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ОСНОВЫ ИНТЕНСИВНОЙ ТЕРАПИИ

BASICS OF INTENSIVE CARE

Учебно-методическое пособие

Рекомендовано Учебно-методическим объединением
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в качестве учебно-методического пособия для студентов
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RESUSCITATION AND INTENSIVE CARE IN THE EARLY POSTOPERATIVE PERIOD

In terms of its duration, the postoperative period (POP) encompasses the period starting from the end of the operation up to the patient's complete recovery or his/her recognition being disabled.

The stages of the postoperative period are identified as follows:

– **early postoperative period** (from the end of surgery till the moment of the patient discharge from hospital);

– **late postoperative period** (from the moment of the patient discharge till the time of his complete recovery fully or his recognition of being disabled).

Both surgery and anesthesia bring about particular pathological changes in the body, which are the manifestations of the body's response to the surgical trauma. This induces defensive mechanisms to eliminate the consequences of the trauma and therefore restore homeostasis. The surgery affects the balance in the rate of metabolic (anabolic and catabolic) reactions rather than launches new metabolic events.

The postoperative state is divided into the four phases:

– catabolic phase;

– resolution phase;

– anabolic phase;

– the body weight gain phase.

The catabolic phase lasts from three to seven days. The period tends to be more acute when the serious changes in the body are caused by the severity of the principal condition or the extent and hazards of the surgery itself. The catabolic stage may also be prolonged and worsened if postoperative complications develop. These include the following:

– bleeding;

– infection;

– hypovolaemia;

– fluid, electrolyte, and acid-base balance disorders.

The improper management (e.g. inadequate analgesia or nutritional support, parenteral nutritional support, pulmonary hypoventilation) is known to contribute to prolonged catabolic phase as well.

The catabolic phase is a defensive body reaction aimed at enhancing the resistance of the body by prompt transfer of the energetic and plastic materials to the vital organs. It is characterised by specific neuroendocrine reactions: activating the sympathetic nervous system and adrenals, hypothalamus and pituitary, intensive synthesis with subsequent release of catecholamines, glucocorticoids, aldosterone and ACTH into the blood. This results in an increase in the amount of glycogen in the circulation, accompanied by a fall in insulin blood levels. Furthermore, intensive synthesis of angiotensin and renin occurs.

The neurohumoral disturbances alter the vascular tone to cause vascular spasm and defects in microcirculation and tissue perfusion, which, in its turn,

leads to hypoxia, metabolic acidosis, electrolyte imbalance, fluid redistribution, an increase in blood viscosity and blood cellular stasis. This further affects the extent of disturbance in the tissue redox processes that take place in the acceleration of anaerobic glycolysis as a result of tissue hypoxia. The myocardium, liver and kidneys are therefore the first to be affected.

The catabolic phase also involves accelerated protein break-down which is manifested by the decrease in muscle and connective tissue protein, and, the depletion in enzymes. The proteolysis in the liver and digestive tract is the fastest to occur, while that in the striated muscles takes significantly longer time to complete.

The resolution phase commonly lasts from **4 to 6 days** and is a gradual transition from the catabolic phase to anabolic one. This period is characterised by the reduction in the overactivity of the sympathetic nervous system and adrenals, including slowing down catabolism which becomes evident as a decrease in nitrogen urinary excretion to as low as 5–8 g/24 hours (as compared with 15–20 g/24 hours in the catabolic phase).

The positive nitrogen balance (the amount of nitrogen excreted is less than the given amount) suggests improvement in protein metabolism. In this period, potassium urinary excretion decreases as the electrolyte starts accumulating to take part in the synthesis of protein and glycogen. The fluid and electrolyte balance is restoring.

As far as the autonomous nervous and endocrine systems are concerned, the parasympathetic activity predominates and blood growth hormone (GH) level is rising, as are those of insulin and androgen.

During **the resolution phase**, the increased waste of energy and plastic materials (protein, fat, carbohydrates) slows down. When this eventually fades away, the active synthesis of protein and glycogen starts with subsequent production of fat, which rises as the intensity of catabolism falls. The persistent predominance of anabolism over catabolism is a sign of the postoperative period transfer to the anabolic phase.

