Handbook of
Critical Care Medicine

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2009

to my father
Dr Sirimananda Rajapakse

who taught me most of what I know
and showed me where to learn the rest

Preface

The management of critically ill patients is an important and integral part of internal medicine practice. Often, junior doctors and medical students receive insufficient training in this area of medicine. There are important differences in the management of critically ill patients when compared with relatively stable patients, and these differences are vital in saving lives.

Critical care medicine is different from most other disciplines in that the approach is more problem oriented, rather than disease or condition oriented. This does not mean that the role of the ICU clinician is simply to correct parameters which are out of normal range. On the contrary, a clear understanding of the basis of the clinical manifestations in critically ill patients is essential to proper management. Anticipation and forward planning in care is also vital, as is the rapidity of response required from the treating team.

While we are often familiar with diseases and conditions, we often feel challenged when faced with having to manage a critically ill patient. This book aims to give junior doctors and medical students an introduction to the practice of critical care medicine, orienting the reader towards a problem-solving approach. It is hoped that this book will serve to make the subject of critical care medicine seem less threatening.

I gratefully acknowledge the assistance from Dr Dinoo Kirthinanda and Dr Sujani Wijeratne, Research Associates, who helped with some of the chapters. Special thanks also go to Dr Dinushi Weerasinghe who meticulously formatted and proofread the final draft.

Senaka Rajapakse

2009

Contents

Clinical approach to the critically ill patient

Critical care medicine is, in principle, very similar to general medicine, except that everything is more intense. Patients' parameters and disease processes change much faster. Decisions have to be taken early and rapidly. Adjustments in care have to be much more dynamic. There is no place for complacency. Things have to be done by the minute and hour, rather than by the day and week. The clinician must be 'on the ball' about his patient. Hence the traditional approach of history, examination, investigations, diagnosis and treatment is not adequate. Often one has to quickly assess the patient, institute life saving measures, correct parameters and start empiric treatment quickly, even before arriving at a definite diagnosis. Knowledge, skills and attitudes are equally important.

This chapter deals with the approach to assessing, stabilising, diagnosing and planning management of a new patient brought into the ICU. The approach is not, however, limited to a new patient; things change so fast in critically ill patients, that the same degree of care and alertness must be maintained throughout the patients' stay in the ICU.

INITIAL ASSESSMENT – IDENTIFY PHYSIOLOGICAL ABNORMALITIES

MAKE SURE THE PATIENT IS SAFE

Acutely ill patients are at great risk of adverse effects and system errors. Life threatening problems are often missed, and safe care is often not instituted early enough. Recognition of alarm features which indicate impending critical events is vital. The clinician must have a clear understanding of these alarm features.

Quickly assess the patient. Do not waste time taking a detailed history; that can be done later.

Assess the clinical setting quickly – the position the patient is in, the availability of monitoring, oxygen, other resuscitation equipment, support staff, documentation etc.

Assessing the patient - ABCDEFG

Airway: Clear the airway. Remove secretions/obstruction if present. (See section on airway management).

Breathing: Is the patient breathing? Is the pattern of breathing regular? Is he tachypnoeic? A respiratory rate of over 25/min is highly suggestive of critical illness, and close monitoring is essential. Give high flow oxygen by mask. (Note: Do not give high flow oxygen if COPD is likely as it can result in respiratory depression and hypercapnoea.) Auscultate the chest, check if breath sounds are equal, and listen for wheezes and crackles. Look specifically for a pneumothorax, and quickly check for chest trauma. If the patient is not breathing, commence advanced cardiac life support (ACLS). Check oxygen saturation if available. Early intubation is preferable if the patient is unable to maintain oxygen saturation above 90%. In the case of COPD, lower levels of oxygen saturation may be tolerated.

Circulation: Assess the pulse rate and volume. Establish IV access. If the patient is hypotensive and the veins are collapsed, a central venous line may be required. If there is no palpable pulse, commence ACLS. Is there tachycardia or bradycardia? Check capillary refill. Check the blood pressure. A mean blood pressure around 65-90mmHg or systolic blood pressure above 90mmHg is adequate for a start. Hypotension could be hypovolaemic, cardiogenic (narrow pulse pressure) or septic (wide pulse pressure). Do not waste too much time checking the JVP; it is not reliable at this stage. If the patient is hypotensive, quick and aggressive fluid resuscitation is vital; in hypovolaemic and septic shock, it is the single most important intervention which will improve survival. If cardiogenic shock or left ventricular failure is likely, appropriate immediate steps should be taken. (See sections on Acute Myocardial Ischaemia and Heart Failure). Auscultate the heart for murmurs, gallop rhythm etc. If bronchospasm is present, start bronchodilator treatment without delay.

Conscious Level: Assess level of consciousness. If the patient is obtunded or confused, what is the reason? Is it pain, breathlessness or something else? If consciousness is reduced, is it due to a primary neurological problem such as stroke, encephalitis, seizure? Is neck stiffness present? (SAH, meningitis) Is there evidence of head trauma? Examine the pupils. Any inequality? Check

the patient's capillary blood glucose, and give IV glucose if low. Is loss of consciousness due to a metabolic problem or drug/toxin overdose?

Drug therapy: What drugs is the patient currently taking? Specifically ask about:

- Drugs which cause sedation – opioids, benzodiazepines
- Overdose – paracetamol, benzodiazepines, neuroleptics, antidepressents
- Drugs which precipitate renal failure – NSAIDs, aminoglycosides
- Drugs which cause hyperkalaemia – ACE inhibitors, potassium tablets, potassium sparing diuretics
- Drugs which can cause hyponatraemia – diuretics, antidepressants
- Hypoglycaemic agents
- Drug allergies

Decide on whether any emergency drugs must be given now.

Excretion: Has the patient passed urine?
If the patient is catheterised, is their urine in the bag? Is it concentrated, blood stained? What has the documented urine output been?
Other sources of fluid loss – diarrhoea? drains?
Is there any evidence of bleeding, especially from the GI tract – haematemesis, malaena?

Fluids: What fluids has the patient had over the past 24 hours and the past few days? Have electrolytes and renal parameters been checked? Is hypovolaemia likely? If so give IV fluids. Check electrolytes, especially potassium urgently.

General features: Does the general appearance suggest a particular disease? Does the patient look ill? Note that an ill looking patient is always ill, while a well looking patient also maybe quite ill. Is the patient febrile? Are the extremities cold (cardiogenic shock, hypovolaemia)? Or warm (sepsis, thyrotoxicosis)? Is there jaundice, pallor, cervical lymphadenopathy, oedema, rashes? Examine the abdomen for distension, organomegaly, masses, distended bladder, and herniae. Are their any intravenous lines, catheters? How long since they were put in (possible sources of infection)? Look for limb cellulitis and skin sepsis. Is there any evidence of endocrine diseases?

IS IMMEDIATE CORRECTION OF ANY PHYSIOLOGICAL ABNORMALITIES REQUIRED?

Start monitoring the patient – pulse, blood pressure, CVP, intra-arterial blood pressure if hypotensive, respiratory rate, pulse oxymetry, urine output. Establish adequate IV access.

By now, the patient's airway has been taken care of. If breathing was not adequate, the patient has been intubated and ventilated. Adjust ventilatory parameters, and make sure that the endotracheal tube is positioned correctly. Make sure that secretions are sucked out, and sputum samples are collected for gram stain and culture.

If the patient is breathing spontaneously, assess whether respiratory support is needed. Check arterial blood gases. Continue oxygen by mask, and consider nasal CPAP (continuous positive airway pressure) if necessary. Secure IV access. Take relevant investigations. The usual initial blood investigations are:

- Full blood count
- CRP and ESR
- Renal function tests
- Electrolytes including calcium, magnesium and phosphate
- Liver function tests
- Clotting profile
- Cardiac enzymes and troponin
- Blood cultures, urine culture

Start IV fluids, depending on your clinical assessment of hydration and cardiovascular status.

Do an urgent ECG – look for:

- Ischaemic changes
- Arrhythmias
- Evidence of hyperkalaemia – if present, give emergency treatment.

Arrange for an urgent in-ward chest radiograph. Look for pneumonia, pneumothorax, pleural effusion, position of the ET tube and central venous lines (adjust these accordingly), cardiomegaly, para-aortic lymph nodes.

Ask yourself the following questions:

- Is the patient in shock? What type – hypovolaemic, cardiogenic, septic?
- Does the patient have acute coronary syndrome? Is he in heart failure?
- Is the patient septic? Tachypnoea, fever, evidence of pneumonia, UTI or other obvious infection, shock with a wide pulse pressure.
- Is the patient in renal failure? Is he producing urine? Is a fluid challenge in order?
- Is the patient in liver failure? Any evidence of encephalopathy? Should a liver failure regime be started?
- If the patient's level of consciousness is reduced, is it due to an intracranial pathology or systemic/metabolic abnormality?

Think of the 'blind spots' – pulmonary embolism, pancreatitis

A more detailed history of the patient's condition can now be obtained from the patient, relatives, and staff previously responsible for the patient's care. Look through the hospital notes, taking care to identify trends in the results of investigations and patient parameters. Examine previous medical records, prescriptions, and investigations. In particular look at previous ECGs, chest radiographs, renal and liver parameters.

Start appropriate initial therapy. Make sure that these are administered; communicate with the rest of the staff. The most essential drugs are

- Antibiotics
- Inotropes and vasoconstrictors
- Sedatives and neuromuscular blocking agents
- Antihypertensives

Check interactions and possible adverse effects relevant to the patient's condition.

MONITOR TRENDS

Is the patient better than since he came in? Have the essential physiological abnormalities been corrected? Are these parameters improving? Are they likely to become deranged again, since only emergency treatment has been given so far? What steps should be taken to prevent them from becoming

deranged again? This usually constitutes specific therapy, i.e. treatment of the underlying clinical condition.

ALWAYS CHECK EVERYTHING YOURSELF. MAKE SURE THAT ALL ASPECTS ARE COVERED. NEVER ASSUME THAT SOMEONE ELSE WILL DO IT.

Homeostasis

Much of ICU management involves correcting and maintaining electrolytes, acid base balance, and hormonal imbalance. Clinicians sometimes make the mistake of simply attempting to correct a biochemical value to normal without identifying and treating the underlying condition which results in the deranged value. Every abnormal value has a reason, and it is vital that that reason is identified, and appropriate measures taken to both correct the abnormality, and to prevent it from occurring again.

Trends are also important, and it is vital that the clinician identifies trends in homeostatic parameters, which though comparatively innocent at the start, may progress to life threatening derangement.

Deranged homeostasis occurs because of the disease as well as the drugs used to treat it, with complex interaction between the two. Before every new therapeutic or diagnostic manoeuvre, ask yourself whether it might interfere with homeostasis. With experience these become commonplace, but there is a definite place for checklists and failsafe measures to prevent potential problems.

Serum electrolytes; sodium, potassium, magnesium, calcium, phosphate, and blood gases must be monitored at least once daily in critically ill patients, and possibly more frequently if deranged.

HYPONATRAEMIA

A serum sodium below 135mEq/L is considered hyponatraemia. It reflects a relative excess of free water to solute. There are several types:

- **Hypotonic hyponatraemia** – this is the commonest type. It can be associated with normal or reduced intravascular volume.
- **Hypovolaemic hyponatraemia** – seen in cirrhosis, congestive heart failure and nephrotic syndrome. Oedema may or may not be present, depending on the use of diuretics.
- **Euvolaemic hyponatraemia –** seen in SIADH and primary polydipsia
- **Hypertonic hyponatraemia** – also known as dilutional hyponatraemia, this most often occurs due to hyperglycaemia or

mannitol administration. Water is drawn into the vascular compartment by the osmotically active molecules, lowering the plasma sodium by dilution.

- To calculate the plasma sodium in hyperglycaemia, use the following formula –
  Corrected PNa = Measured PNa + [(Change in plasma glucose mmol/l) / 3]
- **Isotonic hyponatraemia** – also known as spurious hyponatraemia or pseudohyponatraemia. It occurs in severe hyperlipidaemia or hyperproteinaemia (myeloma). Plasma sodium is determined by measuring the sodium content per litre of whole plasma. When the non-water component of plasma increases, the sodium concentration artefactually falls.

Diagnosis

- In hypotonic hyponatraemia, cerebral oedema occurs due to fluid shift into the cells. Confusion, stupor, convulsions and coma can occur.
- Look for likely precipitants/underlying causes.
- Features of hypothyroidism – myxoedema facies, dry skin, hoarse voice, daytime sleepiness, slow-relaxing ankle jerks.
- Features of adrenal insufficiency – pigmentation, low blood pressure, postural drop, high serum potassium, hypoglycaemia.
- Oedema – evidence of heart failure, nephrotic syndrome, cirrhosis.
- Drugs – diuretics, other drugs listed above, ecstasy.
- Any of the causes of SIADH.
- TURP has a high risk of hyponatraemia, as the prostate bed is irrigated with solutions containing glycine, sorbitol or mannitol. Always check the serum sodium after TURP.
- Plasma osmolality will help categorise the type of hyponatraemia.
- In most cases, urinary osmolality is low, except primary polydipsia where water excretion is normal but intake is high.
- Plasma uric acid level: the initial water retention and volume expansion in the SIADH leads to hypouricaemia.

Causes of hypotonic hyponatraemia
Disorders in which ADH levels are elevated
Effective circulating volume depletion • True volume depletion • Heart failure • Cirrhosis • Thiazide diuretics
Syndrome of inappropriate ADH secretion, including reset osmostat • CNS disorder, including stroke, hemorrhage, infection, trauma, and psychosis • Tumour- small cell lung carcinoma, occasionally other lung tumours, duodenum or pancreas • Drugs – chlorpropamide, carbamazepine, vincristine, vinblastine, cisplatin, thioridazine, haloperidol, amitriptyline, monoamine oxidase inhibitors, bromocriptine, amiodarone, ciprofloxacin • Lung disease – pneumonia, tuberculosis, PCP, rarely other lung diseases • Major abdominal or thoracic surgery • Other infections, particularly in the elderly • Administration of vasopressin or oxytocin • HIV infection
Hormonal changes • Adrenal insufficiency • Hypothyroidism • Pregnancy
Disorders in which ADH levels may be appropriately suppressed
Advanced renal failure
Primary polydipsia, (including Ecstasy)
Alcohol

Treatment of hyponatraemia

In severe symptomatic hyponatraemia (Na <120mEq/L), correction with hypertonic saline is necessary. Give 3% saline in a dose of upto 60ml/hour. The rate of correction must be no more than 2 mEq/L/hour. Serum sodium must be monitored closely, ideally every hour, and 3% saline should be stopped when symptoms resolve. The total increase should be kept below 10-12mEq/day. In asymptomatic hyponatraemia, a rate of correction of 0.5mEq/L/hour is adequate – this can be achieved by fluid restriction alone. Restrict fluids to 1.0-1.2L/day. Oral salt can be added but can worsen oedema if heart failure or cirrhosis is present. IV Furosemide may be of use in hyponatraemia, as it excretes water in excess of sodium. If patients are hypovolaemic and hypotensive, resuscitation with normal saline must be done first.

Why should sodium be corrected slowly?

Too rapid correction (faster than 2mEq/L/hour) can result in osmotic demyelination syndrome (central pontine myelinolysis, and the Marchiava-Bignami syndrome). It occurs from 2 to 6 days after correction of sodium. Symptoms include dysarthria, dysphagia, paraparesis or quadriparesis, behavioral disturbances, lethargy, and coma; seizures may also be seen rarely. It is irreversible. Post-menopausal women are more susceptible.

Cerebral salt wasting: This occurs in cerebrovascular disease, particularly after SAH. Similar to SIADH, however the primary defect is renal salt wasting, resulting in a secondary rise in ADH secretion. It is difficult to differentiate from SIADH, and the main difference is that extracellular volume depletion is present. Signs of volume depletion such as hypotension, decreased skin turgor, elevated hematocrit, possibly increased BUN/serum creatinine ratio should be looked for, despite a high urine sodium concentration. SAH also causes SIADH, and the differentiation is important because cerebral salt wasting is treated with volume expansion.

HYPERNATRAEMIA

Hypernatraemia is more commonly discovered from the laboratory results. It can result in hyper-reflexia, coma or seizures.

It could result from renal water loss– diabetes insipidus, or high doses of loop diuretics, or due to extrarenal water loss– diarrhoea and vomiting. Most of the time, both water and sodium are lost, but water is lost in excess of sodium. Rarely, hypernatraemia occurs following treatment with hypertonic saline or sodium bicarbonate, where the total body sodium is high. Usually the cause is obvious from the history. Polyuria of >10L/day is present in diabetes insipidus. Sometimes a water deprivation test is necessary to make the diagnosis.

Causes of cranial diabetes insipidus	**Causes of nephrogenic diabetes insipidus**
Brain death Neuro trauma Brain tumours Neurosurgery Meningitis, brain abscess	Congenital nephrogenic DI Hypercalcaemia Hypokalaemia Drugs: lithium, demeclocycline, amphotericin B Renal tubular acidosis

Hypernatraemia causes shrinkage of brain cells. If the patient is hypovolaemic, normal saline should be administered to normalise plasma volume, after which the hypertonicity should be brought down by increasing oral water intake, or by administering intravenous half normal saline or dextrose. Rarely, in resistant hypernatraemia, haemodialysis may be necessary.

How much water will the body need?

Calculate the water deficit.

Water deficit = Current body water X [(plasma sodium/140)-1]

Ideal body water is 50-60% of body weight. However, patients with hyponatraemia are water depleted; hence it is reasonable to use a value 10% below, i.e., 40%.
This deficit is the amount of water which should be replaced. However, ongoing insensible and possibly renal water loss is also present, usually around 30-40mL/hour. This should be added to the water requirement.

The rate of correction should not be more than 1mEq/L/hour, and not more than half the water deficit should be given within 24 hours.

HYPOKALAEMIA
Symptomatic hypokalaemia occurs when the potassium level drops below 3mmol/L. The main symptoms are cardiac arrhythmias and muscle weakness.

Hypokalaemia is likely to be present in the following situations:

- Treatment with loop diuretics, osmotic diuretics
- Other drugs – amphotericin B, ticarcillin, beta-2 adrenergic agents (salbutamol)
- Aggressive correction of acidosis, especially with sodium bicarbonate.
- Diarrhoea and laxative use, NG drainage
- Dietary restriction of potassium
- Polyuric phase of acute tubular necrosis
- Patients on large doses of insulin
- Post surgical period
- Liver disease
- Mineralocorticoid excess
- In marked leukocytosis, for example acute leukemia, where intracellular uptake of potassium can result in a low serum potassium
- Hypomagnesaemia

Metabolic alkalosis is a complication of long standing hypokalaemia, as hydrogen ions are excreted in exchange for potassium irons. However, in type I and II renal tubular acidosis, hypokalaemia is present. Hence, if hypokalaemia is associated with metabolic acidosis, consider the possibility of renal tubular acidosis. Hypomagnesaemia leads to potassium wasting,

and unless hypomagnesaemia is corrected, it will not be possible to maintain the potassium level.

Most hypokalaemia cases encountered in the ICU are due to one of the causes given above, and the cause is generally easy to identify. Measurement of 24 hour excretion is not usually required, nor feasible.

Management

Severe hypokalaemia with cardiac arrhythmias can be corrected by giving IV potassium. **NEVER GIVE POTASSIUM AS AN IV BOLUS INJECTION, AS IT CAN CAUSE CARDIAC ARREST.** The recommended rate of intravenous administration of K^+ is 10 mEq/hr in a peripheral line or 20 mEq/hr using a central venous catheter. If the patient is on IV drips, potassium could be added to the IV infusion. IV saline is better than IV dextrose as infusion fluid, because dextrose can drop the serum potassium levels initially. Monitor potassium every 4-6 hours. Correct hypomagnesaemia together with potassium replacement. Moderate or mild hypokalaemia can be corrected with oral potassium. Oral 60-80mEq/day is the usual dose, higher if losses are severe.

The usual salt used is potassium chloride. In acidosis and/or hypophosphataemia (for example, diabetic ketoacidosis), potassium phosphate is preferred.

Anticipate hypokalaemia. Patients with conditions (listed above) which predispose to hypokalaemia must have early potassium replacement. It is also important to stop potassium when the predisposing cause is no longer present, or else, dangerous hyperkalaemia may develop.

HYPERKALAEMIA

THIS IS THE MOST DANGEROUS ELECTROLYTE DISTURBANCE. Dangerous clinical effects, in particular cardiac arrhythmias and cardiac arrest arise when the serum potassium rises above 6.0mEq/L. The rate of rise is important, as a sudden rise is more likely to cause cardiac arrest. Unnoticed hyperkalaemia must be considered a possible cause when sudden unexpected cardiac arrest occurs.

If a high serum potassium value which is not compatible with the clinical picture is received, check if it is correct. First, make sure it is of the same

patient – have the samples got mixed up? The potassium measurement can be spuriously high if the blood sample is not taken correctly and haemolysis occurs: mechanical trauma during venepuncture, long storage time of blood sample. Severe leukocytosis or thrombocytosis can also result in spuriously high potassium levels.

Hyperkalaemia must be anticipated in the following situations:

- Acute oliguric renal failure
- Severe acidosis
- Rhabdomyolysis
- Tumour lysis syndrome
- Digitalis toxicity
- Diabetic ketoacidosis
- Hypoaldosteronism
- NSAIDS reduce potassium excretion
- Type IV renal tubular acidosis

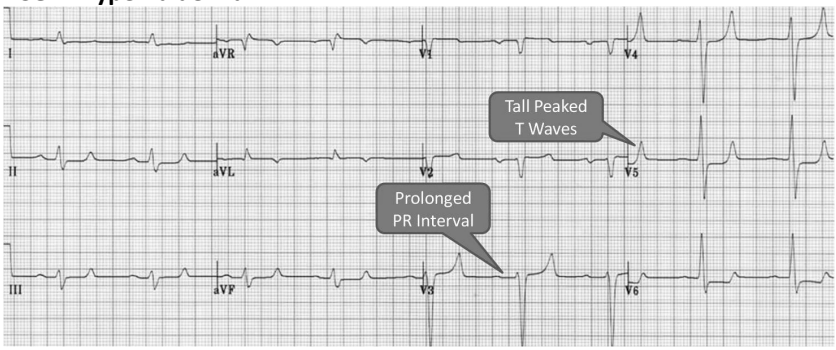
Management:
If cardiac arrest has occurred, resuscitate.
If not, do an urgent ECG. If ECG changes are present, emergency treatment must be given.

- To stabilise cardiac muscle by preventing the cell membrane effects of hyperkalaemia
- IV 10% Calcium gluconate 10ml over 2-3 minutes
- To drive extracellular potassium into the cells
    - 10 units of soluble insulin in 50ml 50% glucose
    - Sodium bicarbonate, especially if metabolic acidosis is present
    - Beta-2-adrenergic agonists – nebulised salbutamol
- These measures are only temporary, since there is nearly always increased body potassium. Hence measures should be taken to remove potassium from the body.
    - Loop or thiazide diuretics
    - Cation exchange resin – Kayexalate(sodium polystyrene sulfonate) 15-30g, given orally or rectally
    - Haemodialysis

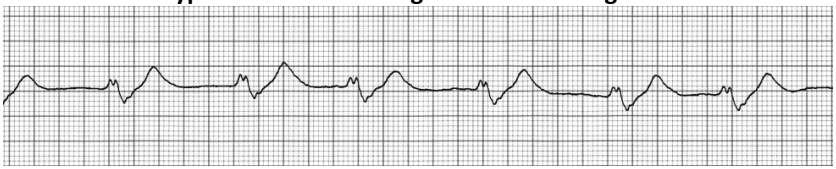
- Check the drug chart to see if any drugs being given might contribute to hyperkalaemia – ACE inhibitors, angiotensin receptor blockers, spironolactone, and even KCl. Digoxin should be stopped.

ECG changes (*These do not correlate well with potassium levels)*	
Hypokalaemia	**Hyperkalaemia**
flattening of T waves T wave inversion prominent U waves ST segment depression QT prolongation In severe hypokalaemia: decreased voltage and widening of the QRS complex prolonged PR interval ventricular ectopics and VT.	Early: tall peaked T waves *In severe hyperkalaemia:* prolonged PR and QRS duration AV conduction delays sine wave pattern ventricular fibrillation or asystole

ECG in hyperkalaemia



ECG in severe hyperkalaemia showing Sine Wave changes



Never attempt to put in internal jugular or subclavian lines in a patient with hyperkalaemia. The tip of the catheter may irritate the hypersensitive right atrium, tricuspid valve or right ventricle and precipitate ventricular tachycardia or fibrillation.

CALCIUM METABOLISM

Most laboratories check the total calcium level, which must be corrected for the plasma albumin level to obtain ionised calcium levels. Add or subtract 0.2mmol/L from the total calcium for each 10g by which the plasma albumin is below or above 40g/L respectively

HYPOCALCAEMIA

Tetany is the main clinical effect. Hypocalcaemia is seen in ICU patients in the following situations:

- Acute renal failure
- Acute pancreatitis
- Septic shock
- Rhabdomyolysis
- Multiple blood transfusions
- Malignancy with bone deposits, or after chemotherapy-phosphates released combine with plasma calcium
- Parathyroidectomy or idiopathic hypoparathyroidism
- Hypomagnesaemia

Treatment

Calcium should be replaced intravenously. Give 10ml of 10% calcium gluconate over 5 minutes. Continue infusion if necessary. Check calcium frequently.

HYPERCALCAEMIA

Hypercalcaemia is not a frequent problem in the ICU, and occurs in:

- Chronic renal failure with secondary hyperparathyroidism
- Malignancy with bone metastases, or myeloma
- Primary hyperparathyroidism
- Thyrotoxicosis
- Sarcoidosis
- Vitamin D toxicity

Patients develop thirst, polyuria and confusion. Constipation is a feature. Severe hypercalcaemia with total calcium over 3.5mmol/L is seen in malignancies with bone involvement.

Treatment:

Rehydrate the patient - Hypovolaemia should be corrected to increase renal excretion of calcium. Oral rehydration of 2-3L per day may be sufficient in milder cases. Patients with severe symptoms should be given IV normal saline 1 litre, 6 or 8 hourly. Forced saline diuresis is necessary only in severe hypercalcaemia with reduced consciousness or cardiac arrhythmias, with serum total calcium >3.5mmol/L. It is carried out as follows:

- Normal saline 1L 2 hourly
- Frusemide 40mg/hour by infusion
- CVP is necessary for monitoring. Slow the infusion and increase dose of frusemide if the CVP rises above 10cm water. Check calcium and potassium 2 hourly. Replace potassium as necessary.
- Forced saline diuresis can be stopped once calcium drops below 3.5mmol/L.

Dialysis maybe necessary in persistent severe hypercalcaemia if renal failure is present, as forced saline diuresis will not be effective.

If hypercalcaemia persists after adequate hydration, consider giving therapy to inhibit bone osteoclastic activity. IV pamidronate (a bisphosphonate) 20-60mg IV over 8 hours for 2 days is usually adequate. Glucocorticoids are also effective in hypercalcaemia secondary to lymphoma, myeloma, vitamin D toxicity and sarcoidosis.

HYPOMAGNESAEMIA

Hypomagnesaemia should be considered in the following ICU situations:

- Malnourished patients
- Chronic liver disease and alcoholics

- Chronic diarrhoea
- Post surgical patients
- Aminoglycosides, amphotericin B, cisplatin, pentamidine, cyclosporine cause urinary magnesium wasting.
- Loop and thiazide diuretics inhibit magnesium reabsorption.

Hypomagnesemia is often associated with hypokalemia due to urinary potassium wasting and hypocalcemia. Correction of magnesium levels is necessary in both these situations.

Consider the possibility of hypomagnesaemia in ventricular arrhythmias, especially in patients likely to have depleted magnesium levels as detailed above. Hypomagnesaemia causes QT prolongation.

Certain genetic conditions such as Gitelman syndrome cause primary magnesium wasting in the kidney.

Treatment:

Correct contributing factors if possible.

If cardiac arrhythmias or QT prolongation is present, and if associated with hypokalaemia, correct with IV magnesium sulphate. Give 1-2 grams over 1 hour. Larger doses may be necessary in severe hypomagnesaemia.

In suspected hypomagnesaemia with cardiac arrhythmias, magnesium can be given empirically, pending the results of investigations. However, care should be taken in renal failure, as hypermagnesaemia may develop.

HYPERMAGNESAEMIA

This is rare. It may be seen in renal failure, and in patients receiving large doses of IV magnesium, for example in pre-eclampsia/eclampsia. Accidental poisoning with Epsom salts is a cause. It is sometimes seen in diabetic ketoacidosis, tumour lysis syndrome, and theophyline or lithium toxicity.

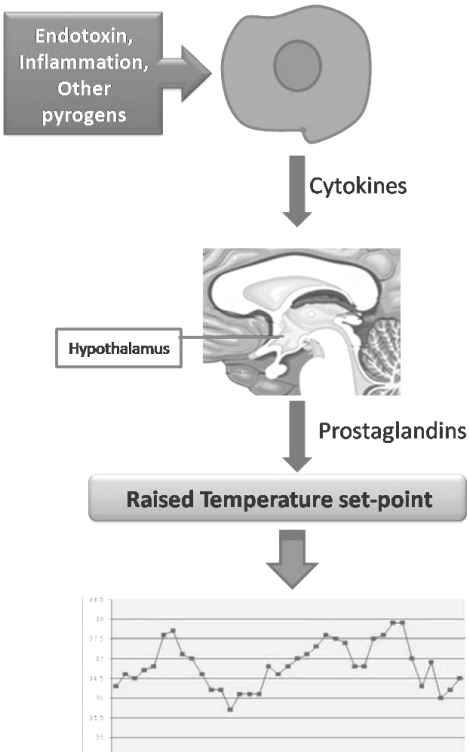
Hypermagnesaemia is usually asymptomatic, but if the levels are very high, can result in neuromuscular paralysis, complete heart block and asystole, and hypocalcemia.

In patients without renal failure, stopping magnesium (in patients being treated with magnesium) or treating other precipitants is adequate. In renal failure, dialysis may be required. If cardiac complications are present, give IV calcium gluconate to reverse the toxic effects of magnesium.

Pyrexia

In the ICU, fever is defined as a core temperature above 38.3˚ C. The presence of fever usually, but not always, indicates the presence of infection. Fever may be transient and trivial, or may indicate serious infection, and the presence of fever must be always be taken seriously.

What causes fever?



The body temperature rises when heat generation increases in excess of heat loss; this usually occurs due to a reset of the hypothalamic thermostat to a higher set-point. The set-point for temperature changes, and the temperature rises accordingly. Several factors can trigger the development of fever, in particular invasion by microorganisms and release of microbial products. Many other conditions can trigger the temperature response of the body. Several humoral factors play a role during infection, including interleukin-1 and -6 and prostaglandin E_2. These factors result in the hypothalamic thermostat being reset. Subsequent events include activation of the vasomotor centre and sympathetic nervous system, leading to increased heat production (by brown adipose tissue), reduced heat loss, and a consequent rise in body temperature.

What else could cause a rise in body temperature?

In certain conditions, the hypothalamic thermostat is not reset; elevated body temperature occurs due to an imbalance between heat production and heat loss. This occurs in, hyperthyroidism, salicylate and anticholinergic drug overdose, skin disease and heat stroke.

Masking of fever

In certain conditions, such as malnutrition, uraemia, immune-suppression and corticosteroid therapy, the body's thermoregulatory mechanisms are disrupted. The patient may not mount a febrile response to infection in this situation. Slight elevations in core temperature may herald the development of serious infection in such patients, and should be investigated and treated early.

Chills and rigors

Sometimes patients complain of chills and rigors. Rigors are associated with a sudden rise in core temperature, with increased energy expenditure. They may result in cardiorespiratory instability, and increase the requirement for inotropic and ventilator support; tachycardia, tachypnoea and hypotension may occur. Sudden bronchospasm may also occur with entry of bacteria into the bloodstream. Chills and rigors must always be taken seriously, as they usually indicate the presence of infection, due to bacteria or viruses, or malaria. Rigors are unpleasant to the patient, and can be controlled with opioids.

What effects does fever have on the body?

Fever increases oxygen consumption by the tissues. In turn, fever may shift the oxygen dissociation curve to the right, resulting in increased oxygen extraction by the tissues. For every degree centigrade increase in temperature, oxygen demand and energy expenditure increase by about 6-10%. Shivering can also increase oxygen demand and energy expenditure. While fever has beneficial effects in combating infection, it can also be harmful; it can cause protein catabolism, and cerebral damage, especially if the temperature is very high, and lasts an hour or longer. Warming the patient rather than cooling the patient is preferable, as warming the patient reduces the temperature gradient between the body and the environment, and this reduces heat generation and metabolic stress. In general, patients

should be nursed at an ambient temperature around 32˚ C; this can be achieved by using blankets or warmers.

How to measure body temperature

Ideally, core temperature should be measured. In practice this is difficult, and rectal, oral or axillary temperature is measured. However, these are less reliable, and temperature changes may lag behind core temperature. Rectal temperature is preferable to oral and axillary temperature; oral temperature can be affected by taking cold or warm liquids.

The importance of 'patterns' of fever

We are often taught about characteristic patterns of fever – alternate day fever in malaria, stepladder fever in typhoid, evening pyrexia in tuberculosis. In critically ill patients these characteristic patterns have very poor predictive value, and diagnosis and decisions should not be based on fever patterns. In critically ill patients, fever often has a diurnal variation, with fever being higher towards the evenings.

Causes of fever in critically ill patients

The causes differ depending on at what point the patient developed fever. If fever was the presenting feature, it could be due to any infective cause, viral, bacterial, protozoal or fungal, or could be due to non-infective causes. Of the infective causes, viral and bacterial infections are more common than fungal and non-infective causes. Dengue and influenza are important viral infections which can result in the patient becoming seriously ill. Bacterial infections could be divided into systemic infections resulting in characteristic syndromes (typhoid, tuberculosis, leptospirosis etc) and organ/region specific infections; pneumonia, urinary tract infection, meningitis, sinusitis, cellulitis, liver abscess, endocarditis are common and important organ specific causes, which can result in the development of severe sepsis. In some situations, the source of infection which results in bacteraemia is unclear, and infection is confirmed by only a positive blood culture. Malaria is an important cause, especially in travellers, and those who have received blood transfusion. Fungal and opportunistic infections are seen in immunocompromised patients.

Fever *developing* in a critically ill patient in ICU is often due to nosocomial (hospital acquired) infection. Bacterial infections are the most common, and

the pattern of organisms as well as their antibiotic sensitivity is different from community acquired infections. Fungal infections are also common, and their incidence is increasing with the increased use of broad spectrum antibiotics.

Nosocomial infections

Nosocomial (hospital acquired) infections complicate the course of illness in around 30% of critically ill patients. Several factors increase the risk of nosocomial infections.

Factors which increase the risk of nosocomial infection
Advanced age
Neutropaenia
Underlying disease – diabetes, renal failure, Liver cirrhosis, Cushing syndrome
Steroids and immunosuppressive drugs, HIV infection
Intravascular catheters
Intubation/mechanical ventilation
Urinary catheters, nasogastric tubes, wound drains
Peritoneal dialysis catheters
Prosthesis /foreign bodies
Previous surgery
Impaired consciousness/neurologic disease
Prolonged ICU stay

It has been suggested that the use of proton pump inhibitors for stress ulcer prophylaxis may increase the risk of infection by abolishing the gastric acid barrier; however, this is not proven.

Fungal sepsis: what conditions predispose to it

Severely ill patients, those with diabetes, renal failure, liver cirrhosis, immunocompromised states, and those who have been on broad spectrum antibiotics are at risk of developing fungal sepsis. Often, fungal infections are superficial, oral thrush due to Candida being the commonest, although systemic fungal infections can occur. Deep seated fungal infections can complicate abdominal surgery, deep or penetrating wounds, and are also seen with prolonged ICU stay.

The common causes of fever in critically ill patients are shown in the table

Infective		**Non-infective**
Community acquired	**Nosocomial**	Connective tissue disorders Antibiotic induced fever Neuroleptic malignant syndrome Malignant hyperpyrexia Neurological causes of hyperpyrexia Trauma Thrombo-embolism Salicylate overdose Anticholinergic overdose Hyperthyroidism Heat stroke Skin disease Pulmonary aspiration Postoperative fever (<48h) Gastrointestinal bleeding Febrile non-haemolytic red cell and thrombocyte transfusion reactions Alcohol withdrawal Gout Transplant rejection Neoplasia Haematoma Myocardial infarction Addisonian crisis, acute adrenocortical insufficiency Acute pancreatitis
Bacterial • Pneumonia, bacteraemia(unknown source) meningitis, urinary tract infection, sinusitis, cellulitis, liver abscess, endocarditis • Typhoid, leptospirosis, brucellosis, tuberculosis Viral • Influenza • Arbo-virus: Dengue, Chikungunya Malaria Infections in immuocompromised patients • Atypical tuberculosis • Pneumocystis carinii pneumonia • Fungal infections	Bacterial • Ventilator associated pneumonia • Infected intravenous devices / catheters • Cutaneous infections • Acute acalculous cholecystitis • Urinary tract infection • Endocarditis • Primary gram-negative bacteraemia Viral (rare) • Herpes virus, • Cytomegalovirus, EBV • Adeno- or respiratory syncytial virus induced pneumonias Fungal infections – often antibiotic induced Transfusion malaria	

Diagnosing the cause of fever

The approach to diagnosing the cause must always be based on a proper history and examination, which should be directed towards suspected sources of infection. Simply running a battery of tests should not be the approach.

Start by trying to answer the following questions

1. **When did the fever start? Was it related to any clinical events?**
   Duration of ICU stay, duration since intubation, duration of intravenous line, urinary catheters, drains, surgical or other invasive procedures. Blood transfusions (transfusion malaria).

2. **How high is the temperature?**
   Higher temperatures are more likely to be due to infective causes. A temperature of over 39˚C or more is more likely to be caused by infection. Chills, rigors, all suggest bacteraemia with a focus of infection/suppuration.

3. **Can a focus of infection be recognised clinically?**
   The source of infection maybe obvious, such as pneumonia, worsening cellulitis/gangrene, wound infection, or may have been revealed by routine clinical examination or routine daily investigations.

4. **Are there risk factors for nosocomial bacterial or fungal infection?**
   These are listed in the box above.

5. **Is the patient immuosuppressed?**
   Opportunistic infection, PCP, Tuberculosis

6. **What are the likely micro-organisms involved?**
   Depends on the site of infection. This is a gross oversimplification, but in general,
   - Pneumonia- pneumococci, Haemophilus, Pseudomonas, Staphylococcus, Klebsiella
   - Aspiration pneumonia – oral anaerobes
   - Urinary tract infection – Coliforms

- Cellulitis of a limb – Staphylococcus, Streptococci, Gas forming organisms
- Meningitis – Meningococcus, Pneumococcus, Listeria,
- Intra-abdominal infection – coliforms, intestinal anaerobes

7. **Is the fever due to a non-infective cause?**
   Thromboembolism, pancreatitis, drug induced fever, neuroleptic malignant syndrome, Cerebrovascular events involving the pons or hypothalamus.

Relevant clinical examination

A relevant detailed clinical examination is of utmost importance.

- Look for skin sepsis, Candida infection, especially in the intertriginous areas.

Next, starting from the head, do a detailed screen of

- Haematomas on the scalp (infected), abscesses
- Neck rigidity and Kernig's sign
- Sinuses – tenderness. (sinusitis maybe caused by an nasogastric tube
- Fundoscopy – emboli, Roth spots - endocarditis
- Otitis media
- Dental infections, Tonsils
- Cervical lymph nodes
- Breasts for abscesses
- Respiratory system for crackles, areas of consolidation, effusions
- Cardiovascular system for new murmurs (endocarditis)
- Abdomen – intercostals tenderness over the liver (liver abscess), tenderness, lumps, free fluid, absent bowel sounds, epigastric masses (pseudopancreatic cyst)
- Genitalia – scrotal abscess, vaginal discharge (intra-uterine infection)
- Limbs for cellulitis, infarction

Look at

- Intravascular cannula sites for redness, warmth, tenderness
- Uribag – turbid urine, haematuria
- Surgical drains for purulent discharge
- Wounds

- If diarrhoea is present, suspect pseudomembranous colitis (Clostridium difficile infection)
- Look at the monitor – tachycardia can indicate infection. Low blood pressure with a wide pulse pressure may herald the development of septic shock. A fall in the pulse oxygen saturation may indicate the development of pneumonia.

Investigations

The most commonly performed investigation is a white blood cell count. A high total count with neutrophil leukocytosis suggests bacterial infection; examination of the blood picture may demonstrate a 'left shift', and toxic granulation of the neutrophils. Remember that a low white cell count (below 4 X 10^9/L) could also indicate infection.

The ESR, CRP and certain other markers such as procalcitonin are generally believed to be useful in detecting infection, although their sensitivity and specificity are still being questioned. In general, a high or rising CRP level indicates ongoing bacterial infection.

Bacterial cultures are the gold standard investigations to demonstrate infection. Blood cultures taken under careful sterile conditions are reliable. If fever occurs, blood culture must be taken before antibiotics are started, or, if the patient is already on antibiotics, before changing the antibiotic regimen. Anaerobic and aerobic cultures should be taken, 2 sets at least 10 minutes apart. If the patient is intubated, endotracheal aspirate should be sent for culture. Urine culture should be taken if urinary sepsis is suspected. If present, any fluid from drains should be sent for culture, together with wound swabs and pus from discharging wounds or abscesses.
Routine throat swabs, nasal swabs, skin swabs (groin, axilla) are of no particular use.

Common mistakes

- Starting antibiotics before taking appropriate cultures
- 'The patient is on antibiotics; therefore I did not take a culture'. If the patient develops a new infection while on a particular antibiotic, it is likely that the current antibiotic therapy is ineffective. Culture will help identify the infecting organisms' antibiotic sensitivity.

Taking cultures from intravenous lines

When line sepsis is suspected, the catheter should be removed, and the tip of the catheter sent for culture, together with a peripheral blood culture drawn at the same time. If only the catheter tip culture grows an organism, it is likely to be simply a colonising organism. If both cultures show the same organism, it is likely that catheter was the source of infection.

Significance of blood culture results

Commonly identified micro-organisms causing nosocomial infection include Gram-negative bacilli such as Enterobacteriaceae, Klebsiella, Pseudomonas, Acinetobacter and Serratia spp, Gram-positive bacteria such as coagulase-negative Staphylococci and S. aureus, and Candida albicans. Staphylococcus epidermidis cultures may not be of clinical significance, unless present in more than one bottle, and rapidly growing in culture. Urine cultures, and sometimes blood cultures, grow Candida spp. which can potentially cause catheter-related blood stream infections, wound infections, and peritonitis. However, culture of Candida spp. may represent colonisation as opposed to infection, and this is difficult to differentiate. Whether to take a Candida culture seriously depends largely on the clinical state and risk factors of the patient. For example, if a long stay seriously ill patient, who has been on multiple antibiotics, produces a blood culture positive for Candida, the clinician may decide to start on antifungal agents.

Radiological investigations

Chest x-ray is the most useful radiological investigation. The appearance of new areas of consolidation could indicate the development of pneumonia. In a ventilated patient, it could mean the patient is getting ventilator associated pneumonia.

CT scan of the chest is more accurate in detecting pneumonia, but the inconvenience of moving a critically ill patient to the CT scan room is often not justifiable. There is a definite place for Spiral CT scan of the chest if pulmonary embolism is suspected.

Ultrasound scanning of the abdomen is useful to detect intraabdominal abscesses, liver abscesses, cholecystitis, pyelonephritis, and pelvic infections. **CT scanning of the abdomen** maybe required where intraabdominal sepsis is strongly suspected. Transthoracic and transoesophageal **echocardiography** are useful in diagnosing endocarditis, when suspected.

Nuclear imaging techniques, such as **Gallium scanning**, are theoretically useful, but often of little practical value in critically ill patients.

SIRS and sepsis

SIRS, the systemic inflammatory response syndrome, is diagnosed by the presence of two or more of the following;

- Fever (>38 °C) or hypothermia (<36 °C)
- Tachycardia (>90 /min)
- Tachypnoea (>20 /min), or fall in arterial PCO_2 (<32 mmHg)
- Leukocytosis (>12.0 x 10^9 /L) or leukopaenia (<4.0 x10^9 /L) or >10% immature (band) forms.

While burns, trauma and various other conditions can result in SIRS, the presence of SIRS with evidence of infection is defined as sepsis.

Starting antibiotics

Empiric antibiotics are generally started if fever is present with other signs of infection, such as neutrophil leukocytosis, elevated CRP, and/or an identified source of sepsis. Antibiotics should be started early in critically ill patients, and broad spectrum antibiotics should be used. The choice of the antibiotic depends on the suspected site of infection, and is based on the common organisms which cause such infection. Where the source of infection is not identified, broad spectrum aerobic and anaerobic antibiotic cover is used. Antibiotics should be chosen carefully, given for at least 3 days before they are deemed not to be effective, by which time culture results should be available. Clinicians often change antibiotics too early and too often, giving inadequate time for them to work. Piling antibiotics with the same range of cover on top of each other should be avoided. The clinician should be clear as to what each antibiotic is intended to cover.

Severe infection

Severe infection is one of the commonest causes of admission to a medical ICU. Patients admitted with other critical illnesses often develop infection while in hospital; this is known as nosocomial or hospital acquired infection. Infection is the most important cause of death in ICU patients.

In some patients, infections respond to simple antibiotics, and resolution is rapid and complete. Other patients go on to develop multi-organ failure, which has a high mortality. It is often difficult to predict how a patient with infection will progress; however, there are certain risk factors which predict that the course of infection will result in complications. Infections are usually more likely to run a complicated course if the patient is of advanced age, if comorbid conditions such as diabetes, chronic liver disease, chronic renal disease, chronic obstructive airways disease, heart failure or malignancy are present, or if the patient is immunocompromised.

The common causes of severe infection needing ICU care are severe community-acquired pneumonia, meningitis, urinary tract infection, cellulitis of a limb, and abscesses. Infection which occurs more than 48 hours after admission to hospital is defined as nosocomial infection. Nosocomial infections comprise about 10 percent of infections in ICU patients. In adult ICU patients, nosocomial pneumonia is the commonest cause of infection, followed by bloodstream infection and urinary sepsis. The risk of nosocomial infection increases because of intubation and ventilation. Intravenous lines are an important source of bloodstream infections, and urinary catheterization increases the risk of urinary tract sepsis. Stress ulcer prophylaxis with proton pump inhibitors, prolonged ICU stay, and immunocompromised states increase the risk of nosocomial pneumonia.

Infection causes a pro-inflammatory cytokine response which results in fever, leukocytosis, tachycardia and increased respiratory rate; this is known as the systemic inflammatory response syndrome or SIRS. SIRS is not limited to infection, and can be caused by a variety of other conditions, such as surgery, burns, trauma, myocardial infarction, pancreatitis, drug reactions, transfusion reactions etc. When SIRS is caused by infection, the condition is known as SEPSIS. If sepsis is associated with organ dysfunction, it is known

as SEVERE SEPSIS, and when refractory hypotension occurs, it is defined as SEPTIC SHOCK. Sepsis, severe sepsis with multiorgan failure, and septic shock are increasingly severe complications of infection, with correspondingly higher mortality.

Early recognition of infection, and early prediction of sepsis and its complications is crucial, though not always easy. Early treatment, with antibiotics and source control (removal of the source of infection) improves mortality and morbidity.

There is no universally reliable tool to diagnose sepsis early or to predict its progression. A high degree of alertness to changing parameters, as well as anticipation of the development of sepsis with initiation of preventive measures is therefore important. For example, the development of tachypnoea or a drop in blood pressure may herald the development of severe sepsis. Biochemical markers such as ESR, C-reactive protein, and neutrophil leukocytosis may predict the development of sepsis, but maybe normal, especially in immunocompromised patients. Newer markers such as procalcitonin levels have been suggested to be useful, but evidence is still forthcoming.

The diagnosis of infection and sepsis in the ICU is made based on clinical judgment and a timely and focused diagnostic work-up. The section on fever discusses the approach to a febrile patient. Worsening clinical parameters will alert the clinician to the development of severe sepsis and multiorgan failure.

Community-acquired Pneumonia

This is one of the commonest reasons for ICU admission. The patient presents with fever, cough with expectoration, sometimes the classical "rusty sputum", pleuritic chest pain, and on examination has either evidence of lobar consolidation (crackles, bronchial breathing, whispering pectoriloquy). Depending on the severity and the infecting organism, as well as the patient's immune status, signs maybe bilateral. Streptococcus pneumoniae, Legionella, Haemophilus influenzae, Klebsiella, gram negative bacteria and Staphylococci are the common 'typical' infections; in up to 40 % of patients, the infecting organism is not identified. Patients with neutropenia are more susceptible to infections with gram negative organisms including Pseudomonas. Patients with HIV and low CD4 counts

are likely to develop *Pneumocystis jiroveci* pneumonia (formerly known as *Pneumocystis carinii*), and also tuberculosis and fungal infections.

The following investigations are required:

- Chest radiograph: multilobar involvement, and the presence of a pleural effusion indicates worse prognosis. Apical involvement is seen in Klebsiella pneumonia, and also in tuberculosis, although the clinical course is different in the two conditions; tuberculosis having a more indolent course. Multiple diffuse infiltrates will be seen in bronchopneumonia. Bilateral alveolar infiltrates are seen in Pneumocystis infection. Chest radiograph may show evidence of a lung abscess.
- Blood culture has high specificity in identification of the causative organism, and gives positive results in up to 30% of patients with CAP.
- Sputum culture is useful, especially since antibiotic sensitivity will guide the choice of antibiotics. It is important to obtain lower respiratory secretions for culture. Many methods are used to obtain specimens; expectoration, hypertonic saline induction, deep tracheal suctioning, bronchoscopic brushings and lavage, and occasionally transthoracic needle aspiration. Secretions should be processed within 2 hours. Gram stain is useful in detecting conventional organisms. Legionella pneumophila can be diagnosed by detection of antigen in urine. Potassium hydroxide wet mount is used for detecting fungi. Zeihl Neelson stain is used to detect tuberculosis and fluorescent stain for Pneumocystis. These special stains must be requested where clinical suspicion of these causative organisms is high. If Influenza A virus is considered likely, enzyme immunoassay must be performed.

