia and transient pyramidal signs
  - Tremors, seizures Signs of thyrotoxicosis (Orbital signs & Goiter)

- Signs of thyrotoxicosis (Orbital signs & Goiter)

WORK-UP

- **Laboratory Studies**
  - Thyroid storm diagnosis is based on clinical features, not on laboratory test findings.

- Thyroid studies
  - Results of thyroid studies are usually consistent with hyperthyroidism and are useful only if the patient has not been previously diagnosed.
  - Test results may not come back quickly and are usually unhelpful for immediate management.

- Usual findings include elevated triiodothyronine (T3), thyroxine (T4) and free T4 levels; increased T3 resin uptake; suppressed thyroid-stimulating hormone (TSH) levels; and an elevated 24-hour iodine uptake. TSH levels are not suppressed in the rare instances of excess TSH secretion.

- Other studies: CBC,LFT,Electrolytes, ABG, Renal function and urinalysis.

- Hypercalcemia: May occur from thyrotoxicosis

DIFFERENTIAL DIAGNOSIS

- Sepsis
- Neuroleptic malignant syndrome
- Malignant hyperthermia
- Acute mania

MANAGEMENT

- Medical tratment
  - If needed, immediately provide supplemental oxygen, ventilatory support, and intravenous fluids. Dextrose solutions are the preferred intravenous fluids to cope with continuously high metabolic demand.

- Correct electrolyte abnormalities.

- Treat cardiac arrhythmia, if necessary.

- Aggressively control hyperthermia by applying ice packs and cooling blankets and by administering acetaminophen (15 mg/kg orally or rectally every 4 h).

- Promptly administer antiadrenergic drugs (eg, propranolol) to minimize sympathomimetic symptoms.

- Correct the hyperthyroid state. Administer antithyroid medications to block further synthesis of thyroid hormones (THs).

- High-dose propylthiouracil (PTU) is preferred because of its early onset of action and capacity to inhibit peripheral conversion of T4 to T3.

- Administer iodine compounds (Lugol iodine or potassium iodide) orally or via a nasogastric tube to block the release of THs (at least 1 h after starting antithyroid drug therapy). If available, intravenous radiocontrast dyes such as ipodate and iopanoate can be effective in this regard. These agents are particularly effective at preventing peripheral conversion of T4 to T3.

- Administer glucocorticoids to decrease peripheral conversion of T4 to T3. This may also be useful in preventing relative adrenal insufficiency due to hy-

perthyroidism.

- Treat the underlying condition, if any, that precipitated thyroid storm and exclude comorbidities such as diabetic ketoacidosis and adrenal insufficiency. Infection should be treated with antibiotics.

- Rarely, as a life-saving measure, plasmapheresis has been used to treat thyroid storm in adults.

- Iodine preparations should be discontinued once the acute phase resolves and the patient becomes afebrile with normalization of cardiac and neurological status.

- Surgical treatment

  - Patients with Graves who need urgent treatment of hyperthyroidism but have absolute contraindications to thioamides may be managed acutely with beta-blockers, iodine preparations & glucocorticoids as described. Subsequently, thyroidectomy can be performed after 7 days of iodine administration which reduce vascularity of the gland & the risk for thyroid storm.Contributor Information and Disclosures

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Pathophysiologic mechanisms of Graves disease relating thyroid-stimulating immunoglobulins to hyperthyroidism and ophthalmopathy. T4 is levothyroxine. T3 is triiodothyronine.

MYXEDEMA COMA

OVERVIEW

- Pathophysiology:Myxedema crisis occurs most commonly in older women with long-standing, undiagnosed or undertreated hypothyroidism who experience an additional significant stress, such as infection, a systemic disease, certain medications, and exposure to a cold environment. When hypothyroidism is long-standing, physiologic adaptations occur. Reduced metabolic rate and decreased oxygen consumption result in peripheral vasoconstriction, which maintains core temperature. The number of beta-adrenergic receptors is reduced, usually with preservation of alpha-adrenergic receptors and circulating catecholamines, causing beta/alpha-adrenergic imbalance, diastolic hypertension, and reduced total blood volume. Myxedema crisis is a form of decompensated hypothyroidism in which adaptations are no longer sufficient. Essentially, all organ are affected.

CLINICAL PRESENTATION

- Metabolic Thyroid hormones are critical for cell metabolism and organ function. With an inadequate supply, organ tissues do not grow or mature, energy production declines, and the action of other hormones is affected. Although weight gain is common, severe obesity is rarely secondary to hypothyroidism alone.

- NeurologicAlthough the condition is called myxedema coma, the absence of coma does not exclude the diagnosis of this disorder. The presenting mental status may be lethargy or stupor. The exact mechanisms causing changes in mental status are not known. Brain function is influenced by reductions in cerebral blood flow and oxygen delivery.

- CardiovascularThe heart is profoundly depressed, with bradycardia and decreased contractility causing low stroke volume and cardiac output.Nonspecific ST- and T-wave inversion changes, low voltage, and ventricular arrhythmias may be noted. Plasma volume is decreased, and capillary permeability is increased, leading to fluid accumulation in tissue and spaces and possibly causing pericardial effusions.

- PulmonaryTypically, the lungs are not severely affected. Respiratory muscle dysfunction may be compromised, and depressed ventilatory drive and increased alveolar-arterial oxygen gradient are common. Fluid accumulation may cause pleural effusions and decreased diffusing capacity. However, hypothyroidism may also have a direct impact, because the condition can cause obstructive sleep apnea that resolves with thyroid replacement.

- RenalKidney function may be severely compromised, partly because of low cardiac output and vasoconstriction that causes a low glomerular filtration rate. Reduced levels of NA^+/K^+ ATPase decrease sodium reabsorption and impair free water excretion, resulting in hyponatremia, which is usually present in myxedema coma.

- GastrointestinalSevere or even mild hypothyroidism decreases intestinal motility. Patients with myxedema coma can present with gastric atony, mega-colon, or paralytic ileus.