The resolution phase starts from **the 3rd to 7th days** after the surgery if the postoperative period is uneventful (i.e. without complications).

The signs suggestive of the resolution stage onset are generally as follows:

– absence of pain;

– normalization of body temperature;

– resumption of appetite.

In addition, patients become active, and their body functions restore (the skin colour returns to normal; breathing becomes deep and its rate reduces; the heart rate returns to the preoperative one; peristaltic bowel sounds and flatus passage resume).

The anabolic phase is characterized by an increase in the synthesis of protein, glycogen, and fat, depleted during the operation and the postoperative catabolic period.

Furthermore, the parasympathetic nervous system tends to be overactive. Similarly, the secretion of anabolic hormones (GH and androgens) increases to allow the protein synthesis. GH, for instance, is responsible for the transport of amino acids from the intercellular space to the cells, while androgens promote the synthesis of proteins in the liver, kidneys, and myocardium directly.

Clinically, the anabolic phase is, in fact, the period of recovery, restoration of the impaired functions of the cardiac, respiratory, excretory, digestive and nervous systems. During this phase, the patient's general condition improves, appetite increases, the heart beat and rate return to normal as do the blood pressure levels, and the digestive functions (food passage, intestinal absorption and spontaneous bowel movements) are restored.

The anabolic phase usually lasts for **2–5 weeks**, which is dependent on the extent of the surgery, the patient's preoperative state and the severity and duration of the catabolic phase.

Phase of body weight gain (3–6 months). This phase of the postoperative period ends with an increase in weight, which occurs after 3–4 weeks and continues till full recovery, which sometimes can take several months.

POSTOPERATIVE INTENSIVE CARE

Immediately after the operation the patient is transferred either to the ward or to the Intensive Care Unit (ICU) which are arranged to monitor the patients and, if needed, to provide them with emergency and intensive care.

Patients may be admitted to the ICU after surgery, either electively or after unexpected peri-operative complications.

Indicatons for elective ICU admission:

– airway monitoring: e.g. major oral, head and neck surgery;

– respiratory monitoring: e.g. cardiothoracic surgery, upper abdominal surgery, prolonged anesthesia, previous respiratory disease;

– cardiovascular monitoring: e.g. cardiac surgery, vascular surgery, major abdominal surgery, prolonged anesthesia, previous cardiovascular disease;

– neurological monitoring: e.g. neurosurgery, cardiac surgery with a circulatory arrest;

– elective ventilation: e.g. cardiac surgery, major abdominal surgery, prolonged anesthesia, previous respiratory disease;

– patients may be admitted to the ICU after surgery, either electively or after unexpected peri-operative complications.

GENERAL CARE

Each patient should be constantly monitored. The emergency laboratory ensures a prompt monitoring of blood haemoglobin, haematocrit, electrolyte and protein levels, as well as circulating blood volume and acid-base balance. The intensive care unit is also equipped with everything necessary to provide the emergency aid: medications and transfusion fluids, a mechanical ventilation

apparatus, sterile sets for venous injections or infusions and tracheostomy, defibrillator, sterile catheters, tubes, a set for change of dressing.

The treatment consists of metabolic disorders compensation, restoration of the body functions, normalisation of the redox reactions in the tissues — oxygen transfer, elimination of the products of incomplete metabolism and carbon dioxide and replenishment of the increased energy waste.

Parenteral and, whenever possible, enteral nutritional support, is a very important method to improve and maintain the protein and electrolyte balance. It is advisable to give fluids and nutrients in the natural way and try to implement it as early as possible.

General care includes:

– ensure surgical and anaesthetic plan has been agreed, e.g. overnight ventilation, special precautions (e.g. wire cutters if mandible wired), movement allowed, haemodynamic targets, etc;

– provide adequate analgesia;

– ensure adequate rewarming;

– maintain euglycaemia;

– provide appropriate thrombosis prophylaxis;

– monitor blood gas, electrolyte and haemoglobin.