Treatment: Intravenous antibiotics should be commenced after cultures are taken. Treatment should be with one of the following regimens:

- beta-lactam antibiotic (usually co-amoxyclav) with a macrolide
  or
- 3rd Generation cephalosporin with a macrolide
  or
- Levofloxacin

Severe infection

If the patient is immunocompromised, anti-pseudomonal cover is required. Either a 4th generation cephalosporin, a carbopenem such as meropenem should be given as initial treatment. If Pneumocystis is suspected, trimethoprim-sulphamethoxazole should be given. Transplanted patients have a high risk of cytomegalovirus infection, and in such patients, ganciclovir should be considered.

Aspiration pneumonia is caused by aspiration of vomited gastric contents. Because of the high acidity, chemical injury occurs, with loss of the alveolocapillary integrity and exudation of fluid and protein, causing pulmonary oedema. The lung is susceptible to secondary infection. Since the stomach contents are usually sterile, and colonic bacteria are not present in vomitus unless distal bowel obstruction is present, the anaerobes often implicated in aspiration pneumonia are the oral anaerobes. These are adequately covered by co-amoxyclav; Clindamycin is also effective, and has the advantage of being associated with a lower rate of post treatment MRSA. Metronidazole, although commonly used in practice, has a failure rate of 50 percent, and should not be given as monotherapy. It could be used in combination with penicillin.

Complications of pneumonia

Lung abscess: Failure to respond to therapy may lead to abscess formation in the lung. Both anaerobic and aerobic organisms can cause lung abscess. The differential diagnosis is cavitating tuberculosis, and a tumour with a necrotic centre. Aspiration pneumonia is a cause of lung abscess; they can also be caused by septic emboli. In the right basal region, an abscess could be caused by extension of a liver abscess, either bacterial or amoebic. The patient usually has high swinging fever with chills, and offensive purulent sputum. On chest radiograph, an abscess appears as a cavity with an air-fluid level, with a varying degree of surrounding consolidation. Surgical drainage is not usually required, and intravenous antibiotics are adequate.

Empyema: Lobar pneumonia is often associated with an exudative pleural effusion. When pus collects in the pleural space, it is known as an empyema. Staphylococcus aureus, Pneumococcus and Streptococcus pyogenes are common organisms causing empyema. The patient has high swinging fever with chills. Drainage by intercostal tube is required.

ARDS: Acute respiratory distress syndrome is a serious complication of pneumonia; it is discussed in greater detail in the section on respiratory failure.

Urinary tract infection (urosepsis)

Community acquired infections in the urinary tract occur either as a result of congenital structural abnormalities of the urinary tract, the presence of calculi, prostatic enlargement causing outflow obstruction, or other structural abnormalities of the urinary tract, or in immunocompromised states such as diabetes mellitus or chronic renal failure. Gram negative bacteria are the common cause. Patients have flank pain and tenderness over the renal angle. Examination of the urine shows leukocytes and granular casts, and culture helps identify the organism. Imaging of the urinary tract by ultrasound scan is required to look for structural abnormalities and obstruction. Intravenous urogram and CT scanning may also be required.

Treatment is usually with empiric therapy pending urine culture reports. Intravenous antibiotics are preferred, usually co-amoxyclav, ceftriaxone or ciprofloxacin. In severe sepsis, an aminoglycoside should be added. Since renal impairment may be present, dose adjustment must be considered. Relief of obstruction, either by percutaneous nephrostomy or ureteric stenting may be required.

Cellulitis and erysipelas

Skin and soft tissue infection is commonly seen in diabetics, patients with peripheral vascular disease, patients with chronic liver disease or hypothyroidism, and immunocompromised patients. They may also occur in healthy individuals after minor trauma, burns, insect bites; tinea pedis is a predisposing cause. Most infections are serious and could progress rapidly, hence early antibiotic therapy and debridement is necessary. Erysipelas is a superficial infection of the skin with painful, erythematous skin lesions and lymphangitis. Cellulitis involves the deeper layers of skin and subcutaneous tissue. Necrotising fasciitis is the disastrous condition which must be excluded in patients with cellulitis. The presence of an anaesthetic area of skin overlying the cellulitis is characteristic in necrotizing fasciitis. Streptococcus pyogenes and Staphylococcus aureus are the usual causative organisms. Anaerobic cellulitis is a necrotizing infection of subcutaneous

tissues, without significant deep spread; myositis is not seen, in contrast to gas gangrene. Clostridium perfringens is the causative organism.

Treatment is with cloxacillin or co-amoxyclav. Clindamycin or cephalosporins are alternatives in patients with penicillin allergy. Anaerobic cellulitis is treated with co-amoxyclav or clindamycin.

Necrotizing fasciitis

This is a rare, but serious infection with a high mortality. At the beginning, the appearance is similar to cellulitis, but the infection extends much deeper than the subcutaneous tissue, into the deep fascia. The patient develops severe sepsis often with septic shock. The affected area changes from dark red to blue-grey, with vesicles and bullae. Subcutaneous gas may be present. Anaesthesia of the surrounding skin occurs due to thrombosis of the small blood vessels and destruction of superficial nerves. Myositis occurs, and CPK levels rise.

The infection is caused by anaerobes and non-group A streptococci. Enterobacteriae may also be present. Sometimes the infection is due to Streptococcus pyogenes and Staphylococcus aureus.

Treatment: Necrotizing fasciitis is a surgical emergency. Extensive debridement of necrotic tissue is done, and the area is left open for secondary closure. Co-amoxyclav and clindamycin are the usual initial antibiotics. Ceftriaxone is used in penicillin allergy.

Gas gangrene

This is caused by infection with Clostridium perfringens, and follows muscle injury with dirt contamination. Intense pain, with necrosis and bullae formation, with a foul odor of the wound is present. Gas bubbles may be seen, and crepitation is present. Septic shock usually occurs. X-ray of the affected area shows gas dissection of the muscle.

Treatment is with debridement or amputation. IV penicillin and clindamycin are recommended treatment. Hyperbaric oxygen is sometimes used, but its benefit is not sufficiently proven.

Meningitis

Fever, headache, photophobia and neck stiffness are the classical features of meningitis. Cranial nerve palsies and focal neurological signs are known to occur; fits and reduced level of consciousness may also be present,

especially in meningo-encephalitis. Bacterial meningitis is the commonest intracranial infection, with significant morbidity and mortality. Diabetes insipidus and SIADH can occur as complications. In Meningococcal infection, DIC may occur, leading to a generalized petechial/purpuric rash. This is sometimes complicated by bleeding into the adrenal glands, resulting in acute adrenal insufficiency and shock (Waterhouse-Friderichsen syndrome). In immunocompromised patients and the elderly, the classical clinical features maybe absent. Meningitis should be suspected in anyone with fever and altered mentation. Infection occurs either by bloodstream spread or by direct spread of bacteria into the CSF from infection in the sinuses or nasopharyngeal passages.

Neisseria meningitidis and Streptococcus pneumoniae are the most common organisms; Haemophilus influenzae is common in immunocompromised patients, as is Listeria monocytogenes. Tuberculous meningitis is seen in HIV infection, immunocompromised patients, alcoholism, diabetics and in malignancy and advanced age.

Investigations: Blood culture must be taken before commencing antibiotics. CSF examination must be performed, but antibiotic therapy should not be withheld if there is delay in performing lumbar puncture. A CT scan is usually performed prior to obtaining a CSF sample, to exclude cerebral oedema, in which case lumbar puncture may be dangerous. In bacterial meningitis, the CSF is cloudy, with elevated neutrophils, high protein and low glucose concentration (less than 50% of the corresponding blood glucose level). Gram stain of CSF is useful in identifying the organism, and should guide antibiotic therapy. In tuberculous meningitis, lymphocytes predominate.

Treatment: Intravenous antibiotics should be started without delay. The chosen antibiotic must have good CSF penetration. Ceftriaxone or Cefotaxime are indicated as first line antibiotics.

- Gram positive cocci:
    - In community acquired meningitis; *Streptococcus pneumoniae*. Initial therapy is adequate. Penicillin used to be the drug of first choice, but resistance is increasing.
    - If after head trauma or surgery, or in the presence of an intracranial device or CSF leak, suspect *Staphylococcus aureus* or coagulase negative streptococci. Add Vancomycin.

- Gram negative cocci: Neisseria meningitidis. Initial therapy adequate. Penicillin G is the drug of choice.
- Gram positive bacilli: Listeria. Use Ampicillin and gentamicin.
- Gram negative bacilli: Klebsiella, E.coli.
    - If after head trauma or surgery, or in the presence of an intracranial device or CSF leak, suspect Pseudomonas. Ceftriaxone should be replaced with Ceftazidime.
    - *Haemophilus influenzae* is covered by 3rd generation cephalosporins.

Treatment is usually continued for 14 days, possibly longer depending on the organism.

Endocarditis

Endocarditis usually develops on valvular heart lesions or intracardiac shunts. The mitral and aortic valves are commonly involved. Right sided endocarditis is seen in intravenous drug abusers. Prosthetic valves are high risk for endocarditis. Fever and changing murmurs should alert the clinician to the possibility of endocarditis. Splenomegaly, clubbing, and signs occurring as a result of septic emboli such as Oslers nodes, Janeway lesions, Roths spots may be present. Mycotic aneurysms in the cerebral circulation maybe a feature and glomerulonephritis can occur. A significant proportion of patients develop congestive heart failure due to valvular dysfunction. Transient bacteraemia during a dental procedure is the usual predisposing event.

Streptococcus viridans and Group D streptococci are the common causes of subacute endocarditis. Staphylococcus aureus is the commonest cause of acute endocarditis. Streptococcus bovis causes endocarditis in patients with inflammatory bowel disease and bowel cancer. Fungal endocarditis is seen in post cardiac surgical patients.

Diagnosis: Diagnosis is based on the Duke Criteria. 3 to 5 sets of blood cultures should be obtained. Echocardiography will demonstrate the presence of oscillating vegetations.

Treatment: While a single agent can be used, there is a high rate of relapse, and combination therapy is used to reduce the duration of treatment.

- Viridans Streptococci or enterococci: Penicillin and gentamicin or Ceftriaxone and gentamicin for two weeks.
- Right sided endocarditis due to staphylococci: Vancomycin. Duration of treatment 4-6 weeks
- Prosthetic valve endocarditis: combination of vancomycin, rifampicin, and gentamicin

Fever in endocarditis usually responds within 4-5 days. Initial empiric antibiotic therapy must be changed once cultures are available. If the fever does not settle, or the patient's clinical conditions worsen, consider

- Myocardial / valve root abscess formation
- Mycotic aneurysm
- Other infections not related to endocarditis
- Fungal endocarditis

Note that it is important to give prophylactic antibiotics for ICU patients with valvular heart lesions undergoing invasive procedures.

Surgery is sometimes required in endocarditis. Indications include

- Development of myocardial/valve root abscess
- Progressively worsening valve destruction
- Persistent sepsis
- Ruptured sinus of valsalva

NOSOCOMIAL INFECTIONS

Nosocomial infections should be considered in patients who develop fever after 48 hours in the ICU. To identify the site of infection, a systematic search must be performed. Consider the following:

- Respiratory sources
- Intravascular line related sepsis
- Urosepsis
- Gastrointestinal infection
- Skin and soft tissue infection
- Surgical infections
- Fungal infections

Nosocomial pneumonia

This is the commonest cause of nosocomial infection, and comprises nearly half of all hospital acquired infections. It is often seen in ventilated patients.

Why do patients get nosocomial pneumonia?

The commonest reason is aspiration of upper airway contents. Aspiration of gastric contents may also occur in, if the patient vomits or because of the nasogastric tube. The cuff of the endotracheal tube does not prevent aspiration. Contamination of respiratory equipment, such as suction tubes can play a role. It is vital that intubation is performed as a sterile procedure. Contamination of respiratory equipment from the hands of doctors, nurses and other healthcare professionals is also a documented cause. The use of proton pump inhibitors is associated with an increased risk of pneumonia.

Causative organisms:

The commonest organisms are organisms which normally reside in the upper airways; Haemophilus influenzae, *Streptococcus pneumoniae*, methicillin-sensitive *Staphylococcus aureus* (MSSA), and non-resistant enteric Gram-negative bacilli (*Escherichia coli*, Klebsiella spp., Proteus spp., Enterobacter spp., and *Serratia marcescens*). *Pseudomonas aeruginosa* is also an important cause, especially in patients with chronic lung disease and in late onset nosocomial pneumonia. MRSA, multiresistant gram negative bacilli, and *Acinatobacter baumanii* are other serious infections. Multi-resistant organisms are seen in patients who have been on broad spectrum antibiotics. Anaerobes are not common. Fungal infections and anaerobic infections should be considered in patients who are repeatedly culture negative.

Diagnosis is based on the appearance of thick purulent secretions and new pulmonary infiltrates on x-ray, with worsening sepsis. It is sometimes difficult to differentiate this from the development of ARDS. Culture of tracheal secretions is unreliable because it is difficult to distinguish colonizing organisms. Bronchoalveolar lavage is sometimes used to obtain better specimens.

Sinusitis

Sinusitis is an important nosocomial infection which is often missed. The risk of sinusitis is increased by intubation, and by the presence of a nasogastric tube.

Pseudomembranous colitis

Diarrhoea occurring in critically ill patient should raise the suspicion of pseudomembranous colitis. Most often, diarrhea is caused by alterations in bowel flora due to antibiotics, and is relatively benign. Pseudomembranous colitis is a serious and potentially fatal complication, caused by *Clostridium difficile* infection. This results in a toxin related acute inflammation of the colonic mucosa. It is caused by the use of broad spectrum antibiotics, in particular clindamycin, broad spectrum beta lactams, and cephalosporins.
Diagnosis: Enzyme immunoassay (EIA) for CD (*Clostridium difficille*) toxin A and B can give rapid diagnosis. Tissue culture toxin assay is mose sensitive.
Treatment is with metronidazole.

Intravascular catheter infection

Suspect this in the following situations

- Spiking of fever with no obvious other source
- Presence of the catheter for more than 3 days
- Local inflammation and purulent discharge
- Resolution of fever when line is removed

Definitive diagnosis is made by culturing the tip of the catheter. Differentiating colonization from infection is important. Hence the diagnosis is made only by demonstrating a positive tip culture with a corresponding culture of the same organism from a blood culture drawn simultaneously from a different site.

Skin and surgical infection

Surgical sites and bed sores should be examined for signs of inflammation and pus discharge. The limbs should be examined for cellulitis. It is of particular importance to examine the perineal region and genitalia, and in women to perform a vaginal examination and look for pus and tenderness.

Fungal infection

Fungal infection is responsible for around 10% of nosocomial infections, and has a high mortality. Candida species are the most common. The use of broad spectrum antibiotics favours colonization of the oropharyngeal, gastrointestinal and genitourinary tracts. Colonization does not equal infection.

Treatment is with Fluconazole or amphotericin B.

Nosocomial infections must be treated promptly and appropriately. Choice of antibiotics must be guided by cultures. Differentiating actual infection from colonization is always a dilemma.

DIAGNOSTIC WORKUP FOR INFECTION IN ICU

Patients with suspected infection or new appearance of fever must have urgent investigations to identify the site of infection and the possible organism. These will guide antibiotic and supportive therapy.

Inflammatory markers

C-reactive protein and procalcitonin are both useful markers of infection. Neutrophil leukocytosis indicates bacterial sepsis; however leukopaenia could be present. Several blood cultures should be taken prior to commencing antibiotics. Urine and sputum should be cultured. Wound swabs and pus should be cultured. If pleural or peritoneal fluid collections are present, these may be aspirated and cultured. If meningitis is suspected, lumbar puncture should be performed; however, if there is any delay in performing invasive procedures, antibiotics should be commenced without delay.

Chest radiography is very useful in demonstrating new infiltrates suggestive of pneumonia. Skull Sinus x-ray may demonstrate inflammation or fluid in sinusitis. Ultrasound scan of the abdomen, or CT scan maybe useful to demonstrate intraabdominal or pelvic abscesses.

General principles of treatment

- Sepsis in the ICU should be considered a medical emergency. Antibiotics should be commenced early. Intravenous antibiotics are nearly always required, and should be given in adequate doses. The choice of antibiotic will most of the time be empiric initially, and will be based on the suspected site of infection and the expected common organisms, as

detailed above. If a source or site cannot be identified, broad spectrum antibiotics are usually commenced, aimed at providing adequate gram negative and gram positive cover.

- Antibiotics should not be changed at too frequent intervals. Often clinicians expect resolution too early. Once antibiotics are chosen based on a rational approach, they should be reviewed every 3 days, unless there is justification in changing therapy based on culture results.
- Source control should be attempted:
    - Abscesses should drained
    - Wounds should be debrided
    - Infected urinary catheters should be removed
    - Infected intravascular cannulae should be removed
    - In the case of necrotizing fasciitis, fasciotomy and debridement should be done
- Chest physiotherapy is of benefit in pneumonia, and regular physiotherapy should be given
- Several interventions are of proven benefit in severe sepsis; namely early and aggressive fluid resuscitation, tight glycaemic control, corticosteroids, renal support, and activated protein C. These will be dealt with in depth in the section on severe sepsis.

Specific disease conditions causing fever

The patient admitted to ICU with the primary presenting symptom of fever may have one of several infective syndromes. These should be considered based on the clinical history.

- Typhoid: step ladder fever, early: constipation, dry cough, headache, malaise. Later diarrhea, obtundation, complications such as intestinal perforation
- Leptospirosis: history of contact with dirty water, high fever with chills and rigors, myalgia and muscle tenderness, conjunctival suffusion, haematuria, jaundice, liver dysfunction, acute renal failure, bleeding tendency
- Malaria: history of travel to malarial area, high fever with chills and rigors, periodicity (may not be present at the start), jaundice, anaemia, confusion, coma, hypotension
- Dengue: fever, backache, retro-orbital pain, myalgia, thrombocytopaenia, shock, effusions, pulmonary oedema, myocarditis, multiorgan failure

Conditions other than infections causing fever in ICU patients

Consider

- Brain stem stroke
- Drug fever
- Transfusion reactions

General principles of antibiotic therapy

As detailed above, antibiotics should be started early, based on

- The most likely source/site of infection
- Relative effectiveness of the antibiotic
- Penetration of the antibiotic to the site of infection
- Local organism and antibiotic sensitivity patterns
- Contraindications and precautions
- Interactions with other antibiotics and other medications
- Age, renal or hepatic dysfunction
- Hypersensitivity
- Cost

Antibiotic therapy should be guided by cultures and clinical response (reviewed every few days). Penetration of the antibiotic into the site of infection should be considered. Vancomycin has poor alveolar penetration and hence has poor efficacy in pneumonia. Teicoplanin may be better. Meropenem has superior CNS penetration compared to imipenem. Certain antibiotics have time dependent killing, and others have peak concentration dependent killing.

Antibiotics with time-dependent killing:

Glycopeptides and beta lactams have time dependent effects. These should be administered to ensure that the baseline antibiotic concentration is above the MIC of the organism. This is achieved by

- administering the antibiotic by continuous infusion or more frequent dosing
- using a drug with a long half life
- co-administration of another drug which blocks the elimination of the antibiotic

Antibiotics with peak concentration dependent killing:
Aminoglycosides and fluoroquinoloes have this property. The drug should be administered at high doses to achieve high peak concentrations, with longer intervals between doses to prevent toxicity.

Vancomycin is best administered as a continuous infusion maintaining a blood concentration several times higher than the MIC.

Hypotension

Hypotension or low blood pressure is a common clinical problem encountered in wards and in the ICU. In general, it is defined as **systolic blood pressure less than 90 mmHg or mean blood pressure below 60 mmHg.**

However, sometimes this depends on the patient's initial blood pressure. Some healthy individuals have a baseline blood pressure which is low. Also, patients who are hypertensive may have symptoms of hypotension when their pressure falls. Because of this, a drop in systolic blood pressure more than 40-50 mmHg from baseline is also considered hypotension.

Ask the following questions:

- What was the patient's baseline blood pressure?
  Ask the patient, relatives; check previous records, physician's notes
- Is the patient on antihypertensive medications? What drugs?
  (For example, patients with chronic heart failure may be on ACE inhibitors and beta blockers titrated to achieve systolic blood pressure as low as 90mmHg)
- Is the patient symptomatic?
  Dizziness especially on standing, syncopal attacks and malaise may be present. Often these are disregarded by the patient unless very severe. Sometimes, features of organ hypoperfusion may present, such as anginal chest pain, hypoxia, or altered level of consciousness.

Always think of unusual but obvious causes of hypotension: consider the following case-vignette: A 60 year old man presented to an outpatient clinic with a history of feeling faintish for a few hours. His blood pressure was 70/40mmHg. He had not been on antihypertensive medication. He has had a similar episode three months ago, and had been investigated by a cardiologist with ECG, echocardiogram, exercise ECG, and Holter monitoring, all of which were normal. He was pale, and on questioning admitted to have had malaena for two days. He was resuscitated with fluids and blood, and was later found to have a hepatoma, with haematobilia.

Differentiate between hypotension and shock

Hypotension can occur without shock. Shock is a serious condition, with ongoing tissue hypoperfusion and tissue dysfunction and, most of the time, metabolic acidosis caused by anaerobic tissue metabolism with lactic acid production.

If a patient has a low blood pressure, look for features of shock (evidence of tissue hypoperfusion and hypoxia), and features which may suggest a cause, namely;

- Tachycardia – this can occur in most forms of shock
- Gallop rhythm – in cardiogenic shock
- Pulse volume – reduced in cardiogenic and hypovolaemic shock, increased in septic shock
- Shortness of breath
- Hypoxia – evidenced by cyanosis
- Skin – maybe pale, mottled or flushed depending on type and degree of shock
- Reduced urine output
- Altered consciousness – reduced cerebral blood flow

Hypotension without shock can occur in the following situations:

- Drug induced hypotension – seen especially in the elderly, common with ACE inhibitors and beta blockers.
- Postural hypotension – also common in the elderly, and patients with autonomic neuropathy (hypertensives, diabetics, patients with thyroid disorders). Can also be caused by certain antihypertensives
- Idiopathic low blood pressure can be seen in some healthy individuals.
- In ICU patients, sedatives and vasodilators can cause hypotension without any significant tissue hypoperfusion. Patients with dengue infection can manifest with low blood pressures without tissue hypoperfusion, although such patients could develop shock and should be watched carefully.
- In severe sepsis, vasodilatation occurs initially resulting in low blood pressure, which is sometimes fluid responsive. Organ dysfunction has not set in yet, and at this point fluid resuscitation alone will normalise the blood pressure and prevent the development of septic shock.

Conversely, shock may be present with an apparently normal blood pressure.

If the patient is in shock, look for a cause

Ask the patient and relatives about

- Premorbid conditions; diabetes, ischaemic heart disease, hypertension, medications, smoking, COPD
- Overt bleeding, malaena, haematemesis
- Anginal chest pain, acute dyspnoea (pneumothorax)
- Fever, any symptoms pointing to infection (cough, dysuria)
- History of allergy. Anaphylaxis could present with sudden hypotension

Examine for

- Features of shock (see above)
- Features to differentiate hypovolaemic, cardiogenic and vasodilatory shock
- Possible correctable causes of shock- pneumothorax, pericardial effusion

Causes of hypotension and shock

All hypotension and shock falls in to one (or a combination) of the following

- Shock due to reduced ventricular filling - **Hypovolaemic shock**
- Shock due to reduced cardiac contractility - **Cardiogenic shock**
- Shock due to a decrease in systemic vascular resistance - **Vasodilatory shock**

The different conditions which result in each of these types of shock are shown in the table.

Hypovolaemic shock could be absolute or relative. Absolute intravascular volume depletion is seen either due to loss of intravascular fluid externally (bleeding, GIT or renal loss), or internally into extravascular compartments (sepsis, burns, dengue shock syndrome). Relative intravascular fluid depletion can occur when the vascular tone is decreased, resulting in increased capacitance and low peripheral vascular resistance (sepsis, anaphylaxis).

Often, in a given patient with shock, more than one type of shock could be present. For example, a patient with vasodilatory septic shock and severe

acidosis will have a cardiogenic component contributing to low blood pressure, and in addition will have relative intravascular hypovolaemia. In dengue shock syndrome, both hypovolaemic and cardiogenic shock maybe present.

Clinical differentiation of the types of shock

The history may suggest the cause of hypotension. If obvious bleeding or other cause of hypovolaemic shock is present, the diagnosis will be obvious. A history of ischaemic or valvular heart disease, together with an anginal chest pain may suggest cardiogenic shock. Both hypovolaemic shock and cardiogenic shock are low cardiac output states. The pulse volume will be low, with peripheral vasoconstriction and activation of the sympathetic system resulting in sweaty peripheries; hence, the classical cold, clammy extremities with a weak, thready pulse. Marked pallor may suggest bleeding to be the cause, although in both cardiogenic and hypovolaemic shock, peripheral vasoconstriction can result in pallor. The pulse pressure is narrow. In contrast, good volume, 'bounding' pulses are seen in vasodilatory shock (characteristically septic shock), with a wide pulse pressure, and warm extremities. The presence of a gallop rhythm, plus or minus murmurs may suggest cardiogenic shock. An elevated JVP can be seen in cardiogenic shock, and also in some patients with septic shock. In hypovolaemic shock, the JVP will be low.

The effects of hypotension

'Time is tissue'. The longer shock persists, the more established the tissue damage becomes. This tissue damage eventually leads to multi-organ failure. The brain is the organ which is most susceptible to ischaemia and hypoxia, and hypoxic brain damage is irreversible. The kidneys are also very vulnerable, and nearly all organs and tissues in the body will be affected with prolonged hypotension. Once ischaemic tissue damage becomes established, reversal of shock does not significantly improve outcome. In early studies, it was found that reverting the blood pressure to normal by using fluids, inotropic agents and blood transfusions did not improve survival in patients who had developed multiorgan failure following prolonged tissue hypoperfusion. However, early restoration of tissue perfusion, with aggressive fluid resuscitation, before tissue damage has taken place, prevents multi-organ failure and improves outcome.

Hypovolaemic shock	Cardiogenic shock	Vasodilatory shock
• Haemorrhage *Overt, or occult (GI haemorrhage, intraperitoneal bleeding)* • Third space fluid loss *capillary leak in sepsis, burns* • GI fluid loss *diarrhoea, fistulae, large gastric aspirates/vomiting* • Transdermal fluid loss *burns, hyperpyrexia* • Polyuria *diabetes insipidus, diuretics* • Inadequate fluid intake or administration • Vasodilating drugs *nitrates, propofol* • Severe tachycardia and arrhythmias • Flow obstruction resulting in diminished left ventricular filling. *pulmonary embolus, tension pneumothorax, pericardial tamponade, lung hyperinflation.*	• Myocardial ischaemia, infarction, stunning • Myocarditis/cardiomyopathy *Viral, leptospirosis* • Systemic inflammation *sepsis, post-cardiac surgery* • Drugs *β-blockers, calcium channel blockers, doxorubicin* • Myocardial contusion from direct trauma • Severe metabolic acidosis causing myocardial depression.	• Systemic inflammation *sepsis, anaphylaxis, post-cardiac surgery* • Drugs *ACE inhibitors, nitrates, calcium antagonists, sedatives* • Endocrine disorders *absolute (Addison's) or relative adrenocortical insufficiency, phaeochromocytoma (may present with paroxysmal hypotension)* • Unopposed peripheral sympathetic activation *epidural anaesthesia, spinal cord injury*

Hypotension

How to monitor a patient with shock

Volume replacement must be started without delay. In general, the following parameters must be monitored:

- Vital signs: pulse, blood pressure, respiratory rate, jugular venous pressure
- Urine output: *If the urine output is satisfactory, i.e., >30-50ml/hour, it indicates that renal perfusion is reasonably adequate.*
- Lung bases for crackles: *While hydrating, care should be taken not to overload the patient, especially if he or she has some degree of compromised cardiac function.*
- Central venous pressure, by insertion of an internal jugular or subclavian line: *External jugular lines are not central venous lines – they may be used for urgent volume replacement where it is not possible to insert a central line, but carry the risk of air embolism. Central venous lines are also required for volume replacement and giving inotropes.*
- Intra-arterial blood pressure, by insertion of an arterial line: *This is more accurate than conventional blood pressure monitoring, although not always necessary at the start.*
- Pulse oxymetry: *A low pulse oxymetry occurs with hypotension, due to reduced mixed venous oxygen saturation. Restoration of this to normal indicates improvement of tissue perfusion*

Baseline investigations should be performed.

- ECG – look for evidence of acute coronary syndromes, arrhythmias
- Chest radiograph- look for pneumothorax, pulmonary embolism
- Arterial blood gas analysis- look for metabolic acidosis, which might suggest sepsis. Severe acidosis can depress cardiac functions and cause hypotension.
- Full blood count, renal profile, liver function tests, septic screen
- Serum lactate is useful for demonstrating tissue hypoxia, and high levels are a poor prognostic marker
- Echocardiography, if possible, will confirm or exclude cardiogenic shock, and is very useful in planning further management.

Restoration of blood pressure and tissue perfusion

Time is tissue!

Therefore, blood pressure and tissue perfusion should be normalised as fast as possible.

If a cause for shock has been identified, such as pneumothorax, pericardial effusion or arrhythmia, it must be corrected. If the patient is actively bleeding this should be arrested if possible.

Establish intravenous access with one or more large bore intravenous cannulae. If possible, a central venous line should be inserted.

Volume replacement

Volume replacement is almost always needed in patients with shock *irrespective of the type of shock.* Even patients in cardiogenic shock almost always have some degree of volume depletion. Fluids should be avoided only in very severe heart failure and pericardial tamponade. If hypovolaemic or septic shock, or dengue shock syndrome is likely, then volume replacement should be started immediately. Large volumes may be required, and boluses of fluids may need to be given. There is no clear evidence as to whether crystalloids or colloids are better; what matters is to give adequate fluids. Crystalloids are generally preferred; 0.9% saline or Hartmann solution is recommended; dextrose solutions should not be used for volume replacement.

If bleeding is present, red cells, plasma, platelet concentrate maybe given; other specific blood or anticoagulant products maybe required in specific situations. Single donor platelets are preferred to single platelet packs in patients with thrombocytopaenia, because they raise the platelet count more rapidly. They are, however, more difficult to obtain, and require greater preparation time.

Blood transfusion is generally not urgent, except in severe haemorrhage, and severe anaemia leading to coronary ischaemia. In general, haemoglobin over 8mg/dL is adequate, although if coronary artery disease is present, a target of 10mg/dL is preferred.

Oxygenation

All patients should be given oxygen by face mask. The target pulse oxygen saturation is 97-99%; in patients with a history of COPD, a target oxygen saturation of around 92% is adequate. Prolonged hypoxaemia will result in muscle fatigue, and myocardial depression, and will worsen tissue damage. Fluid resuscitation will itself increase tissue oxygenation. Sometimes it may be necessary to ventilate the patient to maintain oxygenation.

Shock which does not respond to fluids

Adequate fluids must be given before deciding that the patient's hypotension is unresponsive to fluids. Most clinicians do not adequately resuscitate their patients. Patients with hypovolaemic shock and septic shock need large volumes of fluids, i.e., several litres. If the patient is not clinically overloaded, i.e., his lung bases are clear, and his JVP is not elevated, fluids can safely be given. The CVP should be maintained around 8-10mm of water.

If shock does not respond to fluids, ask the following questions;

- Is the diagnosis correct?
  Reassess the history and examination. What was initially thought to be hypovolaemic shock due to bleeding may have now been complicated by myocardial infarction due to anaemia.
  Echocardiogram will usually resolve this issue. In addition to cardiogenic shock, the patient maybe septic, resulting in vasodilatory shock. In a patient with septic shock, severe acidosis maybe causing myocardial depression.
  Bicarbonate can be given in severe acidosis (pH<7.1) to improve myocardial contractility.

  Septic shock is quite often unresponsive to fluid resuscitation, because of the widespread and profound vasodilatation which occurs.

- Have adequate fluids been given?
  Adequate fluids must be given before deciding that the patient's hypotension is unresponsive to fluids. Most clinicians do not adequately resuscitate their patients. Patients with hypovolaemic shock and septic shock need large volumes of fluids, i.e., several litres. If the patient is not clinically overloaded, i.e., his lung bases

are clear, and his JVP is not elevated, fluids can safely be given. The CVP should be maintained around 8-10mm of water. It is difficult to assess the adequacy of fluid resuscitation by clinical examination alone. A raised jugular venous pressure is not diagnostic of adequate filling; it may be due to right ventricular failure, or decreased venous compliance which can occur due to venoconstriction. Other signs of inadequate volume resuscitation are: thirst, tachycardia, oliguria, and an increased core-toe temperature difference. Postural changes in blood pressure, a big swing in central venous pressure during spontaneous breathing, or an increased systolic, stroke volume or pulse pressure variation in ventilated, and non-spontaneously breathing patients may also be helpful.

A very simple test would be to elevate the patient's legs. If the blood pressure rises, the patient is still fluid depleted. In a ventilated patient, one could try increasing the PEEP. If the blood pressure falls with an increased PEEP, it is likely that more fluids are required. These dynamic measures are more useful than baseline static measures in determining the adequacy of fluid resuscitation.

- Are any of the therapies being used causing hypotension?
  Dobutamine, a vasodilator, can cause an exaggerated Beta-2 adrenergic effect in some patients, and could cause hypotension. Propofol, a commonly used sedative agent in ventilated patients, could cause low blood pressure.

- Think of other causes
  Pericardial tamponade, pneumothorax, pulmonary embolism, continuing gastrointestinal haemorrhage, severe anaphylaxis, drug overdose etc.

Inotropes, vasodilators, and vasoconstrictors

Drugs which improve cardiac contractility or increase vascular tone should be started if fluid resuscitation fails to restore blood pressure to normal. Catecholamines are the usual first line of drugs, as they have a short duration of action and can easily be titrated to achieve the desired effect. They fall into two main groups depending on their action. All

catecholamines have cardiac inotropic action, but different catecholamines have varying effects on the peripheral vessels.

- Ino-constrictors=inotropic+vasoconstrictor: Noradrenaline, moderate to high dose Adrenaline, and high dose Dopamine.
- Ino-dilators= inotropic + vasodilator: Dobutamine (any dose), low dose dopamine.

Vasopressin is another drug which is used, and it has purely vasoconstrictor properties. It has certain side effects; it can precipitate angina, and can cause severe peripheral vasoconstriction leading to gangrene of the extremities. It is therefore used as an add-on drug, and as a noradrenaline sparing agent.

The choice of drug will depend on the cause of hypotension. It stands to reason therefore, that in septic shock, noradrenaline is the preferred drug. In cardiogenic shock, dobutamine or adrenaline is the drug of first choice. If a combination of septic and cardiogenic shock is present, a combination of inodilators and inoconstrictors may be required. However, there is no basis for using two inodilators or two catecholaminergic inoconstrictors in combination, as they all act through the same receptors and saturation of these receptors occur when the drugs are given in high doses. In practice, it is common to see patients on dopamine, noradrenaline and adrenaline, but this practice is illogical. The usual doses of inotropic/vasopressor drugs are given in the table.

Drug	Dose
Dopamine	0-20 micrograms/kg/min
Dobutamine	0-20 micrograms/kg/min
Adrenaline	0-2 micrograms/kg/min
Noradrenaline	0-2 micrograms/kg/min
Vasopressin	0-0.03 Units/min

Note that improving the blood pressure alone does not necessarily translate into clinical benefit. Especially after prolonged tissue hypoxia has been present, normalising the blood pressure will not prevent the progression of

tissue damage which has already begun. Hence, the importance of treating shock as a medical emergency.

Protocol for resuscitation in septic shock

In resuscitation of septic shock, noradrenaline is recommended as the first line inoconstrictor. If the patient's blood pressure does not respond, add dobutamine to boost cardiac output. Maintenance of blood pressure is usually with noradrenaline or dopamine, sometimes with the addition of vasopressin. If cardiac compromise is present, dobutamine should be continued.

Low dose corticosteroids

Low dose corticosteroids are of benefit in septic shock; corticosteroids are probably necessary for catecholamines to act on blood vessels, and it is postulated that certain patients with septic shock have relative adrenal insufficiency. These patients in particular respond to treatment with low dose corticosteroids. While there is some controversy as to their benefit, corticosteroid treatment is currently recommended in sepsis treatment guidelines. This will be covered in greater detail in the following section.

Sepsis, severe sepsis, septic shock and multi-organ dysfunction

The Systemic Inflammatory Response Syndrome or SIRS is discussed in the section on severe infection. To recapitulate,

SIRS: the patient has 2 or more of the following criteria

- Fever (>38 °C) or hypothermia (<36 °C)
- Tachycardia (>90 b/min)
- Tachypnoea (>20 /min), or fall in arterial PCO2 (<32 mmHg)
- Leukocytosis (>12.0 x 10^9 /L) or leukopoenia (<4.0 x10^9 /L) or >10% immature (band) forms

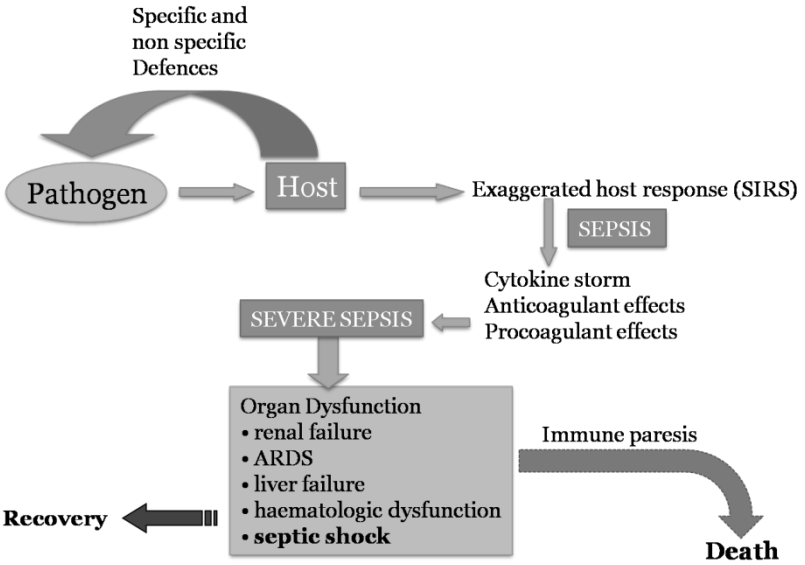
When SIRS is caused by infection, the condition is known as sepsis. In the past, the term septicaemia has been used. The old definition of septicaemia was a condition where bacteria multiply in the bloodstream, resulting in organ damage. It is now known that the manifestations of sepsis are caused by disordered immunity and the cytokine cascade; hence, the term septicaemia no longer has any meaning, and was removed from the definitions in 1992. Hence, the current definitions are;

- Sepsis: SIRS due to infection
- Severe sepsis: Sepsis with dysfunction of at least one organ system
- Septic shock: severe sepsis with hypotension resistant to fluid replacement.

Sepsis, severe sepsis and septic shock form a continuum of disease caused by a complex interaction between the infecting organism and the host response to infection. In the initial stages of sepsis, an exaggerated immune response occurs, with a cytokine storm. Later on, immune paresis occurs, resulting in progressive worsening of the patient's condition and death. Sepsis has a high mortality. Early diagnosis and early and aggressive treatment is as important as in any other acute condition like myocardial infarction or asthma. However, often the signs and symptoms of sepsis are subtle, and missed even by experienced clinicians. The importance of early recognition and quick and aggressive treatment cannot be over-emphasised.

US data in 2000 showed that sepsis has a national incidence rate of 3 per 1000 population. Mortality from sepsis was around 18 percent. However, mortality is very variable, and depends on the severity of sepsis and the number of organs affected. Septic shock has a very high mortality of around 45%. Both the incidence and the mortality due to sepsis rise with increasing age. With better ICU care and greater awareness of the condition, the mortality from sepsis has been falling over the years; however, the incidence of sepsis has been increasing over the years, resulting in larger numbers of people dying from sepsis. While gram negative bacteria were the commoner causative agents in the past, in recent years, gram positive bacteria have become the common. The incidence of fungal sepsis has also increased, in part because of the use of broad spectrum antibiotics.

A simplified diagram of what takes place in severe sepsis



Criteria for diagnosis of sepsis

Infection, documented or suspected, and some of the following:
• General variables ○ Fever (>38.3°C) ○ Hypothermia (core temperature <36°C) ○ Heart rate >90 min ○ Tachypnea ○ Altered mental status ○ Significant edema or positive fluid balance (>20 mL/kg over 24 hrs) ○ Hyperglycemia (plasma glucose >140 mg/dL or 7.7 mmol/L) in the absence of diabetes
• Inflammatory variables ○ Leukocytosis (WBC count >12,000 /mm^3) ○ Leukopenia (WBC count <4000 /mm^3) ○ Normal WBC count with >10% immature forms ○ Plasma C-reactive protein >2 SD above the normal value ○ Plasma procalcitonin >2 SD above the normal value
• Hemodynamic variables ○ Arterial hypotension (SBP <90 mm Hg; MAP <70 mm Hg; or an SBP decrease >40 mm Hg in adults or >2 SD below normal for age)
• Organ dysfunction variables ○ Arterial hypoxemia (PaO_2/FIO_2 <300) ○ Acute oliguria (urine output <0.5 mL/Kg hr or 45 mmol/L for at least 2 hrs, despite adequate fluid resuscitation) ○ Creatinine increase >0.5 mg/dL ○ Coagulation abnormalities (INR >1.5 or a PTT >60 secs) ○ Ileus (absent bowel sounds) ○ Thrombocytopenia (platelet count <100,000/mm^3) ○ Hyperbilirubinemia (plasma total bilirubin >4 mg/dL)
• Tissue perfusion variables ○ Hyperlactatemia (> upper limit of lab normal) ○ Decreased capillary refill or mottling

WBC, white blood cell; SBP, systolic blood pressure; MAP, mean arterial blood pressure; INR, international normalized ratio; a PTT, activated partial thromboplastin time.

Criteria for diagnosis of severe sepsis

Severe sepsis = sepsis-induced tissue hypoperfusion or organ dysfunction (any of the following thought to be due to the infection
• Sepsis-induced hypotension
• Lactate greater than the upper limits of normal laboratory results
• Urine output <0.5 mL/kg hr for >2 hrs, despite adequate fluid resuscitation
• ALI with PaO_2/FIO_2<250 in the absence of pneumonia as infection source
• ALI with PaO_2/FIO_2 <200 in the presence of pneumonia as infection source
• Creatinine >2.0 mg/dL (176.8 mol/L)
• Bilirubin >2 mg/dL (34.2 mol/L)
• Platelet count >100,000
• Coagulopathy (INR >1.5)

Given the increasing mortality due to sepsis with increasing severity, various scoring systems have been devised to predict outcome. Unfortunately, none of these reliably predict prognosis. Various markers have also been suggested for early detection of sepsis, and for prognostication; these include C-reactive protein and procalcitonin. The predictive value of these markers is controversial, and there are no uniformly accepted early markers for diagnosis, although these markers are of some use.

The clinical features of sepsis depend on the organ dysfunction present, and can be very variable. Respiratory tract infection is, however, the commonest site of infection. Undiagnosed bloodstream infection, urosepsis, intraabdominal sepsis, and CNS infections are important causes of sepsis.

Initial investigations

The following initial investigations must be performed in a patient suspected to have sepsis

- ESR, CRP, full blood count: High ESR and CRP suggest infection and sepsis. A high white cell count with neutrophil leukocytosis suggests bacterial sepsis; sometimes neutropaenia is present. A low platelet count also may suggest sepsis; other causes of low platelet count should be considered; dengue haemorrhagic fever, leptospirosis, malaria, background chronic liver disease, malignancy.
- Blood culture: several blood cultures should be obtained BEFORE starting antibiotics

- Renal function tests: blood urea, serum creatinine, serum electrolytes: acute renal failure may be present. Life threatening hyperkalaemia may need urgent treatment.
- Liver function tests: Important to determine coexistent liver disease, leptospirosis, malaria, hepatitis, drug induced liver dysfunction
- Serum calcium, phosphate, magnesium: these may need correction if abnormal
- Serum lactate: a high serum lactate indicates tissue hypoxia, and is a marker of severity of sepsis; the serum lactate may be high in patients with severe sepsis even with a normal blood pressure, due to alterations in tissue microcirculation
- Coagulation profile:to obtain a baseline, diagnose DIC
- Arterial blood gas analysis: sepsis often shows metabolic acidosis. Hypoxaemia may be present if ARDS is developing, and severe hypoxaemia is an indication for ventilation. Renal failure may also result in metabolic acidosis, and may be an indication for dialysis.
- Chest radiograph: to diagnose pneumonia and ARDS
- ECG: as a baseline, and to determine if a cardiac event has occurred. In pulmonary embolism, the classical ECG changes may help diagnosis. A completely normal ECG generally makes significant cardiac dysfunction unlikely, though there maybe exceptions. T wave inversions are also seen in myocarditis.
- Echocardiography: where ARDS is suspected, bedside echocardiographic evaluation is useful in excluding heart failure.

Other investigations maybe required depending on the clinical presentation and suspected diagnosis;

- Blood for malaria parasites – thick and thin films
- Malaria antigen tests
- Leptospira antibody tests
- Blood for viral studies (including dengue)
- Lumbar puncture and CSF examination
- Contrast CT scan of the brain in suspected cerebral abscess
- Ultrasound scan of the abdomen in suspected intra-abdominal infection
- Contrast CT abdomen in suspected intra-abdominal infection
- Blood picture, D-Dimers in suspected DIC

Daily investigations

The following investigations are generally required on a daily basis

- CRP
- Full blood count
- Serum Creatinine, serum electrolytes
- Arterial blood gas analysis
- Chest x-ray in ventilated patients

Liver function tests and coagulation profile maybe required at intervals, depending on the diagnosis.

Treatment

Treatment should be commenced without delay.

Treatment of severe sepsis is largely supportive. However, of recent, several therapies have been shown to have survival benefit in severe sepsis. In summary these therapies are:

- Early aggressive fluid resuscitation
- Low tidal volume ventilation for ARDS
- Tight glycaemic control
- Corticosteroids in septic shock
- Activated protein C
- Renal replacement therapy

The Surviving Sepsis Campaign guidelines were developed with the aim of reducing the mortality from sepsis. The guidelines are evidence based. In addition to the above, specific evidence based recommendations are made on numerous other therapies and interventions which are of benefit in sepsis.

Early aggressive resuscitation

Early aggressive resuscitation according to a protocol aimed at achieving certain haemodynamic goals has been shown to reduce mortality. Resuscitation must begin as early as possible once tissue hypoperfusion has been recognised, and should not be delayed until the patient is transferred

to the ICU. 'Time is tissue'. The aim is to achieve the following goals within the first 6 hours of resuscitation (*the golden hours*):

- Central venous pressure (CVP): 8–12mm Hg
- Mean arterial pressure ≥ 65mm Hg
- Urine output ≥ 0.5mL/kg/hour
- Central venous (superior vena cava) oxygen saturation≥ 70% or mixed venous oxygen saturation ≥ 65%

Crystalloids or colloids are given to achieve these goals. There is no significant difference between colloids and crystalloids in terms of clinical benefit, and crystalloids are considerably cheaper. An initial bolus of 500ml to 1000ml of fluid is given over 30 minutes, and continued until either the haemodynamic goals are achieved or the patient develops features of fluid overload.

If haemodynamic goals are not achieved, blood transfusion could be considered. Dobutamine can be used to augment cardiac output.

Haemodynamic support

After adequate fluid resuscitation if the blood pressure remains low, it will be necessary to start on inotropes. Septic shock is vasodilatory shock; peripheral vasodilatation is present, hence the extremities are warm, and the pulses are bounding. The vessels respond poorly to inotropic agents, and it is postulated that relative adrenal insufficiency may play a role in blunting the adrenergic response of the blood vessels. Usually, cardiac output is normal. However, the cardiac output maybe low in certain situation – for example, if the patient has pre-existing myocardial dysfunction due to ischaemic heart disease or cardiomyopathy, if the patient has developed myocarditis (seen in dengue, leptospirosis) or if severe acidosis is causing myocardial depression. Choice of the appropriate drug to support the blood pressure must be based on these considerations.

Since most adrenergic drugs have positive inotropic effect, but differ in their effects on the peripheral vessel, the terms inodilator, inoconstrictor and pure vasoconstrictor are preferred.

An inoconstrictor has positive inotropic effects on the heart, and causes peripheral vasoconstriction. An inodilator has positive inotropic effects on the heart, and causes peripheral vasodilatation.

- Dopamine(inoconstrictor) has positive inotropic effects on the heart and is a vasoconstrictor
- Noradrenaline (inoconstrictor) has potent vasoconstrictor effects, with comparatively little cardiac inotropic effects.
- Dobutamine (inodilator) has significant cardiac inotropic effects, and vasodilates the peripheral vessels.
- Adrenaline (inoconstrictor) has potent cardiac inotropic and peripheral vasoconstrictor effects.
- Vasopression (pure vasoconstrictor) has potent peripheral vasoconstrictor effects with no cardiac inotropic effect.

Hence, in septic shock which is vasodilatory shock with generally intact cardiac function, noradrenaline or dopamine should be the drugs of first choice. Noradrenaline is more effective, and is more effective in maintaining renal perfusion, than dopamine, and so is the preferred drug. The only advantage of dopamine over noradrenaline is that it can, in the short term, be given through a peripheral vein in a ward setting, until an ICU bed can be arranged.