WORK-UP

- If suspected, treatment must be initiated immediately without waiting for the results.

  - Free T4, T3 and TSH

  - Serum cortisol level

Serum electrolytes & serum osmolality: Na with low serum osmolality is common.

- Serum creatinine: as renal perfusion decreased, the levels are usually elevated.

- Serum glucose: Hypoglycemia is common but may suggest adrenal insufficiency.

- CBC with differential: Bands and/or a left shift may be the only sign of infection.

- Creatine kinase: CK levels are often elevated, and fractionation indicates skeletal (not cardiac) muscle injury unless a myocardial infarction was the precipitating event.

- Arterial blood gases: Increased P_{CO2} and decreased P_{O2} are found.

- Pan-culture for sepsis

MANAGEMENT

- Myxedema crisis/coma is a life-threatening condition; therefore, patients with this disorder must be stabilized in an intensive care unit. The first 24-48 hours are critical. If the diagnosis is considered likely, immediate and aggressive administration of multiple interventions is necessary to lower an otherwise high rate of mortality. Initial priorities include the following:

  - Mechanical ventilation if respiratory acidosis/hypercapnia/hypoxia is significant .

  - Immediate intravenous thyroid hormone replacement while awaiting confirmatory test results (T4 and TSH), even if the diagnosis of myxedema coma is only probable. Because GI absorption is compromised, intravenous therapy is mandatory. The usual conversion to an

intravenous dose of T4 is approximately one half to two thirds of the oral dose. An intravenous loading dose of 500-800 mcg of levothyroxine is followed by a daily I.V. dose of 50-100 mcg; the daily dose is administered until the patient is able to take medication by mouth. Use caution in elderly persons and in patients with coronary artery disease or myocardial infarction, because full-dose T4 therapy may worsen myocardial ischemia by increasing myocardial oxygen consumption.{Ref9}. Some authorities advocate the use of additional intravenous T3, at 10-20 mcg every 8-12 hours, especially in young patients with low cardiovascular risk.

- After a baseline cortisol level is ascertained, initiate hydrocortisone at 5-10 mg/hr, continue therapy unless the random cortisol level on admission indicates adrenal function without abnormalities so hydrocortisone may be stopped without tapering.

- Passive rewarming using ordinary blankets and a warm room (avoid rapid rewarming)

- Treatment of associated infection .

- Correction of severe hyponatremia (Na<120 mEq/L) with saline, free water restriction.

- Broad-spectrum antibiotics with modification of the regimen based on culture results.

- Correction of hypoglycemia with intravenous dextrose.

- Treatment of severe hypotension with cautious administration of 5-10% glucose in half-normal or normal saline (or hypertonic saline if severely hyponatremic).

- Dose adjustment of any medication to compensate for decreased renal perfusion, drug metabolism, etc

- If myocardial ischemia or infarction is diagnosed, or if the patient has significant risk factors for coronary artery disease, institute thyroid replacement at low doses.

- Volume status: hypotension is resistant to the usual drugs until thyroid hormone and glucocorticoids (if insufficient) are administered. If hypotension does not improve with prudent fluid replacement, whole blood can be transfused. Finally, cautious administration of dopamine can be used.

- Diet: motility of the GI tract is usually decreased; therefore, withhold food until the patient is alert and extubated and normal bowel sounds are present; at that time, gradually introduce soft foods.

DISORDERS OF TEMPERATURE CONTROL

HEAT STROKE

OVERVIEW

- Heat stroke is a syndrome of acute thermoregulatory failure in warm environments characterized by central nervous system depression, core temperatures usually above 40 °C, and typical biochemical and physiologic abnormalities.

- Mortality may reach 70%.

- Etiologies

  - Causes of heat stroke involve increased heat production and/or impaired heat loss.

  - Exertional heat stroke is typically seen in younger persons who exercise at higher than normal ambient temperatures.

  - Nonexertional (“classic”) heat stroke affects predominantly elderly or sick persons and occurs almost exclusively during a heat wave. They may take drugs that may adversely affect thermoregulation (anticholinergics, diuretics, alcohol).

- Dehydration and impaired cardiovascular status predispose to heat stroke by decreasing skin or muscle blood flow, thereby limiting transfer of heat from the core to the environment.

- Acclimatization to higher ambient temperatures can greatly increase heat tolerance by increasing cardiac output, decreasing peak heart rate, and lowering the threshold necessary to induce sweating and increase the volume of sweating.

CLINICAL PRESENTATION AND DIAGNOSIS

- Heat stroke should be expected in any patient exercising in ambient temperatures generally >25 °C or in susceptible persons during heat waves.

- Diagnostic criteria for heat stroke includes :
  - Delirium and seizures are associated with temperatures of 40–42*C.
  - Coma is associated with temperatures >42*C.
  - Tachycardia.
  - Tachypnea.
  - Salt and water depletion.
  - Rhabdomyolysis.

- Disseminated intravascular coagulation.
- Heart failure with ST depression and 'T' wave flattening.

MANAGEMENT

- ABC.
- Primary therapy includes cooling and decreasing thermogenesis. Cooling by evaporative (placing a nude patient in a cool room, wetting the skin with water, and encouraging evaporation with fans) or direct external methods (immersing the patient in ice water or packing the patient in ice) has proved effective.
- External methods suffer from inconvenience and the possibility that cold skin may vasoconstrict, thereby limiting heat exchange from the core.
- Active cooling measures should be stopped when the core temperature is <39*C.
- Consider internal cooling using cooled IV fluid, and bladder lavage or peritoneal lavage using cooled fluids.
- Supportive treatment includes fluid replacement by normal saline. Dopamine and α-adrenergic agonists should be avoided. Volume expansion with dextran is contraindicated due to

its anticoagulant effects.

- Control Convulsion.

- Urine output should be closely followed. Patients should routinely receive mannitol 1 to 2 mg/kg intravenously over 15 to 20 minutes to promote urine output and potentially decrease cerebral edema.

- Delays in treatment of as little as 2 hours may increase the risk of death up to 70%.