POSTOPERATIVE RESPIRATORY PROBLEMS

Common problems in those with pre-existing respiratory disease, especially with a reduced vital capacity or peak flow rate include:

– exacerbation of chronic chest disease;

– retained secretions;

– basal atelectasis;

– pneumonia;

– upper airway problems, e.g. laryngeal oedema.

Anaesthesia and surgery (especially upper abdominal surgery) reduce functional residual capacity, thoracic compliance and cough. Reduced macrophage function and systemic inflammatory activation with infection and acute lung injury as possible consequences may be observed.

Postoperative clearance of secretions and maintenance of basal lung expansion are very important. These require effective analgesia and chest physiotherapy. It is necessary to consider early use of non-invasive ventilation in case of spontaneous breathing requiring high FIO_2.

Mechanical ventilation assists basal expansion and secretion clearance where anaesthetic recovery is expected to be prolonged or where surgery ± pre-existing disease increases the risk of secretion retention and atelectasis. Ensure a patent airway prior to extubation in cases where intubation was difficult or after upper airway surgery.

POSTOPERATIVE CIRCULATORY PROBLEMS

Prevention of hypovolaemia is crucial in avoiding inflammatory activation and, therefore, many postoperative complications occur. Haemorrhage is usually obvious and managed by resuscitation, correction of coagulation disturbance and surgery.

Postoperative fluid management requires a high degree of hypovolaemia suspicion; fluid replacement with crystalloids and colloid solutions should be used to confirm and treat hypovolaemia in cases where there is any circulatory disturbance, metabolic acidosis or oliguria.

PAIN

Pain results from many insults, e.g. trauma, invasive procedures, specific organ disease and inflammatory processes. Pain relief is necessary for physiological and psychological reasons, including:

– anxiety and lack of sleep;

– increased sympathetic activity contributing to an increased metabolic demand;

– inadequate capacity of the circulation and respiratory system to meet the demands of metabolising tissues;

– significant risk of myocardial ischaemia;

– exaggerated endocrine response to injury with consequent salt and water retention;

– immobility and muscle splinting, consequent reductions in ventilatory function and cough.

Management of pain. The degree of tissue damage is related to the magnitude of the pain stimulus. The site of injury is also important; thoracic and upper abdominal injury is more painful than injury elsewhere. However, the perception of pain is dependent on other factors, e.g. simultaneous sensory input, personality, cultural background and previous experiences of pain.

***Systemic analgesia*:**

– Opioid analgesics form the mainstay of analgesic drug treatment in intensive care.

– Small, frequent IV doses or a continuous infusion provide the most stable blood levels. Since the degree of analgesia is dependent on blood levels it is important that they are maintained.

– Higher doses are required to treat rather than prevent pain.

– The dose of drug required for a particular individual depends on his perception of pain and tolerance built up after previous analgesic use.

– The use of non-opioid drugs allows the doctors to reduce the dose of opioid drugs or even avoid the opioids. This includes paracetamol and non-steroidals, ketamine and α2-agonists such as clonidine and dexmedetomidine.

***Regional analgesia*:**

– Regional techniques reduce respiratory depression but require experience to ensure safety procedures.

– Epidural analgesia may be achieved with local anaesthetic agents or opioids.

– Opioids allow to avoid vasodilatation and hypotension associated with local anaesthetic agents but do not produce as profound analgesia.

– The combination of opioid and local anaesthetic is synergistic.

– Intravenous opioids should be avoided or close monitoring should continue for 24 h after cessation of epidural opioids due to the potential for late respiratory failure.

– Local anesthetic agents may be used to block superficial nerves, e.g. intercostal nerve block with 3–5 ml 0.5 % bupivacaine plus adrenaline.

Non-pharmacological techniques. Adequate explanation, positioning and physical techniques may all reduce drug requirements.

NAUSEA AND VOMITING

Nausea and vomiting are particularly unpleasant complications of anaesthesia and surgery. The avoidance of these problems is more important to some patients than the provision of adequate analgesia. There are many factors associated with the occurrence of nausea and vomiting.