If the patient has suspected or proven cardiac dysfunction, dobutamine should be added. If there is no response to dobutamine and noradrenaline, consider using adrenaline. Vasopressin is used in patients with refractory septic shock, and is useful as a noradrenaline sparing agent. However, it causes severe peripheral vasospasm and can result in peripheral gangrene.

There is no such thing as ‘renal dose’ or ‘low dose dopamine’. It was earlier believed that dopamine in low doses selectively improves renal blood flow. While this effect is seen in healthy volunteers, there is no evidence that this benefit exists in patients with septic shock. However, clinicians often vouch that dopamine seemed to improve renal perfusion – this is simply because dopamine increases the blood pressure and hence improves renal blood flow.

There is no logic in using multiple inotropes of similar effect, since in the doses that are used, the adrenergic receptors are usually saturated anyway. For example it does not make sense to combine dopamine and noradrenaline, since noradrenaline is more effective and has the same effect as dopamine. Sensible combinations are:

- Dopamine + dobutamine
- Noradrenaline + dobutamine
- Noradrenaline + vasopressin

Vasoactive drugs MUST be given through a central venous line, using an infusion pump. An arterial line must be inserted to monitor the blood pressure whenever possible. Care must be taken to give the correct dose of drugs. Doses must be given in either micrograms per kilogram body weight per minute or micrograms per minute.

The commonly used doses of inotropes are given in the table. Note that there is no defined maximum dose, and the maximum dose of any inotrope is that dose beyond which further increasing the dose either does not help to improve the blood pressure, or beyond which side effects manifest. Clinicians sometimes use suboptimal doses, and care should be taken to ensure that adequate doses are given.

Drug	Dose
Dopamine	0-20 micrograms/kg/min
Dobutamine	0-20 micrograms/kg/min
Adrenaline	0-2 micrograms/kg/min
Noradrenaline	0-2 micrograms/kg/min
Vasopressin	0-0.03 Units/min

The aim should be to maintain a mean arterial blood pressure≥ 65mm Hg. Care should be taken to reduce the dose of vasoactive drugs once target blood pressure is exceeded. It is common in ICUs to see the blood pressure

well above normal, yet the patient still on noradrenaline which has been continued overnight! Drugs should be tailed down gradually, while watching the haemodynamic response.

Corticosteroids

If shock persists despite adequate fluid replacement and inoconstrictors, there may be a place for replacement doses of corticosteroids. Corticosteroids in large doses have immunosuppressant effects, and in the past it was thought that this effect might help modulate the effects of sepsis. However, clinical trials showed that large doses of steroids were of no benefit, and may in fact increase the risk of infections. Cortisol is required to make the blood vessels responsive to adrenergic agents. It was postulated that certain patients with septic shock may have relative adrenal insufficiency, and this was the cause for the lack of effect of adrenergic agents in these patients. Subsequent trials showed that replacement doses of corticosteroids improve haemodynamics and improve survival. The recommended dose of hydrocortisone is 200mg per 24 hours, given either as a continuous infusion or in 4 divided doses.

Antibiotic therapy

Broad spectrum intravenous antibiotics should be commenced as soon as possible after obtaining two or more blood cultures and other cultures as necessary. If pseudomonas is likely, add an antipseudomonal agent. If fungal infection is likely, an antifungal agent should be added. Combination therapy is necessary if neutropenia is present. Source control is important: abscesses and collections of pus should be drained. Antibiotic therapy should be re-assessed every few days and modifications made based on clinical response, suspected sites of infection, regional antibiotic sensitivity patterns, and results of cultures.

Tight glycaemic control

Tight glycaemic control has been shown to be of survival benefit, although the evidence is more for cardiac surgical patients than medical ICU patients. Intravenous insulin is preferred, aimed at maintaining the blood glucose below 150mg/dL. Several regimens are available; the Markovitz regimen is a

popular regimen used in many ICUs. Adequate calories should be given to prevent hypoglycaemia. Once the patient is stable and taking orally, the infusion could be switched over to subcutaneous insulin given three times daily. There is some evidence that insulin may exert anti-inflammatory effects, and hence, be beneficial in sepsis.

Renal replacement therapy

Renal replacement therapy is necessary in patients with acute renal failure; this is discussed further in the section on acute renal failure. Either intermittent haemodialysis or continuous renal replacement therapy could be used, and are equivalent in benefit. Peritoneal dialysis is less effective. The choice of dialysis modality is determined by the haemodynamics of the patient; haemodynamically unstable patients cannot tolerate intermittent haemodialysis, and continuous veno-venous haemofiltration is the preferred modality. This is, however, expensive and not readily available in all centres.

Bicarbonate administration

There is no place for administration of bicarbonate to counteract acidosis or to improve cardiac function in patients with a pH over 7.15. Possible benefit maybe seen if the pH is lower, however, there is no consensus on this.

Low tidal volume ventilation

Ventilation is often required in patients with sepsis and ARDS. Low tidal volume ventilation is known to reduce mortality. This is discussed at greater length in the section on respiratory failure.

Sedation and neuromuscular blockade

Minimum sedation should be given. Intermittent boluses are preferred to continuous infusions, and daily interruption of sedation enables early weaning. Neuromuscular blockade should be avoided as far as possible.

Activated protein C

Human recombinant activated protein C has been shown in a large multicentre trial to improve survival in patients with severe sepsis and a high risk of death. Patients with an APACHE II score of 25 or more are likely to benefit, and the drug should not be used in less severely ill patients.

Bleeding is the most important side effect. The drug is extremely expensive, costing around $7000 per patient.

Correction of haemoglobin and blood product administration

Blood transfusion is not recommended unless the haemoglobin drops to 7g/dL. The target haemoglobin is 7-9g/dL. A haemoglobin of over 10g/dL is required only in patients with ischaemic heart disease. Erythropoietin treatment is not recommended to treat sepsis related anaemia. FFP is not required to correct coagulation abnormalities unless active bleeding is present, or an invasive procedure is planned. Platelet transfusion is required only if the platelet count drops below 5000/mm^3 in the absence of bleeding, and below 30000/mm^3 with active bleeding. Correction to over 50000/mm^3 may be required if surgery is planned.

Deep Vein Thrombosis prophylaxis

Unfractionated or fractionated heparin should be given subcutaneously to prevent DVT. Compression stockings should be used.

Stress ulcer prophylaxis

Stress ulcer prophylaxis should generally be given; proton pump inhibitors are more effective than H2 receptor blockers. However, acid blockade increases the risk of ventilator associated pneumonia.

The above therapies are based on clinical evidence, and contribute to better outcome. Recommendations are based on the **Surviving Sepsis Campaign: International guidelines for management of severe sepsis and septic shock 2008.**

Consideration for limitation of support

In spite of the best of care, severe sepsis and septic shock has a high mortality. As sepsis progresses, more and more organs may fail. During the later stages of the condition, immune paresis occurs. Nosocomial infections often occur as complications. The patient becomes progressively worse, and generally resistant hypotension develops as a terminal event.

It is important to discuss severity of illness and possible adverse outcome with the patient's family, and make sure that expectations are realistic. If recovery seems unlikely, decisions of limitation or withdrawal of support should be considered. Since severe sepsis can suddenly affect previously well patients, this is all the more difficult.

Evaluating respiratory disease & airway management

This section discusses the structure of the respiratory system and how to evaluate respiratory disease, and also deals with how to manage the airway.

The respiratory system is divided into two parts – the upper and lower respiratory tract.

- Upper respiratory tract: nose (nasal cavity, sinuses), mouth, larynx, and trachea
- Lower respiratory tract: bronchi, bronchioles, and alveoli

Respiration is controlled by the respiratory centres in the pons and medulla. These control the rhythm, rate, and depth of respiration. The respiratory centres are stimulated by hypoxia, hypercapnoea, acidosis, and through various receptors within the lungs. The lung receptors respond to stretch and irritation.

Respiratory failure is the most frequent cause of admission to ICU. The history, examination and investigations help to identify the abnormality in the respiratory system, diagnose its cause, and fine tune management appropriate to the patient.

History

Ask for a history of previous lung disease:

- Asthma: duration, severity, compliance with medications, severity of exacerbations, previous intubation.
  A history of previous intubation and ICU admission for acute severe asthma is a risk factor for respiratory failure. Such patients should be intubated without delay.
- COPD: duration, severity, previous hospital admissions and previous intubations
- Previous pneumonia
- Tuberculosis
- Fibrosing alveolitis
- Bronchiectasis

Smoking: How many cigarettes, for how long? Calculate the number of pack years (1 pack or 20 cigarettes for 1 year = one pack year). Has the patient

stopped smoking now? Is there passive smoking? *Smoking is a risk factor for COPD and lung cancer*

Evidence of obstructive sleep apnoea: Snoring, early morning headaches, daytime sleepiness, obesity, collar size over 17 inches. OSA predicts difficult intubation.

Occupational exposure: silicosis, coal, asbestos.

Immune status: neutropaenia, malignancy, HIV.

Rheumatological diseases:

- Rheumatoid arthritis- fibrosing alveolitis, nodules, pleural effusions, Caplan's syndrome
- Systemic sclerosis, ankylosing spondylitis – lung fibrosis
- SLE: pleural effusions, lung fibrosis
- Vasculitides: polyarteritis nodosa, Churg-Strauss syndrome
- Reno-pulmonary syndromes: Wegeners granulomatosis, Goodpastures syndrome

Neurological diseases: motor neuron disease, Guillain-Barre syndrome, myasthenia gravis. Such patients might need prolonged ventilation for ventilatory failure.

Endocrine diseases: Cushing's disease results in impaired immunity and increased risk of lung infections.

Drug induced lung diseases:

- Beta blockers: obstructive airways disease
- Methotrexate, amiodarone: lung fibrosis
- Corticosteroids and other immunosuppressive agents: increased risk of lung infections

Cardiac diseases: valvular and congenital heart disease resulting in cor-pulmonale

Previous lung surgery: patients maybe left with reduced lung reserve.

Family history: Cystic fibrosis, alpha-1 antitrypsin deficiency, Kartegener's syndrome, primary pulmonary hypertension

Symptoms and signs

Cough: the commonest respiratory symptom. It maybe productive or dry. Dry cough is seen in lung fibrosis, certain types of bronchiectasis, and pleurisy. Productive cough with purulent sputum is seen in bacterial infections of the lung. Cough can also be present in upper respiratory infections, such as laryngitis, pharyngitis, tonsillitis, sinusitis with post nasal drip. A chronic cough is defined as cough persisting longer than 3 weeks.

Sputum: most bacterial infections of the lung cause sputum production, which can be very variable depending on the type and severity of infection. The sputum is characteristically yellow in pyogenic infection, and is due to the presence of neutrophils. Yellow sputum is also seen in asthma due to large numbers of eosinophils in the sputum. Green sputum is caused by stagnation of mucus, and is common in bronchiectasis. The sputum in bronchiectasis is copious and purulent. The sputum in pneumonia is characteristically 'rusty', due to the presence of red blood cells. In lung abscess, the sputum is purulent and offensive, and halitosis is often present. In the past, amoebic liver abscesses were known to rupture into the lung, producing the characteristic 'anchovy sauce' sputum. This is rare now with anti-amoebic therapy.

Haemoptysis: small amounts of blood in the sputum are seen in bronchitis. Haemoptysis is always a serious symptom, and may be due to a sinister cause such as pulmonary tuberculosis, bronchial carcinoma, bronchiectasis, or pulmonary infarction. Mitral stenosis may also cause haemoptysis.

Dyspnoea: a subjective state where the patient is conscious of his breathing. Dyspnoea is an important symptom of respiratory disease; it can be caused by anything that stimulates or increases the work of breathing – hypoxia, hypercapnoea, acidosis, consolidation, pneumothorax, pleural effusion, heart failure etc.

Chest pain: Chest pain in lung diseases arises from the pleura. Inflammatory conditions of the lung may involve the pleura and cause pleuritic chest pain, which characteristically worsens on breathing in and out. Pulmonary embolism can cause localised pleuritic chest pain.

Cyanosis: this is the presence of more than 5g/dL of deoxygenated haemoglobin in the blood. Central cyanosis can be caused by any lung

condition which causes severe hypoxia, or by cardiac right to left shunts. Peripheral cyanosis is caused by conditions which slow the peripheral circulation resulting in increased extraction of oxygen from haemoglobin – vasoconstriction, low cardiac output states.

Clubbing: clubbing is seen in squamous cell bronchial carcinoma, suppurative lung disease (bronchiectasis, lung abscess, empyema), fibrosing alveolitis, and congenital or acquired cyanotic heart diseases (where a right-to-left shunt is present).

Examination of the chest: The standard examination of the chest will reveal conditions such as pleural effusions, pneumothorax, localised consolidation, basal fibrosis, bronchiectasis etc. In particular look for:

- Signs of emphysema: barrel shaped / hyperinflated chest, limited chest expansion (less than 3cm), use of accessory muscles of respiration, together with signs of cor-pulmonale (loud second heart sound, parasternal heave, elevated JVP, tender liver, lower limb oedema.

- Lymph nodes in the neck – suggestive of malignancy, sarcoidosis.

Investigations

Chest radiograph

An essential investigation in diagnosing respiratory disease. Consolidations, pneumothorax, pleural effusions are easy to diagnose. Note that most of the time in ICU patients it is not possible to obtain erect posteroanterior views; bedside chest radiographs are anteroposterior views, and distort the anatomy to some extent. It is difficult to diagnose cardiomegaly on such views. Views are often rotated. Because of this, it is prudent to be careful when interpreting subtle and minor radiological appearances which could be artefactual. One should look for clear and gross abnormalities. Whenever possible, chest radiographs in ICU should be obtained with the patient in the seated position.

Ventilated patients must have a chest radiograph done daily. Chest radiographs should also be performed in ICU patients in the following situations:

- After intubation: to check the position of the ET tube
- After subclavian or internal jugular lines are inserted and after any procedures such as pleural aspiration/biopsy, intercostals drain insertion, liver biopsy – in particular to check if a pneumothorax has been created. *It is mandatory that the person who did the procedure checks the chest radiograph.*

The chest radiograph can be normal in:

- Early pneumonia / infection
- COPD, Asthma
- Early lung fibrosis
- Small lesions –tumours less than 1cm in diameter, endobronchial tumours
- Small pulmonary emboli (without infarction)

A small pneumothorax can be easily missed. Always look carefully at the margins of the lung fields for air in the pleural space.

PaO_2

The partial pressure of oxygen determines the degree of oxygen saturation of haemoglobin (SaO_2). The arterial oxygen content is dependent on the oxygen saturation and the haemoglobin. Thus the arterial oxygen content is determined by the following formula:

Arterial O_2 content = (SaO_2 x Hb x 1.34) + (0.003 x PaO_2) mlO_2/dL of blood.
The normal arterial oxygen content is 16-20mlO_2/dL.

Because of the shape of the haemoglobin oxygen dissociation curve, the SaO_2 is a more reliable index of arterial oxygen content than PaO_2. A small fall in PaO_2 will not drop the SaO_2 much, and hence, will not affect arterial oxygen content. However, when the PaO_2 is significantly low, the SaO_2 will fall rapidly. A low Hb will significantly affect arterial oxygen content.

Oxygen delivery to the tissues is dependent on the arterial oxygen content and the cardiac output. If the blood pressure is low, even though the arterial oxygen content is adequate, tissue oxygen delivery will be low. If oxygen utilisation in the tissues exceeds oxygen delivery, the cells revert to anaerobic metabolism, leading to lactic acidosis.

Pulse oxymetry

Pulse oxymetry is widely used to determine oxygen saturation in blood in ICUs. The pulse oxymeter measures phasic changes in the intensity of transmitted light – hence, it works only with pulsating arteries, thus eliminating possible errors created by light reflection from other tissues. It is non-invasive, easy to use, and reasonably accurate. The probe is attached to a finger, and should be shielded from light. Pulse oxymetry can be affected by low perfusion states, skin pigmentation, nail polish, and its accuracy is poor when the saturation drops below 83%. It is not affected by serum bilirubin concentrations.

End tidal CO_2

Measurement of CO_2 levels in expired gases is useful in obtaining information about ventilation, perfusion and tissue metabolism. The content of CO_2 in expired air is determined by:

- Adequate perfusion of the pulmonary circulation: if the cardiac output or perfusion is reduced, the end tidal CO_2 will fall.
- Gas transfer at the alveolar-capillary interface. In conditions where gas transfer is impaired, $ETCO_2$ will fall.
- Adequate ventilation – if ventilation is inadequate, the $ETCO_2$ will fall.
- Tissue metabolism – if tissue metabolism rises, the $ETCO_2$ will rise, for example in malignant hyperthermia.

$ETCO_2$ is usually monitored continuously. Much information can be determined by analysis of the capnograph curve, which is beyond the scope of this book.

CT scanning of the thorax

CT scanning of the thorax is sometimes required, especially

- In suspected pulmonary embolism
- To diagnose the lung pathology (abscess, tumour)
- To diagnose interstitial lung disease
- For assessment of chest trauma
- To diagnose mediastinal masses
- To diagnose aortic dissection

- In ARDS, both for diagnosis as well as for assessment of lung recruitment manoeuvres.

Ultrasound scanning of the chest
This is used mainly for chest tube placement, and to look at pleural pathologies. It is sometimes useful to identify tumours or masses within a collection of fluid in the chest.

Ventilation-perfusion scans
Used primarily to diagnose or exclude pulmonary embolism. Spiral CT scan is easier and yields the same information in most cases.

Bronchoscopy
Used to visual the tracheobronchial tree, and also to obtain specimens for cytology and culture.

Airway Management
The first step in resuscitation is management of the airway,

- Airway patency- remove any obstructions and clear secretions. The tongue falling back is the commonest cause of airway obstruction. Broken teeth, dentures, food and other foreign bodies can obstruct the airway. Secretions, blood and regurgitated gastric contents must be cleared. Sometimes a suction apparatus is required to remove obstruction. Most of the time, neck extension alone will open the airway – sometimes the triple airway manoeuvre is necessary – head tilt, chin lift and jaw thrust. Laryngeal oedema in anaphylactic reactions can obstruct the airway. Upper airway obstruction causes stridor, and is an emergency. If airway patency cannot be quickly established, an emergency tracheostomy must be performed.
- Protective reflexes – these will help keep the airway open and prevent aspiration.
- Respiratory drive – make sure the patient is breathing.

Once the airway has been established, an oropharyngeal airway should be used to keep the airway open. The oropharyngeal airway should be inserted with the convex side towards the tongue and then rotated through 180

degrees. Be careful to avoid pushing the tongue posteriorly and worsening the obstruction.

Oxygen must be given by face mask. Giving 8-12 litres of oxygen will provide approximately 60% oxygen. Patients with COPD must not be given high flow oxygen, as it will knock out the respiratory drive and worsen hypercapnoea. If the patient is not breathing adequately spontaneously, bag and mask ventilation must be performed.

Endotracheal intubation

The indications for intubation in ICU are as follows:

- To provide mechanical ventilation (in patients unable to maintain normal respiration)
- Severe heart failure (to maintain oxygenation)
- Status epilepticus not responding to other therapy
- To secure and protect the airway (in patients unable to maintain an airway –in severe trauma, head injury, stroke)

It is always better to anticipate deterioration and intubate the patient before cardiac arrest or haemodynamic instability occurs. Often, clinicians are reluctant to intubate early. However early intubation prevents the patient from 'crashing'. Sometimes, of course, emergency intubation is necessary.

Preparation

The following equipment is essential

- Laryngoscopes – several sizes. Make sure the light is working.
- Cuffed endotracheal tube of the correct size. In general the largest possible tube will make it easier to ventilate. ET tube sizes are generally given by internal diameter.

  Women: 7.0-7.5 mm

  Men: 7.5 – 9.0 mm

  Test cuff for patency.
- ET tube introducer /guide
- Suction device (make sure these are functioning)
- Syringe to inject cuff
- Oral airway to prevent the patient from biting the tube
- Fixation
- Facilities for ventilation – ambu bag initially, and ventilator
- Sedative and neuromuscular blocking agents, and resuscitation drugs
- Stethoscope (to test position of tube)

Position the patient appropriately. The operator must have sufficient space. Sterile technique should be adhered to.

Pre-oxygenation the patient with 100% oxygen for at least 5 minutes

Sedation and paralysis

Administer an intravenous induction agent. Commonly used drugs are:

- Etomidate 0.2-0.4 mg/kg
- Propofol 0.5 -2mg/kg
- Thiopentone1-5mg/kg

Muscle relaxation may be necessary.

- Suxamethonium 1-2mg/kg.

  Suxamethonium is a depolarising muscle blocker. It acts rapidly. It can cause hyperkalaemia, and the patient's serum potassium should be checked before its use. It can also cause cardiac arrhythmias, increased intracranial pressure, and increased intraocular pressure. Suxamethonium is metabolised by plasma pseudocholinesterase. Certain patients may have a genetic defect in the plasma pseudocholinesterase genes; these patients may

have prolonged neuromuscular paralysis with suxamethonium. Plasma cholinesterase activity may also be reduced by burns, decompensated heart disease, infections, malignant tumors, myxedema, pregnancy and severe hepatic or renal dysfunction.

- Atracurium 0.2-0.5 mg/kg
- Vercuronium 0.05-0.1 mg/kg

Procedure of intubation

- The laryngoscope is held with the left hand near the junction of the handle and blade.
- Insert the blade along the right side of the mouth. Push the tongue to the left and direct the tip of the blade into the midline and into the vallecula between the epiglottis and the base of the tongue.
- Lift forwards and upwards in the direction of the handle of the laryngoscope to lift the epiglottis forward to expose the glottis and visualise the vocal cords. *Do not angulate the laryngoscope using the teeth as a fulcrum.*
- Pass the ET tube smoothly into the trachea until the cuff is seen to pass 2-3 cm beyond the cords. Inflate the cuff.
- Check the cuff pressure.
- Check ventilation with auscultation. Make sure that both sides of the chest expand.
- A chest radiograph is usually performed to check the correct position of the ET tube. The tip of the tube should be 2-3 cm above the carina. Abnormal placement sites are:
    - Tip in the right or left bronchus
    - Tip at the level of the vocal cords with the cuff above the cords.

Asthma and COPD

Severe asthma has a high mortality. Most deaths from acute asthma occur outside hospitals. COPD is the 6th leading cause of death worldwide. Exacerbation of COPD results in transient worsening of chronically altered lung function, and often necessitates ventilator support, either invasive or non-invasive.

Patients with acute severe asthma who fail to improve with initial therapy, and patients with severe exacerbations of COPD should be managed in ICU.

Patients with acute exacerbations of asthma or COPD present with severe respiratory distress, and if untreated, will die of respiratory arrest. Clinicians are often wary of intubating and ventilating patients with COPD, with the fear that it may not be possible to wean them off. However, if signs of imminent respiratory arrest are present, there should be no delay in ventilating the patient, either invasively, or if available, non-invasively.

Assessment

Emergency management of asthma must take place before a full detailed assessment of the patient is performed. This section will deal with evaluation of the severity of asthma or COPD exacerbation, and differentiation between asthma and COPD and other causes of acute dyspnoea.

The clinical features of acute severe asthma and acute exacerbation of COPD are similar; the patient will be very breathless, tachypnoeic, restless, and uses accessory muscles of respiration.

Features of acute severe asthma are

- Inability to complete sentences in one breath
- Respiratory rate (RR) >30/min
- Tachycardia >120/min
- PEFR <50% of predicted normal or of best normal if known (<200 l/min if not known)
- Arterial paradox (the fall in systolic pressure on inspiration) >20 mmHg

The presence of any of the following signs indicates life threatening asthma:

- Silent chest

- Lethargy, feeble respiratory effort, exhaustion
- Cyanosis
- Confusion, coma
- Bradycardia or hypotension
- Peak flow <30% of predicted

If any of these are present, prepare to ventilate the patient. Check if the patient has given an advance directive refusing ventilation. Insert an IV line, and start a drip to maintain IV access.

Details of the patient's previous history will be useful in differentiating COPD from asthma. A history of smoking and chronic dyspnoea suggests COPD.

The severities of attacks of asthma or COPD exacerbation are often underestimated. Any patient admitted with an exacerbation of asthma or COPD must be considered potentially at risk for respiratory arrest. There is no place for complacency.

Predicting the progress of a patient with severe asthma or COPD exacerbation

Acute attacks of asthma have typically two types of clinical course.

- Asthma gradually worsening over a few days, with poor response to therapy. The patient has usually been on bronchodilators for a few days; hence, the bronchospasm is not that severe. However, the inflammatory process is worsening, and mucosal oedema and secretions are responsible for bronchial obstruction.
- Sudden asphyxic asthma. Severe bronchospasm develops over minutes or hours, and can be fatal. Since bronchospasm predominates, the response to bronchodilators is good.

Previous ICU admission and previous ventilation is a poor prognostic factor in asthma, though not in COPD. Clinical deterioration in spite of optimal therapy, with increasing use of bronchodilators, is also a poor prognostic factor. The Peak flow rate is useful in determining progress in asthma, but not in COPD.

Blood gas analysis is very helpful in determining progress and the need for preparing for ventilation. In COPD, a rising $PaCO_2$, with respiratory acidosis, is a poor prognostic sign, and together with other clinical features such as

intercostal recessions, use of accessory muscles of respiration, exhaustion and drowsiness, indicates impending respiratory failure. In asthma, in the early stages, hyperventilation causes a CO_2 washout, hence the $PaCO_2$ is low. Hence, a normal $PaCO_2$ is a danger sign, and indicates impending respiratory failure. Hypoxia also indicates impending respiratory failure and the need for ventilation.

In acute severe asthma, measurement of PEFR should not be attempted as it is known to cause respiratory arrest.

What causes deterioration in patients with acute asthma/COPD exacerbation?

In asthma, inflammatory changes in the airways lead to airway narrowing and resultant increase in resistance of the small airways. This is caused by bronchospasm as well as mucosal oedema and secretions, and results in dynamic hyperinflation of the lung. Dynamic hyperinflation occurs when the expiratory time is not sufficient to allow full expiration. In COPD, expiratory airflow limitation occurs by two mechanisms; airway narrowing similar to asthma, and an increase in lung compliance due to loss of elasticity of lung tissue following emphysematous changes. Loss of elasticity and emphysematous changes result in airway collapse, resulting in air trapping. The so called 'time constant' (i.e., the product of resistance and compliance) is always increased in COPD. Hence in asthma, dynamic hyperinflation occurs, and in COPD, both dynamic hyperinflation as well as air trapping occurs. Some element of air trapping can also occur in asthma by mucosal plugs blocking the airways. In both asthma and COPD this is measured clinically using the FEV_1/FVC ratio. These factors influence ventilator settings in patients with asthma and COPD (see below).

Smoking is the most important causative factor in COPD. Cigarette smoke causes an inflammatory response in the lungs, and in a proportion of smokers, this result in COPD. In both COPD and asthma, mucosal oedema, narrowing of the airways by increased mucous secretions, and increased fluid and cellular exudation into the airways occur. If the inflammation persists, the airways become fibrosed and permanently narrowed; this occurs in COPD, and sometimes in longstanding untreated asthma. Apart from airway narrowing, emphysematous changes also contribute to airflow limitation. Destruction of elastic tissue arises due to an imbalance between

proteinases and antiprotineases, and due to oxidative stress. The result of loss of elasticity causes the small airways to collapse, and also affects elastic recoil of the lung during expiration.

The respiratory muscles play an important role. In COPD, geometry of the chest is altered (flattened diaphragm, increase in anteroposterior diameter of the chest, more horizontal placement of ribs, and shortened intercostals muscles) leading to decreased muscle efficiency. In severe COPD, respiratory cachexia leads to wasting of respiratory muscles. In an acute exacerbation, hypoxaemia and respiratory acidosis can further compromise muscle function, and can also have effects on cardiac output.

The chief difference between asthma and COPD is that the respiratory abnormalities in asthma are fully reversible.

Therapy in asthma and COPD is directed therefore, towards

- Relieving bronchospasm (bronchodilators)
- Reducing inflammation and further damage(steroids, montelukast)
- Improving or supporting respiratory muscle function

Initial therapy

Oxygen therapy: high flow oxygen must be given by nasal mask in all patients with asthma. In COPD, oxygen should be titrated carefully. When high flow oxygen is given to COPD patients, their $PaCO_2$ may rise, leading to carbon dioxide narcosis and worsening respiratory acidosis. The classical explanation for this is that patients with COPD have chronically elevated pCO_2 levels, and their respiratory drive is mainly dependent on hypoxia. Giving high flow oxygen can remove this hypoxic drive; previous teachings warned that the 'patient may stop breathing'. The effect on hypoxic drive is not the only reason for developing hypercapnoea; in fact it may not be even the most important reason. Attenuation of hypoxic pulmonary vasoconstriction by oxygen therapy, with consequent worsening of the ventilation perfusion mismatch, and the decreased binding affinity of haemoglobin for carbon dioxide may be more important reasons for a rise in $PaCO_2$. While oxygen should be given with care, it should not be withheld in patients with COPD who have severe hypoxia. Patients should be observed carefully for carbon dioxide narcosis, and serial arterial blood gas analyses

are useful in determining progress. Preferably, oxygen should be given in low concentrations, to achieve a SpO_2 of 88-92%.

Inhaled bronchodilators: Give salbutamol 5mg or terbuteline 10mg through an oxygen driven nebulizer. If COPD is likely, or if the patient has life threatening asthma, add ipratropium 0.5mg to the nebulizer solution. *Anticholinergics are of greater benefit in patients with COPD.*

Intravenous steroids: Give hydrocortisone 200mg intravenously

Theophyllines: Give aminophylline 250mg IV over 20 minutes. (Check if the patient has taken theophyllines orally or intravenously over the past 24 hours – avoid if so).

If the response is poor,

Intravenous bronchodilators: Give salbutamol 250 micrograms IV, followed by an infusion

Drug	Bolus	Infusion
Aminophylline	250mg IV over 20 minutes	250mg in 500ml of 0.9%Saline over 8 hours (for average adult) Half the dose in CCF or liver disease
Salbutamol	250micrograms IV over 10 minutes	5mg (5ml of 1mg/ml solution) in 500ml of 0.9%Saline or 5% dextrose. Start with 1ml/min (10micrograms per minute), upto 3ml/min.

If the patient does not improve within 15-30 minutes,

- Give continuous nebulisation with salbutamol
- Add ipratropium and repeat 6 hourly
- Repeat hydrocortisone 200mg IV

Look for

- Upper airways obstruction, laryngeal oedema
- Pneumothorax
- Pleural effusion

- Consider other causes of shortness of breath: heart failure, pulmonary embolism, non-cardiogenic pulmonary oedema
- Start aminophylline infusion
- Consider IV magnesium sulphate 1-2 grams given over 20 minutes

If the patient does not improve, and shows signs of life threatening asthma, ventilation should be started.

Close monitoring, both of clinical parameters and of arterial blood gas values is of paramount importance. The patient's symptoms are an excellent guide. If the patient still feels dyspnoeic, irrespective of his other clinical parameters, he should be closely watched, and an arterial blood gas should be performed. If the blood gas analysis shows worsening hypoxaemia and normocapnoea or hypercapnoea with respiratory acidosis in spite of maximum medical therapy, ventilation should be considered before the patient develops respiratory arrest. The outcome is much better if the patient is electively ventilated than if he is ventilated after an arrest.

Ventilation

Mechanical ventilation should be considered if **at least two** of the following are present:

- At least moderate dyspnoea, with use of accessory muscles and paradoxical abdominal motion
- Hypercapnic acidosis (pH <7.35)
- Respiratory frequency >25 breaths per minute

Note that clinical judgement should always take precedence; if the patient is obviously not responding to initial therapy, and is becoming exhausted, there should be no delay in initiating ventilation.

In asthma, invasive ventilation is required. In COPD, provided that the pH is >7.30, a trial of non-invasive ventilation may be given. In intubating the patient, the largest possible endotracheal tube should be used, both to reduce airway resistance and to enable easy suctioning of secretions. Sedation and paralysis may be required.

If invasive ventilation is used, pressure support with PEEP is the usual mode of support required in either situation, although there are no definite guidelines on this. The initial ventilator parameters are as follows:

- Minute ventilation <115 ml/kg
- Tidal volume <8 ml/kg
- Respiratory rate 10 to 14 per minute
- Inspiratory flow 80 to 100 l/min to ensure a short inspiratory time, and a low Ti:Te ratio

Especially in COPD, patients should be weaned off ventilation as soon as possible.

Antibiotic therapy

Most exacerbations of asthma are non-infective, and antibiotics have no place. If the patient has fever with neutrophil leukocytosis, elevated CRP, or consolidation on chest x-ray, then antibiotics could be given. The eosinophil count in sputum in asthma is high, hence the sputum maybe yellow in the absence of infection. On the other hand, upto 50% of COPD exacerbations are due to viral or bacterial infection, and antibiotics should be started. An antibioitic which is effective against *Haemophilus influenzae, Streptococcus pneumoniae, Moraxella catarrhalis*, and atypical bacteria should be used. Levofloxacin or erythromycin/clarithromycin is suitable.

Mucolytic agents

Mucolytic agents such as n-acetyl cysteine have no place in the treatment of asthma or COPD exacerbations.

Sedation

Sedative agents may be required in intubated patients. Benzodiazepines or morphine are used. These should never be given in awake, non-intubated patients with COPD, as they can cause respiratory depression.

Fluid balance

Patients with COPD are at greater risk of developing pulmonary oedema, since the capacity of pulmonary lymphatic drainage is impaired. This is particularly important in patients with pre-existing heart failure.

Nutritional support

Nutritional support is generally required in COPD, since the increased work of breathing results in higher energy expenditure.

Cardiac complications

Patients with asthma and COPD are more likely to have arrhythmias, due to hypoxia, stress and sympathomimetic drugs and aminophylline. Cardiomyopathy is often associated with longstanding COPD (cor-pulmonale); this can also predispose to arrhythmias. Severe hyperinflation of the chest can result in reduced venous return and decreased cardiac output. Severe acidosis and hypoxia can decrease myocardial contractility and reduce cardiac output.

Long term management

Once the patient has improved, long term therapy with inhaled steroids, long acting bronchodilators, pulmonary rehabilitation and immunization should be planned. Often a period of oral corticosteroid therapy with tailing off is required. Smoking cessation is essential. The prognosis for asthma is good, but poorer for COPD.

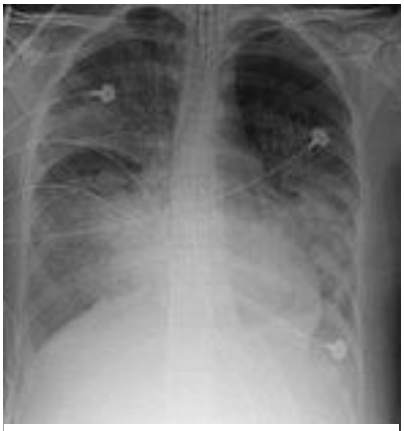
Respiratory failure

Acute respiratory failure is defined as, all acute lung conditions except obstructive lung disease that requires active therapy. It is a common occurrence in ICUs, and is a life threatening complication of a variety of lung conditions, in particular pneumonia, trauma or sepsis. Acute respiratory failure has a high mortality of upto 40%. Pneumonia is the commonest cause.

Acute respiratory distress syndrome or ARDS is the most important type of acute respiratory failure. The current definition is based on the North American – European consensus committee (NAECC) of 1994.

ARDS: an inflammatory process in the lungs with

- Acute onset of respiratory failure
- Bilateral infiltrates on chest radiograph
- Hypoxaemia with a PaO_2: FiO_2 ratio less than 200mmHg
- Absence of left ventricular failure (clinically, or based on a pulmonary artery wedge pressure <18mmHg
- **Acute lung injury (ALI)**: the same as ARDS except with PaO_2: FiO_2 ratio less than 200mmHg



Chest radiograph in ARDS showing bilateral fluffy

The characteristic early histo-pathological change is exudation, resulting in non-cardiogenic pulmonary oedema, with diffuse alveolar damage; this is known as the exudative stage. Over the first week, this gives way to a "proliferative" stage; in this stage, the pulmonary oedema resolves, with proliferation of type II alveolar cells, squamous metaplasia, interstitial infiltration by myofibroblasts, and early deposition of collagen is seen (hyaline membrane formation).

A few patients progress to a third "fibrotic" stage, where obliteration of normal lung architecture, fibrosis, and cyst formation occurs. Although ARDS often occurs in the setting of multiorgan failure, the pathogenesis of ARDS is not necessarily the same, and ARDS can occur in isolation, for example after inhalation of toxic gases. There are many causes of ARDS (see table). ARDS is most often caused by direct injury to the lung, such as occurs in pneumonia, aspiration of gastric contents, near drowning, and inhalation of toxic gases.

Causes of ARDS
Sepsis
Pneumonia
Aspiration
Severe trauma or burns
Multiple blood transfusions
Pancreatitis
Drug overdose / Drug reaction
Near drowning
Inhalation of toxic gases / smoke
Cardiopulmonary bypass
Pulmonary contusion
Multiple fractures
Following bone marrow transplantation
Venous air embolism or Amniotic fluid embolism
Neurogenic pulmonary edema
Bronchiolitis obliterans organizing pneumonia (BOOP)
Miliary tuberculosis

Physiological derangement in the lung in ARDS

- Interstitial and alveolar oedema appears. The pressure at the venous end of the pulmonary capillaries (measured as the pulmonary capillary wedge pressure) is normal. This distinguishes it from cardiogenic pulmonary oedema. As a result, the lungs are stiffer, akin to a sponge soaked in water. The lung compliance is hence reduced and the work of breathing increases. The ‘extravascular lung water’ or EVLW increases; this can be measured using a device called PiCCO.
- As a result of alveolar oedema, intrapulmonary shunting of blood occurs. The functional residual capacity falls.

- The wet heavy lung causes basal atelectasis. This is made worse by increased intraabdominal pressure which occurs in sepsis and other extrapulmonary causes of ARDS.
- These physiological changes become more and more pronounced as ARDS progresses.

Clinical features of ARDS

Hypoxia is the characteristic feature, showing up clinically as cyanosis, or dropping oxygen saturation on pulse oxymetry or arterial blood gas analysis. The patient will become progressively more dyspnoeic and tachypnoeic. Coarse crackles are heard all over the lungs.

Why does the patient become dyspnoeic?

Dyspnoea occurs due to increased work of breathing in an attempt to compensate for impaired gas exchange and shunting.

The classical investigations and changes in monitoring parameters are:

- Hypoxaemia not corrected by oxygen
- Chest radiograph:
- Bilateral diffuse and fluffy interstitial infiltrates which change from day to day
- Basal atelectasis
- Evidence of pneumonia may be present (this may be the precipitating cause)
- Normal pulmonary capillary wedge pressure
- Blood investigations may show evidence of sepsis (high CRP, neutrophil leukocytosis), DIC (prolonged clotting parameters, microangiopathic haemolytic blood picture, elevated D-Dimer and Fibrin degradation products), evidence of renal failure.
- CT scan of the thorax will show infiltrates, pleural effusions and small pneumothoracies more accurately than chest radiography, but is not indicated unless an alternative diagnosis is suspected.

Differential diagnosis

ARDS needs to be differentiated from other conditions which can cause acute hypoxaemia:

- Heart failure (cardiogenic pulmonary oedema)
- Fluid overload after surgery
- Fluid overload due to acute renal failure
- Pulmonary embolism

Heart failure is diagnosed on the history, presence of ECG abnormalities and echocardiography. The patient may give a history of chest pain, and may have a past history of ischaemic heart disease or heart failure, or valvular heart disease. Echocardiography will confirm the diagnosis. B-natriuretic peptide levels are elevated in heart failure. Characteristically, the left ventricular filling pressures are high in heart failure, in contrast to ARDS. Left ventricular failure responds dramatically to loop diuretics. Fluid overload after surgery occurs around the 2^{nd} to 3^{rd} postoperative day, and results from progressively increasing positive fluid balance. The clinical features are similar to ARDS, however filling pressures are high. Fluid overload due to acute renal failure is similar, and the patient will be oliguric, with elevated blood urea and serum creatinine. The condition often responds to diuretics.

Pulmonary embolism results in increased physiological dead space, resulting in a sudden decrease in end-tidal CO_2. Chest radiograph may show a wedge shaped shadow, and ECG may show the classical S wave in Lead I and Q wave and T wave inversion in Lead III (S-one Q-three T-three). D-dimer may be elevated, although this may occur in ARDS too. Spiral CT chest, Ventilation-Perfusion scan or pulmonary angiography will confirm the diagnosis. Evidence of deep venous thrombosis will support (but not confirm) the diagnosis.

Treatment

Effective therapies for ARDS are limited. Treatment is largely supportive, and is aimed at improving oxygenation and preventing ventilator induced lung injury.

Ventilation

All patients should receive oxygen by mask. If the hypoxaemia does not resolve (as often it does not), intubation and ventilation is required. It is better to ventilate early before the patient develops severe hypoxaemia or

exhaustion, which can result in cardiovascular instability and possible cardiac arrest. The patient requires ventilation if any of the following is present:

- Exhaustion
- Respiratory rate is above 30-35/min
- Hypoxaemia (PaO_2<7-8 kPa) on oxygen via mask
- Rising $PaCO_2$
- pH below 7.3

Ventilation itself does not reduce mortality due to ARDS. Ventilation must be fine-tuned to prevent lung injury. Assist control ventilation or Synchronised intermittent mandatory ventilation may be used. Whatever method is used, the following principles should be adhered to;
Low tidal volume ventilation: a tidal volume of 6ml/kg body weight significantly reduces mortality compared to higher tidal volumes. This was demonstrated in the ARDS network clinical trials.
The end-inspiratory plateau airway pressure should be kept <30-35 cm H_2O.
Higher positive end expiratory pressure (PEEP) is of benefit in keeping the airways open.
The lowest possible FiO_2 should be used. High oxygen concentrations damage the alveoli, and may worsen alveolar collapse, as oxygen is absorbed very quickly from the alveoli.
This is based on the principle of maintaining an 'open lung' policy. As a result of the reduced tidal volumes, CO_2 retention may occur, hence this is known as 'permissive hypercapnoea'.

Fine tuning ventilation in ARDS is quite complicated, and requires careful adjustments with careful monitoring of the respiratory parameters.

Treating infection
Appropriate antibiotics should be used to treat pneumonia, if it is the primary cause. Choice of appropriate antibiotics is discussed in the section on severe infection.

Fluid management
Careful fluid management is important, to avoid overhydration and fluid overload, while maintaining adequate cardiac filling pressures.

Nutrition
Patients with ARDS have increased energy expenditure, and need appropriate nutrition.

Corticosteroids
Large doses of steroids have no proven benefit. Smaller doses may be of benefit, but studies are still underway. Steroids are of proven benefit in patients with acute respiratory failure due to Pneumocystis carinii pneumonia, tuberculosis and vasculitis.

Prone position ventilation
Turning the patient over is one way of redistributing blood flow within the lung and recruiting underventilated and collapsed alveoli. While there is little evidence that it improves survival, the method is useful to improve oxygenation.

Inhaled NO
Nitric oxide selectively vasodilates the vessels around the better ventilated alveoli, and can improve oxygenation. It has no evidence of survival benefit.

Extracorporeal Membrane Oxygenation (ECMO)
This has been used experimentally, but benefits have not been proven.

Complications of ventilatory support
Ventilator induced lung injury
Pneumothorax is the most well known complications of ventilation, with an incidence of 10%. It is associated with the use of high PEEP. Mediastinal, retroperitoneal, peritoneal or subcutaneous emphysema can also occur. Pneumothorax may require emergency aspiration, especially in the case of a tension pneumothorax, or an intercostals drainage tube. Subcutaneous emphysema usual resolves spontaneously. Always suspect pneumothorax if the patients respiratory parameters deteriorate suddenly.

Microscopic lung injury
Opening and closing of alveoli and overdistension of alveoli result in damage to the alveoli. This can trigger a local inflammatory reaction, which can become generalised and result in multiorgan dysfunction. Bacteria can spread across the damaged alveoli to the bloodstream, worsening sepsis.
Oxygen induced injury

High concentrations of oxygen are toxic to the lungs. High concentrations of oxygen cause alveolar collapse, as oxygen is absorbed rapidly. The lowest concentration of oxygen should be used.

Haemodynamic effects

Contrary to popular belief, high levels of PEEP do not drop the blood pressure, unless the patient has reduced intravascular volume. If the blood pressure falls when the PEEP is increased, fluids should be given. PEEP can be used to augment cardiac output, as the increased intrathoracic pressure will reduce the transmural pressure of the left ventricle. It is by this mechanism that PEEP helps in acute left ventricular failure, and not, as is commonly thought, by the increased alveolar pressure driving out the intra-alveolar fluid.

Mechanical ventilation

Mechanical ventilation is often required in critically ill patients who develop respiratory failure. While it is a valuable tool to assist ventilation, it can be dangerous if used inaccurately or unnecessarily. Junior doctors often find ventilators and ventilation threatening and shrouded in mystery, with strange bits and pieces of equipment, numerous unfamiliar settings and confusing parameters and values to be monitored. In reality, if one understands the basic concepts of ventilation, it is quite simple.

The basic use of a ventilator is to promote alveolar ventilation; thus helping with CO_2 elimination and correcting impaired oxygenation. The respiratory system has two components:

- The gas transfer mechanism: the lungs -airways, alveoli, and circulatory system supplying the lungs
- The pump which ventilates the lungs: diaphragm, accessory muscles of respiration, and the respiratory centre.

Respiratory failure is due to either pump failure, lung failure or both.

Lung failure occurs due to:

- Alveolar dysfunction – pneumonia, ARDS, lung fibrosis
- Airways obstruction – asthma, COPD
- Vascular dysfunction – cardiogenic pulmonary oedema, pulmonary embolism
- Extrapulmonary obstruction – pleural effusion, pneumothorax

Pump failure occurs due to:

- Neuromuscular disorders – Acute inflammatory demyelinating polyneuropathy, transverse myelitis, poisoning with neuromuscular blocking agents (organophosphates), myasthenia gravis, brain stem strokes.
- Excessive load – any of the causes of lung failure could create an excessive load on the lung, leading to exhaustion of the muscle pump. This is one of the most important causes of pump failure in ICU patients. For example, the compliance of the lung is reduced in ARDS, resulting in excessive workload and exhaustion. Similarly, in acute asthma, the work of breathing increases, and this together

with poor oxygenation results in exhaustion of the respiratory muscles.

Ventilation requires airway access. Usually, this is obtained by endotracheal intubation.

➔ ***See chapter on Airway management***

In certain situations, non-invasive ventilation is used. This is done by application of a closely fitting face mask. Non-invasive ventilation is sometimes tried prior to endotracheal intubation, especially in patients with COPD.

Endotracheal intubation has several advantages over non-invasive ventilation.

- The upper airway is protected against positive pressure from the ventilator
- Aspiration of gastric contents is minimised because of the endotracheal cuff
- Suctioning of secretions is easy
- Dead space is minimised
- The connection between the ventilator and the airway is secure and stable

Critically ill patients are generally ventilated through endotracheal intubation. The disadvantages of invasive ventilation are:

- Higher risk of nosocomial pneumonia
- Loss of cough reflex
- Inability of the patient to speak
- Possible late complication of tracheal stenosis with long duration of ventilation

Early ventilators were simple pumps. They delivered a fixed tidal volume, a fixed number of times per minute. The tidal volume and rate could be adjusted to achieve the necessary minute ventilation. At the start of the inspiratory cycle of ventilation, the valve opens, and a fixed volume of air is delivered into the lungs by positive pressure. At the end of inspiration, the expiratory valve opens and the inspired air is expired by the elastic recoil of the lungs. After a pause, the cycle begins again. Hence the term intermittent positive pressure ventilation (IPPV). Since the patient's own breaths would interfere with the ventilators breaths, patients had to be

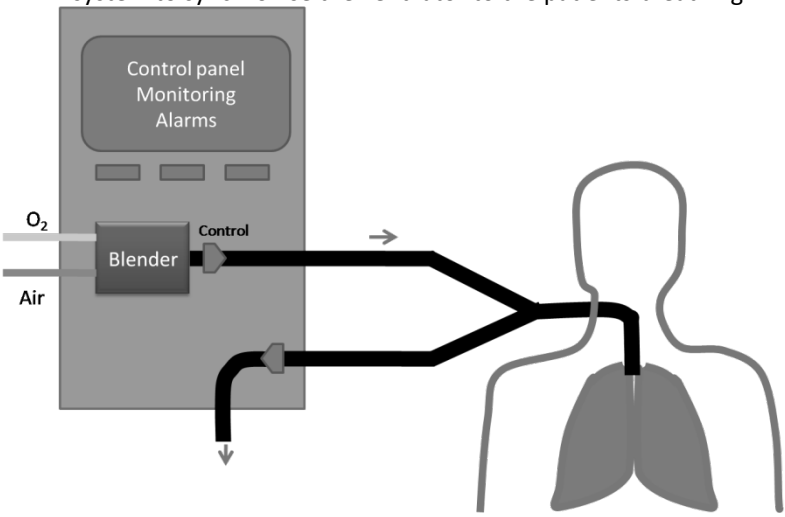
paralysed using a neuromuscular blocking agent. This simple mode of ventilation is known as continuous mandatory ventilation (CMV). Ventilation occurs continuously irrespective of whether the patient is breathing or not. The number of breaths per minute is set by the machine, and is hence mandatory.

This form of ventilation is rarely used now. Modern ventilators nearly always synchronise the delivered breaths to the patient's own breaths. As a result, it is often not essential to paralyse the patient.

The components of a ventilator

A ventilator has several basic components

- A source of pressurised gas with a mechanism for mixing air and oxygen to the desired concentration of oxygen
- A ventilator circuit, with an inspiratory valve and an expiratory valve
- A control system, with a control panel together with monitoring and alarms
- A system to synchronise the ventilator to the patients breathing'



The ventilator is connected to an oxygen supply. Oxygen is mixed with air to achieve the desired oxygen concentration. This is called the FiO_2,

or fraction of inspired oxygen, and is correctly given as a fraction, i.e., 0.4 for 40% oxygen.