HYPOTHERMIA

OVERVIEW

- Hypothermia exists when the core temperature is <35 °C (95°F).
- Etiology
    - Exposure to cold, use of depressant drugs (alcohol, phenothiazines, barbiturates, neuroleptics, paralytics), and hypoglycemia. Other common causes include hyperglycemia, hypothyroidism, adrenal insufficiency, central nervous system disorders, extensive burns, sepsis, and trauma.

CLINICAL PRESENTATION AND DIAGNOSIS

- Mild: <35*C—shivering in an attempt to correct body temperature. Neurological signs of dysarthria and slowness appear.
- Moderate: <32*C—hypertonicity and sluggish reflexes with cardiovascular dysfunction become life-threatening.
- Sever: <28*C—arterial pulses often impalpable. Hypothermic rigidity is difficult to distinguish from death.
- Prognosis depends on the degree and duration of hypothermia.
- Complications

- Hypoxaemia
- Hypovolaemia and metabolic acidosis are common.
- Renaltubular damage may result from renal blood flow reduction.
- Acute pancreatitis,
- Rhabdomyolysis and gastric erosions are common.

WORK-UP

- **ECG changes:**
  - Sinus bradycardia is followed by atrial flutter and fibrillation with ventricular ectopics and fibrillation.
  - Prolonger PR& QT interval, wide QRS Complex

MANAGEMENT

- Oxygen to maintain SaO2 >95%.
- Fluid replacement with careful monitoring.
- Rewarming—all hypothermic patients with no evidence of other fatal disease should be assumed fully recoverable. In the event of cardiac arrest, full resuscitation should continue until normothermia is achieved. VF is resistant to defibrillation between 28–30*C. The technique used for

rewarming depends on core temperature (measured with a lowreading rectal thermometer) and clinical circumstances.

- Rapid Internal rewarming

  - For core temperature <28*C (<33*C with acute exposure hypothermia) or where there is cardiac arrest, rapid rewarming should be instituted.

  - This may be achieved by continous arterio-venous rewarming circuits, peritoneal dialysis, gastric or bladder lavage with warmed fluids.

  - Cardiopulmonary bypass is an effective rewarming strategy for patients with cardiac arrest resistant to defibrillation. These techniques may achieve rewarming rates of 1–5*C/h.

    - If extracorporeal rewarming is available, rates of 3–15*C/h may be achieved with the addition of cardiovascular support.

- Passive rewarming:

    - For mild degree, using blanket and warm drinks.

- External Active rewarming:

  - For moderate degree.

- With good insulation (space blanket), rewarming rates of 0.1–0.7*C/h can be achieved.

- Active surface rewarming with a heated blanket or warm air blanket can achieve rates of 1–7*C/h and is less invasive. Haemodynamic changes and fluid shifts may be dramatic during active rewarming, requiring careful monitoring and support.

OPIOID POSITIONING

OVERVIEW

- The term narcotic specifically refers to any substance that induces sleep, insensibility, or stupor, and it is used to refer to opioids or opioid derivatives.
- Activation of opioid receptors results in inhibition of synaptic neurotransmission in the central nervous system (CNS) and peripheral nervous system (PNS).
- The physiological effects of opioids are mediated principally through mu and kappa receptors and to a lesser extend through sigma and delta receptors .
- Mu receptor effect : analgesia, euphoria, respiratory depression, and miosis.
- Kappa receptor effects : analgesia, miosis, respiratory depression, and sedation
- Sigma receptors effect: dysphoria, hallucinations, and psychosis.
- delta receptor effect: euphoria, analgesia, and seizures.
- Common classifications divide the opioids into agonist, partial agonist, or agonist-antagonist agents and natural, semisynthetic, or synthetic.

CLINICAL MANIFESTATION

- CNS: sedation,euphoria,seizure
- CVS: hypotension ,bradycardia ,QRS prolongation ,QT prolongation
- Pulmonary :respiratory depression ,bronchospasm ,pulmonary edema
- GI: nausea ,vomiting ,constipation ,increase smooth muscular tone (sphincter)
- Urinary tract : retention urethral spasm
- Eye: miosis.
- Skin: urticarial ,flushing

DIFFERENTIAL DIAGNOSIS

- Alcohol or substance abuse
- Toxicity of sedative, local anesthetic ,neuroleptic agent .
- DKA,,Hyperosmolar Hyperglycemic Nonketotic Coma
- Hypoglycemia ,electrolyte disturbance

WORK-UP

- Toxicology screen.

- CBC, chemistry and Arterial Blood Gases .

MANAGEMENT

- General : Airway protection ,breathing and circulation support

- Specific :

  - Activated charcoal is the GI decontamination method of choice for patients with opiate intoxication following ingestion if no contraindication Naloxone

  - The endpoint for naloxone in chronic opioid dependence should be adequate respiration, not complete reversal of sedation.

  - Recommended reversal practice is to start with a very low dose of naloxone of 0.05 to 0.1 mg and titrate it up until reversal of respiratory depression is achieved. (infusion may be started later according to patient condition)

ORGANOPHOSPHATE POISONING

OVERVIEW

- Organophosphorus pesticides are the most important cause of severe toxicity and death from acute poisoning worldwide, with more than 200 000 deaths each year in developing countries
- Organophosphorus compounds inhibit numerous enzymes (most important: esterase)
- Inhibition of acetylcholinesterase leads to the accumulation of acetylcholine at
- cholinergic synapses, interfering with normal function of the autonomic, somatic,
- and central nervous systems.
- This produces a range of clinical manifestations, called (acute cholinergic crisis)

CLINICAL PRESENTATION

- Muscarinic effects by organ systems include the following:
  - Cardiovascular :Bradycardia, hypotension
  - Respiratory :Rhinorrhea, bronchorrhea, bronchospasm , severe respiratory distress

- Gastrointestinal: Hyper salivation, nausea and vomiting, abdominal pain, diarrhea
- Genitourinary :Incontinence
- Ocular :Blurred vision, miosis
- Glands: Increased lacrimation, diaphoresis

- Nicotinic signs and symptoms
  - Musclefasciculations, cramping, weakness, and diaphragmatic failure.
  - Autonomic nicotinic effects include hypertension, tachycardia, mydriasis, and pallor.
  - CNS effects include anxiety, emotional liability, restlessness, confusion, ataxia, tremors, seizures, and coma.