Factors associated with postoperative vomiting:

• ***Patient predisposition*:**

– age, sex, menstrual cycle, obesity;

– history of postoperative vomiting;

– history of motion sickness;

– anxiety, pain;

– recent food intake, prolonged fasting.

• ***Surgical factors*:**

– type of surgery;

– emergency surgery.

• ***Anaesthetic factors*:**

– inhalational agents;

– intravenous induction agents;

– opiates;

– duration of anaesthesia;

– distension of gut;

– oropharyngeal stimulation;

– experience of anaesthetist.

• ***Postoperative factors*:**

– pain;

– hypotension;

– hypoxaemia;

– movement of a patient;
– first intake of fluids/food;
– early mobilization.

This long list indicates that often there is no single, identifiable cause, although opioids are frequently at fault.

Because patients find nausea and vomiting distressing, it should be prevented if possible. The medical consequences of vomiting include the possibility of acid aspiration, electrolyte imbalance and dehydration, inability to take oral drugs and disruption of the wound. A vomiting patient upsets other patients in the recovery area and surgical ward.

Most anaesthetists prescribe antiemetics, but the consensus is that they should not be given prophylactically unless patients are deemed high risk. Drugs used include cyclizine, prochlorperazine, droperidol, metoclopramide and ondansetron.

ACID-BASE DISORDERS IN CRITICAL CARE

Disorders in the acid-base balance are commonly found in critically ill patients. Clinicians responsible for these patients need a clear understanding of acid-base pathophysiology in order to provide effective treatment for these disorders.

DEFINITIONS

pH is used to describe the proton concentration in a solution. It is the negative logarithm of the H^+ concentration, so when the blood pH is normal (7.40) (table 1) the H^+ concentration in blood is 40 nmol/L^{-1}. For every ten-fold increase in H^+ concentration the pH goes down by 1 unit.

Table 1

Nomal ranges of acid-base balance parameters

Parameter	Range
pH	7.35–**7.4**–7.45
$PaCO_2$	35–**40**–45 mmHg
Bicarbonate HCO_3^-	22–**24**–26 mEq/L
Base Excess (BE)	–2.0–**0**– +2.0 mEq/L

Acid is a substance that has the ability to give up a proton (H^+ — a positively charged hydrogen ion), and so when in an aqueous solution acids have a low pH.

Base is a substance that has the ability to accept a proton and has a high pH in solution.

Respiratory acid. Carbon dioxide is the only respiratory acid which can be exhaled. Carbonic acid is only formed when combined with water.

Bicarbonate. In acid-base determinations the concentration (in milliequivalents per liter) of the bicarbonate ion ($\mathbf{HCO_3^-}$) is calculated from the PCO_2 and pH.

Base excess (BE) is a measure of a metabolic acid level (normally zero). BE changes are termed excess or deficit. It is helpful to remember that the phrase "this patient has a base excess of minus ten" means "this patient has a metabolic acid excess (acidosis) of 10 mEq/1".

Acidosis and alkalosis. Acidosis is an abnormality which tends to produce an acid pH unless there is a dominating, opposing alkalosis. Alkalosis is the opposite phenomenon and tends to produce an alkaline pH unless there is a dominating, opposing acidosis.

The body can accommodate significant alterations in acid levels through buffering. The primary buffer in the blood is bicarbonate, which combines with excess acid (hydrogen ions) to make carbon dioxide decreasing the effect of the acid on the blood pH.

Buffering means that metabolic acidosis (a low tissue pH) does not always lead to the presence of metabolic acidaemia (a low blood pH) (figure 1). Blood pH only falls appreciably when the buffering capacity of the blood becomes overwhelmed.