The ventilator circuit consists of an inspiratory tube and an expiratory tube, which are connected to the patient using a Y shaped connector. A short piece of tubing is used to connect the Y piece to the patient's ET tube, and this is a common pathway for both inspired and expired gases. Both the inspiratory line and the expiratory line have valves. Ventilators usually have a synchronisation system to sense the patient's own breathing, and synchronise the machines breaths accordingly. Sensors within the ventilator circuit sense the patient's inspiratory effort, and trigger opening of the inspiratory valve. During inspiration, the inspiratory valve opens and the expiratory valve closes. When inspiratory flow falls below a certain level, the inspiratory valve closes and the expiratory valve opens. Passive expiration occurs driven by the elastic recoil of the lung. The size of the external ventilator circuit must be adequate for the patient, and in an adult, the inner diameter should be 22mm.

The control panel allows the user to set various parameters, including the tidal volume, set rate, PEEP and Pressure Support, and the mode of ventilation. Modern ventilators display most of the required ventilator and patient parameters, sometimes in graphical form. Information usually displayed include the set rate, the actual rate, the FiO2, set tidal volume, actual tidal volume and minute ventilation, PS, PEEP, and whether each breath is a spontaneous or assisted breath. In addition the control panel has various alarms which can be set according to requirements. For example, if the tidal volume drops below a certain level, an alarm would sound. The control panel also allows for certain manoeuvres which are used to assess various respiratory parameters such as peak and plateau pressures, airway resistance and lung compliance. These are more complicated, and will not be dealt with here.

The gas delivered to the patient must be adequately heated to body temperature and humidified. This is achieved by using either a heat and moisture exchanger mounted at the Y-piece, or an Active Heated Humidifier in the inspiratory line. HMEs are simple devices which collect heat and humidity from the expired air and passively humidify

and heat the inspired air. They are relatively cheaper than heated humidifiers. They have the disadvantage of not being very effective if the tidal volume and minute ventilation are high, and tend to increase dead space. If the patient has copious secretions, clogging of the HME could occur, needing frequent changes.

Active humidifiers are more effective and have an active heating device with temperature control and sensors to maintain the correct humidity and temperature. They are more expensive.

Additional parts of a ventilator circuit include

- Water traps for collecting condensate in the tubing
- Antibacterial filters – these are usually located at the inspiratory port
- Nebuliser in the inspiratory line – useful for giving nebulised drugs
- Sensors for pressure, flow, and CO_2 analysis

Setting up a ventilator

As discussed earlier, the two main variables which can be set are

- Tidal volume
- Respiratory rate

Tidal volume (V_t) x Respiratory Rate (RR) = Minute ventilation (MV)

The average tidal volume would be around 6-12 ml/kg body weight, i.e., for a 60kg adult, approximately 360-720ml.
The respiratory rate would be around 10-14/min.
The usual starting point for minute ventilation would be around 100ml/kg/min.

As mentioned above, modern ventilators attempt to supplement and support the patient's own respiration as far as possible. There are two basic ways in which ventilators work, namely:

- VOLUME CONTROL VENTILATION
- PRESSURE CONTROL VENTILATION

In volume control ventilation, a fixed volume of air is delivered into the lungs during each inspiration. Inspiration ends when this volume has been delivered. In pressure control ventilation, a fixed inspiratory pressure is applied during inspiration. Expansion of the lung is limited by the pressure

which is applied. When the recoil pressure of the lung equals the applied pressure, or when the inspiratory time ends, inspiration ends. The volume of air entering the lungs during the inspiratory phase will depend on the compliance of the lung. If the compliance is low, the lung will expand to a lesser degree than if the compliance is high. Volume control ventilation is more widely used in critically ill patients, because the lung volumes are more predictable, and will be discussed here.

Several different modes of ventilation are available. Before we discuss the commonly used modes, there are two other important settings that are briefly mentioned. These will be understood better after the modes of ventilation are discussed.
Pressure support: this is the amount of pressure applied at the start of the inspiratory cycle, i.e., when the inspiratory valve opens. Pressure support makes it easier for the patient to breathe in, and takes away the dead space. Pressure support is not present in ventilator timed breaths, only in spontaneous breaths.
PEEP (positive end expiratory pressure): this is the pressure in the circuit at the end of expiration. It helps to keep the airways open, since if the pressure within the airways fall to zero, the airways will collapse.

The three commonly used modes of volume control ventilation are:

- Assist control ventilation (AC)
- Synchronised intermittent mandatory ventilation (SIMV)
- Spontaneous ventilation with pressure support (Spont+PS)

In all these forms of ventilation, the patient is allowed to breath. Paralysis is required in certain circumstances; however, in general the ventilator supplements and assists the patient's natural breaths. Ventilator breaths are usually triggered by the inspiratory effort made by the patient. When the patient makes a respiratory effort, a negative pressure is applied to the inspiratory valve. When this negative pressure exceeds a certain value (usually around negative 2mmHg), inspiration is 'triggered' - the valve opens and inspiration begins. When the inspiratory flow falls below a certain value, the inspiratory valve closes, and expiration begins.

Assist control ventilation

In this mode, a tidal volume and respiratory rate are set on the machine. Every inspiratory effort triggers the machine to deliver a full breath of the set tidal volume. If the patient's own respiratory rate is less than the set respiratory rate, the ventilator will ensure that the required breaths are given.

Let us take an example where the set rate is 14 breaths per minute, and the tidal volume is 500ml. Let us say the patient is breathing at a rate of 10 breaths per minute.

Each time the patient attempts to take a breath, the ventilator will deliver a tidal volume of 500ml. Since the set rate is 14, the balance 4 breaths will be machine delivered. The minute ventilation will therefore be 14X500=7 Litres.

Take another example where the patient is breathing at 20 breaths per minute. Every breath the patient takes will trigger a full breath of 500ml. Hence, the minute ventilation will be 20X500=10 Litre.

AC is useful in situations where it is preferable to control the patient's ventilation almost completely, especially where one does not want to have any additional stress on the heart, for example after a cardiac arrest or myocardial infarction. The disadvantage is that if the patient's respiratory rate is high, the minute ventilation can be significantly high, resulting in respiratory alkalosis.

If the patient is paralysed, AC is equivalent to CMV!

NOTE: Never paralyse a patient without sedation. Imagine how you would feel if you were fully conscious but unable to move!

Synchronised intermittent mandatory ventilation (SIMV)

This is a more physiological mode of ventilation, and is the most widely used. Here, a tidal volume and rate are set, and also a level of pressure support. The machine will deliver breaths up to the set rate with the set tidal volume. If the patient breaths above the set rate, the patient's breaths will trigger the ventilator, just like in AC. However the *additional breaths will not have the same tidal volume as the set tidal volume, and will be spontaneous breaths. The tidal volume of these breaths will depend on the respiratory effort, and the amount of pressure support applied.* This method prevents high minute ventilation, and prevents respiratory alkalosis.

For example, if the patient has a spontaneous rate of 20, and the set rate is 14 with tidal volume of 500ml, the patient will receive 14 breaths with a tidal volume of 500mL. The remaining 6 breaths will have a tidal volume depending on the patient's respiratory effort, airway resistance, and the pressure support. The higher the pressure support, the larger the tidal volume of these breaths (because in effect these breaths are similar to pressure control ventilation). If respiratory alkalosis develops, the respiratory drive will fall, and the patient will breathe less frequently. Because there is a mandatory set rate, the required minimum minute ventilation is ensured.

Spontaneous ventilation with pressure support

In this form of ventilation, there is no set rate or tidal volume. The patient is connected to the ventilator, and allowed to breathe on his own. The inspired tidal volume depends on the respiratory effort, airway resistance, and the pressure support. Usually however, the machine has a minimum limit, and if the patient does not breathe adequately the alarm will sound, and the machine will take over and ventilate the patient. This mode is an effective weaning mode – if the pressure support is sufficiently low, and the patient's respiratory parameters and blood gases are adequate, he is probably ready for extubation. A pressure support of approximately 8mmHg is just sufficient to take away the dead space effect of the endotracheal tube.

Choice of ventilator modes and settings

These depend on the requirements of the patient. Some general principles apply:

- In general, SIMV is the most widely used form of ventilation because it is more physiological, and allows the patient to breathe comfortably when possible. Some degree of pressure support is necessary.
- AC is used in settings where the patient is haemodynamically unstable, or you wish to minimise the load on the heart. Neuromuscular blockade is usually required, although if the patient has little spontaneous respiration this could be done without.
- Spontaneous modes are used for weaning, or in patients who are breathing comfortably but require some degree of supported

ventilation. The PS provides the additional respiratory support in such patients.

- PEEP helps to keep the airways open, and prevents atelectasis. It is useful in ARDS. Higher levels of PEEP are required in conditions like heart failure, where the PEEP augments cardiac output.
- The minimum possible FiO_2 should be used, as explained in the section on respiratory failure.

How to determine the initial settings in a patient who has just been ventilated

The usual set rate will be between 10 and 14 breaths per minute. The tidal volume is usually between 6 and 12 ml/kg body weight, preferably closer to 6ml/kg. Start with a high FiO_2, and then reduce it to maintain a pulse oxygen saturation of over 95%. SpO_2 over 90 will generally be adequate in patients with COPD. The ratio between the inspiratory time and expiratory time must also be set; this is known as the I:E ratio and is generally between 1:2 and 1:1.5. Longer expiratory time maybe required in obstructive lung disease. On the other hand, in ARDS, a longer inspiratory time maybe required to improve alveolar recruitment and oxygenation. In an average 60kg man, this would be around 360 to 400ml. A PEEP of around 4-5mmHg is usually required, and if the patient is on SIMV, a pressure support of 16 -20 would be generally adequate. Note that these values are just rough guides, and will depend on the individual patient, and underlying condition.

An arterial blood gas analysis should be done after about an hour. The expected targets are:

- PaO_2 over 70mmHg
- Normal $PaCO_2$
- Normal pH

A low PaO_2 is caused by

- Shunt effect, generated in areas of the lung with a low ventilation perfusion ratio: this can be improved by increasing the FiO_2.
- True intrapulmonary shunting, due to perfusion of non-ventilated areas of the lung: the only way to improve oxygenation in this situation is to open up non ventilated areas of the lung. This can be done by the following

- Suctioning out bronchial secretions which are blocking the airways and causing collapse of distal alveoli.
- Increase the PEEP to recruit more alveoli – PEEP opens up airways and increases the number of ventilated alveoli, hence minimising the shunt.
- If pleural effusions or pneumothorax is present, these may need aspiration.

Increasing the minute ventilation is not a useful manoeuvre to improve oxygenation.

If the PaO_2 is higher than 80mmHg, reduce the FiO_2. FiO_2 levels above 0.6 are toxic to the lungs.

If the $PaCO_2$ is high, increase the tidal volume and pressure support, and/or the set rate. CO_2 retention indicates inadequate minute ventilation. In certain situations, such as in ARDS where low tidal volume ventilation is preferable, a higher $PaCO_2$ may be acceptable (Permissive Hypercapnoea). Resultant acidaemia may be tolerated or corrected with bicarbonate if essential. Similarly, in a patient with COPD, the patient's baseline $PaCO_2$ may have been high, and it will be unrealistic to attempt to normalise this.
Sometimes a lower $PaCO_2$ maybe required, for example to reduce increased intracranial pressure.

If the pH is low, it could be due to metabolic acidosis or respiratory acidosis. In either case, increasing the minute ventilation may be required.

If the pH is high, the minute ventilation must be reduced. This can be done by reducing the set rate or reducing the tidal volume and the pressure support.

Biphasic ventilation

Biphasic ventilation is another mode of ventilation where the machine controls only pressure, which moves up and down within a lower and upper baseline. Biphasic Positive Airway Pressure or BIPAP is an example of biphasic ventilation, and this is a commonly used form of non-invasive ventilation. If the patient is breathing spontaneously, the spontaneous breaths are freely superimposed on the moving pressure baseline. Certain machines allow for patient synchronisation, so that the patient could breathe in during the high level of pressure or 'inspiratory positive airway

pressure' (IPAP) and breathe out during the expiratory positive airway pressure (EPAP) level. BIPAP is a useful mode of non-invasive ventilation in COPD patients.

De-escalation of ventilation, and weaning the patient off the ventilator

De-escalation or reduction of ventilator support should be commenced as soon as the patient's respiratory parameters show signs of improvement. However, in patients with severe lung disease, de-escalation should be performed very slowly and carefully. The set rate, tidal volume, PS and PEEP can all be progressively reduced while monitoring the patient's parameters and blood gases carefully. If the patient tolerates a level of reduced support, further de-escalation should be attempted.

Weaning can be considered if several basic criteria are satisfied, namely:

- Improvement in the patient's primary lung disease or underlying condition.
- Haemodynamic stability – normal blood pressure off inotropic agents.
- Ability to protect airway (conscious and alert, brain stem reflexes intact).

Weaning is considered if the patient is on the lowest possible ventilator support. By this time, the patient is usually on spontaneous mode with pressure support. Consider the following when attempting to wean:

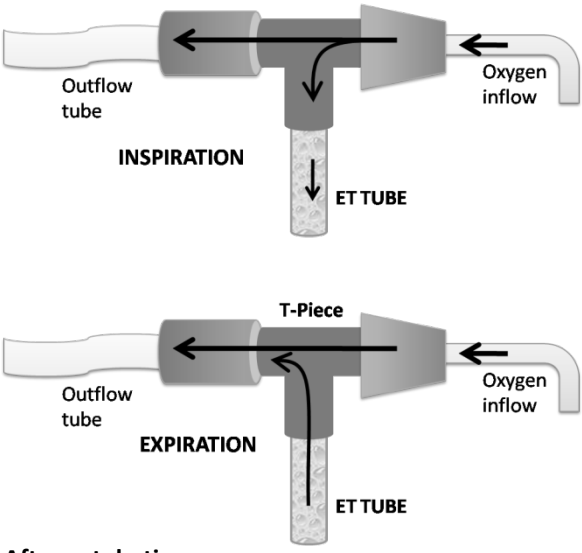
- The patient is breathing spontaneously and comfortably with adequate spontaneous tidal volumes and respiratory rate.
- The PEEP is minimal.
- The PS is around 7-8mmHg (this is the level of pressure support necessary in an intubated patient to take off the dead space of the tube and circuit. Note that a PS below this will increase the patient's dead space.
- Arterial blood gases are adequate. Note that a patient with COPD will not be expected to have normalisation of his $PaCO_2$. Oxygenation and pH must be normal.

If these criteria are met, the patient could be extubated. Usually, this is best done in the mornings, when the full complement of staff is around. There may always be a need to re-intubate the patient, so be prepared for this.

Some people prefer a trial of T-Piece prior to extubation. This is not essential however, if the patient is on spontaneous mode with minimal pressure support, there is no evidence that a T-Piece trial gives better weaning results.

What is a T-Piece trial and what does a T-Piece do

A T-Piece is a tube shaped like a T. It is connected to the patient as shown in the diagram. An oxygen supply is connected to one end of the T, and this drives the expired air out. The need for this oxygen flow is to ensure that expired air is expelled, or else the dead space would be too large.



After extubation

Generally, a repeat arterial blood gas is done about 30 minutes after extubation. If the patient becomes hypoxeamic, a trial of CPAP maybe given provided that the $PaCO_2$ and pH are normal. Sometimes however, the patient may be unable to breathe on his own and may require reintubation. It may not be possible to wean certain patients off the ventilator, especially if their lung disease is progressing, or in patients with COPD or neuromuscular conditions. In this situation, a tracheostomy may be required. Tracheostomy is advantageous in that it makes suctioning easier, reduces the risk of nosocomial infection, and avoids the possibility of tracheal stenosis and tracheomalacia due to prolonged intubation.

Pulmonary embolism

Acute pulmonary embolism is an important and dangerous complication in the ICU. It has a high mortality without treatment. Massive PE can be fatal before treatment can be instituted, and is a cause of sudden cardiac arrest and death. Less severe and recurrent embolism can result in episodic breathlessness and cough with desaturation.

Thrombosis arises in the deep veins of the lower limbs and pelvis in most cases. Risk factors are

- Immobilization
- Recent surgery
- Stroke
- History of venous thromboembolism
- Thrombotic tendency (antiphospholipid syndrome, protein C/S deficiency, factor V leiden)
- Malignancy
- Preexisting respiratory disease
- Chronic heart disease
- Smoking
- Obesity
- Hypertension

The most important issue is to suspect and recognise PE in the ICU. It is a 'blind spot', and is often missed because it was simply not thought of.
Always consider PE in the following situations:

- Sudden onset breathlessness, cough, pleuritic chest pain, haemoptysis.
- Sudden hypotension without any obvious cause
- Sudden decrease in oxygen saturation
- Sudden fever spike

On examination, tachycardia is often present. The blood pressure may be low in massive embolism. A fourth heart sound and loud P2 may be present, and evidence of right heart failure may manifest. Evidence of DVT may be present in less than 30%.

Diagnosis

Since the signs and symptoms are non-specific, a high index of suspicion must be maintained until the condition is excluded.

- ECG: Sinus tachycardia is the commonest manifestation, and is of course non-specific in an ICU patient. The classical changes are the S waves in LI, with Q waves and T wave inversions in LIII (S one Q three T three). Evidence of right ventricular strain and RBBB maybe present, although these are also commonly seen in patients with ARDS and other lung disease.
- Arterial blood gas: Hypoxaemia, hypocapnoea and respiratory alkalosis are present. Hypoxaemia is a bad prognostic sign.
- Chest radiograph: Atelecasis and pleural effusion may be present, but these could be due to so many other causes in ICU patients.
- Echocardiography: may show right ventricular strain and elevated pulmonary artery pressure.
- D-dimer: This is elevated in PE. It has high negative predictive value; patients with normal values have a 95% likelihood of not having PE. However, D-dimer could be elevated for many other reasons in ICU patients, hence it has little practical value.
- Spiral CT with contrast is now the most commonly used investigation to diagnose PE. It is simple and convenient to do, and readily available. While it may not be as sensitive as pulmonary angiography, it has practical value in the ICU in helping to identify other causes that may explain the clinical picture.
- Ventilation/perfusion scan: This is not easily available, and its accuracy in ICU patients with other lung problems is limited.
- Pulmonary angiography is the 'gold standard' test. It is well tolerated, but more complicated to organise and perform than spiral CT, which is gradually replacing it.
- Doppler ultrasound of the lower limbs helps identify DVT. However, the presence of DVT does not necessarily mean that the patient has had a PE.
- BNP levels and Troponin levels are elevated in PE. Their specificity is low however, and they are mainly used for prognostication.
- APTT for monitoring of heparin therapy. PT baseline and as necessary once the patient is started on warfarin.

Treatment

Resuscitate the patient first. Give oxygen by mask. If severe hypoxaemia is present, intubation and ventilation is necessary.

A fluid challenge should be given carefully, as volume overload may result in right heart failure. In general, not more than 500ml to 1L of fluid should be given. Inotropes should be started without delay if there is persistent hypotension.

Consider thrombolysis in the following situations

- hypotension
- severe hypoxemia
- Substantial perfusion defect
- Right ventricular dysfunction associated with PE
- Extensive deep vein thrombosis

Contraindications are detailed in the section on treatment of acute myocardial infarction.

Doses: either streptokinase or tPA can be given.

tPA - 100 mg intravenously over two hours

Streptokinase - 250,000 units intravenously over the initial 30 minutes, then 100,000 units/hour for 24 to 72 hours.

Anticoagulation reduces mortality in PE, and is the mainstay of treatment. IV Heparin is the usual treatment, aimed at achieving an APTT twice the normal. Subcutaneous low molecular weight heparin is an effective alternative.

The patient should be started on warfarin, to maintain an INR around 2.5-3.5. Warfarin must be continued for at least 6 months, possibly longer. Investigations for a thrombotic tendency cannot be correctly interpreted soon after a thrombotic event, and should be delayed.

Prevention

Compression stockings should be used in all patients in the ICU. Patients at high risk should be given prophylactic anticoagulation, usually subcutaneous low molecular weight heparin.

Hypertensive problems in critical care

Severe hypertension can develop in people with chronic hypertension. It can also occur in people with previously normal blood pressure. Severe hypertension can result in life threatening complications, and early and careful therapy is important. Overaggressive therapy can also result in dangerous adverse consequences.

Acute elevation in blood pressure may be the primary presenting feature in a critically ill patient, or may complicate patients with other critical illness.

Cut-off values for severe hypertension

The JNC VII hypertension guidelines define hypertension as a blood pressure of 140/90mmHg or above. There is no clear cut off point for severe hypertension, as severe hypertension is generally defined according to comorbid conditions and complications. The rate of rise of blood pressure, and the prior level of blood pressure are also important. In general, most patients with hypertensive emergencies have a diastolic blood pressure greater than 120mmHg.

Patients can develop hypertensive emergencies with lower diastolic blood pressures. Patients with previously normal blood pressures are more likely to develop end-organ damage and hence hypertensive emergency if their blood pressures rise acutely. This happens in conditions like acute glomerulonephritis, pre-eclampsia/eclampsia, and cocaine or amphetamine induced hypertension.

Conversely, Patients with chronic hypertension may tolerate higher diastolic blood pressures without end organ damage.

Classification

Severe hypertension is classified as follows;

- Hypertensive emergency (emergent hypertension): severe hypertension associated with new or progressive end-organ damage
- Hypertensive urgency (urgent hypertension): severe hypertension without evidence of new or worsening end organ damage

A classification of the different clinical conditions and settings of hypertensive crises is given in the table. Observe that some of the conditions listed are *causes* of severe hypertension, others are conditions which, associated with hypertension, make emergent or urgent treatment of hypertension necessary.

Hypertensive emergency	Hypertensive urgency
• Hypertensive encephalopathy • Acute coronary syndromes • Acute left ventricular failure • Acute aortic dissection • Acute renal insufficiency • Ischaemic stroke • Acute intracranial haemorrhage, SAH • Phaeochromocytoma • Mono-amine oxidase inhibitor-tyramine interaction • Antihypertensive withdrawal • Severe pre-eclampsia/eclampsia • Flash pulmonary oedema with renal artery stenosis	• Accelerated hypertension (progressive hypertension with retinal haemorrhages and exudates, but without papilloedema) • Severe hypertension associated with ▪ stable angina ▪ TIA ▪ congestive heart failure ▪ renal failure • Peri-operative hypertension • Hypertension after renal transplantation

Why is this classification important?

In hypertensive emergency, the blood pressure must be reduced rapidly, over minutes or a few hours, to prevent end organ damage. However, reducing the blood pressure to normal levels very rapidly can result in organ hypoperfusion, and care must be taken to avoid this. Intravenous antihypertensive therapy is often needed. In hypertensive urgency, blood pressure can be lowered less rapidly, and oral antihypertensives are often adequate. Hence, determining whether organ damage is ongoing is vital.

What is the pathological basis of severe hypertension?

A rise in blood pressure takes place if one of the following occurs: a rise in systemic vascular resistance, a rise in cardiac output, or a rise in intravascular volume. Most cases of hypertensive emergency are due to a

rise in systemic vascular resistance, caused by increased adrenergic activity, increased circulating catecholamines, and activation of the renin-angiotensin-aldosterone pathway. Fluid overload can occur in renal disease and over transfusion. Increased cardiac contractility can occur in phaechromocytoma, and cocaine overdose.

The pathogenesis of severe hypertension and end organ damage is not fully understood. Fibrinoid necrosis of arterioles and small arteries is the characteristic histological lesion which causes the clinical manifestations of end-organ damage. Red blood cells are damaged as they flow through vessels obstructed by fibrin deposition, resulting in microangiopathic hemolytic anemia. In patients without hypertension, cerebral blood flow is kept constant over a mean pressure of 60 to 120mmHg. In hypertensive patients, arteriolar thickening occurs, and blood flow is kept constant over a mean pressure of 110 – 180mmHg. When the mean pressure rises over the upper limit of autoregulation, breakthrough of the normal autoregulation of cerebral blood flow takes place. This results in dilatation of cerebral arteries causing cerebral hyperperfusion and cerebral oedema. However, why some patients with severe hypertension develop end-organ damage while others do not, is unclear.

Evaluating hypertension in the ICU

In the ICU, hypertension is often measured using a conventional blood pressure apparatus. Automatic blood pressure devices are also used, with the readings obtained on the monitor. Manual measurement using a standard blood pressure cuff and apparatus is more accurate than automatic blood pressure devices. The arm is the preferred site for the cuff, although thigh, forearm or calf could be used. The cuff of automatic devices should not be placed on an arm being used for intravenous infusions, as intermittent inflation of the cuff will interfere with flow of the infusion. Intra-arterial blood pressure monitoring is the most accurate, and should be used if the patient is haemodynamically unstable.

Pain, anxiety, cold, and even the stress of being moved to the ICU may be the cause of an acute rise in blood pressure, and where there is no emergency, these factors should be corrected prior to starting on medication.

Evaluate whether the patient has hypertensive emergency or hypertensive urgency

If a patient presents with severe hypertension, a quick but directed history and examination should be taken to assess whether the patient has ongoing end-organ damage.

Neurologic damage

Hypertensive encephalopathy is a life threatening syndrome. Symptoms maybe subtle; headache is a common complaint, with nausea, vomiting, visual disturbances, lethargy, and confusion. Ask the family if the patient had subtle abnormalities of mental status. Fits, either focal or generalised, and focal neurological deficits are serious complications, and could indicate intracranial bleeding. A quick but detailed neurological examination must be done, to assess mental status, look for focal neurological signs, neck stiffness, and cerebellar dysfunction. Examine the optic fundi to look for cotton wool exudates, flame haemorrhages and papilloedema.

A non-contrast CT scan brain should be performed, to look for haemorrhages. A cerebral infarct may not be apparent early on a non-contrast CT brain, hence a contrast CT or MRI may also be required if a stroke is suspected. Cerebral oedema is compatible with hypertensive encephalopathy. Intracranial haemorrhage is one of the most dreaded complications of severe hypertension.

Lumbar puncture is generally not indicated or required, and maybe dangerous with increased intracranial pressure. Note that bradycardia may be a sign of increased intracranial pressure. ECG changes, especially T wave and ST segment changes may be seen in subarachnoid haemorrhage, which is not due to active coronary artery disease. It may be caused by a catecholamine surge at the peripheral nerve endings mediated by the brain.

It is crucial to distinguish hypertensive encephalopathy from a haemorrhage or infarct. In hypertensive encephalopathy, immediate blood pressure reduction is essential, while this may be dangerous in the presence of a stroke.

Cardiovascular damage

Angina, dyspnoea, severe tearing chest pain suggestive of aortic dissection will suggest cardiovascular involvement. Elevate JVP, tachycardia, a gallop rhythm and coarse crackles in the lungs maybe present. Carefully examine for pulse deficits in the extremities, a new aortic regurgitant murmur, and a left pleural effusion; signs of aortic dissection. An ECG and a chest radiograph should be done urgently. ECG may show ST segment elevation or new bundle branch block suggestive of acute myocardial infarction, or ST and T wave changes of unstable angina or non STEMI. ST depressions may also be present due to left ventricular strain caused by the high blood pressure. Note that similar ST – T changes maybe caused by the catecholaminergic surge following intracranial events. ST elevation suggesting myocardial infarction can also be seen in aortic dissection, where the dissection cuts through the coronary artery. Chest radiograph may confirm pulmonary oedema, and changes maybe present in aortic dissection. Cardiac enzymes and troponins should also be done to confirm myocardial infarction, if suspected.

If pulmonary oedema is present, it could be due to systolic or diastolic heart failure. In systolic heart failure, the heart is often dilated, with reduced ejection fraction. In diastolic heart failure, the left ventricular myocardium is thickened and stiff. While the ejection fraction is normal, the ventricle does not relax adequately in diastole, resulting in diminished diastolic filling. Pulmonary venous pressures rise, resulting in pulmonary oedema.

Most of the time, the clinical features, ECG changes, and chest radiograph appearances are adequate to make a diagnosis of cardiogenic pulmonary oedema. Echocardiography is very helpful in diagnosing systolic dysfunction- note that left ventricular ejection fraction is normal in diastolic failure, and this may cause confusion; it is important to think of and suspect diastolic dysfunction. B-natruiretic peptide levels are elevated in heart failure, and may help to differentiate heart failure from other causes of pulmonary oedema such as fluid overload and ARDS; however, the test needs further validation.

Systolic heart failure	Diastolic heart failure
Dilatation of the cardiac chambers on echocardiography	Left ventricular hypertrophy without cardiac dilatation on echocardiography
Ischaemic changes on ECG	Left ventricular hypertrophy on ECG Cornell criteria for LVH: sum of R wave in lead aVL and S wave in lead V3. ▪ S in V3 + R in aVL > 28 mm (men) ▪ S in V3 + R in aVL > 20 mm (women)
Evidence of ischaemic heart disease	Evidence of longstanding hypertension
Lower blood pressure elevation	Higher blood pressure elevation

Aortic dissection, if suspected, must be confirmed or ruled out quickly. A pulse deficit in the extremities maybe present. Chest radiography may show a widened mediastinum, and possibly a pleural effusion on the left. Echocardiography, CT scan or MRI scan of the thorax and aortography may be required to confirm the diagnosis. ECG may show evidence of acute myocardial infarction due to involvement of the coronary artery orifice in the dissection.

It is of vital importance to exclude a dissection, as treatment with thrombolytics and anticoagulants for acute coronary syndrome will cause disastrous bleeding in a dissection.

Renal damage

Renal damage is difficult to assess. A reduction in urine output, haematuria and oedema may be the warning features. Urine-analysis (for granular and red cell casts), blood urea, serum creatinine, and serum electrolytes should be done. Renal involvement maybe the result of uncontrolled blood pressures, or maybe the cause of hypertension.

Look for a secondary cause of hypertension

There is a greater likelihood of a secondary cause for hypertension in patients presenting with hypertensive crisis. Therefore, a secondary cause should be looked for;

- Renal disease: acute glomerulonephritis, renal artery stenosis (renal bruits, hypokalaemia) , polycystic kidney disease (enlarged palpable kidneys)
- Cushings syndrome (classic features such as central obesity, moon face, buffalo hump, purple striae)
- Phaeochromocytoma (classically episodic hypertension, with palpitations, panic attacks)
- In a woman of reproductive age – pregnancy (pre-eclampsia/ eclampsia)
- Look for possible cocaine or amphetamine overdose

Investigations in a patient with hypertensive crisis			
Investigation	**Expected findings**	**Investigation**	**Expected findings**
Full blood count and blood picture	Evidence of microangiopathic haemolysis	ECG	Ischaemic changes, left ventricular hypertrophy
Blood urea, serum creatinine	Elevated in renal failure	Chest radiograph	Pulmonary oedema, widened mediastinum and pleural effusion in dissection
Serum electrolytes	life threatening hyperkalaemia, hypokalaemia due to renal artery stenosis	Echo-cardiogram	Left ventricular dysfunction, regional wall-motion abnormalities, left ventricular hypertrophy
Urine-analysis	granular and red cell casts, with dysmorphic red cells in glomerulonephritis	CT scan and MRI thorax	Dissecting aneurysm
		Ultrasound scan abdomen	Polycystic renal disease, renal artery stenosis

In general however, hypertension should be managed during the acute stage, and a possible secondary cause could be looked for later.

Management

The goal of treatment is to lower the blood pressure to avoid continuing organ damage, while maintaining organ perfusion and avoiding complications.

Does the patient have a hypertensive emergency?

If yes, the patient should be managed in an ICU, and the blood pressure should be lowered quickly, using intravenous antihypertensive agents.

Sublingual drugs, such as sublingual nifedipine have no place in the treatment of hypertensive emergency, as they cause drastic, unpredictable lowering of blood pressure which can cause brain damage.

Goal of therapy: 25% reduction in mean arterial blood pressure, or reduction of diastolic blood pressure to 100-110mmHg, over a few minutes to a few hours. The target blood pressure may be much lower, as low as a systolic pressure of 110mmHg in aortic dissection.

Sudden reduction of blood pressure can cause organ damage. When the blood pressure is very high, tissue autoregulation changes, and perfusion is dependent on higher pressures. Lowering the blood pressure rapidly can result in ischaemia, especially to the brain. The brain is particularly susceptible if a stroke has occurred, because a compensatory rise in blood pressure maintains cerebral blood flow. Reduction of blood pressure drastically can result in worsening of the ischaemic penumbra. Sudden reduction of pressure can result in stroke or TIA, altered mental status, myocardial ischaemia, mesenteric ischaemia, and deterioration of renal functions.

Starting antihypertensive medication

Intravenous drugs are used. A single agent is preferred. The choice of drugs is wide, and availability varies from country to country. Ideally, a short acting drug, which can be titrated carefully to achieve and maintain the desired blood pressure is required. Certain specific conditions may influence the choice of the antihypertensive agent.

Drug	Route	Dosage	Onset	Duration
Nitroprusside	IV infusion	0.25-10mcg/kg/min	Immediate	1-2 min
Labetalol	IV bolus IV infusion	Start 10-20 mg upto 80mg 0.5-2 mg/min	3-5 min	3-6 h
Nitroglycerin	IV infusion	5-300 mcg/min	1-2 min	1-3 min
Nicardipine	IV infusion	5-15 mg/h	5-10 min	15-40 min
Fenoldopam	IV infusion	1.0-1.6 mcg/kg/min	15 min	30-60 min
Hydralazine	IV bolus	5-20 mg	10-30 min	3-6 h
Enalaprilat	IV bolus	0.625-1.25 mg	10-15 min	6-8 h
Phentolamine	IV bolus	5-10 mg every 10 min	1-2 min	10-30 min

Sodium nitroprusside is the closest to the 'ideal'drug. It is short acting, easy to titrate, and is an arterial and venous vasodilator. Sometimes, it causes hypotension and reflex tachycardia, but this can be prevented with careful intra-arterial blood pressure monitoring. If hypotension occurs, it is easily treated by stopping the infusion and giving IV fluids. Cyanide or thiocyanate toxicity is also a known side effect. The infusion decomposes on exposure to light, and infusion sets should be shielded from light.

Labetalol is a combined non-selective beta and alpha adrenergic antagonist. Beta blocking action predominates over alpha blocking action, in a ratio of 7:1. It reduces blood pressure by reducing systemic vascular resistance, with minimal reduction in heart rate and contractility. It is particularly useful in patients with high adrenergic activity, and in pregnancy, because it reduces blood pressure without compromising placental circulation. Because it is a beta blocker, it should not be used in asthma and COPD, or in heart block.

Nitrates have coronary vasodilatory and venodilatory effects, and dilate systemic arteries in higher doses. Nitrates are ideal in patients with

hypertensive emergency with acute coronary ischaemia. Headache is a side effect.

Nicardipine is a dihydropyridine calcium channel blocker with coronary and systemic vasodilatory effects. It does not cause heart block, and can be used in most types of hypertensive emergencies, and is safe in pregnancy.

Fenoldapam is a short acting peripheral dopamine -1 blocker. It lowers blood pressure by arterial vasodilatation, renal vasodilatation and natriuresis. It has little side effects, and is an alternative to nitroprusside. It is not widely available.

Hydralazine is an arterial vasodilator, which is not used widely now except in pregnancy. It is difficult to titrate, and since it increases heart rate and contractility, and myocardial oxygen consumption, it is contraindicated in myocardial ischaemia and aortic dissection.

Diuretics have usually no place in the management of hypertensive crisis. The high blood pressures result in natriuresis, and patients often have intravascular volume depletion.

Oral drugs should be commenced, based on the patients co-morbid conditions once blood pressure is controlled.

Does the patient have a hypertensive urgency?
In the absence of ongoing organ damage, the patient has hypertensive urgency.

Goal of treatment: 25 % reduction in blood pressure over several hours to a day.

ICU care is generally not needed. Oral medications are usually adequate. The choice of antihypertensives is based on the patient's co-morbid conditions and compelling clinical indication, based on standard guidelines as for any hypertensive.

Special situations

Hypertensive encephalopathy: if target blood pressure is achieved, but the patient's mental status has not improved, consider other possibilities, in particular SAH, ICH or ischaemic stroke.

Stroke: often it is difficult to determine whether the high blood pressure caused the stroke, or whether the stroke resulted in high blood pressure in an attempt to maintain cerebral perfusion. In general, in stroke, antihypertensive treatment should NOT be commenced unless blood pressures are above the following levels: (mean BP= diastolic BP + one third (systolic-diastolic BP)

Type of stroke	Risk blood pressure
Ischaemic stroke	Systolic BP >220mmHg or mean BP>130mmHg
Haemorrhagic stroke	Mean BP>130mmHg
Ischaemic stroke where thrombolysis has been given	Systolic BP >180mmHg or mean BP>105mmHg

Nitroprusside, labetalol, nicardipine and nitrates are used. Nitroprusside and nitrates, being arterial vasodilators, may increase cerebral blood volume and so, intracranial pressure while lowering mean arterial pressure. Nimodipine is especially useful in subarachnoid haemorrhage, as it prevents secondary cerebral injury due to cerebral vasospasm. It is given orally.

Myocardial ischaemia: Nitrates have the added benefit of coronary vasodilatation. Labetelol and nicardipine are also useful. Unless the blood pressures are very high, oral antihypertensives maybe adequate. Pain relief with morphine is also important.

Left ventricular dysfunction: Nitrates are useful because of their venodilatory effects. Although beta blockers can be dangerous in unstable left ventricular systolic dysfunction, labetalol is useful in diastolic dysfunction, as it slows the heart rate, giving more time for diastolic filling. Diuretics are generally necessary, but should be given carefully in diastolic dysfunction because they may reduce left ventricular filling pressures.

Aortic dissection: The blood pressure must be acutely lowered, to a systolic pressure of 100-110mmHg. The aim is to reduce the shear force on the aorta; a vasodilator must never be used alone as it may worsen the shear force. Labetolol, alone or incombination with a vasodilator is the most common choice. In patients whom beta blockers are contraindicated, trimethaphan may be used, though it has many adverse effects. Aortic dissection of the ascending aorta (type A) requires surgery, and that of the descending aorta (type B) can be managed medically.

Phaeochromocytoma: Alpha blockade must always precede beta blockade. Labetalol has predominantly beta blocking effects, and should be used together with a vasodilator.

Pre-eclampsia/eclampsia: Preeclampsia is diagnosed on the basis of pregnancy-induced hypertension (>140 mmHg systolic or >90 mmHg diastolic blood pressure confirmed by two separate measurements, occurring after 20 weeks gestation in a woman who was normotensive before 20 weeks gestation) and proteinuria (500 mg/l protein in a random specimen or an excretion of 300 mg per 24 h). Oedema is often present. If eclampsia is imminent, pregnancy must be terminated irrespective of the gestational age, as the risk to the mother is enormous. Seizures can be controlled with magnesium sulphate infusion. Labetalol, hydralazine and nicardipine are preferred drugs, as they maintain placental blood flow. ACE inhibitors are contraindicated in pregnancy. The goal is to reduce diastolic blood pressure to 90-100mmHg.

Perioperative hypertension: Often, there is a need to control acute blood pressure elevations in patients undergoing surgery. Pain and anxiety may cause the blood pressure to rise, and reassurance, sedation and analgesia may be adequate. High blood pressures are of concern to the surgeon and anaesthetist however, hence often it is necessary to reduce blood pressures to reasonable levels prior to surgery. If urgent reduction of blood pressure is necessary, nitroprusside or nitrates are preferred, although nearly any of the agents can be used.

Acute myocardial ischaemia

Coronary artery disease accounts for 30% of deaths. This section discusses the evaluation and management of acute coronary syndromes, which can be either the primary reason for admission to the ICU, or may develop in patients already in the ICU. Rapid recognition and diagnosis of acute coronary syndromes is important in the ICU to prevent myocardial damage and complications.

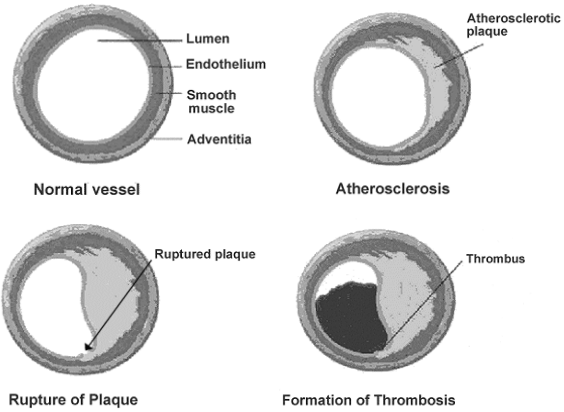
Acute coronary syndromes (ACS) describe the spectrum of conditions which cause acute myocardial ischaemia, resulting in typical anginal chest pain, together with ECG changes and abnormalities in markers of myocardial damage.

ACSs are due to thrombus formation on a ruptured coronary atheromatous plaque, and include the following clinical entities:

- Unstable angina: the following clinical situations are defined as unstable angina
    - New onset angina
    - A change (more frequent, more severe) in the pattern of angina
    - Angina occurring at rest or minimal exertion

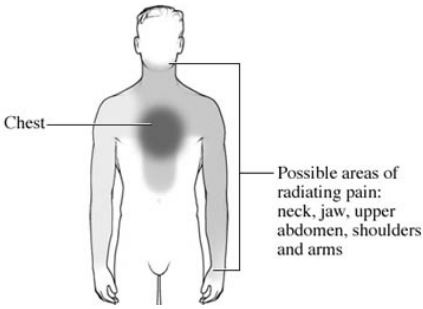
  Cardiac biomarkers such as Troponin and cardiac enzymes are not elevated in unstable angina.
- Myocardial infarction: Ischaemic symptoms occur with raised cardiac biomarkers; cardiac troponin, cardiac enzymes or both. Myocardial infarction maybe further categorised as;
    - Non-ST elevation myocardial infarction (Non STEMI)
    - ST elevation myocardial infarction (STEMI)

The pathological basis of atherosclerosis and thrombus formation is illustrated in the figure below. Typically, an atheromatous plaque has a lipid rich core and a fibrous cap. An ACS occurs when plaque ruptures, exposing the atherogenic lipid rich material to the circulation. A thrombus forms; in the case of unstable angina, this is an unstable clot, which does not fully occlude the vessel. If the thrombus completely occludes the vessel, acute myocardial infarction occurs.



Typically, the pain of myocardial infarction has the following features:

- Severe
- Constant
- Retrosternal
- Spreading across the chest. May radiate to the throat and jaw, down the ulnar aspect of both arms or to the interscapular area
- Duration >20 minutes
- Sweating, nausea, pallor, dyspnoea and anxiety often present



The pain of unstable angina is similar, though often milder. Features of unstable angina often precede myocardial infarction, over a few days or hours. Classically, anginal chest pain waxes and wanes, worsening with exertion, and is associated with sweating.

Sometimes the pain is atypical and hence, more difficult to diagnose. Waxing and waning chest pain is always suspicious, especially if it worsens on exertion, even though the site is not typical. Atypical sites of chest pain include:

- Epigastrium (inferior ischaemia, i.e., ischaemia of the inferior wall of the heart)
- Confined to the jaw, arms, wrist or back (interscapular region)
- Throat (sometimes a tightening sensation in the throat)

Certain patients have silent ischaemia caused by autonomic neuropathy; particularly patients with *longstanding hypertension, diabetes, thyroid disorders, and the elderly*. These patients may not have chest pain during an acute coronary event, but may have other symptoms such as dyspnoea, palpitations or collapse.

In a patient with suspected anginal chest pain,
ALWAYS CONSIDER AND EXCLUDE AORTIC DISSECTION.

Pericarditis also presents with chest pain, although more often the patient complains of pricking chest pain. Other non-cardiac causes of chest pain which are important in the differential diagnosis are:

- Gastro-oesophageal reflux disease
- Pneumothorax
- Pleurisy
- Muscular pain

Recognition of acute coronary syndrome is a vital first step, in both new patients as well as patients already in ICU for other conditions.

'Time is myocardial tissue'....

Immediate management

- Quickly assess the patient:
  - Resuscitate if necessary
  - Evaluate likelihood of ACS – symptomatology, past history, risk factors

  - Check haemodynamic stability – pulse, blood pressure
  - Look for left ventricular failure
  - Exclude aortic dissection – examine all peripheral pulses and look for a difference in pulse volume and blood pressure in the two arms, and between the arm and legs. *This is vital. Giving thrombolytic therapy in a patient with aortic dissection will be fatal.*
- Reassure the patient.
- Give oxygen by mask. If available, connect to pulse oxymeter.
- Obtain intravenous access. Take blood for basic biochemistry and haematology, and cardiac biomarkers. Start a slow drip.
- Check random blood glucose.
- Do a 12 lead ECG: Does the patient have?
  - ST segment elevations in 2 leads or more, or new LBBB → STEMI
  - No ST elevations, but ST, T-wave changes → Non STEMI or unstable angina
  - Normal ECG – ACS not excluded. If clinical history suspicious, keep under observation
- Give sublingual nitroglycerin 0.4mg; this can be repeated.
- Give small doses of morphine - 2-3mg IV, which can be repeated every 10-20 minutes until pain is relieved. Morphine has the advantage of relieving pain, alleviating anxiety, and by causing pulmonary venodilatation, relieving pulmonary oedema. Vomiting is a side effect, and IV metoclopramide can be given. Do not use pethidine for pain relief.
- Give aspirin 300mg to be chewed and swallowed. *This reduced mortality by 25% in the ISIS-2 study.*
- Give Clopidogrel 300mg orally stat.

If the diagnosis is a STEMI, urgent therapy is necessary to re-open the blocked artery. There are two options:

Primary angioplasty- This obtains better results, but needs access to a centre where the procedure is possible without delay. Door to balloon time must be less than 90 minutes.

A balloon catheter is introduced through a peripheral artery (femoral, brachial or radial) and the balloon is passed into the coronary artery. Injection of contrast media will demonstrate the blocked artery. The balloon is passed into the obstruction and inflated. A stent is placed in the affected segment of the coronary artery. Stents may be simple bare metal stents or drug eluting stents.

Thrombolytic therapy- *Exclude contraindications first.* Door to needle time must be less than 30 minutes. Available thrombolytic therapies are:

Streptokinase: can cause anaphylaxis (rare)

Tissue plasminogen activator derivatives

- Recombinant tissue-type plasminogen activator (rt-PA); Alteplase
- Reteplase (r-PA): newer agent, longer half life, more fibrin specific
- Tenecteplase (TNK-tPA)

tPA has somewhat better mortality results and patency rates compared to streptokinase. The major complication with all thrombolytic agents is intracranial haemorrhage.

Which is better; thrombolysis or primary angioplasty?

Primary angioplasty with coronary stenting provides better re-establishment of blood flow in the occluded vessel. However, results are dependent on the expertise of the operator and the centre, and the speed at which the procedure could be arranged (within 90 minutes of admission). If facilities are limited, thrombolysis should be performed without delay. Retrospective community studies have shown that thrombolysis and angioplasty results are comparable. In certain situations however, angioplasty clearly gives better results, or may be preferable, such as:

- In cardiogenic shock
- If thrombolysis is contraindicated
- In elderly patients (over 75 years)
- Previous MI or CABG
- Large anterior MI

Contraindications to thrombolysis

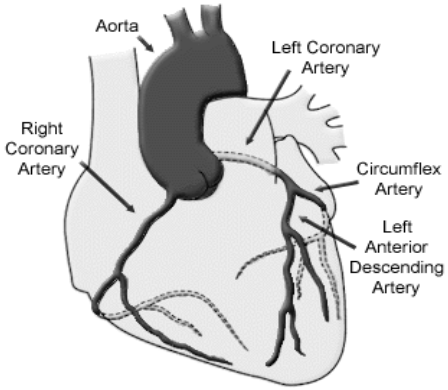
Absolute	Relative
▪ **Previous haemorrhagic stroke** ▪ **Other stroke within the past 6 months** ▪ **Intracranial tumour** ▪ **Active internal bleeding within the past 2 weeks (excluded menstruation)** ▪ **Aortic dissection (known or suspected**	▪ Severe hypertension >180/110mmHg, not controlled after sedation or analgesia ▪ Oral anticoagulation therapy (INR>2.5) ▪ Known bleeding tendency ▪ Recent major trauma, surgery within the past 4 weeks ▪ Traumatic CPR ▪ Pregnancy ▪ Active peptic ulcer disease ▪ Recent streptokinase, or allergy to drug being used ▪ Chronic hypertension

Further management

- Treat pulmonary oedema if present (see section on heart failure).
- Use IV furosemide 40 to 80mg. May need larger doses, or infusion at a rate of 10 to 20mg/hour.
- If no response consider nitroglycerin or isosorbide infusion, especially if the blood pressure is high. CPAP may be required in severe cases.
- Start beta blockers, as soon as the patient is stable. Avoid if bradycardia or heart block is present.
- Start ACE inhibitors as soon as possible.
- Start a statin as early as possible. This has both plaque stabilising as well as long term benefit.
- Heparin:
  IV heparin or subcutaneous low molecular weight heparin maybe necessary to prevent re-thrombosis. Streptokinase has a long duration of action, and generally heparin is not required after

streptokinase. Heparin or LMWH must be given after therapy with tPA. Bleeding and thrombocytopaenia are complications.

- Glycoprotein IIb/IIIa inhibitors: these are used after coronary angioplasty and stenting. Examples are abciximab (Reopro®), tirofiban and eptifibatide.



For practical purposes, the coronary circulation has 3 main branches; Right coronary artery (RCA), Left anterior descending artery (LAD) and left circumflex (LCx). The left main stem is short, but can sometimes be involved, resulting in extensive infarction. Usually the left coronary artery is the more dominant system; however, in some individuals the right coronary artery is dominant.

Interpreting the ECG in a STEMI

The ECG changes depend on the time since the occurrence of coronary occlusion. The earliest change is the appearance of hyperacute tall T-Waves. Upward convex (dome shaped) ST segment elevations are the hallmark of an acute ST elevation MI. T-wave inversions occur later on, and Q waves appear. Subsequently, the elevated STs return to baseline, and the Q waves remain long term. The inverted T waves generally remain for some time but may revert to normal later on.