WORK-UP

- Cholinesterase activity that is less than 80% of the lower reference range is probably indicative of a significant exposure to an organophosphorus compound
- In severe clinical toxicity the erythrocyte acetylcholinesterase activity is less than 20% of normal.

MANAGEMENT

- General : :Airway protection ,breathing and circulation support
- Specific :
  - All patients require decontamination :
  - The three most widely used classes of antidotes are muscarinicantagonists (usually atropine) oximes (usually pralidoxime or obidoxime), and benzodi-azepines.
  - Atropine for :salivation, lacrimation ,nausea , vomiting, bronchospasm and bradycardia
  - Pralidoxime for :muscular weakness
  - Benzodiazepine for: seizure

PARACETAMOL POISONING

OVERVIEW

Groups at risk for paracetamol poisoning:

- underlying hepatic impairment (viral hepatitis ,alcoholic liver disease)
- microsomal enzyme induction: like phenobarbitone, carbamazepine phenytoin ,rifampicin ,oral contraceptives, chronic alcohol ingestion
- acute glutathione depletion states:
- acute illness with decreased nutrient intake
- anorexia / bulimia / malnutrition, chronic alcoholism
- Damage to the liver, or hepatotoxicity, results not from paracetamol itself, but from one of its metabolites, N-acetyl-p-benzoquinoneimine (NAPQI)

CLINICAL MANIFESTATION

- Stage 1 (0-24hrs): asymptomatic or GI upset only
- Stage 2 (24-48hrs): nausea & vomiting, right UQ pain and tendernessprogressive elevation of aminotransaminases,, bilirubin, PT
- Stage 3 (48-96hrs): signs / symptoms of progressive hepatic failure including jaundice, hypoglycemia , coagulop-

athy or encephalopathy, renal failure

- Stage 4 : normalization of LFTs & complete resolution of hepatic architecture by 3 months OR progression of hepatic failure then death

- Rarely, after massive overdoses, patients may develop symptoms of metabolic acidosis and coma early in the course of poisoning.

DIFFERENTIAL DIAGNOSIS

- Alcoholic hepatitisDrug-induced or toxin-induced hepatitis

- Hepatobiliary diseaseHepatorenal syndrome

- Ischemic hepatitis (shock liver)Viral hepatitis

WORK-UP

- CBC,LFT, coagulation profile ,RFT, electrolyte ,toxicology screen

- Blood paracetamol level :(Rumack-Matthews or the Acetaminophen nomogram)

  - Nomogram, estimates the risk of toxicity based on the serum concentration of paracetamol at a given number of hours after ingestion

  - A paracetamol level drawn in the first 4 hours af-

ter ingestion may underestimate the amount in the system because paracetamol may still be in the process of being absorbed from the GIT. Therefore a serum level taken before 4 hours is not recommended.

MANAGEMENT

- General : : Airway protection ,breathing and circulation support
- Specific :
    - Activated charcoal dose 1 g/kg (maximum dose 50 g) by mouth in all patients who present within four hours of a known or suspected acetaminophen ingestion.
    - N-Acetylcysteine:Oral at 140 mg/kg loading dose followed by 70 mg/kg every four hours for 17 more doses OR infusion at 150 mg/kg loading dose over 15 to 60 minutes, followed by a 50 mg/kg infusion over four hours; the last 100 mg/kg are infused over the remaining 16 hours of the protocol.
    - Hemodialysis : - If NAC not availableMetabolic acidosis with serum level more than800mq/ml

INHALED POISONING CO

OVERVIEW

- CO is a colorless, odorless gas and is produced by burning material containing carbon.
- Toxicity results from cellular hypoxia caused by impedance of oxygen delivery
- CO reversibly binds Hb 230-270xs more avidly than oxygen .
- Binding of CO to Hb causes an increased binding of oxygen at the other
- 3 Oxygen binding sites resulting in a leftward shift of oxy-Hb dissociation curve &
- decreased availability of oxygen the already hypoxic tissues
- CO binds cardiac myoglobin with even greater avidity than Hb resulting in myocardial depression and hypotension that further exacerbates tissue hypoxia

CLINICAL MANIFESTATION

- Acute CO poisoning:
  - COHb>10% tightness across forehead, possible headache

- COHb>20% throbbing headache
- COHb>30% severe headache, dizziness ,nausea and vomiting
- COHb>40% above symptoms + tachycardia ,tachypnea and collapse.
- COHb>50% collapse ,tachycardia ,tachypnea and convulsion
- COHb>60% respiratory failure , convulsion ,cardiac depression and coma
- COHb>70% cardiopulmonary arrest and death

- Chronic CO poisoning :similar symptoms to acute poisoning but gradual onset of neuropsychiatric symptoms and cognitive impairment.

DIFFERENTIAL DIAGNOSIS

- Toxic alcohol ,Toxic narcosis,Methemoglobinemia and DKA

WORK-UP

- Pulse oximetry overestimate oxyhemoglobin
- Diagnosis is confirmed by measuring the levels of carbon monoxide in the blood by CO –oximetry

- ABG: PaO2 should remain normal(Oxygen saturation is accurate only if measured
- But not if calculated from PaO2)
- CBC, chemistry and coagulation profile.
- Lactate level (lactic acidosis from tissue hypoxia)
- Hyperglycemia and hypokalemia occur with severe intoxication.