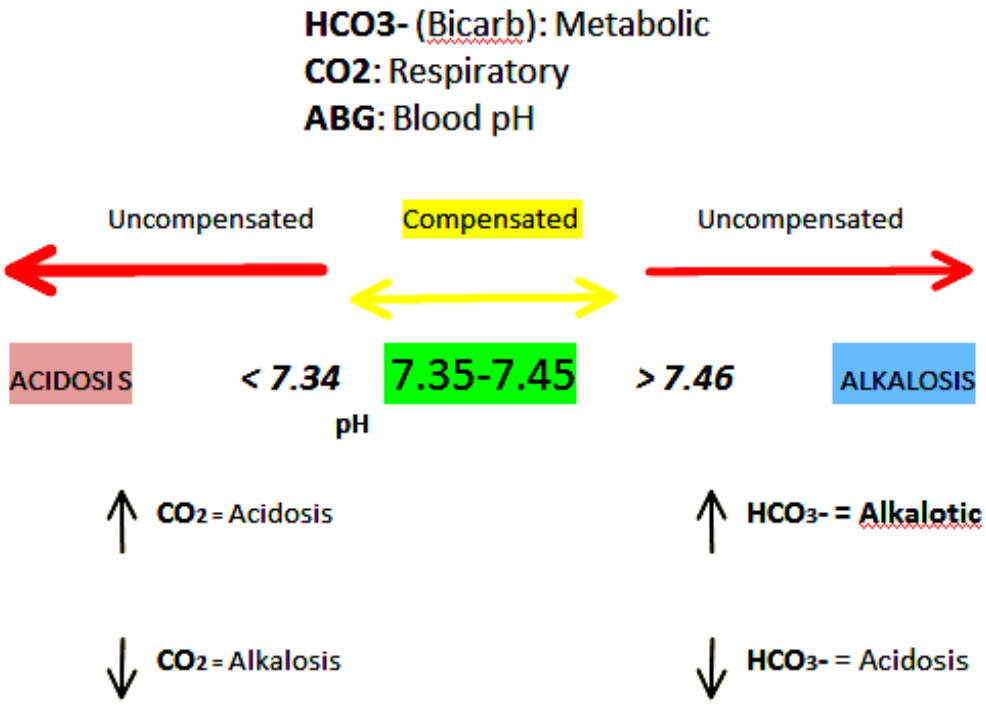

Fig. 1. Acid-base balance disorders

A drop in bicarbonate concentration is the hallmark of metabolic acidosis.

Pure **respiratory acidosis (high PCO_2)** implies a normal metabolic state and increases both the $[HCO_3^-]$ and $[H^+]$. Similarly, pure metabolic acidosis implies a normal PCO_2; the high $[H^+]$ is associated with a reciprocal fall in the $[HCO_3^-]$. In practice respiratory compensation promptly lowers the PCO_2, which reduces both the $[H^+]$ and the $[HCO_3^-]$.

ACID BASE CALCULATION. RULES AND PRACTICAL APPLICATION

An overview of the six sequential steps involved is outlined. A check of pH, pCO_2 & HCO_3 against the Henderson-Hasselbalch equation is usually difficult without a calculator. However, a quick check of the logical consistency of the results is often possible. For example, pH must be less then 7.4 if PCO_2 is high & HCO_3 is low. It is preferable to review the result print-out from the machine.

The six steps of systematic acid-base evaluation:

1. **pH**: assess the net deviation of pH from normal.
2. **Pattern**: check the pattern of bicarbonate & pCO_2 results.
3. **Clues**: check for additional clues in other investigations.
4. **Compensation**: assess the appropriateness of the compensatory response.
5. **Formulation**: bring the information together and make the acid base diagnosis.
6. **Confimation**: consider if any additional tests to check or support the diagnosis are necessary or available & revise the diagnosis if necessary.

The **first step** is to look at the arterial pH (table 2). A net acidaemia means that acidosis must be present. A net alkalaemia means that alkalosis must be present. A normal pH gives 2 possibilities: no acid-base disorder or a mixed disorder with alkalosis compensating acidosis.