The appearance of new left bundle branch block also indicates a STEMI, and should be treated accordingly.

Sequence of ECG changes in MI

Hyperacute (0 - 20 minutes) Tall peaking T waves and progressive ST elevation

Acute (mins - hours) ST-segment elevation persists, gradual loss of height of the R wave in the infarcted area. T waves may be inverted.

Early (hours to days) Q waves appear (broad and deep) in area of ischaemia. STs return to baseline. T wave inversions persist.

Indeterminate (days to weeks) Q waves now maximal size. T wave inversions persist. ST-segments normalize

Old (weeks to months) Deep Q waves with normal ST-segments and T waves

NB: persistent ST elevations indicate the presence of a left ventricular *aneurysm.*

The ECG leads in which these changes occur help diagnose the region of the MI, and hence the likely coronary artery which is occluded:

- LII, LIII, aVF → inferior MI (RCA)
- V2 – V4 → anterior MI (LAD)
- V1 – V3/V4 → anteroseptal MI (LAD)
- V5, V6, LI, aVL → lateral MI (LCx)
- V1-V6, LI, aVL → extensive anterior MI (proximal LAD or left main stem)
- V3R, V4R (usually with inferior MI) → right ventricular MI (RCA)

Posterior MI

True posterior MI is diagnosed by finding mirror image changes of an MI in the anterior leads. If the ECG were to be turned upside down and held in front of a mirror the typical changes would be apparent. Hence, in V1 and V2, the following changes are seen:

- Tall R waves (equivalent to Q waves)
- ST segment depressions
- Upright T waves

Usually, when ST depressions are present, the T waves are inverted. If ST depressions are present with upright T waves, suspect a posterior MI. Posterior MI is due to occlusion of either the posterior descending branch of the RCA or the posterolateral branch of the LCx.

Reciprocal changes

In any MI, while the classic ST elevations, Q waves and T inversions are seen in the leads corresponding to the affected area, the 'opposite leads' may show reciprocal ST depressions. These usually denote more extensive infarction.

Non-ischaemic conditions which can mimic the ECG changes of MI

- Hyperkalaemia – tall T waves
- Early repolarisation syndrome – ST elevation and tall T-waves – seen in Asians, particularly men. Normal variant. Look for a slight notching at the start of the ST segment.
- Conduction defects - LBBB may be confused with Q waves

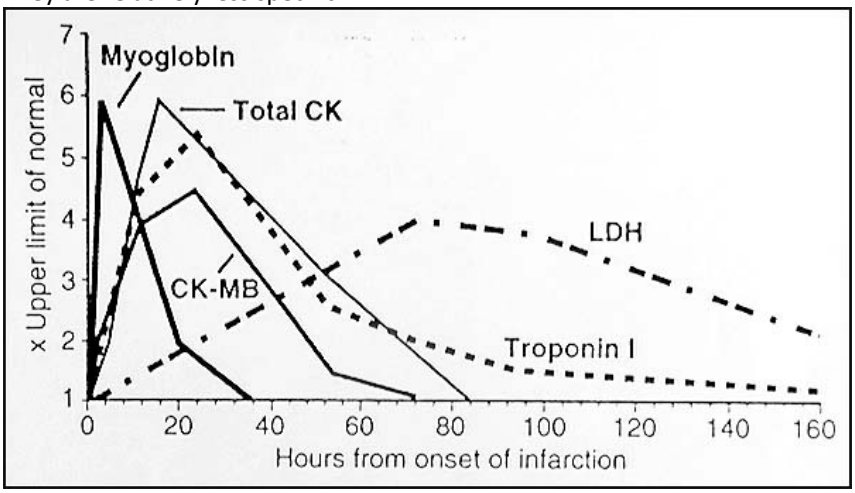
- Pericarditis – ST segment elevations – usually saddle shaped (upward convex) in comparison to the dome shaped ST elevations of MI
- Left ventricular aneurysm – persistent ST segment elevations
- Subarachnoid haemorrhage and other types of stroke – large tall T waves (cerebral T waves) non specific ST segment changes, and Q waves can occur. QT prolongation may be seen

Biochemical markers of ischaemia

Blood must be sent for cardiac troponins and cardiac enzymes on admission and at 6-8 hour intervals.

Cardiac troponins: these are the most sensitive markers of myocardial damage. They begin to rise about 6-8 hours after MI, and remain elevated for approximately a week. Higher troponin levels are associated with worse prognosis.

Cardiac enzymes: the earliest biomarker to rise is the serum myoglobin, which rises within 2 hours. It has poor specificity. Creatine kinase-MB rises after 6 hours and returns to normal within about 48 hours. It is less sensitive than troponin. LDH levels rise late but remain elevated for around 10 days. They are relatively less specific.



Cardiac biomarkers are elevated in myocardial injury. Hence other causes of myocardial injury apart from ischaemia, such as myocarditis, cardiac surgery, trauma and massive pulmonary embolism can result in elevated biomarkers.

Troponin levels can be elevated in ICU patients for reasons other than ischaemia. Increased levels are seen in renal failure, multi-organ failure, severe bacterial sepsis and due to vasoconstrictors. It is likely that all these conditions result in a degree of myocardial damage; hence, they are not really 'false positives'.

Other investigations

- Check the patient's haemoglobin. Anaemia contributes to cardiac ischaemia, and severe anaemia can even cause an MI.
- Low platelets (due to haematological disorder or liver disease) may preclude the use of aspirin and clopidogrel. Heparin can cause thrombocytopaenia.
- Blood glucose – hyperglycaemia worsens outcome after MI, whether stress induced or due to pre-existing diabetes mellitus. Tight glycaemic control with insulin, given initially as an infusion and later in divided subcutaneous doses improves outcome after an MI.
- Liver enzymes – gross abnormalities of liver function may preclude the use of certain drugs, in particular statins.
- Chest radiograph – this must be performed after the patient is stable, to determine if there is cardiomegaly and also to look for chest infections.
- Echocardiography: Echocardiography in the acute stage can help diagnose MI; regional wall motion abnormalities may be seen. This is particularly useful where the ECG changes are not typical, for example in LBBB. It is also useful to assess left ventricular function, especially if LVF is present, and to diagnose RV infarction. Echocardiography is also used to diagnose complications of MI, such as pericardial effusion, acute mitral regurgitation, and acquired ventricular septal defect, and also to identify aneurysm formation and consequent left ventricular thrombus formation.

Complications of MI

Left ventricular failure: (see section on heart failure)

Cardiogenic shock: (see section on hypotension)

Arrhythmias: (see section on arrhythmias). During and soon after thrombolysis or angioplasty, ventricular arrhythmias are commonly seen. These are known as re-perfusion arrhythmias and have a good prognosis. Non-sustained VT does not usually need treatment, other than correction of any electrolyte abnormalities. Sustained VT is treated with lignocaine or amiodarone. Atrial fibrillation is also treated with amiodarone, or sometimes digoxin is given for rate control. Ventricular fibrillation occurring within the first 24 hours is known as primary VF, and while it must be treated (with defibrillation) it does not indicate worse outcome.

Heart block: This maybe present in the acute stage, and maybe first degree, second degree or complete.
The treatment and outcome depends on the region of infarction.

- Inferior infarction – due to involvement of the AV bundle with right coronary ischaemia. Good prognosis, usually responds to atropine bolus. May need temporary pacing if no response.
- Anterior infarction – poorer prognosis for recovery, as it indicates extensive damage to the myocardium involving a large part of the conducting system. Usually needs temporary, and sometimes permanent cardiac pacing.

Post infarction angina: Usually, after the initial pain of the MI has settled, the patient will be free of pain. Recurrence of chest pain, either at rest or on mild exertion could be due to post infarction angina or re-infarction. Hypertension or anaemia could also cause post infarction angina. Treatment is usually by increasing antianginal therapy – nitrates, beta blockers and calcium channel antagonists. Post infarction angina is an indication for early coronary angiography, to determine if re-occlusion has occurred, and to exclude other critically narrowed coronary artery branches.

Right ventricular infarction: Patients present in the acute stage with hypotension, congested neck veins, and clear lungs. ST elevation in V4R is characteristic. Low blood pressure is due to reduced right ventricular contractility resulting in reduced left sided filling pressures. Careful administration of fluids will normalise the blood pressure; inotropes are sometimes needed. Diuretics should be avoided. The prognosis is good, with full recovery often taking place.

Acquired mitral regurgitation: Mild papillary muscle dysfunction is common after an MI. A pansystolic murmur will be present. Papillary muscle rupture is a serious complication, presenting suddenly with pulmonary oedema and hypotension. Echocardiography is diagnostic. Initial treatment is with afterload reduction by vasodilator drugs. Intra-aortic balloon pumping may be necessary; surgical repair is mandatory, without which the mortality is high.

Acquired VSD: Patients present with sudden severe heart failure. Surgical repair is essential, without which the mortality is extremely high.

Ventricular rupture: this is an uncommon but extremely serious complication. Cardiac tamIt is more common in the elderly, and in patients who did not receive thrombolyis. Surgery is of benefit, but the condition has a high mortality.

Pericarditis: Pericarditis may occur early after an MI (infarction pericarditis). It presents with pricking chest pain and saddle shaped ST elevations on ECG. Often it does not require treatment.
Dresslers syndrome, or post myocardial infarction syndrome occurs weeks to a few months after an MI, rarely within the first week. Pleuritic chest pain, pericardial friction rub, fever, leukocytosis, and sometimes pleural effusion or pulmonary infiltrates are seen. Treatment with NSAIDs maybe required.

The Killip classification is a useful way of classifying patients after an MI, and gives an idea about prognosis

Killip Class I	**Killip Class II**
Normal blood pressure No left ventricular failure *Good prognosis*	Hypotension No left ventricular failure Elevated JVP Usually due to a right ventricular MI. Look at V4R on ECG for ST elevations. Treatment: IV fluids to increase right ventricular filling pressures. If pressure remains low, will need inotropes.
Killip Class III	Killip Class IV
Normal blood pressure Left ventricular failure *Prognosis significantly worse than I or II* Treatment: IV frusemide, nitrates etc.	Hypotension and left ventricular failure. Treat with inotropes (dobutamine, adrenaline) and diuretics and nitrates. *Very poor prognosis. Indicates severe myocardial damage.*

Heart failure

Patients may be admitted to the ICU with acute heart failure, and patients already in ICU being treated for other illnesses may have their course complicated by heart failure.

Definition: The rapid onset of symptoms and signs secondary to abnormal cardiac function.

Acute heart failure is a dangerous and life threatening condition, which requires early recognition and aggressive treatment. Causes of acute heart failure are:

- Acute myocardial infarction
- Decompensation of chronically depressed cardiac function
- Valvular heart disease
- Myocarditis – viral, bacterial, sepsis induced, autoimmune
- Cardiomyopathies – HOCM, restrictive/infiltrative, autoimmune, endocrine (thyrotoxicosis, myxoedema)
- Arrythmias – tachycardia shortens diastole and reduces left ventricular filling
- Severe anaemia

In a patient with pre-existing heart disease, the following could precipitate acute heart failure:

- Anaemia
- Uncontrolled hypertension
- Chest infection
- Severe sepsis
- Fluid overload (after fluid therapy, in renal failure)
- Pericardial effusion
- Tachy and brady arrthythmias
- Medications: beta blockers, calcium channel blockers

Acute heart failure could be

- Diastolic or systolic
- Forward or backward
- Left ventricular or right ventricular (or biventricular)
- Low output or high output

Evaluation of a patient with suspected heart failure

The most common symptom is dyspnoea and orthopnoea. The patient will be tachypnoeic, and will have bilateral fine crackles, and may have a wheeze. Tachycardia is often a feature, and a gallop rhythm may be present. The JVP may be elevated. Pulse oxymetry may show hypoxaemia.

Clinical differentiation is mainly from

Acute asthma (predominant wheeze, past history)
Pulmonary embolism
Severe anaemia
Fluid overload or acidosis in acute renal failure
Severe pneumonia and ARDS

How do patients with heart failure develop wheeze?

In the airways, mucosal oedema occurs due to venous congestion. This results in airway narrowing and rhonchi.

Management

Monitoring – connect the patient to a continuous cardiac monitor and pulse oxymeter.

Have the emergency drug trolley and defibrillator close at hand.

Resuscitate the patient first.

Airway: clear secretions, open the airway (see section on airway management), if necessary use an oral airway. If the patient is near arrest, intubation may be necessary.

Breathing: dyspnoea and tachypnoea are the cardinal features of acute heart failure. Give supplemental oxygen by face mask.

Circulation: if the patient is hypotensive, fluid resuscitation and inotropes may be necessary, bearing in mind that fluid resuscitation may worsen pulmonary oedema.

Obtain IV access. Take blood for routine investigations (full blood count, renal profile, liver function tests, cardiac biomarkers, random blood glucose, BNP)

Plasma BNP – B-natriuretic peptide is useful in diagnosing heart failure where doubt exists. It is elevated in systolic and diastolic failure, but not in other causes of acute dyspnoea. BNP has high negative predictive value.

Diuretics: loop diuretics must be given without delay. IV frusemide, 40-80 mg by slow bolus injection should be given. Even if in doubt of the diagnosis, if the patient's blood pressure is stable, diuretics will do little harm. Frusemide is oto-toxic, and the rate of injection should be no more than 4mg/min. Doses up to 400mg of frusemide maybe necessary in severe left ventricular failure.

Frusemide can be given as a continuous infusion of 10-20 mg/hour, with dose reduction according to response. The immediate action of frusemide is through vasodilatation rather than diuresis. Watch for and correct hypokalaemia.

While treatment is being given, arrange for an urgent 12 lead ECG and inward chest radiograph.

ECG: look for evidence of acute coronary syndrome. Changes of old myocardial infarction may suggest chronic heart disease. T wave inversions and conduction defects may be seen in myocarditis.

Chest radiographs: since a PA view cannot be obtained, it will be difficult to identify cardiomegaly – however, the classical features of pulmonary oedema will be apparent. These are:

Upper lobe diversion of blood
Perihilar congestion
Kerley B lines
Pleural effusion

Afterload reduction:

If the blood pressure is high, it will increase the load on the heart and worsen heart failure. Sublingual and intravenous nitrates are used to lower systemic vascular resistance and improve heart failure. Intravenous ACE inhibitors can also be used.

Morphine, 2-4 mg IV is also effective. It acts by causing pulmonary venodilatation, and also by alleviating anxiety and calming the patient. It has the additional advantage of analgesic effect if the patient has angina.

Oxygenation: if hypoxaemia persists in spite of emergency therapy, CPAP will be of benefit. CPAP helps by reducing the work of breathing. It also improves cardiac output by reducing ventricular transmural pressure and thereby reducing afterload. If CPAP does not succeed, intubation and mechanical ventilation may be necessary. Application of PEEP has a similar effect to CPAP, and in addition, mechanical ventilation reduces the work of breathing and reduces systemic oxygen demand.

Fluid therapy: It is important to ensure that circulating volume is adequate, as this will affect preload. Many patients with heart failure with low blood pressure are volume deficient. A fluid challenge should be given with care. Failure to optimise fluid volume will result in a further drop in blood pressure with diuretics. Some patients will, however, be volume overloaded; especially patients with chronic heart failure, and patients who have been in ICU for some time.

Correction of arrhythmias: Tachyarrhythmias compromise cardiac output and worsen heart failure. Ventricular filling occurs in diastole. When the heart rate increases, diastole shortens more than systole, resulting in reduced ventricular filling time, and hence reduced preload. Atrial fibrillation, in addition, results in further reduction in ventricular filling because the atrial 'kick' is lost. Tachyarrhythmias should be treated (see section on arrhythmias). Amiodarone is a useful agent to control tachyarrhythmias, but can drop the blood pressure.
Bradyarrhythmias may also reduce cardiac output. Temporary cardiac pacing maybe required to improve cardiac output in severe bradycardia.

The different types of heart failure:
Left ventricular vs right ventricular failure- isolated left ventricular failure is seen most commonly following acute ischaemia. It can also be due to outflow tract obstruction or volume overload. Right ventricular failure can occur as a consequence of longstanding left heart failure, or can occur due

to chronic lung disease (cor pulmonale) or primary pulmonary hypertension. The clinical features vary accordingly. In left heart failure, bilateral basal crackles are heard, with rhonchi. Mitral regurgitation may be present. In right heart failure, the JVP is elevated, the liver is enlarged and tender, and maybe pulsatile if tricuspid regurgitation is present. Dependent oedema and ascites may be present. In chronic congestive cardiac failure, features of both right and left heart failure are present.

Systolic vs diastolic heart failure – in the majority of cases, heart failure is due to reduced contractility of the myocardium, due to ischaemic damage. This results in reduced left ventricular ejection fraction during systole, and is referred to as systolic heart failure. Often however, there is reduced relaxation of the heart during diastole, especially if left ventricular hypertrophy is present. This is particularly common in the elderly and patients with hypertension. As a result, left ventricular filling is impaired, resulting in congestive heart failure. Clinically, the patient presents with all the clinical features of heart failure, but on echocardiography his left ventricular ejection fraction is normal. Plasma BNP levels are useful in this situation as they are elevated in both systolic and diastolic failure.

Forward vs backward failure – this describes whether the predominant features are of forward flow (low cardiac output states resulting in hypotension and poor tissue perfusion) or backward congestion (resulting in pulmonary oedema and other congestive features).

Low output vs high output failure – in most instances of heart failure, the cardiac output is low. In certain conditions however, there is low peripheral resistance and a hyperdynamic circulation. The cardiac output is high, although the increased output is inadequate to meet the requirements. Thyrotoxicosis, pregnancy, Beri-Beri, arteriovenous malformations, Paget's disease are examples of high output failure. In septic shock, the cardiac output is normal or high, in a sense similar to high output failure.

Treating the patient with resistant heart failure

If the patient is in cardiogenic shock, cardiac inotropes such as dobutamine and adrenaline can be tried. However, these increase myocardial oxygen consumption, and if ischaemic heart disease is the cause, can make things worse.

Intra-aortic balloon counterpulsation can be used in resistant cardiogenic shock. It is not always available, except in specialised centres. A balloon pump is inserted via the femoral artery into the descending aorta. The balloon inflates during diastole to improve coronary and cerebral blood flow and deflates immediately prior to systole resulting in a reduction in afterload. *It is not a long term treatment, and should be used only in situations where the underlying cause can be corrected, such as valve repair or coronary revascularisation.*

Once the patient is stable, consider the following issues:

Was heart failure due to acute coronary syndrome? Does the patient require angiography?

Was the heart failure a de novo occurrence, or was it on the background of chronic heart disease?

Are any medications likely to have made the heart failure worse?

Long term treatment

Once stabilised, the following drug therapy should be considered:

- ACE inhibitors or Angiotensin receptor blockers -these reduce mortality. Maximum tolerated dose should be used.
- Loop diuretics – often required if left ventricular function is impaired. No direct evidence of survival benefit, but of symptomatic benefit.
- Spironolactone – reduces mortality. Usual dose is 25mg daily.
- Digoxin – no survival benefit, probably symptomatic benefits but controversial. May interact with other drugs in ICU patients. Can cause hyperkalaemia and other features of toxicity. Toxicity made worse by hypokalaemia. Indicated in atrial fibrillation.

- Beta blockers – improve long term survival. Should not be commenced in unstable patients. Carvedilol is best; metoprolol and bisoprolol also show survival benefit.
- Amiodarone – maybe required for arrhythmia control.
- Anticoagulation – maybe required if evidence of an akinetic or dyskinetic myocardial segment is present, and definitely indicated in atrial fibrillation. When anticoagulation is indicated, initially heparin or low molecular weight heparin is given, and long term anticoagulation is obtained with warfarin.
- Other anti-ischaemic medications are indicated if the patient's heart failure was due to ischaemic heart disease.

Other issues:

- Anaemia must be corrected. The Hb must be maintained at least over 10g/dL.
- Salt restriction is necessary.
- Valvular heart disease may need surgical correction.
- Underlying metabolic conditions must be treated.

Arrhythmias

Abnormal cardiac rhythms often occur as complications in ICU patients. Tachyarrhythmias or bradyarrhythmias with haemodynamic instability may be the primary reason for ICU admission.

In the ICU, it is important to identify potentially dangerous cardiac rhythm abnormalities early, before haemodynamic instability manifests. Certain rhythm abnormalities such as ventricular fibrillation or ventricular tachycardia require emergency treatment. The ICU clinician must be conversant with interpretation of the common rhythm disturbances on ECG, and be able to determine their clinical significance in relation to the clinical condition of the patient. Certain rhythm disturbances will require urgent referral to an interventional cardiologist or cardiac electrophysiologist.

Patients in the ICU are nearly always on continuous ECG monitoring. The staff should be alert to recognise changes in rhythm which might be life threatening or which might herald the onset of life threatening complications.

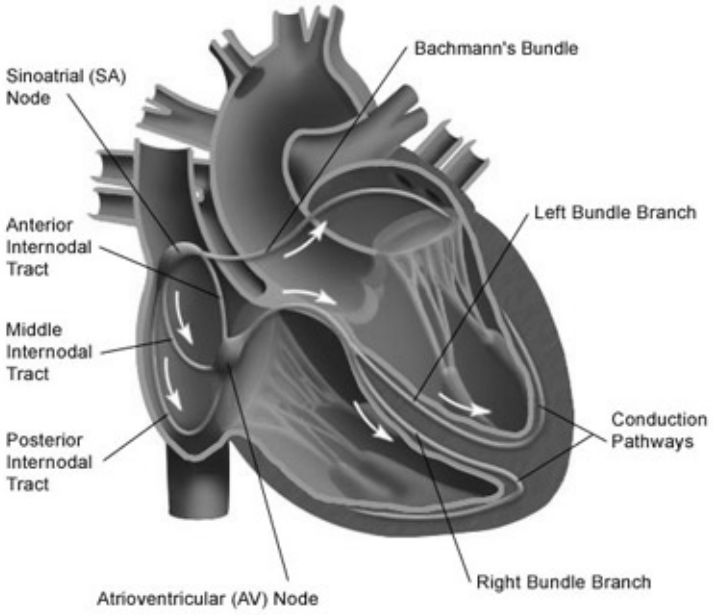
What are the difficulties encountered in ECG monitoring in ICU patients?

Burns and chest trauma can make lead positioning difficult. Shivering can result in a muscle artefact. Leads may be displaced in patients in the prone position. Restless patients may pull of the leads from the chest.

Certain conditions put patients at higher risk of developing rhythm abnormalities:

- Ischaemic heart disease
- Valvular or congenital heart disease, and cardiomyopathies
- History of arrhythmias and pro-arrhythmic states
- Certain drugs which may predispose to arrhythmias
- Stroke
- Drug overdose and poisoning
- Electrocution
- Thyrotoxicosis

In order to understand the different rhythm abnormalities, it is necessary to have an understanding of the conducting system of the heart.



The main components of the conducting system are the sinuatrial node, the atrioventricular bundle, the bundle of His, its branches and the Purkinjie fibres.

The sinuatrial node (SA node) – situated at the junction of the SVC and the right atrium. Blood supply is from the right coronary artery in 55%, and by the left circumflex in the rest.

The atrioventricular bundle – formally thought to be a node, is connected to the SA node by three channels in the atrial wall. Situated in the interventricular septum, it is supplied by the distal branch of the right

coronary artery in 90-95%. Hence, it is often affected in inferior MI which is due to infarction in the right coronary artery territory.

Bundle of His- passes through the membranous interventricular septum to the muscular interventricular septum, and divides into bundle branches. Supplied by both coronary arteries.

Bundle branches –the bundle of His divides into right and left bundles. The right bundle extends down the right side of the septum to the base of the anterior papillary muscle where it divides into the Purkinjie system. . The left bundle divides early into the left anterior and left posterior hemibundles, which then join the Purkinjie system. The bundle branches are supplied by both coronary arteries.

The SA node and AV bundle have good autonomic innervations. The bundle of His, branches and Purkinjie fibres have little autonomic innervation.

Normal conduction begins in the SA node, and spreads to the atria resulting in atrial contraction. Impulses then travel to the AV bundle, which delays conduction before the impulse travels to the ventricles. In the normal patient, the AV bundle is the only pathway connecting the atria and ventricles; apart from this, the atria and ventricles are electrically separate. This arrangement enables the delay between atrial and ventricular conduction.

All areas of the heart have automaticity, i.e., the ability to act as independent pacemakers. The rate of the pacemakers is lower the further one goes down the heart. Because the SA node has the highest rate, it overdrives the other parts of the conducting system. If the SA node is not functioning, the AV bundle will take over as pacemaker, with a lower rate. If the AV bundle is not functioning, the bundle of His or parts lower down will take over, with correspondingly lower rates.

On the ECG, the depolarisation of the SA node, the AV bundle and the bundle of His do not appear. The waves on the ECG are a result or atrial and ventricular depolarisation. The normal timings within the heart are as follows: (note that a small square on an ECG is equal to 0.04 seconds, and a large square is equal to 0.2 seconds)

Structure	Segment on ECG	Normal time (sec)	No of small squares on ECG
Atrial depolarisation	P-wave	<0.1	<2.5
Time to conduct through AV bundle and bundle of His	PR interval	0.12-0.20	3-5
Depolarisation of septum and ventricles	QRS duration	<0.12	<3
Ventricular repolarisation	QT interval (corrected)	0.38-0.42	Calculated value. Depends on heart rate

Cardiac arrhythmias are caused by two mechanisms:

- Abnormalities of conduction
- Conduction blocks: result in various types of bradyarrhythmias
- Aberrant conduction pathways- result in re-entrant tachyarrthythmias
- Abnormal automaticity – result in tachyarrhythmias due to impulses arising from sites other than the SA node.

The rest of this section will take you through a stepwise sequence of identifying different types of arrhythmias. The pathogenesis of each of the arrhythmias will be discussed in each case.

Arrhythmias are best diagnosed using a rhythm strip, usually obtained from Lead II. The first step in identifying an arrhythmia is to determine the heart rate.

How to determine the heart rate:

- If the rhythm is regular, divide 300 by the number of 'large squares' between two QRS complexes.
- Example: number of large squares = 3, therefore rate:300 / 3 = 100
- If the rhythm is irregular, count the number of QRS complexes over 30 large squares (6 seconds) and multiply by 10.

Heart rate >100 beats per minute → tachycardia

Heart rate <60 beats per minute → bradycardia

Bradycardias

The common causes of bradycardia are:

- Sinus bradycardia
- Nodal bradycardia
- Atrial fibrillation with a slow ventricular response
- Sick sinus syndromes
    - Type I – sinus bradycardia
    - Type II – sinus node dysfunction and sinuatrial exit block
    - Type III – tachycardia/bradycardia syndrome
- Second degree heart block
    - Mobitz type I
    - Mobitz type II (Wenckebach block)
- Complete heart block

Use the following algorithm to diagnose the bradycardia.

Are P waves present?

No (atrial fibrillation, nodal bradycardia)

Regular rhythm? → Nodal bradycardia

Irregular rhythm? → Atrial fibrillation with slow ventricular response

(Also consider atrial flutter with varying block. The classical flutter waves will be present)

Yes (sinus bradycardia, sick sinus syndromes, heart block)

The presence of p waves indicates a functional (albeit not necessary perfectly) sinus node.

Are the P waves regular?

No (sick sinus syndrome)

Yes (sinus bradycardia, heart block):

Is each P wave followed by a QRS complex?

Yes → sinus bradycardia

No (heart block) – now to differentiate types:

Is there any relationship between the P waves and QRS complexes?

No → complete heart block

Yes →Second degree heart block

Differentiate the two types of second degree heart block by the following:

Progressive prolongation of the PR interval, ending with a missed beat→Mobitz type II (Wenckebach) block

PR interval remains fixed, however, intermittently or at fixed intervals, there are no QRS complexes following the P-waves
→ Mobitz type I block

By using this sequence it should be possible to identify which rhythm abnormality is causing the bradyarrhythmia.

Sinus bradycardia: this may be harmless and normal for certain individuals, particularly well trained athletes. Beta blockers and calcium channel blockers can also cause sinus bradycardia. Many other conditions can cause sinus bradycardia; viral myocarditis, poisoning with digitalis glycosides (digoxin, oleander seeds), very high bilirubin levels, hypothyroidism, and sick sinus syndrome type I.

Look for prolongation of the PR interval – i.e, first degree heart block. By itself it is harmless, but it could herald the development of greater degress of block, depending on the underlying condition. Ischaemia, Beta blockers and calcium channel blockers are common causes in the ICU. It is a diagnostic criterion for acute rheumatic fever.

Heart block: The most important condition to consider in an ICU patient with heart block is whether it is due to acute coronary syndrome. Myocarditis, drugs (beta blockers and calcium channel blockers), and toxicity with digitalis glycosides are other causes. In endocarditis, the appearance of heart block may indicate the development of an aortic root abscess. Certain patients may have pre-existing heart block due to degenerative conditions of the conducting system, chronic valvular disease, or congenital heart disease.

Sick sinus syndrome: This too, may result from coronary ischaemia, myocarditis, drugs including digitalis, and pre-existing degenerative conditions. It may also be congenital.

Nodal bradycardia: The causes are similar to heart block and sick sinus syndrome.

Atrial fibrillation: The causes are numerous. Most importantly, acute ischaemia, myocarditis, and chronic atrial enlargement due to valvular heart disease should be considered. A slow ventricular response could be due to treatment with digitalis or amiodarone. Signs on the ECG of digitalis toxicity should be looked for, namely downsloping ST depressions (the inverted tick sign).

Bradyarrhythmias may also be caused by accidental vagal stimulation. ICU patients are at risk, because airway manipulation, bronchoscopy, and even suctioning may cause vagal stimulation and life threatening bradycardia.

The significance of bradyarrhythmias
Asymptomatic bradyarrhythmias may not need treatment, although a careful watch should be maintained for possible deterioration and development of greater degrees of block. Patients with congenital and pre-existing heart block or sick sinus syndrome are less likely to develop complications. The main issues are:

- Haemodynamic instability – low heart rate may make heart failure worse.

- Development of escape rhythms - When the heart rate is slow, escape rhythms from the ventricular muscle may take over, resulting in ventricular tachycardia

Treatment:

- Remove any drugs which are likely to contribute to bradycardia (beta blockers, verapamil, diltiazem, amiodarone, digitalis)
- In the acute situation, for example after a myocardial infarction, boluses of atropine may revert the rhythm to normal.
- In severe bradycardia (heart rate below 40 beats per minute) or haemodynamic instability, temporary cardiac pacing is required.

Tachyarrhythmias

As detailed earlier, tachyarrhythmias arise due to the presence of re-entrant pathways, or due to increased automaticity. The most common tachyarrhythmias are supraventricular tachycardia, ventricular tachycardia, polymorphic ventricular tachycardia (torsades de pointes), atrial fibrillation with a rapid ventricular response, atrial flutter with fixed block and multifocal atrial tachycardia.

The following algorithm helps diagnose the tachyarrhythmia

Is the rhythm irregularly irregular?

Yes → Atrial fibrillation with a rapid ventricular response

Note: the rhythm may be irregular in multifocal atrial tachycardia. Here, P waves will be present, but of varying size and orientation.

No → consider supraventricular or ventricular tachycardia

Are the QRS complexes broad? (>3 small squares)

No→ Supraventricular tachycardia

Yes →Ventricular tachycardia

This is a general rule. However, there are exceptions:

If there is either a pre-existing left or right bundle branch block, or aberrant conduction between the atria and ventricles, it is possible to have a broad complex supraventricular tachycardia.

If the focus of ventricular tachycardia occurs high up in the ventricular conducting system, the complexes may be narrow, although this is rare.

Supraventricular tachycardia

The different types of regular narrow complex (supraventricular) tachycardias are:

- Sinus tachycardia
- Atrioventricular nodal re-entrant tachycardia (AVNRT)
- Atrioventricular re-entrant tachycardia (AVRT)
- Atrial tachycardia & multifocal atrial tachycardia
- Atrial flutter with fixed block

Sinus tachycardia is caused by fever, sepsis, inotropes, pain, anxiety etc. It usually does not cause significant haemodynamic instability, and often does not need treatment apart from correcting the underlying cause.

AVNRT and AVRT are causes of paroxysmal SVT. The onset and termination of these arrhythmias are sudden.

AVNRT – common and responsible for nearly two thirds of paroxysmal SVTs. A re-entrant circuit is present within the AV node and surrounding perinodal tissue.

AVRT - here an accessory pathway connects the atria and ventricles. The impulse travels down the normal bundle of His and re-enters the atria through the aberrant pathway, setting up a continuous circuit of excitation which results in tachycardia. This is called orthodromic conduction. Rarely, the impulse travels from the atria to the ventricles through the aberrant pathway, re-entering the atria through the normal pathway. This is known as antidromic conduction, and is an example of an SVT which could have broad complexes. AVRT occurs in Wolff-Parkinson-White syndrome, where an abnormal bundle of Kent connects the atria and ventricles.

Atrial fibrillation with a rapid ventricular response can be caused by coronary ischaemia, pneumonia, conditions which cause atrial enlargement

such as valvular heart disease or cardiomyopathy, pulmonary embolism, thyrotoxicosis, alcohol and caffeine. It could occur with no identifiable cause (lone atrial fibrillation)

Atrial flutter is similar in aetiology to atrial fibrillation. The atria contract at a rate of 300 beats per second. Since the ventricles cannot contract at this rate, there is invariably some degree of heart block, which maybe fixed or variable. If variable block is present, the ventricular rhythm will be irregular. Fixed block is usually 2:1 or 3:1; hence, the ventricular rate will be either exactly 150 beats per minute, or exactly 100 beats per minute. Always suspect atrial flutter with 2:1 block, if the rate is exactly 150 beats per minute. Carotid sinus massage may increase the AV block and slow the ventricular rate, making the characteristic flutter waves obvious.

Atrial tachycardia is caused by abnormal automaticity in a focus in the atria outside the SA node. It may originate from a single focus, in which case the P waves will be morphologically similar, or from multiple foci (multifocal atrial tachycardia) where the P waves will have varying morphology. It is caused by coronary ischaemia, cardiomyopathies, lung disease, sepsis, hypokalaemia, hypoxia, alcohol excess, and theophylline.

Ventricular tachycardia

A ventricular rhythm with a rate over 120 bpm is a ventricular tachycardia. A ventricular rhythm with a rate between 100 and 120 beats per minute is called an accelerated idioventricular rhythm (AIVR). VT could be sustained or non-sustained.

Nonsustained VT: 3 or more consecutive ventricular beats with a rate of >120bpm with a duration of less than 30 seconds. Its incidence is higher with structural heart disease. Inotropes and theophylline may contribute. In general, the prognosis is better than that with sustained VT.

Sustained monomorphic VT: here, the ventricle beats at a rate of >120bpm for more than 30 seconds. This is a more serious arrhythmia; causes include acute coronary syndromes, chronic valvular disease and cardiomyopathy, digitalis toxicity, cocaine abuse, and sepsis.

Sustained polymorphic VT: this is characteristically seen in congenital or acquired long QT syndrome.

Congenital long QT syndrome: two types exist; the Romano Ward syndrome, with purely cardiac involvement, and the Jervell Lange Neilsen syndrome which is associated with sensorineural deafness.

Acquired long QT syndrome: caused by hypokalaemia, hypomagnesaemia, hypocalcaemia, hypothyroidism, structural heart disease, and most importantly, drugs.

Drugs which cause QT prolongation
Quinolones (levofloxacin)
Macrolides (erythromycin, clarithromycin)
Pentamidine
Newer Antihistamines (astemizole, terfenadine)
Phenothiazines
Tricyclic antidepressants
Domperidone
Quinine
Cocaine
Organophosphates
Antiarrhythmic drugs – class IA and III (quinidine, procainamide, disopyramide, amiodarone, sotalol)

The characteristic polymorphic VT or Torsade de pointes is a ventricular rhythm with a rate >100bpm, with frequent variations of the QRS axis and morphology (twisting of points).

Accelerated idioventricular rhythm (AIVR): this is caused by gradual failure of the conducting system above the ventricles. Commonly seen after thrombolysis (re-perfusion arrhythmia).

Ventricular fibrillation
This is the most dangerous arrhythmia, and results in no effective cardiac output, or cardiac arrest. For practical purposes it is categorised together with pulseless VT. The ventricular electrical activity is completely irregular. Immediate defibrillation is the only treatment. In pulseless VT, ventricular complexes are seen, but there is no effective cardiac output.

Asystole
The ECG shows a flat line. Seen in cardiac arrest, this has a poor prognosis, and does not respond to defibrillation. Note that it is important to differentiate asystole from fine ventricular fibrillation.

Pulseless electrical activity (Electromechanical dissociation)
Here, the ECG monitor shows complexes, however, there are no effective contractions of the ventricle. The condition occurs in severe myocardial damage, and in pericardial effusion. The prognosis is extremely poor.

The management of VF, pulseless VT, asystole and PEA are discussed in the section on ACLS. These rhythms often occur as a terminal event in ICU patients. They are potentially reversible, especially when occurring in the setting of an acute coronary event.

Many factors predispose ICU patients to tachyarrthythmias:

- Pre-existing chronic ischaemic or valvular heart disease
- Acute coronary syndrome
- Sepsis
- Treatment with pro-arrhythmic antiarrhythmic drugs (class Ic antiarrhythmics)
- Acid base abnormalities
- Hypercapnoea
- Electrolyte imbalance – potassium, calcium, magnesium
- Excessive catecholaminergic activity
- Inotropes
- Pain, anxiety

- The presence of intracardiac guide catheters and pacing wires, and incorrect placement of central venous lines and dialysis lines in a way in which they irritate the myocardium
- Drugs which cause QT prolongation

Treatment
All tachyarrhythmias do not need treatment. Determine the following:

Is the tachyarrhythmia causing haemodynamic compromise? Hypotension indicates definite haemodynamic compromise. In tachycardia, diastole shortens more than systole. Ventricular filling occurs during diastole; shortening of diastole results in reduced end-diastolic volume, and hence reduced cardiac output. Left ventricular failure is also a form of haemodynamic compromise. The presence of angina also indicates haemodynamic instability, as coronary perfusion is getting compromised. If there is haemodynamic compromise, the arrhythmia must be reverted quickly.
In SVT or VT with haemodynamic compromise, synchronised electrical cardioversion should be performed without delay.

Is the patient haemodynamically stable at present, but likely to become unstable with time? Persistent tachycardia will eventually tire out the myocardium. If there is existing myocardial dysfunction, tachyarrhythmias are likely to be less well tolerated. Such arrhythmias should be identified early and treated. Medical cardioversion, with antiarrhythmic drugs should be attempted.

Supraventricular tachycardia:

- Try carotid sinus massage. Be careful in elderly with possible carotid plaques. Do only one side at a time
- Adenosine 6mg IV as a rapid bolus (give as fast as possible and flush with saline). Repeat 12 mg if no effect.
- Verapamil can also be used in a dose of 5-10mg IV. It is vital to make sure that the arrhythmia is definitely an SVT, as verapamil is dangerous in VT.
- If there is no response, electrical cardioversion must be considered.

Atrial fibrillation:

- Rate control should be the priority. Conversion to sinus rhythm is desirable, but measures must be taken to prevent possible embolisation. Intravenous beta blockers or verapamil (never both together) are the drugs of first choice for rate control. Digoxin can also be given. Amiodarone is effective, and can convert the atrial fibrillation to sinus rhythm. If the AF has been present for >24 hours, the patient must be anticoagulated first to prevent thromboembolism. TOE is useful to exclude the presence of atrial thrombi. DC cardioversion may be required. Do not give digoxin in WPW syndrome, as it shortens the refractory period of the accessory pathway and accelerate the rate.

Doses:

- Digoxin: Loading: 10-15 mcg/kg total dose given 50% initially and remainder at 4-8h intervals, maintenance: 0.0625-0.375 mg qd.
- Verapamil:0.075mg/kg slow IV
- Amiodarone: 300mg IV over 1 hour, followed by 900 mg over the next 24 hours.

Sustained monomorphic ventricular tachycardia:

Amiodarone (dose as above) is the drug of first choice. Lignocaine is an alternative. If there is no response, electrical cardioversion should be considered.

Polymorphic VT:

Intravenous Magnesium Sulphate is effective in most cases. Lignocaine is given in post MI situations.

Is the patient not likely to become haemodynamically compromised? Is no treatment necessary?

Sinus tachycardia usually does not require treatment. While most other tachyarrhythmias are likely to cause problems if left too long, careful observation with attention to other precipitant factors may be adequate.

- Check blood gases and correct acidosis.

- Check potassium levels and maintain potassium at the upper range of normal (especially in ischaemic heart disease and post cardiac surgery).
- Check and replace magnesium levels. Magnesium levels are often low in ICU patients. Blood levels can be normal, but tissue levels maybe low. If in doubt, and the urine output is adequate, a bolus dose of magnesium should be administered empirically.
- Optimise anti-ischaemic treatment: maximise anti-ischaemic drugs. Consider if the patient needs intra-aortic balloon counterpulsation or coronary angioplasty or surgery.
- Try to stop all medications which could be causing the arrhythmia.
- Check thyroid function.
- Check whether the central venous line is irritating the atrial myocardium or tricuspid valve. A chest radiograph might be helpful. If in doubt, withdraw line a few centimetres.

In patients with hyperkalaemia who require urgent dialysis, avoid cannulating the internal jugular or subclavian lines. The tip of the line (either for CVP or for dialysis) can irritate the overly irritable myocardium and precipitate dangerous arrhythmias.

Bundle branch block

New onset bundle branch block often indicates ischaemia or other pathological process. The QRS duration is greater than 0.12 sec (3 small squares)

LBBB	RBBB
Deep slurred S waves in V1 and V2	Tall R waves in V1 and V2
Left axis deviation	Right axis deviation
Dominant R waves in LI, aVL and V6	Deep slurred S waves in LI, aVL and V6

The ST segments are directed away from the baseline in the direction opposite to the predominant QRS deflection, i.e., in LBBB, there are ST elevations in V1, and in RBBB, there are ST depressions in V1.

LBBB is more likely to be pathological than RBBB. New LBBB is diagnostic of STEMI. RBBB can be harmless, although it can occur in ischaemic heart disease and lung disease, including pulmonary embolism.

This general overview of arrhythmias will guide you through the common rhythm problems arising in the ICU. The topic is very wide, and there is much more to learn.

Acute Renal Failure

Acute renal failure is the sudden (and usually **reversible**) failure of the kidneys to excrete nitrogenous and other waste products causing loss of homeostasis and retention of these products within the body.

Acute renal failure (ARF) is a common and serious complication in ICU patients. Many factors affect the kidney in ICU – hydration, hypotension, nephrotoxic drugs, contrast media, and in many instances, the primary disease process itself, such as severe sepsis and acute liver failure. Sepsis is the leading cause of ARF in ICU patients, and renal failure is the leading cause of death in sepsis.

ARF may also be caused by specific diseases affecting the kidney – for example various types of glomerulonephritis, especially rapidly progressive glomerulonephritis, Goodpasture's disease, SLE, systemic vasculitis (polyarteritis nodosa), acute infections like leptospirosis, dengue and other types of haemorrhagic fevers, malaria , snake bite, paracetamol poisoning. These conditions may be identifying based on their accompanying symptoms and signs.

Oliguria is defined as a urine flow of less than 500 ml/day; less than 50-100 ml/day is termed anuria. However, in the ICU, a reduction in urine output must be recognised eary; more rapid assessment of urine output than can be achieved with a 24 hourly assessment is required. Hence, for adults, oliguria can also be defined as a urine flow of less than 0.5 ml/kg/hr for two consecutive hours. In infants, renal concentrating ability is less developed and a urine flow of less than 2 ml/kg/hr (for two hours) is considered oliguria.

Oliguria is classified as being pre-renal, renal, or post renal.

If the urine output drops, first exclude a blocked or misplaced urinary catheter.

Primary renal causes of acute renal failure
Primary glomerulonephritis • Post streptococcal GN • Anti-glomerular basement membrane disease (Goodpasture's) • Crescentic glomerulonephropathy • IgA nephropathy
Connective tissue diseases • SLE • Systemic sclerosis
Vasculitis • Polyarteritis nodosa • Microscopic polyangiitis
Infections • Leptospirosis • Dengue& other haemorrhagic fevers • Typhus • Malaria
Snake bite – vipers, cobra
Poisoning • Paracetamol
Malignancy – myeloma
Pyelonephritis, renal abscess

Pre-renal oliguria: Renal blood flow comprises 20% of cardiac output. Hypotension for any cause results in renal vasoconstriction and reduced renal blood flow. Hence, the urine output is reduced. At this stage, no structural damage to the kidney has occurred. If renal perfusion is re-established, kidney function returns to normal, urine output normalises, and no long term sequelae occur. Blood urea may rise, but creatinine remains normal or mildly elevated. If hypotension is prolonged, acute tubular necrosis occurs, resulting in established renal failure which leads to renal oliguria.

Renal oliguria: structural damage to the kidney has occurred, usually acute tubular necrosis. The renal cortex is more resistant to ischaemic damage,

but severe prolonged hypotension can result in cortical necrosis, which has a worse prognosis. Renal oliguria results in acute renal failure, which will not immediately return to normal. Hypotension and renal hypoperfusion is not the only cause of acute tubular necrosis in ICU patients; many other factors contribute such as;

- Cytokines in severe sepsis
- Nephrotoxic drugs
- Radiological contrast media
- Tubular damage due to rhabdomyolysis

Often in acute tubular necrosis leading to established renal failure, oliguria persists. Blood urea and serum creatinine rise, and hyperkalaemia can occur. In some patients, urine output improves - but the blood urea and serum creatinine continue to rise – this is known as non-oliguric renal failure. The urine which is passed is of poor quality, and excretion of toxins is inadequate. The kidney's concentrating ability is lost.

Non-oliguric renal failure lulls the treating team into a false sense of complacency. Clinicians delay intervention despite rising renal parameters because the urine output is satisfactory. While non-oliguric renal failure does have a better prognosis than oliguric renal failure, decisions to commence renal replacement should be based on clinical and biochemical parameters other than the urine output.

Post-renal oliguria: This is due to obstruction to urine flow. Anuria is often due to obstruction, although renal oliguria can also result in anuria. Intermittent flow of urine is also likely to be due to obstruction. Obstruction is caused by:

- A blocked or misplaced in-dwelling urinary catheter
- Urethral obstruction or disruption
- Ureteric obstruction with solitary kidney
- Bilateral ureteric obstruction

Oliguria is most commonly pre-renal, and hence resuscitation will prevent the patient developing established renal failure, hence should be attempted in all patients. Even patients with established renal failure may have an ischaemic element, and resuscitation may help.

Diagnosing pre-renal, renal and post-renal oliguria

- Assess intravascular volume status.
- Clinical features of dehydration – thirst, loss of skin turgor, sunken eyes, dry tongue.
- Look for factors which might have caused hypovolaemia such as,
  - Bleeding – overt, gastrointestinal, into the peritoneal or pleural cavities, into muscles (haematomas), through drains
  - Reduced fluid intake – anorexia, vomiting, fasting for procedures or surgery, reduced consciousness, dysphagia, diarrhoea, purgation for colonic preparation before colonoscopy or barium enema
  - Diuretics
  - Poor glycaemic control resulting in osmotic diuresis and dehydration
  - Chronic renal failure with inadequate intake – diuresis due to loss of renal concentrating ability
  - Third space loss after trauma
  - Increased insensible water loss- fever, burns, exfoliative dermatitis
- Evaluate fluid balance over the last few days – look at the intake output charts. It is not surprising to find that the patient has been in persistent negative balance over the preceding few days, although intake over the last 24 hours may be adequate.
- Is the patient hypotensive? If so is it hypovolaemic, septic or cardiogenic shock? In septic shock, relative hypovolaemia due to widespread vasodilatation occurs.
- Is intra-abdominal hypertension present resulting in reduced renal blood flow? Look for ascites, post abdominal surgery.
- Is a primary condition causing renal damage?
- Does the patient have severe sepsis?
- Has the patient received nephrotoxic drugs? Aminoglycosides, cephalosporins, amphotericin, cyclophosphamide, NSAIDs, cytotoxic drugs.
- Is there rhabdomyolysis?
- Has contrast media been used? Were reno-protective precautions (hydration, N-acetylcysteine) taken?

- Does the patient have a degree of underlying renal impairment and is this acute on chronic renal failure? Look for previous renal function reports and medical records. Evaluation of renal size using ultrasound may help. In chronic renal failure the kidneys are shrunken. However, in diabetes, and amyloidosis the kidneys are normally larger- when chronic renal failure occurs in these conditions the kidneys maybe of normal size.
- Biochemical evidence
  - Blood urea – elevated in dehydration and in established renal failure.
  - Serum creatinine- a rise indicates established renal failure.
- High blood urea with normal creatinine suggests pre-renal failure. If both are elevated, established renal failure is likely.
- Calculate the creatinine: urea ratio (in SI units). Generally, the ratio is 10:1.
- High creatinine:urea ratio = rhabdomyolysis or other catabolic states
- Low creatinine: urea ratio (i.e., high urea) = high nitrogen load (concurrent gastrointestinal bleed, recently started artificial nutrition) or dehydration.
- Calculate estimated creatinine clearance using the Cockcroft-Gault method (ml/min). This is necessary for making dose adjustments of drugs.
  males – GFR = (140-age) X Weight (Kg) / (72 X serum creatinine)
  females – GFR (males) X 0.85
- Actual measurement of 24 hour creatinine clearance is not done in ARF, as it assumes steady state renal functions.
- Hyperkalaemia can occur in established renal failure due to the inability of the kidney to excrete potassium. This can be life threatening.
- Alkalosis is a feature of intravascular volume depletion. However, in hypovolaemia and hypotension resulting in tissue hypoxia, anaerobic metabolism in the tissues results in lactic acidosis.
- Hyperphosphataemia occurs in established renal failure.
- Examination of the urine is helpful in differentiating pre-renal oliguria from established renal failure. In pre-renal oliguria, the

concentration ability of the kidney is preserved, while it is lost in intrinsic renal failure.