MANAGEMENT

- General : Airway protection ,breathing and circulation support
- Specific :
  - 100% oxygen until patient is asymptomatic and levels of percent carboxyhemoglobin (COHb) in the bloodstream are below 10% (some have suggested continuing until below 2%in patients with cardiovascular or pulmonary compromise).
  - Consider immediate transfer of patients with cardiovascular or neurological impairment to a hyperbaric facitiliy(persistent symptoms after 4 hours of normobaric oxygen necessitate transfer to a hyperbaric center)
  - Supportive management

- Hyperbaric oxygenation indicated in :COHb more than 20 %
    - Pregnancy
    - Cardiac ischemia
    - Unconscious after exposure
    - Neurological ,psychiatric features

ALCOHOL TOXICITY

OVERVIEW

- Toxic Alcohols traditionally refers in particular to methanol and ethylene glycol, which are the most important chemicals in the class because they are both of high potential toxicity and wide availability, third toxic alcoholic chemical is Isopropanol.

- Methanol is commonly found in windshield wiper fluid and ethylene glycol in automobile antifreeze and isopropanol is a ubiquitous topical disinfectant.

- It is not the toxic alcohols themselves that produce significant toxicity, but their metabolites. Methanol and ethylene glycol are metabolized to the clinically important metabolites formic acid (methanol) and glycolic and oxalic acid (ethylene glycol).

- Patients may be obtunded and require therapeutic medication infusions and hemodialysis that cannot be accomplished in general inpatient units so patient may require ICU.

CLINICAL MANIFESTATION

- All of the toxic alcohols can produce significant CNS depression, and a compensatory tachypnea may be present if there is a metabolic acidosis.

- Methanol (MeOH)

    - Neurologic: CNS dysfunction/depression, coma.

- Ophthalmologic: Blindness

- Ethylene glycol (EG)
  - Neurologic: CNS dysfunction/depression, coma; multiple cranial nerve deficits.
  - CV: Cardiopulmonary failure.
  - GU: Renal failure.

- Isopropanol
  - Neurologic: CNS dysfunction/depression, coma.
  - CV: Hypotension; myocardial depression.

WORK-UP

- General: toxicology screen, urea &electrolyte ,blood gas, serum osmolality and osmolar gap .
- Specific :
  - (Methanol)high anion gap metabolic acidosis, high osmole gap
  - (Ethyleneglycol) high lactate &osmole gap, acidosis ,Ca oxalate crystalluria,low Ca,Fluorescence of the urine on exposure to ultraviolet radiation
  - (Isopropanol) Acetonemia, acetonuria; anion gap

metabolic acidosis (mild)

MANAGEMENT

- General : Airway protection ,breathing and circulation support
- Specific :

ETHANOL

ETHANOL

OVERVIEW

- Between 2% and 10% of ingested ethanol is excreted intact by the kidneys and lungs, but the major fraction is metabolized by the liver.
- Intoxicationmanifestation: depend on amount and concentration of ethanol , acute or chronic stage and the patient co-morbidity .

CLINICAL MANIFESTATION

- Intoxication:(according to blood alcohol concentrations)
  - 20–79 mg/dL - Impaired coordination and euphoria
  - 80–199 mg/dL - Binge drinking: Ataxia, poor

judgment, labile mood.

- 200–299 mg/dL - Marked ataxia, slurred speech, poor judgment, labile mood, nausea and vomiting
- 300–399 mg/dL - Stage 1 anesthesia, memory lapse, labile mood
- 400+ mg/dL - Respiratory failure, seizure, coma

- Withdrawal*:*
  - Stage 1: occurs 6 to 24 hours or more after the last drink (anxiety, restlessness, decreased attention, tremulousness, insomnia,)
  - stage 2: occurs about 24 hours after the onset of abstinence, (hallucinations, misperceptions, irritability, delusional ,confused)
  - stage 3: occurs 7 to 48 hours after cessation of drinking(seizures)
  - stage 4 :manifests 2 to 6 days, or more, after initiation of abstinence (confusional state ,severe autonomic hyperactivity, Tremors, hallucinations, and seizures ,Hyper adrenergic manifestations like diaphoresis, mydriasis,,tachycardia, hypertension)

- *Wernicke–Korsakoff syndrome:* due to thi-

amin deficiency in chronic ethanol intake.

WORK-UP

- CBC, electrolyte, RFT, LFT, blood gas, coagulation profile and lactic acid.
- Toxic screen and ethanol level.
- Serum osmolarity and the osmolar gap.

DIFFERENTIAL DIAGNOSIS

- DKA , Hypoglycemia
- Carbon Monoxide Toxicity
- Other alcoholic substance toxicity
- Oral Hypoglycemic Agents toxicity

MANAGEMENT

- General: Airway protection, breathing and circulation support.
- Specific :
  - Intoxication: IV thiamine (50 or 100 mg) is given during the initial phase.Dextrose administration is traditionally preceded by thiamine dosing .Correction of electrolyte.

- Withdrawal: benzodiazepine Barbiturates clonidin.

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وزارة الصحة
Ministry of Health

M . O . H
DRUG LIST

ALPHAPITICAL
DRUG INDEX

(A)
abacvir sulfate + lamivudine + zid-ovudine
acetazolam ide
acetylcholine chloride
(acetyl salicylic acid (asprine
acitren
acyclovir
adalimumab
adefovir dipivoxil
adenosine
adrenaline hcl
(adrenaline (epinephrine
albendazole
albumen human
alemtuzumab
alendronate sodium
alfacalcidol
allopurinol
alprazolam
alprostadil (prostaglandin e1) pediatric dose
alteplase
aluminum hydroxide + magnesium hydroxide
atracurium besylate
atropine sulphate
azathioprine
azelaic acid
azithromycin
(B)
bacillus calmette-gue rin
bacitrin zinc + polymixin b sulphate
baclofen
basiliximab
bcg vaccine (bacillus calmette – Guer-(in
beclomethasone
bnzhexol hcl
benzoyl peroxide
benztropine mesylate
beractant,phospholipid
betahistine dihydrochloride
betamethasone
betaxolol hcl
bevacizumab
bicalutamide
bimatoprost

amantadine hcl	bisacodyl
amethocain	bisoprolol fumarate
amikacin sulfate	bleomycin
amiloride hcl + hydrochloridethiazide	bortezomib
aminoacids for adult	bosentan
aminocaproic acid	botulinum toxin type a
aminoglutethimide	bretulium tosylate
aminophyline	brimonidine tartrate
amiodarone hcl	brinzolamide
amlodipine besilate or felodephne	bromocriptine
ammonium chlorhde	b-sitosterol
amobarbitol	budesonide
amoxicilline trihydrate	budesonide 3mg capsules
amoxicilline trihydrate + clavulanate potassium	budesonide turbuhaler
amphotericin b liposomal	Bulk-forming laxative
mpicilline sodium	bupivacaine hcl
anagrelide	buprenorphine
anastrozole	bupropion
antihemorroidal / without steroids	busulfan
(anti rabies serum (horse origin	**(C)**
anti-rho(d) immunogloblin	cabergoline
(antithymocyte globulin(atg	calcipotriol
apracloidine hcl	calcipotriol + betamethasone dipropionate
aripiprazole	(calcitonin (salmon)-(salcatonin

artemether + lumefantrine	calcitriol
artemisinin	calcium carbonate
artesunate	calcium chloride
artesunate + sulfadoxine + pyrimethamine	calcium gluconate
artificial tears eye dropper	calcium lactate
(ascorbic acid (vitamin c	capecitabine
(sparaginase (crisantaspase	capreomycine
atazanavir	captopril
atenolol	carbamazepine
atorvastatin	carbimazole

carboplatin	cyclophosphamide
carboprost tromethamine	cycloserine
carboxymethyl-cellulose	cyclosporine
carmustine	cyprotone acetate + ethinyl estradiol
carteolol hcl	cytarabine for injection
carvedilol	**(D)**
caspofungin acetate	dabigatran
cafaclor	dacarbazine
cefepime hydrochloride	dactinomycin
cefixime	dalteparin
cefixime sodium	danazol
ceftazidime pentahydrate	dantrolene sodium
ceftriaxone sodium	dapsone

cefuroxime	darunavir
celecoxib	dasatinib monohydrate
cephalexin monohydrate	daunorubicin hcl
cephradine	desmopressin acetate
cetuximab	dexamethasone
chloral hydrate	Dextran (dextran40) + sodium chlorid
chlorambcil	dextromethorphan
chloramphenicol	dextrose
chlordiazepoxide hcl	diazepam
chlorhexidine gluconate	diazoxide
chloroquine	diclofenac
chlorpheniramine maleate	didanosine
chlorpromazine hcl	diethylcarbamazine citrate
chlorthalidone	digoxin
chlorzoxazone	dihydralazine mesilate or hydralazine hcl
(cholecalciferol (vitamine d3	diloxanide furoate
cholestyramine	(diltiazem hcl (sustainad release
cincalcet hydrochloride	dimenhydrinate
cinnararizine	dinoprostone
ciprofloxacin	diphenhydramine hcl
cispltin	(diphetheria,tetanus,pertussis (dpt
citalopam hydrobromide	diphetheria,tetanus vaccine for adult
clarithromycin	diphetheria,tetanus vaccine for children
clindamycin	diphetheria antitoxine

clindamycin or erythromycin for acne	dipyridamol
clindamycin phosphate	disodium pamidronate
clofazimin	disopyramide phosphate
clomiphene citrate	distigmine bromide
clomipramine hcl	dodutamine hcl
clonazepam	docetaxel
clonidine hcl	docusate sodium
clopidogral	domperidone
clotrimazole	dopamine hcl
cloxacillin or flucloxacillin sodium	dorzolamide&1
clozapine	doxorubicin
codeine phosphate	duloxetine
colchicine	dydrogesterone
colistin sulphomethate sodium	**(E)**
conjugated estrogen + norgestrel	econazole
corticorelin (corticotrophin-releasing (factor,crf	edrophonium chloride
cromoglycate sodium	efavirenz
(cyanocobalmin (vit b12	(electrolyte oral rehydration salt (ors
cyclopentolate hcl	emtricitabine

cyclophosphamide	carboplatin
cycloserine	carboprost tromethamine
cyclosporine	carboxymethyl-cellulose
cyprotone acetate + ethinyl estradiol	carmustine
cytarabine for injection	carteolol hcl

(D)	carvedilol
dabigatran	caspofungin acetate
dacarbazine	cafaclor
dactinomycin	cefepime hydrochloride
dalteparin	cefixime
danazol	cefixime sodium
dantrolene sodium	ceftazidime pentahydrate
dapsone	ceftriaxone sodium
darunavir	cefuroxime
dasatinib monohydrate	celecoxib
daunorubicin hcl	cephalexin monohydrate
desmopressin acetate	cephradine
dexamethasone	cetuximab
Dextran (dextran40) + sodium chlo-rid	chloral hydrate
dextromethorphan	chlorambcil
dextrose	chloramphenicol
diazepam	chlordiazepoxide hcl
diazoxide	chlorhexidine gluconate
diclofenac	chloroquine
didanosine	chlorpheniramine maleate
diethylcarbamazine citrate	chlorpromazine hcl
digoxin	chlorthalidone
dihydralazine mesilate or hydralazine hcl	chlorzoxazone

diloxanide furoate	cholecalciferol (vitamine d3)
diltiazem hcl (sustainad release)	cholestyramine
dimenhydrinate	cincalcet hydrochloride
dinoprostone	cinnararizine
diphenhydramine hcl	ciprofloxacin
diphetheria,tetanus,pertussis (dpt)	cispltin
diphetheria,tetanus vaccine for adult	citalopam hydrobromide
diphetheria,tetanus vaccine for children	clarithromycin
diphetheria antitoxine	clindamycin
dipyridamol	clindamycin or erythromycin for acne
disodium pamidronate	clindamycin phosphate
disopyramide phosphate	clofazimin
distigmine bromide	clomiphene citrate
dodutamine hcl	clomipramine hcl
docetaxel	clonazepam
docusate sodium	clonidine hcl
domperidone	clopidogral
dopamine hcl	clotrimazole
dorzolamide&1	cloxacillin or flucloxacillin sodium
doxorubicin	clozapine
duloxetine	codeine phosphate
dydrogesterone	colchicine
(E)	colistin sulphomethate sodium
econazole	conjugated estrogen + norgestrel