Test	Pre-renal oliguria	Renal oliguria
Urine osmolality	High >350mOsm/L	Low <350mOsm/L
Urinary sodium	Low <10mmol/L	High >20mmol/L
Fractional excretion of Na	Reduced <1%	Increased >1%
Urinary sediment	No cells or casts	Proteins, cells, casts Muddy brown casts – ATN. Red cell casts in glomerulonephritis. Eosinophils in interstitial nephritis.

- Is post-renal oliguria present or contributing? Always consider obstruction if sudden anuria occurs.
- Is the bladder distended? If so, is the urinary catheter blocked?
- If the patient is not catheterised, is there any history of trauma which could have damaged the urethra? If so, do not attempt to catheterise– call in a genitourinary surgeon.
- Is prostatic enlargement likely? (Elderly patient, history of prostatism, digital examination of the rectum). If so, attempt catheterisation. If not possible, do suprapubic bladder puncture.
- Is there obstruction of the ureters? This is unlikely to occur all of a sudden. Consider retroperitoneal fibrosis, ureteric calculi.
- Do a plain radiograph of the abdomen (to look for calculi and renal outline) and ultrasound scan of the abdomen which may show hydronephrosis.
- Obstruction, if present, will impede renal perfusion by back pressure. Relief of obstruction is urgent. This will depend on the cause, and urgent referral to a genitourinary surgeon is necessary.

Treatment of pre-renal oliguria

Look for features of acute circulatory impairment; tachycardia, hypotension, cold extremities, lactic acidosis, high blood urea – these are present after loss of more than 10-15% of blood volume.The patient may complain of thirst, the tongue will be dry, and skin turgor lost. Note that a fluid challenge should be tried in oliguric patients even if the patient is normotensive, if other signs of intravascular volume depletion are present.

Acute circulatory impairment could be classified as being with either distended neck veins, or flat neck veins. Flat neck veins indicate hypovolaemia, and fluid resuscitation is indicated. Distended neck veins will be seen in cardiogenic shock; associated hypovolaemia may still be present – however, fluids should be given with care, as the patient could be pushed into pulmonary oedema. It may be necessary to treat heart failure concurrently, with diuretics and inotropes.

Note that even in cardiogenic shock, fluids may be required; hypovolaemia will result in reduced preload and (based on the Frank-Starling Law) further reduce cardiac contractility.

Give a fluid challenge: 10-15ml/kg (around 500-750ml) of 0.9% saline or Hartmann solution rapidly. Colloids – hetastarch is an alternative, however,

- There is no proven benefit of colloids over crystalloids, although theoretically colloids stay in the intravascular compartment, and crystalloids are distributed equally in the intravascular and extravascular compartments.
- Dextran-40 has been associated with a higher chance of ARF.

Look for haemodynamic improvement – rise in blood pressure, fall in tachycardia, rise in oxygen saturation, rise in jugular venous pressure, and most importantly, improvement in urine output.

Larger volumes of fluids may be required, especially in septic shock. If some improvement occurs, continue to give fluids boluses. In the study by Rivers et al on early and aggressive fluid resuscitation in critically ill patients, large volumes (upto several litres) were given effectively and safely. Watch carefully for over hydration and pulmonary oedema, which is the main risk involved in giving fluids; the patient may complain of dyspnoea and become tachypnoeic, and develop fine basal crackles. Should pulmonary oedema

develop, fluids should be stopped. If not, continue to give fluids. Fluids should be given with greater care in elderly patients.

Most clinicians under-resuscitate, because of the fear of pulmonary oedema. Pathetically low volumes of fluids are given, and lack of response is interpreted as failure of the fluid challenge test. It is much easier to manage pulmonary oedema than it is to manage the disastrous complications of renal and multi-organ failure resulting from prolonged tissue hypoperfusion caused by inadequate intravascular volume. At the most, ventilation will be required.

Ventilated patients are relatively protected from pulmonary oedema due to fluid overload, and hence larger volumes of fluids can be safely given. Application of PEEP can easily control pulmonary oedema.
Hypotension due to hypovolaemia will generally respond to adequate fluids. If the blood pressure does not respond to fluids, cardiogenic or septic shock is likely. In cardiogenic shock, the neck veins are likely to be distended, and pulmonary oedema may be present. In septic shock, the blood pressure may not respond to fluids; this is because of the profound vasodilatation that occurs. Vasopressors should be commenced. Noradrenaline is the most effective in terms of raising blood pressure and improving renal perfusion. Dopamine is less effective. Dobutamine worsens vasodilatation, and should only be added to noradrenaline if cardiac dysfunction is present. Replacement doses of corticosteroids may be necessary to restore vascular sensitivity to vasopressors (see section on *Severe Sepsis and septic shock).*

Reno-protection
Apart from fluid resuscitation, the following steps should be taken to prevent renal damage

- Avoidance of nephrotoxic drugs.
- Prevention of contrast nephropathy.
    - Where possible, avoid contrast altogether.
    - If essential, hydrate with half normal saline and give N-acetylcysteine 600mg 12 hourly starting 12 hours before administration of contrast.
- Tight glycaemic control may play a role in preventing renal failure and treat urinary tract infection if present.

Management of Renal oliguria

The initial evaluation has been dealt with above. In addition to blood urea and serum creatinine, other important investigations in management of ARF are:

- Serum electrolytes – hyperkalaemia is a life threating complication in ARF. Potassium levels rise because the kidneys are unable to excrete potassium. The rate of rise of potassium is more critical than the actual level. A patient with CRF who has had persistently high potassium levels may tolerate hyperkalaemia better than a patient who had a large rise of potassium over several hours.
- Arterial blood gas analysis: metabolic acidosis may be caused by acute renal failure, due to inability of the kidney to excrete hydrogen ions. The base excess will be negative, with a widened anion gap. Lactic acidosis may contribute to the acidosis. Acidosis makes hyperkalaemia worse.
- Serum calcium, phosphate and magnesium: hyperphospataemia occurs as a result of the kidneys' inability to excrete phosphate, and hence the serum calcium falls. Hypomagnesaemia may also be present.
- ECG – should be done urgently in hyperkalaemia. Hyperkalaemia with ECG changes needs emergency management.
- Serum creatine phosphokinase (CPK) and serum myoglobin levels should be done in suspected rhabdomyolysis.
- Full blood count: low Hb may occur in previous chronic renal disease, bleeding etc.
- Blood glucose: tight glycaemic control improves renal outcome.
- Certain investigations are required to diagnose primary conditions which might have resulted in renal damage, such as ESR, CRP (myeloma, glomerulonephritis), ASOT (post-streptococcal GN), antinuclear factor, anti-double stranded DNA, complement levels (SLE), ANCA (vasculitis), Anti-GBM antibodies (Goodpasture's disease), blood picture (myeloma), blood for malaria parasites, malaria antigen tests, Leptospira antibodies.

Treatment

Most of the time, acute tubular necrosis has occurred. In addition, patients may be hypovolaemic which contributes to oliguria, and a cautious trial of fluids could be given. The patient with renal oliguria is unable to excrete fluids, and hence can easily develop fluid overload.

The main problems in renal failure are:

- Uraemia:
    - Uraemic encephalopathy- anorexia, nausea, vomiting, malaise, confusion, coma.
    - Uraemic pericarditis, together with coagulopathy due to various causes can result in haemopericardium and cardiac tamponade.
- Fluid overload due to oliguria. Space is often necessary to give inotropes, antibiotics, blood and blood products. Fluid overload also results in pulmonary congestion, increased risk of lung infections, and difficulties in ventilation, and can make cardiac failure worse.
- Hyperkalaemia – can result in life threatening cardiac arrhythmias.
- Acidosis

Fluid management:

Optimal management of intravascular fluid status is vital. If the patient is euvolaemic, then the aim is to maintain euvolaemia, by replacing urinary and insensible losses. Usually, daily intake should be the previous day's urine output + around 500-600ml (insensible loss). If the patient is hypovolaemic, this can be increased or reduced, if overloaded. Daily intake will include the volume of all drugs and inotropes. However, in the ICU, it may be necessary to replace fluids based on hourly urine output. On average, the required hourly output is – the previous hour's urine output + 20-25ml. This should be balanced off every 4 hours, as administration of drugs and blood products will result in different obligatory intakes at different times of the day.

How to determine volume status:

Clinical indices – tachycardia, blood pressure, JVP, lung bases, features of dehydration.

Central venous pressure is the most widely used index of filling. It is not completely reliable, especially if cardiac dysfunction is present. Other methods include pulmonary capillary wedge pressure measurement and PiCCO. Dynamic studies of blood pressure and CVP variation during cycles of respiration are increasingly thought to be accurate measures but, will not be dealt with here. Fluid balance over the last few days must be assessed.

Correction of metabolic acidosis:

Severe acidaemia must be corrected. Acidaemia causes cardiac compromise, resulting in hypotension, which recovers on correction. Whether correction of acidosis improves renal function per se is not clearly established. Acidosis is corrected with IV 8.4% sodium bicarbonate solution.

1ml of 8.4% sodium bicarbonate solution contains 1mEq of bicarbonate.

Note that lactic acidosis should not, in general, be corrected with bicarbonate.

If blood gases are available, the bicarbonate dose should be calculated as follows:

Bicarbonate requirement (mEq) = 0.2 x weight (kg) x base deficit (mEq/L)

Half the total dose should be administered initially, followed by the rest of the dose given over the next 24 hours. If the base excess is not known, administer as an IV infusion of 2-5 mEq/kg over 4-8 hours.

Hyperkalaemia

If hyperkalaemia is present, do an urgent 12 lead ECG. If ECG changes of hyperkalaemia are present, treat as follows;

- To stabilise cardiac muscle by preventing the cell membrane effects of hyperkalaemia
    - IV 10% Calcium gluconate 10ml over 2-3 minutes –to stabilise cardiac muscle
- To drive extracellular potassium into the cells
    - 10 units of soluble insulin in 50ml 50% glucose
    - Sodium bicarbonate, especially if metabolic acidosis is present
    - Beta 2-adrenergic agonists – nebulised salbutamol

- These measures are only temporary, since there is nearly always increased body potassium. Hence, measures should be taken to remove potassium from the body.
    - Loop or thiazide diuretics
    - Cation exchange resin – Kayexalate 15-30g, given orally or rectally
    - Haemodialysis
- Check the drug chart to see if any drugs being given might contribute to hyperkalaemia – ACE inhibitors, angiotensin receptor blockers, spironolactone, and even KCl. Digoxin should be stopped.

Furosemide therapy

Furosemide is widely used by clinicians in the vague hope that creating a diuresis is equivalent to improving renal function. There is no evidence of any benefit in terms of improvement in renal functions, prevention of ARF, or long term renal recovery or survival with frusemide. Sometimes, giving frusemide by bolus or infusion seems to provoke a diuresis. However, the urine passed in this situation is of poor quality (non-oliguric renal failure). It will be noticed in this situation that, in spite of a good diuresis, the patient's biochemical and clinical parameters seem to worsen. The only use of Furosemide may be in the short term, in creating space for medications until dialysis can be arranged. Mannitol is similarly useless, and can in fact, worsen renal functions.

Inotropic support and the 'renal dose dopamine' controversy

In the past, it was thought that dopamine in low doses improves renal blood flow and hence renal functions. While it is true that this effect does occur in healthy individuals, it does not happen in critical illness. It is now proven beyond doubt, that there is no benefit of low or renal dose dopamine, and it should not be used. This does not mean that dopamine is contraindicated. Conventional doses of dopamine aimed at raising the blood pressure are effective in improving renal blood flow and urine output. Noradrenaline is however more effective in raising the blood pressure and improving renal blood flow. Hence, if the blood pressure is low, a noradrenaline infusion should be given.

Alkalinisation of urine

The only situation this is necessary is in rhabdomyolysis. However, there is now evidence that saline diuresis is as effective, and currently saline diuresis is recommended for rhabdomyolysis.

Nutrition in renal failure

If the patient is not being dialysed, it is prudent to reduce protein intake to around 40g per day. However, if the patient is on dialysis, a normal protein intake should be given. Potassium rich food (fruit juices) should be avoided in hyperkalaemia.

Renal replacement therapy

The definitive treatment of ARF is renal replacement therapy. RRT should begin early. The available modalities of RRT are

- Intermittent haemodialysis
- Continuous renal replacement therapy (continuous veno-venous haemofiltration)
- Peritoneal dialysis

In ARF, peritoneal dialysis is less effective, more likely to result in complications, may be technically difficult in the case of intra-abdominal complications, and is more expensive. It is not recommended except in haemodynamically unstable patients in centres where continuous renal replacement therapy is not available.

There is no proven difference in terms of efficacy between continuous and intermittent haemodialysis. The dose of haemodialysis rather than the modality is what matters. However, intermittent haemodialysis is not possible in hypotensive patients, and CVVH is the preferred modality. CVVH is not routinely available in all centres.

Indications for urgent dialysis:

- Uncontrollable hyperkalaemia.
- Salt and water overload causing or worsening severe pulmonary oedema.
- Need to create intravascular space for medications and blood products.
- Severe metabolic acidaemia.

- Blood urea over 30mmol/L (the exact cut off varies depending on the clinical situation.
- Complications of uraemia such as pericarditis, encephalopathy, neuromyopathy or bleeding disorders.
- Hypercalcaemia, severe hyponatraemia.
- Removal of a dialyzable toxin – Lithium carbonate

Two main processes are carried out in renal replacement therapy – haemofiltration and haemodialysis.
Haemofiltration is a convective process. A hydrostatic pressure gradient is used to filter plasma water and solutes across a semi permeable membrane. The driving force is hydrostatic pressure. The amount of fluid removed can be changed by changing the driving pressure. This fluid is discarded, and the lost fluid is replaced with sterile isotonic fluid. Rate of fluid removal depends on:

- Rate of blood flow
- Hydraulic conductance (permeability) of the membrane
- Hydrostatic pressure gradient across the membrane
- Surface area of the haemofilter membrane

Haemodialysis is based on diffusion. Blood is passed over a semi-permeable membrane which separates it from an electrolyte solution flowing in the opposite direction. Waste solute moves out of the blood into the electrolyte solution (the dialysate) along a concentration gradient. Efficacy of haemodialysis depends on:

- Rate of blood flow through the haemodialyser
- Membrane properties
- Rate of flow of dialysate
- Membrane surface area

A standard nomenclature is used in RRT- e.g. CVVH, CAVH, CVVHD, CVVHDF. The C stands for 'Continuous'. VV or AV stands for the type of extracorporeal circuit. VV is veno-venous, where blood is taken out through a vein and reintroduced to the body through veins. AV is arteriovenous, where blood is taken out from an artery and reintroduced to the body though a vein. VV requires a pump for blood flow, and hence can be used even if the blood pressure is very low. H stands for haemofiltration, HD for

haemodialysis and HDF for haemodiafiltration, where haemofiltration is combined with haemodialysis.

The commonly used modalities in the ICU are CVVH and CVVHDF. Most ICUs are moving towards haemofiltration rather than haemodialysis, or methods which combine both.

Anticoagulation of the extra-corporeal circuit is necessary in CRRT, or else the filter or dialyser will get clotted. Heparin is used.

The buffer in the dialysate solution can be acetate, lactate or bicarbonate. Acetate can cause vasodilatation and is not suitable for patients with severe sepsis. Lactate is converted in muscle and liver to bicarbonate. It is suitable for critically ill patients except those with severe liver dysfunction or severe sepsis where lactate metabolism is affected. Bicarbonate is ideal but is not always easily available.

Filter/dialysis membrane – older membranes such as the cellophane based membranes have been shown to activate complement and worsen inflammation. Newer membranes, such as those based on polyacrylonitrile (PAN), polysulphone and polycarbonate may be better, although this is still controversial. Newer artificial membranes also allow passage of larger 'middle' molecules which play an important role in uraemic manifestations. They also allow higher filtration rates.

There is no convincing evidence yet that RRT improves sepsis itself.

RRT should be continued until the native kidneys recover sufficiently to be able to maintain the blood urea below 30mmol/L and an adequate urine output is present.

Effect of ARF on drugs

Doses of nephrotoxic as well as other drugs should be adjusted according to estimated creatinine clearance. In particular, opiate analgesics can accumulate, resulting in worsening renal function and respiratory suppression. Naloxone infusion is sometimes necessary to reverse this

effect. IV penicillin can cause seizures due to accumulation in renal failure. Digoxin should be stopped or the dose reduced to a minimum if essential.

Aminoglycosides are nephrotoxic but may be essential in severe sepsis with ARF. Aminoglycosides act by peak concentration dependent killing, and hence should be given in single daily doses. Vancomycin levels should be monitored and therapy adjusted accordingly.

Management of post-renal oliguria (urinary tract obstruction)

Relief of the obstruction is necessary. This usually requires referral to a genitourinary surgeon. Patients with obstruction are predisposed to urinary tract infection. Urine culture should be performed and empiric antibiotics commenced, especially if the clinical features of infection are present and the urine contains pus cells. It may be necessary to change the urinary catheter.

Intravenous urography may be required to diagnose the site and cause of urinary tract obstruction. However, care must be taken in giving IV contrast, as detailed above.

Altered consciousness

Altered consciousness is a commonly encountered problem in ICU patients. The ICU clinician must be able to:

- Diagnose coma and altered consciousness using a quick neurological examination.
- Initiate management of the patient with altered consciousness.
- Determine specific underlying causes of altered consciousness.
- Determine outcome and prognosis
- Plan out long term care.

What is consciousness? What are the different altered levels of consciousness?

Consciousness is a state of awareness of self and environment in an individual provided with adequate stimuli. A person who is fully conscious is fully responsive to stimuli, and displays appropriate behavior and speech. Patients who are asleep can be roused to this state, and are then able to perform normally.

Consciousness depends on integrated activity in both the

- ascending reticular activating substance (ARAS) of the brain stem
- cerebral cortex

The ARAS determines arousal, which is shown by the phenomena of awakening with eye opening, motor responses and the possibility of verbal communication. The cortex is responsible for the content of consciousness (the combination of psychological responses to feeling, emotions and mental activity).

Unconsciousness is a condition of being unaware of one's surroundings and/or unresponsive to stimulation. It could be due to a variety of causes.

Altered consciousness includes all stages in which normal consciousness is altered, either qualitatively or quantitatively. There are many types of altered consciousness; confusion, somnolence, stupor, delirium, coma.

- **Coma:** A state of unarousable unconsciousness without any psychologically understandable response to external stimuli or inner need. Patients may appear to be asleep, and are incapable of responding normally to external stimuli other than by eye opening, flexion or extension of the muscles in the limbs or occasionally grunting or groaning in response to pain.
- **Stupor:** Strong external stimuli can temporarily/transiently restore partial wakefulness. The patient falls back into stupor as soon as the stimulus is removed.
- **Somnolence (lethargy):** Drowsy but requires only moderate stimuli for arousal. Once awake, the patient speaks and acts slowly, but otherwise normally.
- **Delirium:** An altered state of conscious characterised by restlessness, hallucination, disorientation, delusions. Patients are often frightened and irritable.
- **Confusion:** Bewildered patients who have difficulty following commands; disorientation to persons, in place and time; disturbed memory. Drowsiness is common and may alternate with night-time agitation.
- Delirium is an abnormal mental state reflected in disorientation, fear, and misperception of sensory stimuli. It is often accompanied by visual hallucinations. Delusion, a personal belief not based on reality, such as paranoia, also occurs in some psychotic states.

Coma is the most severe form of altered consciousness and is life threatening. Any type of altered consciousness can, depending on the cause, progress to coma. Early evaluation and diagnosis is therefore essential in any type of altered consciousness. Coma results from either damage to the ARAS or from extensive damage to both cerebral cortices. Localised lesions of the hemispheres, such as infarcts, haemorrhages or tumours result in focal neurological deficits, and for coma to occur, the damage has to be extensive.

For practical purposes, the causes of coma can be divided into structural causes, and non-structural (metabolic, toxic) causes.

Structural causes	Non-structural causes
Mass lesions: Acute lateral shift of the brain due to haemorrhage or oedema, results in either herniation and compression of the brain stem, or compression of both hemispheres.	Electrolyte imbalance: hyponatraemia or hypernatraemia, hypocalcaemia or hypercalcaemia, hypophosphataemia or hypomagnesaemia.
Trauma	Hypoglycaemia, hyperglycaemia, diabetic ketoacidosis
Primary or secondary neoplasms	Hypothyroidism, Addisons disease
Cerebral abscess with mass effect	Organ failure: uraemic encephalopathy, hepatic encephalopathy, post-cardiac arrest anoxic encephalopathy
Extensive cortical infarction or brain stem infarction with involvement of the ARAS	Infections: encephalitis, meningoencephalitis, cerebral malaria, severe sepsis
Increased intracranial pressure, e.g. hypertensive encephalopathy	Toxin induced: drug overdose, ethanol.
	Deficiency states: pellagra, Wernickes
	Post epileptic , non-convulsive status
	Hypothermia, hyperthermia
	Psychogenic states
	Vascular: hypertensive encephalopathy, DIC, Systemic vasculitis, TTP

How do you differentiate between structural and non-structural causes?

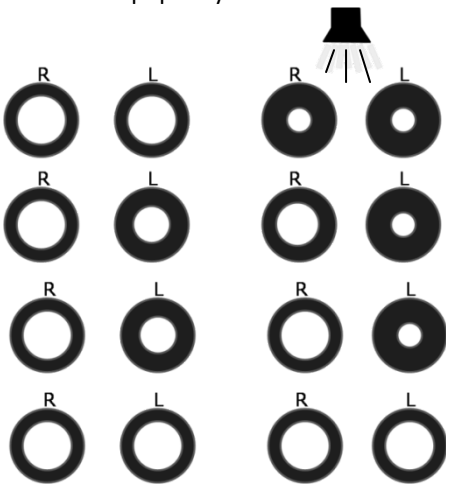
It is important to identify structural causes for the simple reason that they might require surgery. Look for

- Focal neurologic deficits such as unilateral weakness, flaccidity.
- Unilateral dilated non-reactive pupils.
- Evidence of increased intracranial pressure.

However, there are exceptions; patients with hepatic encephalopathy can develop increased intracranial pressure. Barbiturate poisoning can result in fixed, non-reactive pupils.

A brief, relevant neurological examination should be performed as follows;

- Talk to the patient;
  If there is no response,
- Test the response to painful stimuli, such as pressing firmly on the fingernail bed or sternum
- Check pupillary size and reaction to light



Pupils equal and react equally to light.
Normal

Left pupil normal and reacts to light.
Right pupil wide, reacts sluggishly.
Right sided mass lesion.

Left pupil reacts normally. Right pupil fixed and dilated.
Worsening increased intracranial pressure, coning imminent.

Both pupils fixed and dilated
Brain death likely.

- Evaluate the patient's degree of coma on the **Glasgow Coma Scale.** This is based on assessing the **BEST** eye, verbal and motor response to verbal or painful stimuli. The GCS is given as a score out of 15. The minimum is, obviously, 3.

Eye (E)	Spontaneous	4
	To voice	3
	To pain	2
	None	1
Verbal response (V)	Oriented	5
	Confused	4
	Inappropriate words	3
	Incomprehensible sounds	2
	None	1
Motor response (M)	Follows commands	6
	Localises pain	5
	Withdraws from pain	4
	Abnormal flexion	3
	Abnormal extension	2
	None	1

- Look at the pattern of breathing
  Cheyne-Stokes breathing is an abnormal pattern of breathing characterized by periods of breathing with gradually increasing and decreasing tidal volume interspersed, as the brain trys to compensate quickly for changing serum partial pressure of oxygen and carbon dioxide. It usually suggests serious brain injury, and is seen close to death.

  Kussmaul's breathing, or air hunger, where deep and rapid regular breathing is seen, is a feature of acidosis. It is often seen in diabetic ketoacidosis.

- Assess eye movements. Look for spontaneous eye movements, resting eye position and dolls eye movements.

Look for the ABC : airway, breathing, circulation.

If the GCS is below 8, the patient must be intubated and ventilated. Patients who are comatose are unable to protect their airway, and can aspirate.

Airway: Evaluate the airway and protect the cervical spine, if there is a suspicion of possible cervical spine injury. Assume and check for signs of upper airway obstruction, open airway; administer oxygen immediately. Document the oxygen saturation by pulse oximetry. If ventilation remains inadequate despite clearing the upper airway by suctioning, perform mask ventilation and proceed to tracheal intubation.

Breathing: Use auscultation, percussion, and palpation to rule out or confirm pathology which may interfere with oxygenation and ventilation, such as pneumothorax, haemothorax and flail chest. If there is any relevant pathology it should be treated before proceeding to an assessment of the circulation.

Circulation: Hypotension is a significant cause of secondary brain injury. The blood pressure should be maintained to ensure adequate cerebral perfusion pressure. Restore circulating volume with normal saline solution. A systolic arterial pressure equal to or higher than 100 mmHg is adequate and safe for most patients. Note that hypotension itself, can be a cause of coma.

Check for neck stiffness (suggestive of subarachnoid haemorrhage, meningitis).

Look at the optic fundus. *What do you look for?*

Papilloedema – evidence of increased intracranial pressure, space occupying lesions

Subhyaloid haemorrhage – suggestive of subarachnoid haemorrhage. Rare but pathognomonic.

Hypertensive changes, diabetic changes – if a history is not available, these might help in determining the patient's past history.

Check the patient's blood glucose. If the blood glucose is low, a bolus dose of 50ml 50% glucose must be given. If the patient is suspected to be thiamine deficient (malnourished, alcoholic), then thiamine must be given before the glucose, or else Wernicke's encephalopathy may be precipitated.

If the patient is having repeated generalised seizures, then it is important to stop the fits. Repeated generalised seizures causes brain damage.

Altered consciousness

The recommended drug is **Lorazepam 0.1mg/kg IV**

After initial evaluation, a detailed history must be taken to identify a possible cause for altered consciousness, bearing in mind the list of possibilities listed above. Since the patient will not be in a position to give a history, a history must be sought from bystanders, relatives, paramedics, the police etc. Ask about the following;

- Witnessed events? Falls, trauma, fits.
- Evolution of coma? Rapid, slow, accompanied by complaints like headache, vomiting.
- Recent medical history: surgical procedures, infections, current medication.
- General medical history.
- Psychiatric history.
- Access to drugs: sedatives, psychotropic drugs, narcotics, illicit drugs, empty medicine bottles, drug paraphernalia.

The general examination may give some clues. Examine for evidence of trauma, especially head injury. The smell may give a clue – alcohol, organophosphates. Look for injection marks (IV drug abuse), cut injuries, self mutilation etc. In Addisons disease, there may be marked pigmentation. The patient may have typical clinical features of myxoedema. Look for evidence of sepsis; cellulitis, abscesses, pneumonia, sinus tenderness.

Management

Having looked for and if necessary corrected the blood glucose level, the next thing to be considered is a drug overdose. This is a very common cause of admission with coma. Unless the patient has evidence of trauma or an obvious cerebrovascular event, you should assess and treat for opioid or benzodiazepine overdose, these being the most likely to cause coma.

Having stabilised the patient, the following laboratory tests must be requested. Given the wide range of possible causes, many other tests may be required, but these would be the basic tests to start off with.

- Serum electrolytes- hyponatraemia or hypernatraemia, both of which could be due to a variety of causes. If hyponatraemia is present, urinary and serum osmolality should be checked.

- Full blood count – an elevated white blood cell count, with high neutrophils will suggest– infectious causes and sepsis. The platelets may be low in sepsis and viral thrombocytopaenias such as Dengue.
- Liver function tests – elevated transaminases and bilirubin will be seen in liver failure; serum ammonia should be done if liver failure is suspected.
- Blood urea and serum creatinine – acute renal failure
- Arterial blood gas analysis – hypoxia, acidosis, hypercapnoea
- If poisoning is suspected, a urinary toxicological screen will be required.

If myxoedema coma (hypothyroid appearance, slow relaxing ankle jerks) is suspected, or if the patient is hyponatraemic, a TSH test should be done. If the patient is pigmented, suspect Addisons disease, and do a random serum cortisol. In Addisons disease, the patient will often present with hypotension. Serum electrolytes will show a low sodium and upper range potassium, with low blood glucose levels. If liver failure is suspected, derangement of clotting maybe present; do a prothrombin time.

Conditions which result in low platelets (below 10000/mm2) and coagulation abnormalities may cause intracranial bleeding.

CT scan brain: A CT scan brain is essential in any patient with altered level of consciousness. A non-contrast CT scan brain will help in identifying a haemorrhage, and is essential. If possible, this should be followed by a contrast CT brain, to identify other causes such as infarcts and space occupying lesions (Tumour, abscess)

If there is a history of fever, headache, seizure, with or without neck stiffness, then a lumbar puncture is required. If there is suspicion of raised intracranial pressure (papilloedema, focal neurological signs), then a CT scan must be done first to assess the risk of herniation.

What to look for in a lumbar puncture and CSF examination:
Opening pressure, appearance, red blood cell count, white blood cell count, differential, CSF glucose, CSF protein, CSF gram stain, CSF for growth of microorganisms. Some extra fluid should be taken for special studies if necessary, such as viral studies, electrophoresis.

If meningitis or cerebral abscess is suspected, intravenous antibiotics should be started immediately.

EEG: If the patient has had seizures, an EEG must be done. Sometimes, seizure activity can be present in the brain without apparent seizures, resulting in coma – known as non-convulsive seizures. This can only be diagnosed by an EEG. Diffuse slowing in the EEG may indicate metabolic encephalopathy. Triphasic waves suggest hepatic encephalopathy. Periodic lateralized epileptiform discharges suggest herpes simplex encephalitis. Finally, an EEG might be necessary to confirm brain death.

ECG: An ECG may show evidence of a recent myocardial infarction or arrhythmia which could have resulted in a cardiac arrest with hypoxic brain damage. Atrial fibrillation might suggest the possibility of an embolic stroke.

Hypothermia may be seen in Wernicke's encephalopathy, drug overdose, near-drowning, hypothyroidism, or profound sepsis.

Hyperthermia usually occurs in infection, and meningitis, encephalitis, cerebral abscess, and malaria, should be considered. It also occurs in subarachnoid haemorrhage, intracranial haemorrhage, anticholinergic drug overdose and heat exposure.

Non structural causes need ICU monitoring and care. Sometimes a cause cannot be found. Cerebral vasculitis, HIV related conditions need to be considered.

The management of individual conditions is dealt with in the relevant sections.

Stroke

Acute stroke is a medical emergency. Early revascularisation therapy can even reverse primary damage, and careful management can minimise secondary damage.

Stroke is a focal neurological deficit of vascular origin.

Classification

- Transient brain ischaemia (transient ischaemic attacks): arbitrarily defined as a focal neurological deficit of vascular origin lasting less than 24 hours. Mostly due to embolism and the majority last less than 30 minutes.
- Ischaemic stroke: due to thrombosis or embolism of a cerebral vessel, or due to severe systemic hypotension. Risks factors for thrombotic stroke are similar to those of acute myocardial ischaemia. Embolic stroke is caused by emboli from cardiac sources (chronic valvular heart disease, old myocardial infarction, atrial fibrillation, endocarditis) or from the main extracranial vessels (carotid or vertebral atherosclerotic plaques. Systemic hypotension can result from cardiogenic, septic or hypovalaemic shock.
- Haemorrhagic stroke: due to intracranial bleeding from arterioles or small arteries. Causes are hypertension, bleeding tendency, amyloid angiopathy, and ruptured intracranial aneurysms. Bleeding from a tumour is a rare cause.
- Subarachnoid haemorrhage: due to rupture of a berry aneurysm in the circle of Willis.

Once an area of the brain loses its blood supply, death of neurons ensue rapidly. Early revascularisation will minimise death of neurons. 'Time is brain'. The area surrounding the stroke is known as the ischaemic penumbra, and is very susceptible to secondary damage. Careful management of perfusion and oxygenation, temperature, glycaemic control and electrolytes will prevent further damage to the ischaemic penumbra.

The main aims of management of acute stroke are:

- Determine the type and cause of acute stroke.
- If due to ischaemic stroke, decide if thrombolysis is indicated.
- Prevent early recurrences.
- Monitor and treat factors which will improve outcome –look after the ischaemic penumbra.

Initial evaluation

Resuscitate the patient. Check ABC.

Take a quick relevant clinical history from the patient or relatives. The patient maybe unable to give a clear history due to reduced level of consciousness or dysarthria / dysphasia.

In most cases, the onset of weakness will be sudden. The presence of headache, with nausea and vomiting suggests haemorrhage, though many patients with haemorrhage may not complain of headache. Severe occipital headache of very sudden onset, with vertigo and sometimes loss of consciousness is characteristic of subarachnoid haemorrhage. Transient loss of consciousness is more common in haemorrhage but can occur in any stroke. In general, the relationship of the level of consciousness to the neurologic deficit will give an idea of the type of stroke. Most infarcts occur in the internal capsule, and such infarcts will cause significant neurological weakness without affecting the level of consciousness. A reduced level of consciousness with unilateral weakness occurs either with a massive cortical infarct, haemorrhage, or a brain stem infarct or haemorrhage.

Ask for a history of trauma to the head. Relevant past medical history includes smoking, hyperlipidaemia, hypertension, diabetes mellitus, ischaemic or valvular heart disease, arrhythmias (embolic stroke), malignancy, headaches or seizures (brain tumour, AV malformation), liver disease, chronic renal disease, coagulopathy, recent surgery (possible contraindication to thrombolysis). The presence of widespread malignancy may preclude the benefit of aggressive therapy. History of bleeding diathesis or warfarin therapy may indicate the possibility of a bleed.

Draw blood for basic investigations: blood glucose, full blood count, PT, APTT, liver function tests, renal profile, serum lipids, and cardiac troponin. Obtain a 12 lead ECG. Monitor the patient's vitals and pulse oxymetry.

Why cardiac troponin?
Stroke may have occurred as a result of a cardiac event (shock or arrhythmia) resulting in a period of hypotension.

Start a slow IV drip
Quick neurological examination should include the following:

- Level of consciousness (see section on *Altered consciousness)*
- Neck stiffness, Kernig's sign – positive in SAH
- Pupils, visual field, gaze -helps to lateralise stroke. Pupillary irregularities may suggest increase intracranial pressure.
- Dysphasia, apraxia, orientation
- Facial and limb pareses, reflexes – crossed hemiplegia is due to infarction of the pons. If the patient is unconscious, muscle tone and reflexes may be helpful in localisation.
- Coordination, gait - cerebellar involvement
- Fundoscopy – papilloedema (? Intracranial space occupying lesion), sub-hyaloid haemorrhage (SAH)

Examination of other systems:

- Cardiovascular – blood pressure, pulse (Is there atrial fibrillation?), bruits over carotids, cardiac murmurs.
- Respiratory – Is there pulmonary oedema? Has the patient aspirated?
- Abdomen – polycystic kidneys –associated with hypertension, berry aneurysms.

The following patients with stroke require ICU care:

- The presence of severe impairment of vital functions such as respiratory problems, severe bradycardia, tachycardia and arrhythmias, severe hypo or hypertension
- Patients in whom thrombolysis is indicated
- Subarachnoid haemorrhage
- ICH with reduced level of consciousness, cerebellar haemorrhage
- High risk lesions: basilar occlusion/brainstem infarction, large hemispheric stroke, cerebellar infarction

The common patterns of neurologic deficit and the likely arterial supply involved are given in the table.

Artery	Functional importance
Anterior cerebral artery	UMN leg>arm; cortical sensory loss leg only; urinary incontinence
Middle cerebral artery **Main Branch** **Infarction of middle third of hemisphere** **Perforating artery** **Internal capsule infarction**	UMN face, arm>leg; homonymous hemianopia; aphasia or non-dominant hemisphere signs (depends on side); cortical sensory loss UMN face, UMN arm>leg
Posterior cerebral artery **Infarction of thalamus and occipital cortex**	Hemianaesthesia (loss of all modalities);homonymous hemianopia (complete)
Basilar artery	Occlusion results in quadriplegia and death unless there are good anterir collaterals
Posterior inferior cerebellar artery	Lateral medullary syndrome, usually secondary to occlusion of the vertebral artery from which it arises

Management

Administer oxygen by face mask. Aim at keeping the oxygen saturation over 96%.

If the patient's level of consciousness is reduced, take all precautions to prevent aspiration. Place in the left lateral position; insert an airway and nasogastric tube. Intubate if unable to maintain airway.

Circulation: Cerebral blood flow is dependent on blood pressure. Cerebral blood flow must be maintained at an optimal level. If the blood pressure is too high, it may 'flood' the ischaemic penumbra resulting in oedema and cellular hypoxia. If too low, the vessels may dilate, leading to 'stealing' from the penumbra, worsening ischaemia.

In ischaemic stroke, the blood pressure should be maintained between 160-220/95-120mmHg. There is no need to start antihypertensives if the blood pressure is below 220/120mmHg. If the patient has been on

antihypertensives previously, they should be continued unless the blood pressure is low. Hypotension must be treated, with IV fluids, and if necessary, inotropes.

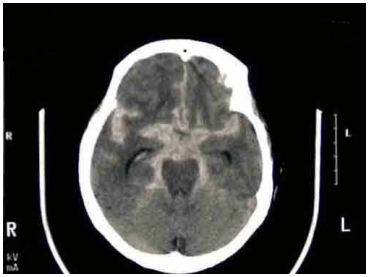
In intracranial haemorrhage, the systolic blood pressure should be reduced to between 140-160mmHg. IV nitroprusside, nitrates or labetalol maybe used to lower the blood pressure to target levels. The management of blood pressure in SAH is dealt with separately.

Arrhythmias may be present and need treatment only if they result in low blood pressure. Atrial fibrillation does not need immediate treatment unless the rate is very high and compromise blood pressure. Bradyarrhythmias may result in a drop in blood pressure, and temporary cardiac pacing maybe required.
Certain conditions warrant tight control of blood pressure - aortic dissection, hypertensive encephalopathy, severe heart failure, acute myocardial infarction or unstable angina. (See section on *Hypertension*)

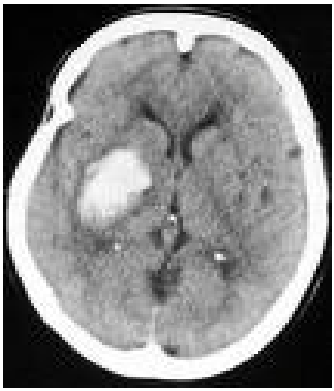
Body temperature: normal body temperature must be maintained, to minimise damage to the ischaemic penumbra. Fever must be treated with antipyrexial agents (paracetamol).
Normoglycaemia must be maintained. If necessary, a glucose-insulin infusion should be commenced.
Urgent CT scan must be performed. The main purpose of this, is to exclude an ICH. The following makes an ICH more likely;

- Very rapid onset and progression of symptoms
- Early profuse vomiting
- Loss of consciousness
- Very high blood pressure, or onset during hypertensive crisis

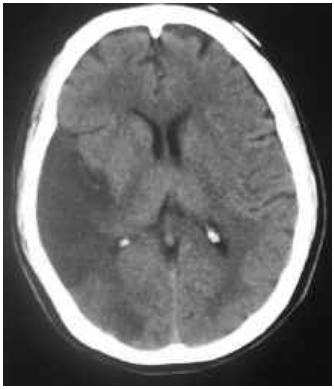
A non-contrast CT brain is the most appropriate initial investigation.
Non contrast CT scan will show an ICH immediately. An infarct may take up to 24 hours to become apparent on a non contrast CT. However, once a haemorrhage is excluded, therapy can begin. Contrast CT will pick up an infarct earlier, but it is difficult to differentiate a haemorrhage. MRI will diagnose both haemorrhage and infarct early, but is more expensive, and takes longer to arrange and to perform. A CT scan will take around 10 minutes, where as an MRI takes around 45 minutes to an hour. Shorter duration is an advantage, especially if the patient is unstable.



CT scan appearance of a subarachnoid haemorrage



CT scan appearance of an intracerebral haemorrage



CT scan appearance of a cerebral infarction

In confirmed ischaemic stroke, the indications and contraindications for thrombolysis are as follows;

INCLUSION CRITERIA	**EXCLUSION CRITERIA**
Clear onset of symptoms within 3 hours	Onset >6h
Onset of symptoms between 3-6h*	Time of onset unclear*
Cranial CT excluding intracerebral haemorrhge	Extended infarction of more than 1/3 of the MCA territory(early signs in cranial CT)
	Severe neurological deficit with fixed conjugated eye deviation, hemiplegia and reduced conscious level
	Increased bleeding risk such as: Recent surgery, pregnancy, metastases, bacterial endocarditis, recent gastrointestinal bleeding
	Rapid improvement in signs during the diagnostic procedures
	Arterial blood pressure > 190/100 refractory to antihypertensive treatment
	Pre-existing oral anticoagulation (antiplatelet agents: no contraindication)
	Severe subcortical arteriosclerotic encephalopathy (SAE)
	Age limits are controversial; there may be beneficial effects even in patients >80 years

(*relative)

Thrombolysis: rtPA is the drug of choice. Dose: 0.9 mg/kg; maximum of 90 mg. Administer through a peripheral vein. 10% of the drug should be given as a bolus, the balance being given over 90 minutes by infusion pump. Intra-arterial thrombolysis can be given in specialised centres.

If the patient shows any neurological deterioration after thrombolysis, an urgent repeat non-contrast CT brain should be performed to exclude a bleed.

Further management
Once the initial management is complete, attention should be given to the following:

Assessment of swallowing: Usually performed by giving the patient small amounts of water to drink. If the patient coughs, a nasogastric tube should be inserted and the patient fed through it for the first 2 weeks after the stroke. If the patient is able to tolerate fluids, feeds maybe given orally.

If evidence of aspiration is present, IV antibiotics should be given. Co-amoxyclav is a suitable antibiotic.

The presence of visual field defects and aphasia make rehabilitation more difficult. Limb physiotherapy should be commenced early. Speech therapy maybe required, if dysphasia is present.

Other complications which may occur include urinary tract infections, decubitus ulcers and deep vein thrombosis. Urinary tract infections should be treated with appropriate antibiotics according to culture. Decubitus ulcers occur in relatively immobile patients, with severe neurologic deficit. Proper nursing with frequent turning of the patient and the use of an air mattress will prevent them. Low molecular weight heparin given subcutaneously and pressure stockings to the legs will prevent DVT.

Seizures: While there is no indication for prophylaxis to prevent seizures, should seizures occur after an acute stroke, treatment is necessary. IV lorazapam is the drug of choice for acute seizures, followed by phenytoin or carbamazepine orally.

Haemorrhagic transformation of an infarct may occur, especially after thrombolysis. Usually, it has no serious clinical effects, and can be managed conservatively. Anticoagulants and antiplatelets must be stopped. Large bleeds may need surgical evacuation.

Increased intracranial pressure occurs in haemorrhages, and in large infarcts where swelling of the infarct occurs. CT scan will help confirm the presence of cerebral oedema and midline shift. Clinically, the patient will show deterioration of consciousness. Untreated increased ICP will result in coning and brain stem death. The aim is to maintain cerebral perfusion pressure. Invasive intracranial pressure monitoring is necessary.

Cerebral perfusion pressure = mean arterial pressure – intracranial pressure

Hence, to maintain CPP, the following measures should be instituted;

- Careful blood pressure control – lower only if systolic blood pressure >220mmHg or diastolic blood pressure >120mmHg.
- Avoid hypovolaemia; give adequate volumes of crystalloids and colloids.
- Hypotension must be treated. If decreased systemic vascular resistance is present, vasopressors such as dopamine and noradrenaline maybe necessary.
- In patients with impaired cardiac output, consider dobutamine.
- The head should be kept straight at 20-30%
- Ensure adequate pain relief. Avoid noxious stimuli which can provoke a rise in blood pressure.
- Fever should be treated vigorously
- Correct hyponatraemia
- Give mannitol
- Short acting barbiturates such as thiopentone are useful where rapid reduction is necessary when mannitol has not had effect.
- Hyperventilation – blood and CSF alkalosis induces cerebral vasoconstriction, and reduces cerebral oedema
- Mild hypothermia (33 centrigrade) also lowers ICP
- Steroids are of no benefit
- Surgical decompression is necessary in extreme cases

In posterior fossa infarcts and haemorrhage, and in ICH and SAH where blood has tracked into the aqueduct, obstructive hydrocephalus can occur. A ventriculo-peritoneal shunt is required.

Secondary prevention

Aspirin: doses of 150 to 1500mg daily have, in various trials, shown to be effective in secondary prevention. Dipyridamole or clopidogrel may give additional benefit.

In embolic stroke, where a source of cardiac or arterial embolisation has been identified, and in atrial fibrillation, anti-coagulation is necessary. IV Heparin should be commenced aimed at maintaining the APTT twice normal and warfarin should also be commenced, targeting an INR around 2-3. Carotid stenosis greater than 70% in the artery of the affected territory is an indication for carotid endarterectomy. Statins reduce the risk of repeat stroke. Smoking cessation is essential.

What is the differential diagnosis of stroke?

- Tumour – slow onset of neurological features, early morning headaches with vomiting, headaches worsening with anything which increases intracranial pressure (laughing, sneezing, coughing, straining), papilloedema.
- Venous sinus thrombosis – headache, seizures. Risk factors: thrombotic tendency, vasculitis, severe hyperglycaemic states, dehydration, malignancy, head or neck trauma.
- Meningitis – fever, neck stiffness.

Subarachnoid haemorrhage

Diagnosis is suspected on the clinical history and is confirmed by non-contrast CT scan, which shows blood in the subarachnoid space. Lumbar puncture is performed if the clinical suspicion is high but the CT normal. CSF contains blood in the early stages and xanthochromia later on.

ECG changes suggestive of cardiac ischaemia may occur after an SAH (see section on *Acute myocardial ischaemia)*

An immediate carotid angiogram is necessary to identify the aneurysm.

Prevention of cerebral oedema: as detailed above, steps should be taken to optimise cerebral perfusion and reduce increased intracranial pressure.
The blood pressure should generally be controlled to 140mmHg. Take care not to drop the blood pressure too much, especially in patients who have reduced level of consciousness, as cerebral perfusion pressure may drop.

After an SAH, secondary cerebral damage occurs due to secondary vasospasm. Nimodipine has been shown to improve outcome in SAH, presumably by reducing cerebral vasospasm. Treatment should be started within 4 days of the event, at a dose of 60mg daily orally, and continued for 21 days.

The risk of rebleeding is high. Hence, surgery for the aneurysm is often essential, unless the patient's condition is too unstable or the patient has already suffered severe cerebral injury. Early surgery (between 48-72 hours) is preferred, before rebleeding occurs. Placement of a clip across the neck of the aneurysm is the treatment of choice.

Complications and their management

- Re-bleeding – poor prognosis.
- Hyponatraemia due to SIADH or cerebral salt wasting. The two are managed differently.
  Cerebral salt wasting is characterized by volume depletion, which leads to the release of ADH. It is usually treated with isotonic saline - restoration of normo-volaemia will suppress the release of ADH and allow the excess water to be excreted. Patients with SIADH are normo-volaemic; since water restriction is not desirable in SAH, the hyponatremia is treated with isotonic saline or, if necessary, hypertonic saline.
- The risk of seizures is high, and prophylactic anti-epileptics should be continued for at least 6 months.
- Obstructive hydrocephalus will require a ventricular shunt.

Neuromuscular disorders

Neuromuscular disorders in the ICU can be classified as:

- Primary neuromuscular disorders which require ICU care, particularly because of involvement of respiratory muscles.
- Neuromuscular disorders which develop in patients in the ICU for other conditions.

Involvement of the respiratory muscles leading to ventilator failure may require assisted ventilation, or may delay weaning from ventilation. Neuromuscular disorders may also delay mobilisation, increase the risk of pneumonia and delay transfer out of the ICU. Neuromuscular disorders can also be missed while the patient is in the ICU, and hence can result in readmission and even death in the wards.

Diseases of the upper motor neuron do not usually cause ventilatory failure. Neuromuscular weakness arises due to disorders in the motor unit. The motor unit is composed of the alpha-motor neuron (located in the anterior horn of the spinal cord or brain stem nuclei), the axon, the neuromuscular junction, and the muscle fibres innervated by a single neuron. Different conditions affect each of these components.

Localisation of the defect

Anterior horn cell	Peripheral nerve	Neuromuscular junction	Muscle
Muscle tone increased or decreased. Muscle wasting present. Fasciculations present. Tendon reflexes depressed or absent, or maybe increased in MND. Weakness variably distributed. Sensory deficits absent.	Predominantly distal weakness and wasting. Symmetrical in generalised neuropathies. May be asymmetrical (e.g. in diabetes). Reduced tone. Reflexes usually absent. Autonomic dysfunction. Sensory deficits often present.	Distribution varies. Reduced tone. Reflexes diminished. Fatigability . Sensory deficits absent	Distribution varies, but often predominantly proximal weakness. Reflexes usually preserved. Sensory deficits absent. Maybe associate with pain, and muscle tenderness

Specific investigations in neuromuscular disease

- Serum Creatine Kinase (CPK) and myoglobin: elevated in myopathies, grossly elevated in rhabdomyolysis and polymyositis.
- Elevated ESR and CRP: suggest inflammatory process (inflammatory myopathies, vasculitis, severe sepsis)
- Chest radiograph: to exclude lung cancer – Eaton-Lambart Syndrome, paraneoplastic neuropathy
- CT scan and MRI brain: maybe needed to exclude alternative diagnoses
- CSF analysis: cytoprotein dissociation in Guillain-Barré syndrome. Useful to exclude other conditions such as meningitis, HIV infection.
- Neurophysiological studies:
    - Nerve conduction velocities: slowed nerve conduction occurs in demyelination, eg- Guillain-Barré syndrome.
    - Compound muscle action potential (CMAP): Reduction suggests a loss of motor nerve or neuron function, or sometimes a loss of muscle bulk.
    - Repetitive stimulation: Decrement suggests neuromuscular failure due to persistence of NMBAs or myasthenia gravis. It may also be used to monitor the response to edrophonium in myasthenia gravis.
    - Electromyography (EMG): In myopathy, short duration low amplitude potentials occur, while in neuropathy, fibrillation potentials and positive sharp waves are present.
    - Single-fibre electromyography (SFEMG): demonstrates increased fluctuation ('jitter') in myasthenia gravis. Useful when there is doubt about the diagnosis.
    - In disease of the neuron, the amplitude of the nerve action potential will be low, and conduction velocity is

normal. In demyelinating conditions, the amplititude is normal, and conduction velocity is reduced.