edrophonium chloride	corticorelin (corticotrophin-releasing factor,crf)
efavirenz	cromoglycate sodium
electrolyte oral rehydration salt (ors)	cyanocobalmin (vit b12)
emtricitabine	cyclopentolate hcl

enalapril malate	Gemfibrozil
enfuvirtide	gentamicine
enoxaparin	glibenclamide
entecvir	gliclazide
ephedrine hydrochloride	glipizide
epirubicin hcl	glucagon
epoetin (recombinant human eryth- (ropoietins	glycrine
ergotamine tartarate	glycopyrrolate bromide
erlotinib hydrochloride	gonadorelin (gonadotrophine-releas- (ing hormone, lhrh
erythromycin	goserlin acetate
escitalopram	granisetron
esmolol hcl	griseofulvin micronized
esomeprazole magnesium trihydrate	(H)
estradiol valerate	haemophilus influenza vaccine
etanercept	haloperidol
ethambutol hcl	heparinecalcium for subcutaneous injection
ethanolamine oleate	(heparine sodium (bovine
ethinyl estradiol	(hepatitis b vaccine (child
ethionamide	homatropine

ethosuximide	human chorionic gonadotrophin
etomidate	human fibrinogen
etoposide	(human isophane insulin (nph
etravirine	human menopausal gonadotrophins,-follicle
(F)	stimulating hormone + luteinizing hormone
factor ix fraction for injection, which is sterile and free of hepatitis, hivand any other infectious disease agent	human normal immunoglobulin for i.m injection
factor viii (stable lyophilized con-(centrate	(human soluble insulin (regular
fat emulsion	hyaluronidase
(felodipine retard (modified release	hydralazine hcimesilate
fentanyl citrate	hydrochlorothiazide
ferrous salt	hydrocortisone
ferrous sulphate or fumarate + folic acid	hydroxurea
filgrastim g-csf	hydroxychloroquine sulphate
finasteride	ydroxyprogesterone hexanoate
fluconazole	hydroxypropyl methylcelulose
fludarabine phoaphate	hyocine butylbromide
fludrocortisones acetate	(I)
flumazenil	ibuprofen
fluorescein	ifosfamide
fluorometholone	iloprost
fluorouracil	imatinib mesilate

fluoxetine	imidazole derivative
flupenthixol	imipenem + cilastatin
fluphenazine decanoate	imipramine hcl
flutamide	(indapamide (sustaind release
fluticasone	indinavir
fluvoxamine malate	indomethacin
follitropin	infliximab
formoterol + budesonide turbuhaler	influenza virus vaccine
foscarnet	injectable polio vaccines (ipv) (salk (vaccine
fosinopril	insulin aspart
furosemide	nsulin detmir
fusidic acid	insulin glargine
(G)	insulin lispro
gabapentine	interferon alpha
ganciclovir	interferon beta 1a
gemcitabine	ipratropium bromide

medroxyprogesterone acetate	irbesartan
mefenemic acid	irintecan hydrochloride
melfloquine hcl	iron saccharate
megestrol acetate	isoniazid
meloxicam	isoprenaline hcl (isoproterenol hcl)
melphalan	isosorbide dinitrate
memantine hcl	isosorbide dinitrate

meningococcal polysaccharide sero group (a,c,y,w-135)	isotretinoin
mercaptopurine	itraconazole
meropenem	ivabradine
mesalazine	ivermectin
mesna	**(K)**
metformin hcl	kanamycin
methadone hcl	kaolin + pectin
methotrexate	ketamine hcl
methoxsalen + ammidine	ketoconazole
methoxy polyethylene glycol-epoetin beta	ketotifen
methyldopa	**(L)**
methylerrgonovine maleate	labetalol hcl
methylphenidate	lactulose
methylperdnisolone	lamivudine
metoclopramide hcl	lamotrigine
metolazone tartrate	lansoprazole
metolazone	latanoprost
metolazone tartrate	l-carnitine
etronidazole	leflunomide
mexiletine hcl	lenalidomide
micafungin sodium	letrozole
miconazole	Leucovorin calcium
midazolam	leuprolid depo acetate
miltefosine	levamizole

minocycline hcl	levetiracetam
mirtazapine	levofaoxacin
misoprostol	levothyroxine sodium
mitomycin	lidocaine + fluorescein sodium
mitoxantrone hydrochloride	Lidocaine hcl
mixed gas gangrene antitoxin	linezolid
moclopemide	liquid paraffin
mometasone furoate	lisinopril
montelukast sodium	lithium carbonate
orphine sulphate	lomustine
moxifloxacin hydrochloride	Loperamide hcl
ultienzyme (pancreatic enzymes:protease200-600u;lipse5,000-10,000u and amylase5,000-10,000u) /capsule or enteric coated tablet	lopinavir + ritonavir
multivitamins	lorazepam
mupirocin	losartan potassium
muromonab-cd3	lubricant
mycophenolate mofetil	(M)
(N)	magnesium oxide
nafarelin	mannitol
nalbuphine hcl	maprotilline hcl
naloxone hcl	measles vaccine
naphazoline	mebendazole
Naproxene	mebeverine hcl
natalizumab	mechlorethamine hcl
natamycin	meclozine + vitamine B6

phenylephrine hcl	nateglinide
phenytoin sodium	nelfinavir
phosphate enema	neomycin sulphate
phosphate salt	neostigmine methylsulpfate
phytomenadione	niclosamide
pilocarpine	nicotine(24-hour effect dose)
pioglitazone	nifedipine retard (modified release)
piperacillin + tazobactam	nilotinib
plasma protein solution	nimodipine
pneumococcal polyvalent (23 valent) vaccine	nitrazepam
poliomyelitis vaccine live oral: (sabin strain)	nitrofurantoin
polyacrylic acid	nitroglycerin
polyethylene glycol,3350-13.125g oral ppowder, sodium bicarbonate 178.5mg,sodium chloride350mg , potassium chloride 46.6mg/sachet	isosorbide dinitrate
polymyxin b sulphate + neomycin sulphate + hydrocortisone	non sedating antihistamine tablet (cetirizine or noratadine)
polystyrene sulphate resins (calcium)|	noradenalin acid tartrate
potassium salt	norethisterone
pramipexole	norfloxacin
pravastatin	nystatin
praziquantel	(O)
prazosin hcl	octreotide
prednisolone	ofloxacin

pregabalin	oily phenol injection
Prilocaine + felypressin	olanzapine
Primaquine phosphate	olopatadine hcl
Primidone	omeprazole sodium
Procainamide hcl	ondansetron
Procarbazine	orienograstim (g-csf)
Procyclidine hydrochloride	oxaliplatin
Progesterone	oxybuprocaine
Proguanil hcl	oxybutynin hcl xl
Promethazine hcl	oxymetazoline
proparacaine	oxytocin
propfol	(P)
propylthiouracil	paclitaxel
Propranolol hcl	paliperidone
Protamine sulfate	palivizumab
prothionmide	pancuronium bromide
Protirelin (thyrotrpphin-releasing hormone,trh)	pantoprazoole sodium sesquihydrate
Pseudoephedrine hcl 30mg + anti-histamine	papaverin
Pumactant phospholipid	para-amino salicylate sodium
Pura aluminum hydroxide	paracetamol
Pyrazinamide	pegaspargase
Pyrethrins	pegylated interferon alpha 2a
Pyridostigmine	pemetrexed
Pyridoxine hcl (vitamine b6)	penicillamine

Pyrimethamine	penicillin benzathine (penicillin g)
Prilocaine + felypressin	pentamidine isethionate
primaquine phosphate	pentavalent vacc.(hbv+hib+dtp)
(Q)	pentoxifylline
quetiapine	perindopril
quinidine sulfate	permethrin
quinine dihydrochloride	pethidine hcl
quinie sulphate	phenobarbital (phenobarbitone)
(R)	phenoxymethyl penicillin (penicillin v potassium)
rabies immunoglobulin for i.m injection	phentolamine mesylate
stibogluconate sodium (organic pentavalent antimony)	rabies virus vaccine
streptokinase	racemic epinphrine
streptomycin sulfate	raltegravir
strontium ranelate	ranitidine
succinylcholine choloride	rasburicase
sucralfate	recombinant factor via
sulfacetamide	repaglinide
sulfadiazine	reteplase
sulfadoxin500mg + pyrimetha-mine25mg	retinoin (vitamine a)
sulfasalazine,500mg/tablet	ribavirin
sulindac	rifabutine
sulpiride	rifampicin
sumatriptan succinate	riluzole

(T)	ringer's lactate solution
tacrolimus	risperidone
tamoxifen citrate	ritonavir
tamsulosin hcl (modified release)	rituximab
telmisartan	rivaroxaban
temazepam	rocuronium bromide
tenofovir disoproxil fumurate	ropivacaine hcl
terbinafine	rose bengal
teriparatide	rosuvastatin
terlipressin acetate	(S)
tetanus antitoxin	salbutamol
tetanus immunoglobulin for i.m injection	salmeterol + fluticasone propionate
tetanus vaccine	scorpion anti – venin
tetracosactrin (corticotrophin)	selegiline hcl
tetracycline hcl	senna
thalidomide	sevelamer
theophylline	sevoflurance
thiacetazone	sildenafil
thiamine (vitamine b1)	silver sulfadiazine (steril)
thioguanine	simethicone
thiopental sodium	simvastatin
tigecycline	sirolimus
timolol	sitagliptin phosphate
tinzaparin sodium	snake anti-venin

tiotropium	sodium acetate
tirofiban hydrochloride	sodium aurothiomalate
tobramycin + dexamethasone	sodium bicarbonate
tobramycin sulfate	sodium chloride
tolterodine tartrate	sodium cormoglycate
topiramate	sodium hyaluronate
trace elements additive (pediatric dose)	sodium hyaluronate intra-articular (mw over 3 sillion)
tramadol hcl	sodium nitropruprusside
tranexamic acid	sodium phosphate
trastuzumab	sodium valpproate
trazodone	somatropin (human growth hormone)
tretinoin	sorafenib
triamcinoloneacetonide	sotalol hydrochloride
triamterene + hydrochlorthiazide	spectinomycin hcl
trifluperazine hcl	spiramycin
trifluridine	spironolactone
trimetazidine dihydrochloride (modified release)	sterile balanced salt solution (bss)
trimethoprim + sulfamethoxazole	sterile water for injection
triple virus vaccine (measles-mumps-rubella)	verapamil hcl
triptorelin acetate	verapamil hcl (sustaind release)
tropicamide	vigabatrin
tuberculin ppd skin test	vinblastine sulfate

typhoid vaccine	(W)
(U)	warfarin sodium
urea	water for injection (sterile)
urofollitrophine f.s.h	wax removal
ursodeoxycholic acid	(X)
(V)	xylometazoline hcl
valaciclovir hcl	(Y)
valganciclover hcl	yellow fever vaccine
valsartan	(Z)
vancomycin hcl	zidovudine (azidothymidine,AZT)
varicella-zoster virus (chicken pox vaccine)	zidovudine + lamivudine
vasopressine	zinc sulfate
vecuronium bromide	zolledronic acid
venlaxine hcl (sustaind release)	zolpedem tartrate
vincristine sulfate	zuclopenthixol acetate
vinorelbine	
vitamine B1 & B6& B12	
vitamine B complex	
vitamine E	
voriconazole	

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Illustration

Flowchart by Hassan Adnan Bukhari

Medication Table by Faisal Ahmed Al-Wdani