- Muscle biopsy: not often useful, except in diagnosing severe inflammatory myopathy which may warrant treatment with steroids.

- Spirometry: the following are urgent indications for ventilation:

- Vital capacity – less than 1 litre or

- Negative inspiratory force – less than minus 20cmH2O

- If spirometry is not available, the single breath count can be used. The patient is asked to take a deep breath and count to 20. Inability to do so indicates a vital capacity of less than 1 litre.

- Arterial blood gases – unreliable in deciding on the need for ventilation in neuromuscular weakness.

Decision to ventilate should be made on the clinical condition of the patient, and the vital capacity and negative inspiratory force, and should not be delayed because of normal blood gases.

Other tests which are useful in individual conditions are discussed in the relevant sections.

Conditions affecting different parts of the motor unit:
Motor neuron: 3 conditions cause disease of the motor neuron – poliomyelitis, tetanus and motor neuron disease (amyotrophic lateral sclerosis). Characteristically, sensory loss is absent.

Motor neuron disease: This is a degenerative disorder, ultimately fatal. Degeneration occurs in the upper motor neurons in the corticospinal tracts, and the lower motor neurons in the brain stem nuclei and spinal cord, thus characteristically resulting in a combination of upper and lower motor neuron signs in the same myotome – for example flaccid weakness, wasting, with brisk reflexes and up going plantars. Muscle fasciculations are prominent, due to formation of giant motor units. The onset is usually in the 6^{th} decade and the condition is fatal within 2 years in most cases. A tropical

variant with longer survival has been identified. Diagnosis is by exclusion of other disorders. Respiratory muscle weakness or pneumonia may necessitate ICU admission, but at this stage of the illness ventilation is futile, unless the patient has developed concurrent illness which is reversible. Riluzole, a glutamate release inhibitor, may prolong survival for around 3 months and may make weaning possible.

Poliomyelitis: New cases are extremely rare, thanks to the effective vaccination program. Typically presents with asymmetrical flaccid weakness and wasting. A significant number of patients have post-polio sequelae. New or progressive disability occurs in a minority of patients, usually decades after the disease itself. These new symptoms are quite variable, and include increased muscle weakness, focal or generalized muscle atrophy, fatigue, pain, and decreased ambulatory abilities. Respiratory muscle paralysis and swallowing difficulty may occur.

Tetanus: Much less common now because of effective vaccination. Caused by the toxin of the anaerobe *Clostridium tetani.* Infection occurs in contaminated wounds. Tetanospasmin blocks neuro transmission in the brain and spinal cord. Disinhibition of neurons that modulate excitatory impulses from the motor cortex results in disinhibition of anterior horn cells and autonomic neurons. Hence, increased muscle tone, painful spasms and widespread autonomic instability occurs. Prolonged mechanical ventilation may be required. Other treatments are:

- Wound debridement to remove Clostridium spores and necrotic tissue.
- IV penicillin to eradicate the organism. Cephalosporins are alternatives.
- Neutralisation of toxin with human tetanus immunoglobulin.
- Sedatives (benzodiazepines) are generally effective in controlling spasms.
- Neuromuscular blocking agents maybe required. Vecuronium infusion is preferred, as it is associated with less autonomic instability.
- Magnesium sulphate is an effective treatment for autonomic instability. It acts as a presynaptic neuromuscular blocker, blocks catecholamine release from nerves, and reduces receptor responsiveness to catecholamines.

- Active immunisation with tetanus toxoid is necessary, as the disease does not confer immunity.

Peripheral nerve: Polyneuropathies present as symmetrical flaccid paralysis, with wasting and absent reflexes. Respiratory muscle involvement can occur. It may be associated with sensory loss, cranial nerve involvement, and autonomic neuropathy.

Causes of polyneuropathy in ICU
Prolonged critical illness, sepsis, multi-organ failure
Metabolic or nutritional • Alcohol • Diabetic neuropathy • Uraemia • Porphyria • Vitamin B12 deficiency • Chronic malnutrition
Infections • Bacterial:Leprosy, Lyme disease, Diphtheria • Viral :CMV, Hepatitis, HIV
Drug induced: nitrofurantoin, isoniazid, vincristine, cisplatin, reverse transcriptase inhibitors)
Immune mediated: Acute inflammatory demyelinating polyneuropathy
Vasculitis – polyarteritis nodosa, Churg-Strauss
Toxins • Heavy metals: arsenic, thallium, lead, gold • Organophosphates • Hexacarbons • Shellfish (sasatoxin)
Paraneoplastic neuropathy – this can occur with a variety of malignancies, especially lung cancer, breast cancer and bowel cancer.

Management of polyneuropathy depends on the cause. Offending drugs should be stopped. Pralidoxime may be of use in organophopate poisoning. Vitamin B12 should be given if deficiency is likely. Dialysis will help in patients with uraemic polyneuropathy. Vasculitis will require pulsed steroids

and other immunosuppressants such as cyclophosphamide and cyclosporine. Paraneoplastic neuropathy may respond to resection of the tumour, or radiotherapy /chemotherapy.

Guillain-Barré syndrome: Acute demyelination occurs following an inflammatory process. Usually preceded by bacterial (Campylobacter) or viral infection. Classically, weakness occurs symmetrically in the legs and progresses proximally. Respiratory muscle paralysis will require ventilation. Bilateral facial nerve weakness can occur.

Diagnosis: Nerve conduction tests show a demyelinating neuropathy. Sometimes an axonal neuropathy is seen, with poorer prognosis. CSF examination done during the second week of illness shows the classical cyto-protein dissociation – elevated proteins with normal cell count. Antibodies against GQ1b ganglioside are associated with the Miller-Fisher variant, where ophthalmoplegia with ataxia and areflexia occurs.

Treatment: Either plasma exchange or intravenous immunoglobulins are equally effective. Intravenous immunoglobulin is given for five days at 0.4 gram/kg per day. Acute renal failure is a complication. Plasma exchange is usually given for four to six treatments over eight to 10 days, for a total of 200 to 250 mL/kg. Hypotension, electrolyte imbalance and IV access are associated problems. Corticosteroids have no clear place. Supportive treatment is equally important.

- Ventilation: 30 % of patients need ventilatory support. Atelectasis due to poor respiratory effort can hasten respiratory failure, and chest physiotherapy must commence early. Inability to stand, to cough, or to lift elbows or head may predict the need for ventilation, and the following are indications for intubation and ventilation-
    - Forced vital capacity <20 mL/kg
    - Maximum inspiratory pressure <30 cmH2O
    - Maximum expiratory pressure <40 cmH2O

      Because the patient may have inadequate ventilator effort to trigger the ventilator, assist-control may be the preferred mode at the start. This can later be changed to SIMV. (See section on Ventilation) Tracheostomy may be necessary if the patient cannot be weaned after 2 weeks.

- Management of autonomic dysfunction is important
    - Quadriplegic patients should not be left unattended in the sitting position as they can have postural hypotension.
    - Intravascular volume should be maintained, particularly during positive-pressure ventilation.
    - Drugs which cause hypotension should be avoided.
    - Hypotension should be managed with IV fluids. Phenylephrine can be used if fluids are inadequate.
    - Episodes of severe hypertension (mean arterial pressure>125mmHg can be treated with labetolol, esmolol or nitroprusside.
    - Arrhythmias can occur during suctioning.
    - Succinylcholine should be avoided.
    - Catheterise if urinary retention occurs.
    - Nasogastric feeding is generally adequate- sometimes autonomic dysfunction can result in reduced gastric and intestinal motility, in which case parenteral nutrition is necessary.
- Give prophylaxis for deep vein thrombosis
- Start physical and occupational therapy early.
- Patients are usually alert, yet unable to move. Psychological support, especially talking to other patients who have recovered from Guillain-Barre syndrome is helpful.
- Pain relief – exquisite muscle tenderness can occur. The pain is neuropathic, and responds poorly to NSAIDs and paracetamol. Opiates maybe necessary. Gabapentin or carbamazepine is effective.

The majority recover completely. A few patients have persistent weakness, especially those with axonal neuropathy.

Critical illness polyneuropathy: This is a complication of severe sepsis. Axonal injury occurs, possibly following ischaemia due to injury to the vasa nervorum of distal nerves. It is associated with critical illness myopathy discussed below. Sensorimotor polyneuropathy occurs, with limb muscle weakness and atropy, diminished reflexes, and peripheral numbness. The cranial nerves are spared. Hyperglycaemia increases the risk of the condition. The main clinical effect is delay in weaning from the ventilator. Nerve conduction tests show diminished motor amplitudes suggestive of axonal neuropathy. CSF examination and creatine kinase is normal. No specific treatment is available, and spontaneous recovery occurs over weeks

to months. Tight glycaemic control with insulin has been shown to lower the incidence.
The main differential diagnosis is from Guillain Barre Syndrome (demyelinating pattern on nerve conduction tests, CSF shows cytoprotein dissociation), and critical illness myopathy (see below).

Neuromuscular junction: May be affected in myasthenia gravis, Eaton-Lambert syndrome, and botulism, and a variety of drugs.

Myasthenia gravis: Most patients will have an established diagnosis. The condition is characterised by intermittent weakness and fatiguability, involving, in order of severity:

- Ocular muscles – ptosis and diplopia
- Facial muscles
- Bulbar muscles – difficulty in swallowing, chewing, clearing secretions
- Upper limb girdle and respiratory muscles
- Limb muscles

The disorder is an autoimmune condition with acetylcholine receptor antibodies. These antibodies can be measured in the blood in 85% of patients. Thymic hyperplasia is present in most young patients and thymoma in 10%. The Edrophonium test, where administration of edrophonium reverses muscle weakness, is diagnostic. Bradycardia can occur; hence, test must be done in a setting where resuscitation facilities are available.
ICU admission is required for myasthenic crisis, post-surgical or postpartum exacerbation, or for management of cholinergic crisis.

Myasthenic crisis: Fast appearing deterioration in muscle strength. Occurs in undiagnosed patients and those on inadequate doses of anticholinesterases. Exacerbating factors include severe mental strain, infection, trauma, or surgery and certain drugs such as quinidine.
Treatment: Ventilatory support maybe necessary. Increase doses of anticholinesterase drugs (neostigmine, pyridostimine). Treat underlying infection. Rarely, plasma exchange or immunoglobulins may be necessary.

Post-operative patients: Patients with myasthenia after surgery are often admitted to the ICU. They usually need prolonged ventilatory support for 24-48 hours. Anticholinesterase drugs are withheld during the first 24 hours,

as they increase secretions and delay weaning. They can be re-introduced at lower doses after 24 hours. Weaning is done with careful clinical assessment and measurement of vital capacity. Although myasthenia is associated with thymoma, no immediate improvement is seen after thymectomy.

Cholinergic crisis: occurs in patients over treated with anticholinesterases. Increased salivation, colic, diarrhoea, sweating and small pupils are present, with worsening weakness and ventilatory failure. Anticholinesterases should be stopped for 24 hours, and gradually re-introduced at a lower dose.

Eaton-Lambert syndrome: Similar to myasthenia, without significant fatiguability. Associated with lung cancer, does not respond to anticholinesterases.

Botulism: Caused by ingesting food contaminated with *Clostridium botulinum*. Neurotoxins produced by the bacteria cause nausea, vomiting, double vision, slurred speech, difficulty in swallowing and widespread paralysis. There are no sensory symptoms or signs. Symptoms usually occur 1-3 days after ingestion. Respiratory paralysis can be quite prolonged. Treatment is with supportive care, and administration of anti-toxin.

Neuromuscular blocking agents (NMBAs): ICU patients receiving NMBAs can develop prolonged neuromuscular blockade due to reduced hepatic and renal excretion of the drugs. There use should be monitored carefully. The minimum necessary dose should be used, and the dose should be reduced daily. The effect of NMBAs can be monitored in the ICU by peripheral nerve stimulation (Train-of-Four response). If prolonged neuromuscular blockade is present, the drugs should be discontinued.
Suxamethonium can cause dangerous hyperkalaemia, especially in patients with critical illness polyneuropathy, and should be avoided.

Patients with muscular dystrophies may require ICU admission for management of respiratory muscle failure or cardiac arrhythmias. Prolonged respiratory depression after anaesthesia for even minor surgery can occur. Decisions to ventilate must be taken with care, and after discussion with the patient, carers, and the treating team, as weaning is difficult. Non-invasive ventilation is preferable.

Muscle disorders

A wide variety of muscle disorders can cause paralysis and require ventilatory support.

Causes of muscle disorders in ICU patients
Rhabdomyolysis • Traumatic (e.g. crush syndrome) • Drug induced – statins, fibrates • Neuroleptic malignant syndrome • Malignant hyperthermia
Inflammatory myopathies • Polymyositis and dermatomyositis
Infective myopathies • Viral – dengue, other haemorrhagic fevers • Bacterial - leptospirosis • Parasitic
Endocrine • Hypothyroidism and hyperthyroidism • Cushing's syndrome • Osteomalacia
Muscular dystrophies • Duchenne's and Becker's • Limb girdle • Myotonic
Critical illness myopathy

Rhabdomyolysis: Results in respiratory muscle weakness. Toxins released by muscle damage can cause acute renal failure. Large amounts of fluid are extravasated into the inflamed muscle, which can result in shock; this can in turn worsen renal failure. Common causes in the ICU are:

- Drug induced: statins
- Infection induced rhabdomyolysis – particularly seen in leptospirosis, severe dengue
- Ischaemic rhabdomyolysis induced by prolonged recumbency
- Exertional rhabdomyolysis
- Compartment syndrome
- Rapidly progressive inflammatory myopathy

Muscle pain, stiffness and tenderness are present. CPK and myoglobin are grossly elevated. Treatment is largely supportive. Drugs, such as statins should be stopped. Inflammatory myopathies may require pulsed corticosteroids. Surgical decompression and debridement is necessary for compartment syndrome.
Adequate intravenous fluid resuscitation must be given. Hypokalaemia and hyponatraemia can occur. Severe depletion of body potassium can occur, with falsely elevated serum potassium levels due to release from damaged muscle. Forced mannitol-alkaline diuresis aimed at maintaining the pH >6.5 is a widely used approach, but is controversial, as mannitol itself can worsen renal impairment, and alkalinisation can precipitate or worsen hypocalcaemia. Simply maintaining adequate hydration and adequate diuresis is probably safer and as effective. Acute renal failure must be managed (see section on *Acute renal failure).* The prognosis is good.

Critical illness myopathy: This is the commonest form of ICU acquired myopathy. Use of corticosteroids is the biggest risk factor. SIRS and severe sepsis, hyperglycemia, hyperthyroidism may also be additional triggers. It is associated with higher illness severity scores. Neuromuscular blockade may aggravate the condition. It usually begins several days after commencement of IV corticosteroids, although the illness is often missed in the early stages because the patient is ventilated or sedated. Flaccid quadriparesis affecting proximal more than distal muscles is characteristic. Difficulty in weaning occurs. Facial weakness commonly occurs, but ophthalmoplegia does not. Deep tendon reflexes are normal or diminished.

Diagnosis: The following features are seen:

- History of treatment with IV corticosteroids.
- Sensory nerve amplitudes >80 % of the lower limit of normal in two or more nerves on NCS. Needle EMG with short-duration, low-amplitude MUPs with early or normal full recruitment, with or without fibrillation potentials.
- Absence of a decremental response on repetitive nerve stimulation.
- Muscle biopsy shows muscle fibre atrophy due to myosin loss.
- Elevated CPK levels

Treatment: recovery is usually spontaneous. Corticosteroids should be discontinued. Tight glycaemic control with insulin may be of benefit.

Cachectic myopathy: This occurs due to protein catabolism and disuse. Common in elderly and malnourished patients. It is a diagnosis of exclusion. Nutritional therapy is required.

Electrolyte imbalance is an important cause of neuromuscular weakness. (See section on *Homeostasis).*

In practice, critical illness polyneuropathy and myopathy, and complications due to NMBAs are the commonly encountered neuromuscular disorders encountered in ICU patients being treated for other disorders. Guillain-Barre syndrome and myasthenia are common conditions requiring ICU admission for ventilation. Note that Gullain Barre syndrome can occur in patients already on treatment for other disorders. Always keep an open mind to exclude treatable disorders before arriving at the diagnosis of critical illness polyneuropathy and myopathy.

Abdominal problems

Abdominal problems are common in the ICU, and often develop as complications, although they may be the primary reason for admission. The important abdominal problems are,

- Peritonitis and other infections
- Intra-abdominal hypertension
- Abdominal compartment syndrome
- Bowel ischaemia and infarction
- Intestinal obstruction
- Constipation and paralytic ileus
- Gastroenteritis and antibiotic associated colitis
- Upper gastrointestinal haemorrhage

Clinical History

The main presenting symptom is abdominal pain. The severity of the pain is often related to the severity of the problem. Abdominal pain maybe missed in patients who are sedated, and also in elderly patients and those who are immunosuppressed (either by corticosteroid therapy, or due to chronic illness such as cirrhosis, diabetes mellitus etc.) The location of the pain may give a clue to the source of the pain, allowing for the following:

- Visceral pain is pooly localised and has a dull aching character. It is caused by distension or spasm of a hollow viscus. Intestinal obstruction, ureteric colic and biliary colic or cholecystitis are examples.
- Parietal pain arises from irritation of the parietal peritoneum and is well localised and sharp. Acute appendicitis, diverticulitis are examples.
- Referred pain is referred to the dermatome which has a common innervation with the visceral structure. It is perceived superficially, and has an aching character. Examples include central abdominal pain in appendicitis, shoulder tip pain in cholecystitis, loin pain with testicular problems, and right hypochondrial pain with basal pneumonia.

- Right upper quadrant: cholecystitis, cholangitis, liver abscess, hepatitis, pancreatitis, right basal pneumonia
- Left upper quadrant: peptic ulcer, splenic abscess, infarction or rupture, pancreatitis.
- Right lower quadrant: appendicitis, hernia, inflammatory bowel disease, ureteric colic, pelvic inflammatory disease, twisted ovarian cyst, ectopic pregnancy.
- Left lower quadrant: diverticulitis, inflammatory bowel disease, hernia, ureteric colic, pelvic inflammatory disease, twisted ovarian cyst, ectopic pregnancy.
- Epigastric: peptic ulcer, reflux oesophagitis, pancreatitis, inferior myocardial infarction, abdominal aortic aneurysm (ruptured)
- Periumbilical: early stage of appendicitis, mesenteric lymphadenopathy, ruptured abdominal aortic aneurysm, umbilical and paraumbilical hernia
- Suprapubic: Pelvic inflammatory disease, cystitis.
- Diffuse: peritonitis, *do not forget the 'medical' causes of diffuse abdominal pain: diabetic ketoacidosis, porphyria*

Certain other features of pain may be helpful: the pain of appendicitis classically begins in the periumbilical region, and then moves to the right iliac fossa. Pain of pancreatitis radiates to the back. Cholecystitis is associated with pain referred to the shoulder tip.
The onset and frequency of pain is important: Gradually increasing cramping colicky pain is seen in intestinal obstruction. A ruptured viscus presents with sudden sharp pain.

Associated symptoms

- Diarrhoea: gastroenteritis, antibiotic associated colitis, bowel infarction; also primary conditions such as typhoid, inflammatory bowel disease.
- Constipation: intestinal obstruction
- Vomiting: maybe in response to pain. Treatment with opiates can also cause vomiting. Persistent vomiting is a feature of intestinal obstruction. The nature of the vomitus will suggest the site of

obstruction; bilious vomiting in small bowel obstruction, faeculant vomitus in large bowel obstruction. Consider diabetic ketoacidosis.

- Haematemesis: bleeding oesophageal varices, portal gastropathy, or a bleeding peptic ulcer are the usual causes. Rarely, haematobilia, caused by bleeding from liver cancer into the biliary tract can occur. Melaena is often associated and patients should be specifically asked about the colour of the stools.
- Genito-urinary symptoms: dysuria, haematuria, loin pain and tenderness (pyelonephritis), vaginal discharge in pelvic inflammatory disease.
- Fever, chills: high fever with chills is caused by abscesses. Sites include the liver, spleen, subphrenic space, pancreas (and pseudopancreatic cysts), kidneys, retroperitoneal space.
- Medications: NSAIDS and corticosteroids predispose to peptic ulceration. Analgesics and sedation may suppress abdominal pain hence, analgesics may be minimised when an acute abdomen is suspected.
- History of macrovasular disease: predisposes to mesenteric ischaemia. Diabetes mellitus increases the risk of most infections. Cirrhosis, chronic renal failure and nephrotic syndrome are associated with reduced immunity and increased risk of infections, in particular, peritonitis especially as they cause ascites.
- Recent surgery: primary or secondary intraabdominal haemorrhage may occur. This is the first thing to consider in post surgical patients who suddenly develop haemodynamic stability. Always consider bowel perforation which might have occurred as a result of endoscopic procedures.

  A 70 year old patient with breast cancer, who was on a PEG, was brought in as an outpatient for replacement of the PEG, which was done without endoscopic guidance. Soon afterwards she became hypotensive and septic. Further investigation showed that inappropriate inflation of the balloon had resulted in a ruptured stomach wall, leading to peritonitis and septic shock. She developed multiorgan failure and died a few days later.
- Jaundice, itching – signs of intrahepatic or extrahepatic cholestasis. Intrahepatic cholestasis is caused by viral hepatitis, leptospirosis and dengue. Extrahepatic cholestasis is commonly caused by biliary

calculi, obstruction from liver or pancreatic malignancy or by lymph nodes at the porta hepatis.

Examination

- Regional tenderness may help localise the site of the problem. Examine for organomegaly:
- Is there abdominal distension? Look for a cause. Is it gas, liquid (blood or ascites) or solid mass?
- Ascites: could be due to a transudate (heart failure, nephrotic syndrome, cirrhosis, renal failure, hypoproteinaemia) or an exudate (bacterial peritonitis, tuberculous peritonitis, malignant deposits in the peritoneum)
- Liver: maybe enlarged in hepatitis and other diseases which involve the liver, such as leptospirosis. Tenderness over the liver, together with intercostals tenderness is present in liver abscess. A right basal pleural effusion may be present.
- Gall bladder: a palpable gall bladder is not due to gallstones, unless the stone is in the cystic duct (Courvoisier's Law). Cholecystitis following obstruction by a pancreatic tumour or stricture results in an enlarged gall bladder which can be palpated distinct from the liver. Often, it can be grasped between the thumb and fingers and moved from side to side; this clinical sign helps to differentiate it from an abnormal lobe of the liver.
- Pancreas: a pancreatic cyst or large tumour, or pseudopancreatic cyst maybe palpable in the epigastrium.
- Stomach: tumours arising from the stomach may be palpable.
- Spleen: enlargement of the spleen is most often due to systemic causes (haematological malignancy, chronic malaria, Kala-azar: large spleen; endocarditis, typhoid, viral infections: small spleen). Portal hypertension can also result in splenomegaly. The spleen may be enlarged in splenic abscess.
- Kidneys: bilateral enlarged kidneys are found in bilateral hydronephrosis and polycystic kidney disease. Unilateral enlargement is found in unilateral hydronephrosis and renal cell carcinoma. In pyelonephritis, renal angle tenderness will be present.
- Pelvic lumps: these usually arise from the pelvis, and characteristically it is not possible to get under the lump. In

women, large fibroids, uterine and ovarian malignancies maybe felt.

- Bowel masses can be either, tumours or inflammatory lumps. These may occur anywhere in the abdomen. Appendicular abscess, which occurs if appendicitis is not treated surgically early, is felt in the right iliac fossa. Hernias may give a clue to possible obstruction and strangulation.
- Rectal examination: may reveal a rectal tumour. Helpful in determining if malaena is present, if the patient has not yet had a motion.
- Vaginal examination may be required in certain cases, to look for vaginal discharge, infected tampons or pessaries, and cervical cancer. Tenderness in the vaginal fornices is present in pelvic inflammatory disease; an abscess or ectopic gestation may be felt by the experienced clinician. It is best therefore, to have a proper vaginal examination performed by a gynaecologist in patients where a pelvic pathology is strongly suspected. Do not forget that the commonest pelvic mass is normal pregnancy!

In addition to the above, look for signs and symptoms of developing or worsening sepsis and organ failure. Abdominal infections are important cause of severe sepsis. Increased abdominal pressure and abdominal pain can restrict respiratory movements and predispose to respiratory infection. Peritonitis results in 3rd space fluid loss which can result in hypotension. Intravascular fluid depletion can easily be tested by passively raising the legs - a rise in blood pressure indicates volume depletion.

Investigations and monitoring

- Full blood count and C-reactive protein: look for signs of infection – neutrophil leukocytosis, elevated CRP.
- Renal functions, electrolytes: look for sepsis induced renal failure. Pyelonephritis is a cause of acute renal failure. Diarrhoea, vomiting and 3rd space loss can result in electrolyte abnormalities. Hypomagnesaemia is more common in patients with chronic liver disease.
- Liver profile: the pattern of liver enzymes help in the diagnosis of different liver diseases:

  - Elevation of serum bilirubin, serum alkaline phosphatase and serum gamma GT with relatively normal transaminases suggests cholestasis.
  - Markedly elevated transaminases with relatively normal bilirubin, alkaline phosphatase and gamma GT suggest hepatocellular damage.
  - Low serum proteins together with elevated transaminases suggest chronic liver disease.
  - High serum ammonia levels are seen in decompensated liver disease. Low platelets are also a feature.

- Serum amylase and lipase: always look for pancreatitis in any patient who deteriorates or shows features of an abdominal problem. It is, like pulmonary embolism, the other 'blind spot', and is often missed until late. (q.v. section on pulmonary embolism)
- Blood cultures
- Urine full report and culture – a high pus cell count with granular casts suggests urinary tract infection.
- Ascitic fluid aspiration. Send for:
  - Culture (in blood culture bottles)
  - Cell count and differential
  - Tuberculosis polymerase chain reaction (TB-PCR) (when suspected)
  - Biochemistry (total protein, albumin, glucose, LDH, amylase, bilirubin, triglycerides (TG) and cholesterol)
  - Gram stain
  - Cytologic exam (where malignancy is suspected)

Characteristics of ascitic fluid in various disease states.

Condition	Gross appearance	Protein, g/dl	Serum-ascites albumin gradient g/dl	Cell Count		Other tests
				Red blood cells, >100,00/µL	White Blood cells, per µL	
Cirrhosis	Straw-coloured or bile-stained	<25 (95%)	>1.1	1%	<250(90%), mesothelial predominantly	
Neoplasm	Straw-coloured, hemorrhagic, mucinous, or chylous	>25(75%)	<1.1	20%	>1000(70%) usually>70% lymphocytes	Cytology, cell block, peritoneal biopsy
Tuberculous peritonitis	Clear, turbid, hemorrhagic, chylous	>25(50%)	<1.1	7%	>1000(70%),>70% Lymphocytes	peritoneal biopsy, stain and culture for AFB
Pyogenic peritonitis	Turbid or purulent	If purulent, >25	<1.1	Unusual	Predominantly PMN leukocytes	Positive Gram's stain, culture
Congestive heart failure	Straw-colored	Variable, 15-53	>1.1	10%	<1000(90%)usually mesothelial, mononuclear	
Nephrosis	Straw-colored or chylous	<25(100%)	<1.1	Unusual	<250, mesothelial, mononuclear	If chylous, ether extraction, Sudan staining
Pancreatic ascites	Turbid, hemorrhagic, or chylous	Variable, Often >25	<1.1	Variable, may be blood-stained	Variable	Increased amylase in ascetic fluid and serum

- Vaginal swabs for culture and ABST
- Chest and Abdominal radiograph: its main use is to detect gas under the diaphragm. This is best done in the erect position, but this is often not possible in ICU patients. A lateral decubitus abdominal x-ray is an alternative. Multiple air-fluid levels are seen in intestinal obstruction.
- Ultrasound scanning of the abdomen: this is very useful for detecting tumours, other lumps, abscesses, collections of pus, pyelonephritis, pancreatitis etc. Best done with a full bladder – remember to clamp catheter in advance.
- CT scan abdomen: this is considerably useful in identifying various abdominal pathologies, and is worth the trouble of shifting the patient out of ICU to radiology. In addition, therapeutic procedures such as aspiration of abscess can be performed under CT guidance. The main issue is with contrast and possible nephropathy. Adequate hydration, use of non-ionic contrast, and pre-treatment with N-acetylcysteine will prevent this to an extent.
- Monitoring of pulse oxymetry and haemodynamics are necessary.
- Abdominal girth should be measured if intra-abdominal hypertension or compartment syndrome is suspected, when intraperitoneal bleeding is suspected and in post abdominal surgery patients.

Peritonitis

Spontaneous bacterial peritonitis (SBP) or primary peritonitis is a bacterial infection of the peritoneal fluid in the absence of bowel perforation, trauma, infection or abscess formation in the gastrointestinal tract. It is most commonly seen in patient with ascites; liver cirrhosis is the commonest cause; it can also occur in patients with nephrotic syndrome or chronic renal failure.

Secondary peritonitis is bacterial infection of the peritoneal fluid secondary to bowel perforation, infection or abscess formation in the gastrointestinal tract or trauma.

Tertiary peritonitis is where peritoneal inflammation persists due to nosocomial infection.

Peritonitis is diagnosed by finding a positive ascitic fluid bacterial culture and an elevated ascitic fluid absolute polymorphonuclear leukocyte count (250 cells/mm^3). Protein concentration >1 g/dL, low ascitic fluid glucose concentration (<50 mg/dL) and Lactate dehydrogenase greater than the upper limit of normal for serum are also supportive.
If SBP is suspected, treatment should be started empirically immediately. Suspect SBP in any patient with ascites with any of the following:

- Fever
- Abdominal pain and/or tenderness
- A change in mental status (especially important in cirrhosis, as patients can develop hepatic encephalopathy
- Sudden hypotension/septic shock
- Ascitic fluid PMN count 250 cells/mm3

Patients with a past history of SBP are at greater risk.

Ascitic fluid, blood and urine culture should be taken, and antibiotics started. IV cefotaxime 2 grams 8 hourly is the usual first line antibiotic. Ciprofloxacin 200mg IV 12 hourly is also effective. Secondary bacterial peritonitis should be treated with cefotaxime and metronidazole. Treatment should be given for at least 5 days, and reviewed based on clinical recovery and cultures. Aminoglycosides should be avoided; hepato-renal syndrome may result.
Intravenous albumin is of proven benefit in patients with cirrhosis and SBP in terms of survival and prevention of renal failure.

Intra-abdominal hypertension

Intra-abdominal pressure is the pressure within the abdominal cavity. It normally fluctuates with respiration. While assessment of tenseness of the abdominal wall can give a rough idea of intra-abdominal pressure, it is usually estimated by measuring intravesical pressure. Intra-abdominal hypertension is a sustained increase in intra-abdominal pressure above 12mmHg. Changes in tissue microcirculation occur when intracranial hypertension occurs. Intra-abdominal hypertension may progress to abdominal compartment syndrome.

Abdominal compartment syndrome (ACS)

This is defined as a sustained increase in intra-abdominal pressure above 20mmHg, with associated new onset organ failure. It can occur due to injury or disease within the abdominal cavity (primary ACS) or as a complication of sepsis, major burns or capillary leak (secondary ACS). ACS is most common

after abdominal trauma, and also occurs after surgery and less commonly in medical ICU patients. It can result in gut dysfunction; increased bacterial translocation occurs across the gut wall, causing multi-organ failure and death.

Treatment of intra-abdominal hypertension

- Improvement of abdominal wall compliance by sedation and neuromuscular paralysis
- Nasogastric aspiration
- Gastric prokinetics: metoclopramide, erythromycin
- Rectal tube and enemas
- Colonic prokinetics: neostigmine
- Endoscopic decompression of large bowel
- Drainage of ascitic fluid
- Reduction of capillary leak of fluid
    - optimise serum protein levels by giving albumin
    - diuretics
- Surgical or percutaneous drainage of intra-abdominal abscesses

If abdominal compartment syndrome occurs, laparotomic decompression of the abdomen is necessary. This means that the abdomen would be kept open. Various methods are used to temporary close the abdominal wall. Later on, once the condition has settled, the laparotomy can be closed.

Bowel ischaemia

Acute mesenteric ischaemia

This is sudden onset of intestinal perfusion due to either arterial embolism, arterial or venous thrombosis, or vasoconstriction with low blood flow. The condition has a very high mortality. Embolism is the commonest cause, often due to valvular heart disease, atrial fibrillation and myocardial infarction. Advanced age, atherosclerosis, low cardiac output states, intra-abdominal malignancy are risk factors. Venous thrombosis, due to acquired or inherited hypercoagulable states is an important cause in young patients. Factor V Leiden is the most common cause of hypercoagulability; other causes include protein C /S deficiency, hyperhomocysteinaemia and antiphospholipid syndrome. Vasculitis is another rare cause.

The colon is the most common site to be involved. Fortunately, colonic ischaemia is often non-gangrenous, which resolves without sequalae.

Around 15% of patients with ischaemic colon will develop gangrene and its life threatening complications.

Patients classically develop rapid onset severe periumbilical pain, with relatively little physical signs. Nausea and vomiting maybe present, with forceful bowel evacuation. Blood in the stools may be present. The condition may have a more insidious onset in venous thrombosis. Initially, guarding and rigidity are absent. Later on, as bowel infarction occurs, the abdomen becomes grossly distended, bowel signs disappear, and features of peritonitis appear. The patient develops severe sepsis and multiorgan failure. It is vital that the diagnosis is made early, as outcome is much better if interventions are taken early; unfortunately the early features are easily missed. A high index of suspicion should be maintained in any patient with risk factors for bowel ischaemia presenting with rapid onset central abdominal pain. Secondary vasoconstriction often occurs, worsening the ischaemia.

Plain abdominal radiograph may show evidence of intestinal obstruction. CT scan abdomen should be obtained without delay; it may show the affected bowel loops, and will also be helpful in identifying alternative causes for abdominal pain. If the CT findings do not warrant immediate surgery, a mesenteric angiogram should be performed, in order to make a diagnosis and to determine the site of occlusion prior to surgery.

Treatment: resuscitation is important, as hypotension will make ischaemia worse. However, inotropes may worsen vasoconstriction. Dobutamine is the best choice because it is thought to have the least vasoconstrictor effect on the splanchnic circulation. Digitalis should also be avoided. Anticoagulation should be commenced unless the patient is actively bleeding. IV heparin is best, as its effect can be reversed rapidly if surgery is required.
Specific therapeutic options are;

- Papaverine infusion given intra-arterially following cannulation of the mesenteric artery. This relieves secondary vasospasm
- Thrombolysis
- Angioplasty and stenting
- Embolism is usually treated with surgical embolectomy
- If bowel infarction has developed, laparotomy and surgical resection is required

Long term anticoagulation with warfarin is usually required.

Intestinal obstruction

This is often due to mechanical obstruction. Paralytic ileus is also an important problem in the ICU.

Common causes are:

- Small intestinal obstruction
  - adhesions from previous surgeries
  - hernias
  - intussusception
  - malignancy
  - Crohn's disease
- Colonic obstruction
  - Colonic carcinoma
  - Sigmoid volvulus
  - Diverticular disease

Clinical features are of colicky abdominal pain, vomiting and absolute constipation (no passage of stools or flatus). Vomiting is more profuse in small bowel obstruction, and may even be absent in large bowel obstruction. Examination reveals abdominal distention with increased bowel sounds. Sometimes a tumour lump maybe palpable. Marked local tenderness maybe present in strangulation. Examine the hernial orifices for possible obstruction, and do a rectal examination.

Investigations: plain abdominal radiograph may show distended bowel with multiple fluid levels in small bowel obstruction. In large bowel obstruction, grossly distended large bowel loops are seen. CT scan of the abdomen may help localise the lesion and identify the underlying pathology. Barium enema is useful to demonstrate the site of obstruction. Air-insufflation during barium enema (to obtain a double contrast barium enema) is risky and must be performed only with care. Sigmoidoscopy or colonoscopy must also be performed with great care.

Management: initial management is usually conservative. Resuscitate the patient with IV fluid and potassium replacement. Prophylactic antibiotics are usually given; cephalosporins with metronidazole provide reasonable cover. Sigmoid volvulus can sometimes be treated by passage of a flexible sigmoidoscope to un-kink the bowel. If the patient is deteriorating and developing signs of severe sepsis with increasing pain, exploratory laparotomy is indicated. Surgical removal of the obstruction is usually performed. In the case of strangulation or intussusception, the gangrenous

bowel is resected and anastomosis peformed. Most large bowel obstruction is due to colon cancer, and resection of the affected bowel is necessary; if possible primary anastomosis is performed. In severely ill patients, a defunctioning colostomy is performed, with secondary anastomosis later, once the patient has recovered.

Constipation and Paralytic ileus

Patients in ICU may become constipated for various reasons. If bowel sounds are normal, and there are no signs of obstruction, this may not be of any serious consequence. Opiate analgesics cause constipation, and calcium channel antagonists such as verapamil are also a cause. Hypercalcaemia is also a cause of constipation. Most of the time, simple laxatives such as lactulose, liquid paraffin, or enemas are adequate treatment. Irritant purgatives such as bisacodyl can cause cramping abdominal pain.

Paralytic ileus is common after abdominal surgery, and usually resolves spontaneously. It can also be caused by severe sepsis and major trauma. Gaseous abdominal discomfort is a feature. Since hypokalaemia worsens paralytic ileus, it is important to maintain the potassium levels near upper normal – IV potassium replacement maybe necessary. A nasogastric tube is usually inserted to decompress the stomach. If paralytic ileus persists for longer than 5 days, a plain x-ray abdomen should be performed to exclude mechanical obstruction.

Acute colonic pseudo-obstruction or Ogilvie syndrome mimics acute large bowel obstruction, except that there is no mechanical obstruction. Symptoms and signs are similar to mechanical obstruction, and massive dilatation of the large bowel can occur, with perforation. Severe sepsis, electrolye imbalance, abdominal surgery, and steroid use are causes. An imbalance in the autonomic innervation appears to be the cause of this.

CT scan abdomen will help exclude a mechanical obstruction.

Treatment: underlying medical problems should be treated. Surgical decompression maybe required if the colonic diameter exceeds 10cm on plain abdominal radiograph. Treatment with neostigmine is effective.

Diarrhoea and antibiotic associated colitis

Gastroenteritis is sometimes severe enough to warrant ICU admission. Severe dehydration can even lead to acute renal failure. Toxin-induced gastroenteritis is usually self limiting and rehydration is adequate. If

persistent vomiting is present, IV fluids are required. If the patient can tolerate oral fluids, oral rehydration solution composed of water, electrolytes and glucose is more effective, as the sodium-glucose co-transport overrides the usual sodium pump.
Infective gastroenteritis requires appropriate antibiotics. Suspected shigella infection is treated with ciprofloxacin. Amoebic dysentery is treated with metronidazole. Tetracycline is the treatment for cholera.

Antibiotic associated colitis or pseudomembranous colitis is a dangerous complication occurring in patients who have been on treatment with broad-spectrum antibiotics. It is a nosocomial infection caused by *Clostridium difficile,* which colonises the gut when the normal bacterial flora has been altered by antibiotics. Penicillins, cephalosporins and clindamycin are the antibiotics most likely to cause antibiotic associated colitis. Clinical features are watery diarrhoea with lower abdominal pain, fever and leukocytosis starting a few days after antibiotic therapy. The usual time of onset is between 5 and 10 days of starting antibiotics, but may develop earlier or even after cessation of antibiotic therapy. Fulminant colitis can occur, with toxic megacolon and perforation. Sigmoidoscopy reveals pseudomembranes, which appear as raised yellow plaques ranging up to 1 cm in diameter scattered over the colorectal mucosa.
Diagnosis is often by bioassay, immunoassay or ELISA for Clostridium difficile toxin in the stools. Endoscopy is not usually necessary. Treatment is with metronidazole 500mg 3 times daily. Oral vancomycin is an alternative – it is not systemically absorbed.

Severe ulcerative colitis
Patients with severe ulcerative colitis can have a fulminant course. Pancolitis is usually present. Massive haemorrhage, toxic megacolon and perforation can occur.
Treatment is with bowel rest, parenteral nutrition, and systemic corticosteroids. Methylprednisolone is preferred. Patients should also be given broad spectrum antibiotics with metronidazole, especially if high fever and leukocytosis are present. Those with toxic megacolon lasting more than 72 hours may need colectomy. Cyclosporine is also effective.

Upper gastrointestinal haemorrhage
Stress ulceration is a common complication in patients in the ICU. Prophylactic acid blockade is recommended, and proton pump inhibitors are

the most effective. Minor bleeding is easily managed with IV proton pump inhibitors. Major bleeding can be difficult to control. The common causes are: peptic ulcer disease, bleeding oesophageal varices, Mallory-Weiss tears, tumours and arteriovenous malformations.
The following clinical features indicate significant bleeding:

- Systolic blood pressure below 100 mmHg
- Postural blood pressure drop of more than 20 mmHg
- Pulse rate above 100 beats/min

Management

- Establish IV access with two large bore cannulae. Send blood for full blood count, renal and liver profile.
- Give IV fluids until blood is available
- Transfuse packed cells and fresh frozen plasma as required. Platelet transfusion is required if platelet count is below 50000/$mm^{3.}$
- *Note: the haemoglobin level will not drop soon after an acute bleed, until haemodilution occurs.*
- Give intravenous omeprazole or pantoprazole 80mg IV as a bolus, and continue 8mg/hour.
- If oesophageal varices are the likely cause (where the patient has cirrhosis for example) intravenous vasopressin or terlipressin is effective. Octreotide or somatostatin is also effective. A Sengstaken-Blakemore tube can be used as a temporary measure for up to 24 hours. Antibiotics therapy with norfloxacin or ciprofloxacin is of benefit in reducing infections in cirrhotic patients with upper gastrointestinal bleeding.

Urgent upper gastrointestinal endoscopy must be performed if significant bleeding is present. Bleeding from a peptic ulcer can be treated with injection sclerotherapy or thermal coagulation. Endoscopic band ligation is the preferred treatment for oesophageal variceal bleeding.

Acute Hepatic Failure

Acute liver failure (ALF) is defined as the development of severe hepatic dysfunction within six months of the onset of symptoms, resulting in encephalopathy, coagulopathy and jaundice.

It can be subdivided into:

- Hyperacute, in which encephalopathy occurs within seven days of jaundice.
- Acute, with an interval of eight to 28 days from jaundice to encephalopathy.
- Subacute, with encephalopathy occurring five to 12 weeks after jaundice.

Without transplantation, the prognosis is worse in the subacute group. The incidence of cerebral oedema is highest in hyperacute liver failure.

Chronic liver disease is more common than ALF; common causes are alcohol abuse, chronic hepatitis B and C virus infection, chronic autoimmune hepatitis, primary biliary cirrhosis, haemochromatosis, Wilson disease. If ALF occurs on top of chronic liver disease /cirrhosis which has been present for more than 6 months, the condition is known as Acute on Chronic Liver Disease.

Why has the patient with chronic liver failure decompensated or deteriorated?
Gastrointestinal bleeding, spontaneous bacterial peritonitis, other sepsis, dehydration, electrolyte abnormalities, sedative drugs, portal vein thrombosis, or development of liver carcinoma can cause deterioration, and should be actively looked for.

ALF is uncommon. Paracetamol overdose and viral hepatitis are the commonest causes.

Causes of acute liver failure
Viral hepatitis • Hepatitis A, B, C, D, E, seronegative hepatitis • Herpes simplex, cytomegalovirus • Chickenpox – only in immunocompromised hosts
Drug related • Paracetamol (acetaminophen) • Antituberculous drugs • Amoxycillin-clavulanate • Amiodarone, methotrexate • Recreational drugs -ecstasy, cocaine • Idiosyncratic reactions-anticonvulsants, antibiotics, NSAIDs • Aspirin in children (Reye syndrome) • Kava Kava
Toxins • Carbon tetrachloride • Phosphorous • *Amanita phalloides*
Vascular events • Ischaemia • Budd–Chiari syndrome (hepatic vein thrombosis) • Hyperthermic liver injury
Pregnancy related • Acute fatty liver of pregnancy • HELLP syndrome • Liver rupture
Miscellaneous: • Wilson disease • Auto-immune • Lymphoma • Carcinoma • Haemophagocytic syndrome

Clinical evaluation

ALF presents with jaundice, encephalopathy and coagulopathy, usually preceded by nausea and vomiting. Patients may appear well initially, but can rapidly progress to develop multi-organ failure. Jaundice usually precedes encephalopathy, although occasionally encephalopathy can occur before jaundice, especially in paracetamol poisoning.

A precipitating cause for ALF, together with diagnosis of the underlying cause of liver disease (in the case of acute on chronic liver disease) must be sought. Simultaneously, resuscitation of the patient must commence. Hypoglycaemia must be looked for and corrected. Acute bleeding must be controlled.

All patients with poisoning must have blood paracetamol levels measured, as immediate treatment with N-Acetyl cysteine prevents ALF.

History

Ask about:

- History of past liver disease.
- Alcohol abuse – assess amount and duration. It is easy to assume that drinking is the cause of liver disease, when it might be due to other causes.
- Paracetamol ingestion; note that taking large numbers of paracetamol tablets over a few hours or days could be dangerous in a patient with chronic liver disease.
- The duration of symptoms before the development of encephalopathy - relates to the incidence of cerebral oedema and prognosis without transplantation.
- Contact with viral hepatitis.
- Drug history – including prescribed, over-the-counter, herbal and recreational drugs.
- Travel history – hepatitis is more common in certain countries.
- Family history of liver disease - haemochromatosis, α-1 antitrypsin deficiency, Wilson disease and cystic fibrosis.
- Blood transfusion and sexual promiscuity – hepatitis B, C.

- History of gallstones or biliary tract surgery.
- Features of auto-immune disease – autoimmune hepatitis.
- Itching for several years preceding jaundice – primary biliary cirrhosis.

Examination

- Jaundice is the cardinal feature of liver disease.
- Altered consciousness in a patient with jaundice should always be considered to be a manifestation of hepatic encephalopathy. Features of early encephalopathy are;
    - Altered sleep pattern – patients sleep in the day and stay awake at night
    - Constructional apraxia
    - Flapping tremors

  Varying degrees of altered consciousness right up to deep coma can occur surprisingly rapidly.
- Check capillary blood glucose level. Hypoglycaemia can cause altered consciousness, which dramatically responds to intravenous glucose.
- The liver may be enlarged in acute hepatitis and other causes of acute liver failure. Enlargement of the spleen suggests chronic liver disease. A shrunken liver is a bad prognostic sign in patients with acute and subacute liver failure.
- Ascites and oedema can occur in both acute and chronic liver disease.
- Spider naevi usually occur in chronic liver disease, but can be present in ALF.
- Look for other stigmata of chronic liver disease; jaundice, ascites, pigmentation, gynaecomastia, testicular atrophy, female hair distribution (in men), white nails, palmar erythema, clubbing.
- Marked pigmentation occurs in haemochromatosis
- Kayser-Fleisher rings are seen in Wilson disease; may require slit lamp examination. Extrapyramidal signs maybe present, but cirrhosis can occur without extrapyramidal signs.
- Bruising and subconjunctival haemorrhages may be signs of acute coagulopathy.

At the end of the clinical evaluation, decide whether ALF or AoCLD is more likely.

Investigations

Liver function tests

- Serum bilirubin: in ALF, bilirubin levels are high. Measure the direct and indirect fractions, although both maybe elevated in ALF, very high indirect bilirubin levels may be due to co-existent haemolysis.In leptospirosis, marked elevation of bilirubin with relatively normal ALT occurs.
- Alanine transaminase (ALT) and aspartate transaminase (AST) are also present in extra-hepatic tissues. ALT is more specific for the liver, and elevation indicates damage to liver cells. In ALF, the ALT is grossly elevated, to several 1000 units/L. In chronic liver disease, the elevation is modest, and levels may be normal. Characteristically, in alcoholic liver disease the AST is twice that of ALT.
- The ALT can fall in massive liver cell necrosis with a falling liver volume.
- Serum alkaline phosphatase and gamma GT are elevated in biliary obstruction– in the setting of ALF, consider primary and secondary biliary cirrhosis.
- A low plasma albumin is seen in CLD, but is non-specific in critically ill patients.
- Prothrombin time and APTT – coagulation factors I, II, V, VII, IX, X are synthesised in the liver. Prolonged PT and APTT which are not corrected by intravenous vitamin K repletion, signify severe acute liver dysfunction.
- Full blood count – in chronic liver disease, hypersplenism may cause pancytopaenia. Macrocytosis and thrombocytopaenia are also features. Anaemia maybe present in chronic blood loss due to oesophageal varices. Overall, the haematological changes occur in chronic liver disease rather than ALF. Eosinophilia may be a feature of drug induced liver disease.
- Renal function tests and electrolytes: hepatorenal failure is an important complication. Serum creatinine levels predict outcome. Electrolyte imbalance is common and requires careful monitoring and correction.
- Other specific tests for various aetiologies include: plasma immunoglobulin profile, hepatitis virus serology (A (IgM), B (sAg, eAg, core IgM and DNA), C (antibody and viral load), delta, E),

autoantibodies, viral serology (CMV, EBV, HSV, zoster), caeruloplasmin, serum copper, urinary copper (pre and post penicillamine), α-1 antitrypsin phenotype, ferritin and iron studies and alpha fetoprotein.

- Liver biopsy is rarely required or performed in ALF as it does not change management. Malignancy is the only indication, where a decision on chemotherapy or therapeutic embolisation may be necessary. Because of coagulopathy, transjugular biopsy is performed if essential.
- Chest radiograph will identify effusions and lung infection which might have precipitated acute liver failure in CLD.
- Ultrasound scan of the abdomen is the most useful radiological examination. It allows assessment of the shape, size and morphology of the liver, identifies biliary obstruction and calculi, and primary and secondary malignancy. It is possible to assess the vascular supply, especially to diagnose Budd-Chiari syndrome.
- CT scan and MRI scan may be necessary in suspected biliary obstruction, suspected primary malignancy or secondary deposits. MRCP is preferred when visualisation of the biliary tree is necessary.
- ERCP – necessary when extrahepatic biliary obstruction is present, both to identify the site and cause of obstruction and for relief of obstruction.
- Upper gastrointestinal endoscopy – necessary in cases of upper gastrointestinal bleeding due to varices (see section on *Abdominal problems)*

Haemolysis (Coomb's negative) in a young patient with stigmata of chronic liver disease suggests the possibility of acute Wilson disease. The prognosis of this presentation is poor, and it should be treated as ALF. It indicates sudden liver necrosis with release of copper into the circulation, which causes haemolysis.

Management of ALF

Staff must be immunised and have confirmed immunity to hepatitis B infection. Universal precautions must be applied, together with appropriate eye protection and face shields. Strict infection control strategies should be in forced as patients are more susceptible to infection.

The key complications which occur in ALF (apart from encephalopathy which is the primary manifestation) are:

- cerebral edema
- renal failure
- hypoglycaemia
- metabolic acidosis
- sepsis
- coagulopathy
- multiorgan failure

ALF has a very high mortality. Liver transplantation is the only therapy proven to improve patient outcome.
Whether the patient has ALF or AoCLD is important; patients with ALF, even with multi-organ failure are possible candidates for liver transplantation. However, the presence of multi-organ failure may preclude consideration for liver transplantation in patients with AoCLD.

Assessment of severity of CLD
The Child-Pugh score or MELD (Model Endstage Liver Disease) score are used.

Child-Pugh score

	1	**2**	**3**
Encephalopathy	0	I/II	III/IV
Ascites	absent	mild	>moderate
Bilirubin(µmol/l)	<34(<2mg/dl)	34-51(2-3mg/dl)	>51(>3mg/dl)
Albumin	>35(>3.5g/dl)	28-35(2.8-3.5g/dl)	<28(<2.8g/dl)
INR	<1.3	1.3-1.5	>1.5

A total score of:
5-6=Grade A (well-compensated disease)
7-9=Grade B (significant functional compromise)
10-15=Grade C (decompensated disease)

MELD score
$3.8 \times \log_e$ (bilirubin (mg/dl) + $11.2 \times \log_e$ (INR) + $9.6 \times \log_e$ (creatinine (mg/dl)) + 6.4X (aetiology: 0 if cholestatic or alcoholic, 1 otherwise)

In broad terms, dysfunction and failure of other organs have adverse prognostic implications in both ALF and AoCLD.

The MELD score is useful to predict mortality in patients with CLD being considered for transplant, but should not be used for ALF.

The prognostic factors differ depending on whether the aetiology is paracetamol toxicity or not. Poor prognostic factors in ALF are as follows:

- Age less than 10 years or more than 40 years.
- Causes other than paracetamol toxicity or hepatitis A and B virus infection.
- Long period between the development of symptoms and encephalopathy.
- Persistent acidosis, INR >3.5 and increasing serum bilirubin and creatinine concentrations also suggest a worse prognosis in those with non-paracetamol aetiologies.

Various prognostic models have been developed from retrospective data; the King's College Hospital Criteria, the O'Grady criteria, and the French (Clichy) criteria are used. Determination of prognosis is important in identifying those patients who have a high risk of death, and hence who will require liver transplantation. However, none of the models have high reliability, and decisions should not be based on these prognostic models alone. The decision to transplant (if available) should be made early, based on the clinical condition and estimated prognosis.

Monitoring:

- Heart rate, blood pressure and CVP. Hypovolaemia must be corrected with saline infusions. Usually, in hypovolaemia the mixed venous oxygen saturation is low due to increased oxygen extraction in the tissues. However, vasodilatation occurs in liver failure leading to a hyperdynamic circulation, together with reduced oxygen extraction by the failing liver, leading to relatively normal mixed venous oxygen saturation.
- Respiratory rate and oxygen saturation.
- Arterial blood gas analysis and lactate levels.

- Urine output.
- Intra-abdominal pressure monitoring if tense ascites is present.
- Temperature. Patients are more susceptible to infection.
- Appropriate blood, urine, sputum and ascitic fluid cultures.
- Regular liver function tests, full blood count, renal profile, blood ammonia, INR.

Give specific therapies where indicated:

- Paracetamol poisoning: Activated charcoal and N-acetylcysteine
- Amanita phalloides mushroom poisoning: Forced diuresis and activated charcoal. Consider penicillin G and silymarin which have been shown to be effective
- Acute Budd-Chiari syndrome: Transjugular intrahepatic portosystemic shunt, surgical decompression or thrombolysis
- Herpes virus infection: Acyclovir

Note:

- Corticosteroids are not effective and can increase the risk of sepsis. Charcoal haemoperfusion, prostaglandins, and hepatic regeneration using insulin and glucagon are all ineffective therapies.
- Antivirals have no place in the management of viral hepatitis A, B, C, D or E.

Discontinue all drugs which are likely to have induced, or to have worsened liver failure. Amoxycillin-clavulanate is hepatotoxic and must not be used. If antibiotics are required, cephalosporins, quinolones and carbapenems are safe.

Encephalopathy

Confusion, agitation, irritability, and drowsiness are signs of encephalopathy.

Check the blood glucose level – it maybe the cause of drowsiness.

The modified Parsons-Smith scale is used to measure the grade of hepatic encephalopathy.

Grade	Clinical features	Neurological signs	Glasgow coma scale
0/subclinical	Normal	Only seen on neuro-psychometric testing	15
1	Trivial lack of awareness, shortened attention span	Tremor, apraxia, incoordination	15
2	Lethargy, disorientation,personality change	Asterixis, ataxia, dysarthria	11-14
3	Confusion, somnolence to semi-stupor, responsive to stimuli, fits of rage	Asterixis, ataxia	8-10
4	Coma	±Decerebration	<8

What causes hepatic encephalopathy? What changes take place in the brain?

Decreased metabolism of ammonia by the liver leading to high blood levels of ammonia is one of the most important causes. However, there is no direct relationship between blood ammonia levels and grade of encephalopathy. Increased activity of the inhibitory GABA-benzodiazepine neurotransmitter system in the brain is also thought to play a role. Hepatic encephalopathy can be temporarily reversed by administration of the benzodiazepine antagonist flumazenil. Increased cerebral uptake of certain amino acids such as tryptophan, tyrosine and phenylalanine may alter the synthesis of neurotransmitters. Cerebral oedema also occurs in encephalopathy, possibly due to an increase in intracellular osmolality in astrocytes brought about by metabolism of ammonia to glutamine. Cerebral vasodilatation also probably contributes.

Cerebral oedema can result in coning and decerebration; hence, hourly monitoring of pupils is recommended in suspected increased intracranial pressure, and if possible intracranial pressure monitoring must be commenced.

Hepatic encephalopathy is precipitated by

- Acute liver failure
- Gastrointestinal - haemorrhage, constipation, increased protein load
- Infections – spontaneous bacterial peritonitis, pneumonia, UTI, cellulitis
- Metabolic disturbances -electrolyte abnormalities, excessive diuretic therapy or fluid restriction, excessive paracentesis, uraemia, alkalosis, anaemia, hypoxaemia
- Hepatic - disease progression, portal vein thrombosis, ischaemia, hepatoma, spontaneous portosystemic shunting , TIPS or surgical shunts
- Benzodiazepines

Treatment of encephalopathy:

- Treat infection if present.
- Normalise serum sodium levels.
- Prevent fever.
- Patients should be nursed in the head up position.
- Normovolaemia should be maintained.
- Protect the airway. Intubation may be necessary in coma.
- Reduce protein intake to 1-1.5 g protein/kg/day. A 'no protein' diet can be given transiently. Vegetable protein is preferable to animal protein.
- Branched-chain amino acids have some benefit in chronic encephalopathy.
- Lactulose given orally, 10-30ml three to four times daily, induces diarrhoea which removes ammonia-generating compounds from the bowel, and creates an acidic environment that retains ammonia within the bowel lumen and prevents bacterial growth.
- Intestinal decontamination with antibiotics - Metronidazole given orally helps make sterile the gut, which reduces ammonia generation by bacterial action on blood and protein in the gut. Neomycin is not recommended because of the risk of nephrotoxicity – it can precipitate hepato-renal failure. *Antibiotics are not of proven benefit, although they are used widely.*

- Zinc supplementation – zinc is necessary for conversion of ammonia to urea which is much less toxic, and patients are often zinc deficient.
- Benzodiazepine antagonists may demonstrate transient improvement in level of consciousness, but are not recommended in treatment. They are too short acting, and have no effect on outcome.

Preventing rise in intracranial pressure: Cerebral oedema has a high mortality. An ICP above 25mmHg and cerebral perfusion pressure <50mmHg are associated with high mortality. Cerebral autoregulation is poor in encephalopathy, and rises in mean arterial blood pressure result in increased ICP. Agitation, seizures, and coughing associated with endotracheal suction increases ICP, and should be avoided.Increased ICP correlates with increased ammonia levels. Fever increases ammonia uptake into the brain, and worsens cerebral oedema. Hypothermia may reduce ICP. Routine ICP monitoring is not always required. ICP monitoring should be considered, if facilities exist, in the following circumstances:

- Hypotension, on vasopressor support
- Renal failure
- Arterial ammonia >150 μmol/l
- Pupillary abnormalities
- Hyperacute liver failure
- Jugular bulb saturations outside the normal range (55% to 80%)

If a sustained rise of ICP above 25mmHg occurs, or pupillary abnormalities occur (unilateral dilatation), coning maybe impending. The following measures are used to reduce ICP:

- Mannitol bolus: 0.5-1.0 g/kg 20% mannitol. Monitor serum osmolality, maintain below 320 mosmol/kg.
- Hypertonic saline: slow infusion to maintain a sodium level of 145-155 mmol/l.
- Hypothermia to 32-33 °C has some evidence of benefit.
- Thiopentone may be beneficial, though hypotension may occur.
- Hyperventilation: may be used for short periods.

Hypotension

Correct hypovolaemia. Persistent hypotension can be caused by severe vasodilatation. Noradrenaline is the drug of first choice. Vasopressin can be added if the response to noradrenaline is inadequate. *Consider the possibility of bleeding from oesophageal varices if the blood pressure drops suddenly, or continues to drop in spite of fluid resuscitation and vasopressors.*

Relative adrenal insufficiency maybe present, as in sepsis. When possible, a Synacthen test or random cortisol should be performed. Replacement doses of hydrocortisone 200mg daily as continuous infusion or in 4 divided doses may be considered in patients on vasopressor support only.

Hypoglycaemia

Common in ALF. Give IV dextrose infusions, 5% - 10%; if necessary supplemented with boluses of 25%.

Nutrition

Nutrional requirements are high. Protein intake should normally be between 1 and 1.5 g protein/kg/day. NG feeding can be given unless severe variceal bleeding is present.

Upper gastrointestinal bleeding

Intravenous omeprazole or pantoprazole is effective prophylaxis. They may be given as twice daily boluses of 40mg or as an infusion of 8mg/hour.

If GI bleeding is present, the infusion of 8mg/hr, preceded by a bolus of 80mg, is more effective. Fresh frozen plasma should also be given to correct the INR to less than 1.5. IV vitamin K is also routinely given, but will not be effective in ALF. If bleeding is severe, blood transfusion is often required, and endoscopic band ligation therapy must be performed. Sengstaken-Blakemore tube insertion maybe used as a temporary measure (see section on *Abdominal problems).*

Pulmonary problems

Pleural effusions are common, and sometimes require drainage if they cause respiratory compromise. Aspiration and hypostatic pneumonia occur, and need appropriate antibiotics. Amoxycillin-clavulanate, the drug of choice in aspiration pneumonia, is contraindicated.

Intubation may be required for airway protection or pulmonary oedema.

Porto-pulmonary hypertension may occur in cirrhotics, resulting in the hepatopulmonary syndrome.

What is the hepato-pulmonary syndrome?
It is caused by the appearance of intrapulmonary vascular dilatations (IPVDs). These cause intrapulmonary arteriovenous shunting, causing right to left shunting of blood and consequent hypoxia. IPVDs are thought to be formed due to failure of the damaged liver to clear circulating pulmonary vasodilators, and possibly due to the production of a circulating vasodilator and inhibition of a circulating vasoconstrictive substance by the damaged liver. Patients develop dyspneoa, and have platypnoea (worsening dyspnoea on sitting up from the lying down position-the opposite of orthopnoea), and orthodeoxia (arterial desaturation on sitting upright). It is associated with spider naevi. Contrast echocardiography is diagnostic. No specific treatment is effective other than liver transplantation.

Renal failure
Acute tubular necrosis is the commonest cause of renal failure. Prevention is important:

- Prevent and treat hypovolaemia.
- Avoid nephrotoxic drugs- neomycin, aminoglycosides, NSAIDs. Prostaglandins are essential for maintaining renal perfusion.
- Avoid IV contrast. Adequately hydrate and give N-acetylcysteine if using contrast.
- Avoid increased intra-abdominal pressure – it may compromise renal perfusion. Drainage of ascites may help dramatically.

Sometimes, the cause of ALF may cause renal failure as well – paracetamol, carbon tetrachloride, hepatitis B and C.

Hepatorenal syndrome is a condition where patients have an acute reduction in renal perfusion pressure resulting from ALF. It is caused by abnormal renal auto-regulation and decreased renal prostaglandin synthesis, in addition to stimulation of the sympathetic nervous system and an increase in synthesis of humoral and renal vasoactive mediators. It is reversible and improves if liver failure improves. The kidneys are structurally normal.
Many therapies have been tried, but have not been effective. Terlipressin combined with albumin as volume therapy, milrinone in combination with

octreotide infusion, noradrenaline infusion in combination with albumin and furosemide, *N*-acetylcysteine infusion and TIPS may have some benefit.
Dialysis is the mainstay of management, and should be started earlier than in acute renal failure not related to ALF. Bicarbonate dialysis is preferred. Continuous renal replacement therapy is preferred; intermittent haemodialysis can cause hypotension and subsequent drop in cerebral perfusion pressure. Minimal dose heparin should be used.

Coagulopathy

PT and INR are markers of prognosis in ALF, but not in CLD. Correction of coagulopathy with fresh frozen plasma is not required unless active bleeding is present, or the risk of bleeding is high. The risk of bleeding is high even with mild coagulopathy in acute fatty liver of pregnancy and HELLP syndrome; FFP must be given in these conditions. In ALF, a*void correcting coagulopathy unless active bleeding is present, as INR is an important index in determining prognosis and the need for transplantation. This does not apply to AoCLD.*

The prognosis of ALF is poor without liver transplantation, and better with AoCLD. Survival in ALF without transplantation is around 10%. The criteria for liver transplantation are shown below.

Transplantation criteria

Paracetamol induced ALF	ALF due to other causes
• pH <7.3 following volume loading and at greater than 24 hours post overdose. • Grade III/IV encephalopathy + creatinine >300 µmol/l (or oligo-anuria) + prothrombin time >100 seconds (INR 6.5). All of these events must occur within a 24-hour time frame.	• Acidosis (pH <7.3) or prothrombin time >100 seconds (INR >6.5) *Any three of the following in association with encephalopathy:* • Age less than 10 or greater than 40 • Bilirubin >300 µmol/l (17.52 mg/dl) • Jaundice to encephalopathy time >7 days • Aetiology either non-A, non-B (seronegative hepatitis) or drug-induced • Prothrombin time >50 seconds

MARS (Molecular Adsorbents Recirculation System)

This is also known as extracorporeal albumin dialysis. This is an artificial system designed to remove bilirubin and other toxins from the body in ALF. The method is based on the assumption that bilirubin and other albumin-bound substances and toxins will move across a concentration gradient from the patient to a circulating 25 percent albumin solution. The ultrafiltrate then courses through another cartridge to undergo conventional renal dialysis, thus providing both hepatic and renal support. Survival benefit has not been shown. MARS is used as a bridging method until liver transplantation is performed. It is considerably expensive and is available only in a few centres.

Various other extra-corporeal liver assist devices have been tried out, but none have shown significant survival benefit.

Pancreatitis

Acute pancreatitis is a serious condition, with a mortality of up to 15%. It is slightly more common in men, and the mortality is highest in the elderly.

Diagnosis is not always easy, and is sometimes missed altogether – it is another one of those 'blind spots' where sometimes the clinician simply does not think of it as a possibility, and the diagnosis comes as a surprise when the serum amylase results come back high. Patient outcome is often hard to predict. The aim should be to make an early diagnosis, assess severity, identify any underlying cause and anticipate complications by careful monitoring.

The main presenting features are acute upper abdominal pain and tenderness, with nausea and vomiting. These are non-specific, and the differential diagnosis includes peptic ulcer disease, cholangitis/cholecystitis, inferior myocardial infarction, and mesenteric infarction. *Always do a serum amylase or serum lipase in any patient with upper abdominal pain.* Sometimes, pain is not prominent, especially if the patient is on analgesics or sedatives. In such patients, severe pancreatitis may present with features of SIRS, shock, multi-organ failure or diabetic ketoacidosis.

Diagnosis and monitoring:

Always have a high index of suspicion for pancreatitis in patients with SIRS and multi-organ failure, especially in unconscious patients.

Serum amylase is elevated markedly. Serum lipase is more sensitive and specific than serum amylase and remains elevated longer.

Plain abdominal radiograph will show regional ileus and will also help to exclude intestinal perforation.

Abdominal ultrasound may show swelling of the pancreas and pseudocyst formation. However, CT scan with contrast is the most accurate radiological test. It should be performed if there is doubt as to the diagnosis, or if there is no improvement within 3 days. CT scanning usually shows swelling of the

pancreas with areas lacking contrast enhancement due to necrosis, and peripancreatic fluid collection. CT scanning may also show evidence of gallstones or pancreatic obstruction which may be the cause. There are also various scoring systems to categorise severity based on the CT scan appearance. Unless urgent, it is better to delay the CT scan for 3 days after onset of disease, in order to identify necrosis better.

Neutrophil leukocytosis maybe present, especially if there is superadded infection. The blood glucose level may be elevated due to involvement of the islet cells. Hypocalcaemia can occur, and daily calcium/phosphate levels must be performed. A rise in C-reactive protein over 150mg/dL indicates severe pancreatitis with necrosis. Since the rise in CRP is delayed 48-72 hours, daily CRP measurement should be done. Liver function tests should be done; a high serum ALT, and elevated gamma GT and alkaline phosphatase may suggest gallstones as the cause. Standard respiratory monitoring and daily renal function tests are necessary. Check blood glucose levels.

Assessment of severity

Clinical evaluation can be misleading early on. Patients appear clinically better than they actually are. However, within 48 hours, the full clinical picture develops, and clinical assessment is an accurate measure of severity.

Age over 60 years, obesity and medical co-morbidity are risk factors for severe pancreatitis. Confusion, hypotension, tachycardia, hypoxaemia and low urine output are signs of impending multi-organ failure. A tense abdomen and the appearance of periumbilical (Cullen's sign) and flank (Grey Turner's sign) ecchymoses may indicate the degree of the inflammatory process.

Two prognostic scoring systems are used in acute pancreatitis – the Glasgow Scoring System, and the Ranson Scoring System. The APACHE II score also has good negative predictive value, and can be performed daily, unlike the Glasgow and Ransom scores which have to be evaluated over a 48 hour period. An APACHE II score > 8 classifies patients in the severe category.

Consider the worst value during the first 48 hours. If >2 adverse criteria are present → considered severe attack.

Glasgow Scoring System	
Arterial PO_2	<60mmHg (8.0 kPa)
Serum albumin	<32g/l
Serum calcium	<8 mg/dl (2 mmol/l)
White cell count	>15x 10^9/l
AST	>200 iu/l
LDH	>600 iu/l
Blood glucose	>180 mg/dl (10 mmol/l)
Plasma urea	>45 mg/dl (16mmol/l)

Ranson Score

0 hours	**48 hours**
Age >55	Hematocrit fall by ≥ 10%
White blood cell count > 16,000/mm^3	Blood urea nitrogen increase by ≥5 mg/dl (1.8mmol/L) despite fluids
Blood glucose >200 mg/dL (11.1 mmol/L)	Serum calcium < 8 mg/dl (2 mmol/L)
Lactate dehydrogenase >350 U/L	pO_2 < 60 mmHg
Aspartate aminotransferase(AST) >250 U/L	Base deficit > 4 meq/L
	Fluid sequestration > 6000 ml

4 or more criteria – severe disease

Identification of aetiology

Alcohol abuse and gallstones are the two most important causes. It can be a complication of biliary tract surgery or ERCP. In females over 40 years, suspect a gallstones, especially if the serum ALT is elevated 3 times normal. Ultrasound scan is highly sensitive in diagnosing gallstones; bile duct stones are more difficult to see, and may require MRCP or ERCP for diagnosis. Hypertriglyceridaemia is a known cause, especially if the serum triglycerides are over 1000mg/dL (11 mmol/L). Hypercalcaemia is also a possible cause, although the incidence of pancreatitis in patients with hyperparathyroidism is low.

Acute biliary pancreatitis is due to impaction of a gallstone in the sphincter of Oddi. In severe pancreatitis due to biliary obstruction, endoscopic sphincterotomy with removal of the stone must be performed. The procedure may increase the risk of infection, and broad spectrum antibiotic cover must be given.

Disease progression

Severe pancreatitis has 2 phases – the early 'toxaemic' phase, characterised by SIRS and remote organ dysfunction, and the later 'necrotic' phase, where local complications occur. A lot of vasoactive substances, activated enzymes and inflammatory mediators are generated locally, and this sets up a systemic inflammatory cascade which results in multi-organ dysfunction, which in turn makes the local necrosis worse.

Management

There is no specific therapy for pancreatitis.

Supportive therapy: careful supportive therapy is of paramount importance and will prevent the development of multi-organ dysfunction.

Most patients are fluid depleted, due to vomiting and reduced intake. Fluid and electrolyte replacement must be given. Central venous pressure monitoring is usually necessary. Adequacy of resuscitation must be judged by haemodynamic responses and urine output. If hypotension persists, inoconstrictors must be started.

Insert a nasogastric tube to prevent aspiration. Correct hypoxia with supplementary oxygen. Pleural effusions may occur (especially on the left), and may need drainage if they compromise respiration. Regular chest physiotherapy should be given. CPAP maybe necessary to maintain oxygen

saturation, and sometimes invasive mechanical ventilation may be required if ARDS develops, though this is not usually the case.

If acute renal failure develops, start haemodialysis early. This will ensure adequate metabolic and fluid control. If the patient is haemodynamically unstable, continuous renal replacement therapy will be the preferred modality. IV contrast given for CT scanning may push the patient into acute renal failure, and hence precautions should be taken (see section on *ARF*).

Severe abdominal distension due to paralytic ileus resulting in significant intra-abdominal hypertension may take place. Decompression of the colon with a rectal tube or surgically may be required, if abdominal compartment syndrome is developing.

Give Stress ulcer prophylaxis with intravenous pantoprazole or omeprazole, usually 40mg twice daily or as a continuous infusion of 8mg per hour. DVT prophylaxis with low molecular weight heparin is necessary, together with compression stockings to the legs.

Analgesia: provide adequate pain relief. Intravenous morphine is effective. Thoracic epidural block is effective and safe, and will help reduce the dose of systemic opioids, although it is not widely used.

Antibiotic prophylaxis: although at the beginning, pancreatitis is a non-infective condition, prevention of secondary bacterial infection in the necrotic areas is essential. If severe necrosis is apparent on the CT scan, broad spectrum antibiotics should be commenced. The risk of giving prophylactic antibiotics is that it may speed up the selection of certain strains of Staphylococci and Enterococci, and may result in fungal overgrown and multi-resistant gram negative bacteria. Aspiration and culture of the necrotic areas should be performed, and if infection is confirmed, appropriate antibiotics must be given.

Blood glucose control: hyperglycaemia must be controlled, usually using an insulin infusion.

Hypocalcaemia often occurs, and must be corrected with infusions of calcium gluconate. Other electrolyte imbalances must be corrected.

Surgical drainage: indications for surgery are limited:

- Infected pancreatic necrosis.
- Intestinal perforation resulting in an acute abdomen: this occurs usually at the left and transverse colon.

- Severe retroperitoneal haemorrhage: this occurs due to erosion of a blood vessel by proteases.
- Pseudocyst formation.
- Biliary obstruction, where endoscopic sphincterotomy has failed.

Surgery for removal of large sterile necrosis does not improve survival and is not recommended. However, if multi-organ dysfunction is persisting, presumably because of the toxins being released from the necrotic material, surgical drainage maybe necessary, although this is controversial.

Nutrition: adequate nutrition is important in pancreatitis; protein and energy requirements are high because of the hypercatabolic state. Alcoholic patients may be malnourished to begin with. Patients may be unable to take orally because of gastric atony and paralytic ileus. Total parenteral nutrition was advocated in the past – the aim being to rest the pancreas. However, jejunal feeding through a jejunal tube is safe and adequate in patients without paralytic ileus, intestinal obstruction or rupture. Enteric feeding is usually given as a 24 hour infusion, starting with around 500ml/day, and increasing according to requirements.

Oral feeding can be started once the patient's condition improves and ileus has resolved. A low fat diet should be given.

Various other treatments have been evaluated, such as octreotide, somatostatin, glucagon and plasma exchange, but none are of proven benefit. Patients with severe hypertriglyceridaemia may benefit from plasma exchange.

Pancreatic pseudocyst formation

This is a collection of pancreatic juice enclosed by a wall of granulation tissue – it is formed from an area of tissue necrosis with rupture of a pancreatic duct into the area. It may cause local compression, rupture, bleeding, and may get infected. Surgical or percutaneous drainage maybe required.

Follow up

After clinical recovery, the cause must be dealt with. If gallstones were present, cholecystectomy must be performed. Hypertriglyceridaemia must be controlled. Alcoholics should stop alcohol.

Diabetic Ketoacidosis

Diabetic ketoacidosis (DKA) is a metabolic emergency caused by absolute or relative deficiency of insulin. It is characterized by hyperglycemia (>300 mg/dL), metabolic acidosis (pH <7.30) low bicarbonate level (<15 mEq/L), with ketonaemia and ketonuria.

In the absence of insulin, peripheral tissues [muscle, fat, and liver] do not take up glucose. Counter regulatory hormones, Eg: glucagon, growth hormone, and catecholamines, lead to breakdown of triglycerides into free fatty acids accelerates gluconeogenesis, resulting in an elevation in serum glucose level in DKA. Hyperglycaemia itself reduces any residual insulin secretion and further impairs peripheral glucose uptake. Beta-oxidation of these free fatty acids produces ketone bodies. Ketone bodies [acetone, acetoacetate and β-hydroxybutrate] deplete extracellular and cellular acid buffers producing acidosis. Excess fatty acids and lactic acidosis, as a consequence of poor tissue perfusion are two other important contributors.

Hyperglycemia (exceeding the renal threshold for glucose) as well as ketonaemia produces osmotic diuresis which depletes sodium, potassium, phosphates, and water. Hyperventilation and vomiting are two other important contributors for dehydration. Dehydration and hypokalaemia are two important problems to be considered in patients with DKA.

When respiratory compensation is no longer sufficient, the metabolic acidosis and dehydration lead to renal failure and circulatory collapse resulting in coma and death.

Clinical assessment

History

The patient may present with classic symptoms of hyperglycaemia:

- Thirst
- Polyuria, polydipsia
- Nocturia

Or, other non specific symptoms like:

- Confusion
- Generalized weakness
- Malaise/lethargy
- Nausea/vomiting

- Fatigue
- Dramatic weight loss due to rapid breakdown of protein and fat stores [especially in children]
- Muscle pains and cramps
- Abdominal pain can be so severe that patient might present as a surgical emergency
- Symptoms of associated with precipitating illness such as infection

In young children, however, early signs are often easily missed. When DKA is developing as a result of another illness, it may mask the underlying problem. Therefore high index of suspicion is the key to diagnosis.

Examination

- The patient will appear ill, and may be drowsy

Dehydration

- Dry skin
- Decreased skin turgor
- Hypotension & Tachycardia
- Dry mucous membranes
- Capillary refill may be initially normal because of the vasodilator effect of acidosis until severe dehydration causes poor tissue perfusion.

Features of acidosis/ketosis

- Labored respirations
- Acidotic breathing [Kussmaul breathing or deep sighing respiration]
- Ketotic breath (fruity, with acetone smell)
- Abdominal tenderness

Other

- GCS if patient is in a state of altered level consciousness
- Decreased reflexes
- Hypothermia or Fever, if infection is present

Causes

The most common scenarios are infection (about 40%), malcompliance with insulin treatments (nearly 25%), and previously unknown diabetes presenting for the first time (approximately 15%).

Other associated causes

- Myocardial infarction [remember that diabetes causes silent infarctions]
- Cerebrovascular accident
- Complicated pregnancy
- Stress, trauma, surgery
- Alcohol
- Emotional disturbances
- Illicit drugs such as Cocaine
- Heavy use of concentrated carbohydrate beverages such as sodas
- Acromegaly
- Idiopathic (20-30%)

Investigations & their implications

- Random capillary blood glucose is acceptable for monitoring changes in blood glucose levels as treatment progresses, but it is wise to measure at least one whole blood glucose at presentation. Keep in mind that high triglyceride levels may lead to false low glucose level.
- Serum Electrolytes:
    - Sodium: For each 100 mg/dL of glucose over 100 mg/dL, the serum sodium concentration is reduced by approximately 1.6 mEq/L. When glucose level falls, the serum sodium level rises by a corresponding amount. Hence true sodium levels can be calculated by adding 1.6 mEq/L sodium for every 100 mg/dL glucose (ie, 1 mmol/L sodium for 3 mmol/L glucose). Sodium levels should rise with treatment. Absence of a rise of sodium levels is shown to be associated with an increased risk of cerebral edema. The possibility of dilutional hyponatremia in the presence to hyperglycemia should be borne in mind.
    - Potassium: close monitoring of potassium levels is essential, as the levels drop quickly with insulin treatment. Initial potassium levels are usually normal or high due to the leakage of intracellular potassium due to acidosis, despite considerable deficits of total body potassium.

- Blood urea and creatinine: Presence of ketones can cause a false elevation of measured creatinine. Hence, blood urea would be a better measure of dehydration and renal function.
- Full blood cell (FBC) count: High white blood cell (WBC) counts (>11 X 109/L) or marked left shift may suggest underlying infection.
- In case of the presence of an infection, necessary investigations should be carried out. Perform blood culture and other cultures as indicated clinically (eg, urine/blood). Chest radiography may be necessary to rule out pulmonary infection. Urinalysis (UFR) may provide clues to underlying urinary infection.
- Arterial blood gas (ABG) analysis:
- pH is often <7.3. It has been shown that venous pH is 0.03 lower than that of arterial in the presence of DKA & the difference is reliably consistent. Since the difference is not of any clinical significance, venous blood pH measurements can be used for monitoring purposes.
- Ketones: Commercial kits are available to measure blood and urine acetone and acetoacetic acid. Specific testing for beta-hydroxybutyrate can be performed by many laboratories. In a less privileged setting Rothera's test can be used to detect ketonuria and Benedict's test to demonstrate glycosuria.

Repeat laboratory tests are critical. Potassium level needs to be checked every 1-2 hours during initial treatment. Glucose and other electrolyte levels should be checked every 2 hours or so during initial aggressive volume, glucose, and electrolyte management. If the initial phosphorous level was low, it should be monitored every 4 hours during therapy.

- CT scanning of the head should be considered in patients with altered level of consciousness, especially in children as this may be caused by cerebral edema.
- Amylase: Serum amylase levels often are elevated in DKA and can be misleading in the presence of abdominal pain. This should be borne in mind when managing patients with acute abdomen. In addition acute pancreatitis can occur in nearly 10% of patients with DKA.
- Electrocardiography (ECG):
  DKA may be precipitated by a cardiac event, and the physiological disturbances of DKA may cause cardiac complications. An ECG is also a rapid way to assess significant hypokalemia or hyperkalemia (see section on homeostasis).

Management of DKA

Treatment of DKA is as dangerous as DKA itself. It may cause life-threatening, predictable hence avoidable acute complications such as:

- Hypokalemia
- Hypoglycemia
- Hyponatremia
- Fluid overload

Airway management is the primary concern in any patient with a significantly lowered level of consciousness. Breathing and circulatory stability should also be established before proceeding to specific management.

General measures

- Gain IV access by a large bore cannula
- If patient's level off consciousness is altered, insert a NG tube to prevent vomiting & aspiration
- If the patient is in a state of respiratory decompensation, consider intubation and ventilation
- If oliguria is present, catheterize and monitor urine out put
- patient should be kept nil by mouth at least 6 hours as gastroparesis is common in DKA.

There are three main problems which should be reversed in DKA.

1. Hyperglycaemia
2. Dehydration
3. Acidosis

Hence insulin treatment & fluid replacement are the mainstay of treatment. As the half life of soluble human insulin is short, continuous replacement is essential.

Fluid replacement:

Time [duration]	0.9 NaCl	KCL*
30 minutes	1L	20 m mol
1 hour	1L	20 m mol
2 hours	1L	20 m mol
4 hours	1L	20 m mol
6 hours	1L	20 m mol

If the serum K^+ exceeds 5.5 mmol/L, K^+ should not be to the replacement fluid. However the levels should be monitored closely as it may drop suddenly due to insulin treatment. If the K^+ level is below 3.5 m mol/L at the beginning, consider giving 40 meq of KCl per each litre of fluid replaced.

If the blood pressure drops below 90 mmHg, consider giving a colloid. Clinically monitor the following:

- Blood pressure
- Pulse rate & volume
- Hydration status
- Apperarence of pulmonary oedema
- Urine out put

The Insulin infusion should be continued until the acidosis resolves, i.e., until the pH and anion gap are normal, even if the blood glucose levels are normal.

Complications

The main complications of DKA and its treatment are:

Complications of DKA & its treatment

- Hypokalemia
- Hypophosphataemia
- Metabolic acidosis
- Hypoglycaemia
- Cerebral oedema especially in children
- Thromboembolism due to dehydration & sluggish perfusion

Insulin replacement

Blood glucose concentration [mmol/L]	**Rate of Insulin [units/Kg/hour]**	**Rate of Insulin for a 60 Kg person [units/hour]**	**Route of insulin**	**Comments**
>20	0.1	6	Use IV infusion	Up to 11 mmol/L use NaCl as the replacement fluid
20-15	0.07	4		
15-11	0.05	3		This is the ideal blood sugar level to maintain until ketonaemia is corrected
11-07	0.03	2		Use 5% dextrose to replace volume.
07-05	0.02	1	Switch to subcutaneous insulin	
<05		**Stop infusion**	**Stop insulin**	

Hypoglycaemia

Hypoglycaemia is defined as serum decreased glucose level below less than 50 mg/dL in men <45 mg/dL in women or <40 mg/dL in infants and children. This leads to signs or symptoms of altered level of consciousness and/or sympathetic over stimulation. The glucose level at which an individual develops symptoms is variable. If not treated quickly and adequately hypoglycaemia would result in coma, cardiac dysrhythmias, and death. The long term outcomes associated with prolonged hypoglycemia are permanent neurological deficits which could manifest as hemiparesis, memory impairment, decreased abstract thinking capabilities, and ataxia etc.

Causes for hypoglycaemia

Hypoglycaemia is commonly seen in diabetic patients. Hypoglycemia may result from changes or overdoses of hypoglycaemic drugs, missed diet, infection, metabolic changes of the body, or activity changes. However, in a significant number of patients no acute cause can be found.

In addition to insulin or hypoglycaemic drugs, many other drugs can precipitate hypoglycaemia. Some of them are listed below.

- Sulphonamide
- Salicylates
- Haloperidol
- Fluoxetine
- lithium
- tricyclic antidepressants
- Isoniazid
- thiazide diuretics
- angiotensin converting enzyme (ACE) inhibitors

In addition, other causes of hypoglycaemia include:

- Hepatic disease (eg, cirrhosis, galactose intolerance, fructose intolerance, glycogen storage diseases)
- Islet cell tumour/ extrapancreatic tumour
- Exercise (in diabetic patients)
- Sepsis
- Pregnancy

- Endocrine disorders (eg, Addison disease, glucagon deficiency, hypopituitarism)
- GI surgery
- Large tumors [eg, mesenchymal tumors, epithelial tumors]
- Starvation
- Idiopathic
- Alcohol and Substance Abuse

Clinical assessment

A history of insulin injection or ingestion of an oral hypoglycemic agent and their correlation with meals should be considered. Possible toxic [deliberate/ accidental] ingestion should be borne in mind. Inquire if the patient was prescribed any new medications. The medical history should include diabetes mellitus, renal failure, alcoholism, hepatic cirrhosis/failure, other endocrine diseases, or recent surgery. Symptoms suggesting infection may also be found. The clinical features are mainly due to sympathetic over stimulations and hypoglycaemic effects on the CNS.

Symptoms of hypoglycaemia are as follows:

- Headache
- Confusion
- Personality changes
- Diplopia
- Fits
- Palpitations
- Hunger
- Nausea
- Vomiting
- Belching
- Sweating
- Anxiety
- Tremulousness
- Nervousness
- Hypoglycaemia may even present as hemiparesis

Assess vital signs for hypothermia, tachypnoea, tachycardia, and hypertension. Respiratory signs may include dyspnoea, tachypnoea, and acute pulmonary oedema. Look for signs of chronic liver disease, Addison's disease, hypopituitarism etc.

However, it must be borne in mind that in severe hypoglycaemia, correcting the glycaemic status should be done prior to a thorough clinical assessment.

Investigations

- Random capillary blood glucose can be used for diagnosis as well as frequent monitoring. If the cause of hypoglycemia is other than oral hypoglycemic agents or insulin in a diabetic patient, other lab tests may be necessary.
- C-peptide measurement: This measurement is elevated in insulinoma, normal or low with exogenous insulin, and elevated with oral sulfonylureas.
- Liver function tests, serum insulin levels, and cortisol and thyroid hormone levels may also be needed. Appropriate investigations should be considered to rule out the possibility of a concurrent occult infection contributing to the new hypoglycemic episode. This includes urinalysis & blood cultures as baseline investigations. Chest X-ray would also be a vital investigation to rule out lung infections.
- Abdominal CT scan or an ultrasound scan to rule out an abdominal tumor may be justifiable in patients with new-onset hypoglycemia and no clear etiology.

Treatment

- Airway management is the primary concern in any patient with a significantly lowered level of consciousness. Breathing and circulatory stability should also be established before proceeding to specific management. Prolonged hypoglycaemia [of >4hours] causes permanent brain damage. Therefore, early management is crucial.
- Blood should be withdrawn for glucose and C-peptide prior to the administration of glucose. If there is a history of alcohol abuse, liver failure, severe starvation or malnutrition, thiamine 1-2mg/Kg IV should be administered to prevent precipitation of Wernicke's encephalopathy.

- If the patient is not fully conscious and poorly tolerates oral feeds, 50ml of 50% Dextrose IV should be given. With repeated blood glucose measurements, this may be repeated as required.
- If hypoglycaemia is the sole cause of patient's illness, with dextrose therapy patient should regain consciousness within 10 minutes. But there may be a lag period of nearly 1 hour before gaining the complete cognitive recovery. If the patient doesn't recover consider other causes of coma.
- In diabetic nephropathy, the insulin resistance improves. This leads to reduced insulin requirement. In patients with severe/recurrent hypoglycaemia the possibility of diabetic nephropathy should therefore be excluded.
- Review the hypoglycaemic drugs and doses patient is currently given. In case of malcompliance/ missed diet, patient should be educated about the dose and timing of hypoglycaemic drugs. If self inflicted hypoglycaemia, a psychiatric referral is essential before discharge.

Sedation, analgesia and neuromuscular paralysis

Sedation and analgesia

Sedation is often needed in ICU patients, especially those who are being ventilated. There are several aims of sedation:

- To relieve pain caused by trauma, surgery, infection, and cardiac and limb ischaemia.
- To relieve the pain and discomfort caused by intravenous lines, catheters, drains.
- To relieve the discomfort and facilitate tolerance of mechanical ventilation.
- To prevent pain and discomfort during procedures such as intubation, defibrillation/cardioversion, IV line insertion, catheterisation.
- To relieve fear and anxiety.
- To achieve sleep – patients in the ICU find it difficult to sleep, because day-night cycles are not apparent, and often there is disturbance from staff and other patients.

Decide on whether, what is required is simply sedation or sedation with analgesia. Analgesia for procedures would usually require short acting drugs with sedative and analgesic properties. On the other hand, discomfort caused by lines and tubes and by simply lying in bed for a long period would need longer acting drugs. Reversibility of the sedative effect is also important, as often it may be necessary to reverse the effect at short notice. The metabolism of drugs is altered by interaction with other drugs and by co-existent liver, renal and cardiac dysfunction. Sedative and analgesic drugs may also cause haemodynamic compromise and cause respiratory depression. All these factors must be taken into consideration when choosing an appropriate drug/s.

Levels of stress are high in ICU patients. Many patients think they are going to die. Reassurance is extremely important. The treating team should avoid discussing the patient's condition at the bedside if the patient is conscious and able to understand; in particular this is important where issues of

worsening prognosis, withdrawal of therapy and cancer are being discussed. The strange environment in the ICU, with strange apparatus, strange noises and being surrounded by strange people can be considerably unnerving, and attention must be paid to this by the treating team, to try to make the patient feel comfortable and cared for. Allowing the patient's family to be in communication, will be of help. Patients being ventilated are unable to talk because of the tube, and their inability to communicate makes anxiety worse.

Patients in the ICU are frequently disturbed. Frequent monitoring of blood pressure, attention to body, eye and oral care, and also events happening around other patients, are a source of disturbance. Sleep deprivation often results. This can be prevented by switching off lights in the ICU at night, and minimising noise made by staff.

Fear and anxiety, the strange environment, sleep deprivation, together with metabolic derangements can result in severe psychosis in some patients.

Discuss with the patient regarding the need for sedation and sleep. Ask the patient if he or she had a good nights sleep, and whether there is anything in particular which is making him/her uncomfortable.

Commonly used drugs are:

- Benzodiazepines – diazepam, lorazepam, midazolam
- Thiopentone
- Propafol
- Opiates – morphine, pethidine, fentanyl
- Ketamine

Benzodiazepines cause sedation, sleep and amnesia. In the past, amnesia was thought to be harmless and even desirable. It is now considered potentially harmful towards long term psychological well-being. However, benzodiazepines are widely used for sedation in the ICUs. Midazolam is short acting. It is often used during procedures where short term sedation is required, such as cardioversion. Diazepam is inexpensive, but its metabolites are very long acting. Lorazepam is also long acting, but metabolism is much less affected by disease. Midazolam is water soluble. The others require a special solvent. In hepatic and renal disease, these solvents could accumulate causing toxicity; hence midazolam is more suitable for prolonged use. Doses are given below:

	Midazolam or diazepam	Lorazepam
Bolus dose	2.5mg	2 to 4 mg
Infusion rate	2-10mg/hour	2-4mg/hour

Oversedation with benzodiazepines can cause respiratory depression. Sometimes, reversal of the effects of benzodiazepines may be necessary. Flumazenil is a benzodiazepine antagonist. It is very short acting, and repeated doses or infusion may be necessary. Start at an IV dosage of 0.2 -1 mg and titrate according to response. It can cause benzodiazepine withdrawal seizures.

Propafol is a general anaesthetic. It acts on the GABA receptor. It has good sedative effects. It is quickly metabolised, and has inactive metabolites. Its onset of action is rapid, and actions wear off quickly when discontinued, which is an advantage. It causes significant cardiac and respiratory depression, and can result in hypotension in patients with septic or cardiogenic shock, and hypovolaemia. It is made soluble in soya bean extract. It is usually given by infusion; maximum dose 4mg/kg/hour.

Thiopentone is an anaesthetic induction agent. When given for induction of anaesthesia, it has a short duration of action because of redistribution into fatty tissue. When given by infusion, however, the drug accumulates, and recovery can be delayed, especially in patients with liver dysfunction. It is rarely used in the ICU, except when sedation for mechanical ventilation cannot be achieved with other drugs. Small bolus doses can be used for treatment of convulsions (25mg). It is given as an infusion at a dose of 2-5mg/kg/hour.

Ketamine is a short acting drug with sedative and significant analgesic properties. It releases catecholamines, resulting in an increase in heart rate and blood pressure. It causes bronchodilatation, and can be used in asthma. It can cause nightmares, hence, must be given in combination with a benzodiazepine. The bolus dose is 25-50 mg, and can be given at an infusion rate of 10-30 mg/h. When given as an infusion, it may be mixed with midazolam in a 10:1 mixture (ketamine: midazolam).

Opiates cause sedation and analgesia. Morphine is the gold standard of opiates, and is widely used in the ICU. It is particularly effective in the management of pain of acute coronary syndrome, and has the added benefit of relieving pulmonary oedema. It is metabolised in the liver, and the metabolites are active. The metabolites accumulate in renal failure. The usual bolus dose is 2-5mg, and it can be given as a continuous infusion at a rate of 1-10 mg/h.

Pethidine is a synthetic opioid. Its metabolite norpethidine can accumulate in renal failure and result in seizures. Hence it is not usually used in critically ill patients. The bolus dose is 10 mg with an infusion rate of 10-50 mg/h.

Fentanyl is a synthetic opioid with a rapid onset of action. It is much more potent than morphine. It does not cause histamine release, and is the most suitable agent for analgesia and sedation in haemodynamically unstable patients. The bolus dose is 50-100 µg and the infusion rate 100-200 µg/h. With prolonged infusion accumulation and slow recovery can occur.

Tramadol is an atypical opioid, and is widely used orally, rectally or intravenously in post surgical ICUs.

All opioids can cause constipation, and laxatives may be necessary with their use. Opioid activity can be reversed with naloxone. The dose is 0.1 mg intravenously every 3-4 minutes. It must be used with care, as it can cause sudden reversal of analgesia. Opioid induced respiratory depression can be reversed with doxapram, which is a respiratory stimulant. The dose is 1-1.5 mg/kg.

Haloperidol is a neuroleptic. It can be used to sedate agitated patients with little risk of cardiorespiratory depression. It is the recommended drug for delirium. The dose is 2.5-5.0mg repeated as necessary. The action lasts 4-8 hours. It can cause extrapyramidal side effects and QT prolongation.

NSAIDS are rarely used in the ICU because of numerous undesirable side effects – risk of gastrointestinal bleeding, antiplatelet effects, renal failure by their anti-prostaglandin effect, and bronchospasm. They are sometimes used in trauma, and in post cardiac injury (Dressler's) syndrome.

Paracetamol is a simple analgesic and antipyretic and is used for simple pain relief and for fever.

Neuromuscular blocking agents

Muscle relaxants maybe required in the following situations:

- During intubation
- During ventilation, where patient relaxation is necessary. Most ventilatory modes are triggered, but if the patient cannot synchronise with the ventilator, or it is necessary to reduce cardiovascular work by using a controlled mode of ventilation, it is necessary to paralyse the patient.
- Raised intracranial pressure

Most of the time, sedation is adequate for ventilation.

Never paralyse a patient without sedation. Neuromuscular blocking agents must only be given if adequate sedation has not been adequate to maintain ventilation

Several complications of neuromuscular blockage are:

- Life threatening hypoxia if accidental extubation occurs.
- Critical illness polyneuropathy – this is due to many factors (see section on *Neuromuscular disorders*). Muscle relaxants may be contributory.
- Protective reflexes are usually lost.
- Immobility can lead to DVT, decubitus ulcers and muscle wasting.

Atracurium is one of the most widely used agents. It undergoes spontaneous (Hoffman) elimination, with inactive metabolites. Histamine release occurs with bolus injection, leading to hypotension. Tachyphylaxis occurs with prolonged use. Reversal of neuromuscular blockade occurs in less than one hour, regardless of the duration of the infusion. The metabolite can accumulate in hepatic and renal failure, but does not cause significant problems. It is less likely to cause critical illness polyneuropathy. The dose of atracurium is 0.5 mg/kg for tracheal intubation and 0.5 mg/kg/h as an infusion.

Vecuronium has a steroid structure. It has an active metabolite which accumulates in renal failure. Its biggest advantage over atracurium is that, it does not cause cardiovascular instability. The dose is 0.1 mg/kg as a bolus (which will last for about 45 min) and 0.8-2.0 µg/kg/min or 5-10 mg/h as an infusion.

Hoffman elimination is a physiochemical reaction causing spontaneous breakdown of the drug. It is independent of enzyme action. The drug is thus reliably eliminated in hepatic and renal failure.

Suxamethonium is a depolarising neuromuscular blocking agent. It is short acting, with a duration of action of 3 minutes. At the start of action, it causes muscles to depolarise, resulting in twitching. This may cause release of potassium from muscle cells. Always check the serum potassium before its use- it should not be used if hyperkalaemia is likely. It should not be used in increased intracranial pressure as the muscle fasciculations can further increase intracranial pressure. The usual dose of suxamethonium is 75-100 mg.

……. the physicians tell us of hectic fever, that in its beginning it is easy to cure, but hard to recognize; whereas, after a time, not having been detected and treated at the first, it becomes easy to recognize but impossible to cure.

Machiavelli, 'The Prince'

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