Table 2

Systematic approach to blood gas analysis

Steps	Principle	Guidelines
pH: check arterial pH	The net deviation in pH will indicate whether an acidosis or an alkalosis is present (but will not indicate mixed disorders)	If an acidaemia is present then an acidosis must be present. If an alkalaemia is present then an alkalosis must be present. If pH is normal pH then either (no acid-base disorder is present) or (Compensating disorders are present i.e. a mixed disorder with an acidosis and an alkalosis)
Pattern: look for suggestive pattern in pCO_2 & $[HCO_3]$	Each of the simple disorders produces predictable changes in $[HCO_3]$ & pCO_2	If both $[HCO_3]$ & pCO_2 are low then suggests presence of either a metabolic acidosis or a respiratory alkalosis (but a mixed disorder cannot be excluded). If both $[HCO_3]$ & pCO_2 are high then suggests presence of either a metabolic alkalosis or a respiratory acidosis (but a mixed disorder cannot be excluded). If $[HCO_3]$ & pCO_2 move in opposite directions then a mixed disorder must be present. Which disorder is present is dependent on which change is primary and which is compensatory, and this requires an assessment based on the history, examination & other results

Steps	Principle	Guidelines
Clues: check for clues in the other biochemistry results	Certain disorders are associated with predictable changes in other biochemistry results	See separate list of "Aids to Interpretation" below
Compensation: assess the compensatory response	The 6 bedside rules are used to assess the appropriateness of the compensatory response	If the expected & actual values match => no evidence of mixed disorder If the expected & actual values differ => a mixed disorder is present
Formulation: formulate the acid-base diagnosis	Consider all the evidence from the history, examination & investigations and try to formulate a complete acid-base diagnosis	
Confirmation: check for specific biochemical evidence of particular disorders for confirmation	In some cases, further biochemical evidence can confirm the presence of particular disorders. Changes in these results may be useful in assessing the magnitude of the disorder or the response to therapy	Lactate, urinary ketones, salicylate level, aldosterone level, various tests for renal tubular acidosis

The **next step** is to determine whether any disorder is of the respiratory or metabolic type by reviewing the pattern and magnitude of the bicarbonate and pCO_2 results. If the disorder is minor (i.e. only one primary disorder present) then the acid-base disorder is diagnosed at this step. But the real problem is difficult to define, so a mixed disorder must always be checked. This is an important part of steps 2, 3 and 4.

Step 3 involves reviewing of other results looking for specific evidence of particular disorders. Some of these "clues" are outlined in the table 3.

Table 3

Some aids to interpretation of acid-base disorders

"Clue"	Significance
High anion gap	Always strongly suggests a metabolic acidosis.
Hyperglycaemia	If ketones also present in urine -> diabetic ketoacidosis
Hypokalaemia and/or hypochloraemia	Suggests metabolic alkalosis
Hyperchloraemia	Common with normal anion gap acidosis
Elevated creatinine and urea	Suggests uraemic acidosis or hypovolaemia (prerenal renal failure)
Elevated creatinine	Consider ketoacidosis: ketones interfere in the laboratory method (Jaffe reaction) used for creatinine measurement & gives a falsely elevated result; typically urea will be normal
Elevated glucose	Consider ketoacidosis or hyperosmolar non-ketotic syndrome
Urine dipstick tests for glucose and ketones	Glucose detected if hyperglycaemia; ketones detected in case of ketoacidosis

In most circumstances, these clues are confirmatory of the expected diagnosis but on occasion can alert to the presence of an unanticipated second disorder. An elevated anion gap can be particularly useful. Most of these "clues" are obtained from the biochemistry profile. An alert clinician can often correctly pick the diagnosis before the gas results are back.

The 4th step is to assess acid-base compensation. The approach discussed here involves the application of six rules. Much of the emphasis is made here to pick the presence of a second acid-base disorder.

Step 5: this stage is reached when overall acid-base assessment can be made.

Step 6: Sometimes the diagnosis suggests additional tests that can be used to confirm the diagnosis or at least allows doctors to make a more precise diagnosis (eg. measurement of the blood salicylate level in a child. In case it is high it can confirm a clinical suspicion of a salicylate overingestion). If a diagnosis of renal tubular acidosis is suspected then further specific tests should be done to specify further diagnosis.

The method of acid-base disorders assessment uses a set of six rules which are used primarily to check the magnitude of the patient's compensatory response. The rules should always be kept in mind — with practice this is not difficult.

A full assessment of blood-gas results must be based on a clinical assessment of each patient and understanding of the pathophysiology of the clinical conditions underlying the acid-base disorder. Do not interpret the blood-gas results as an intellectual exercise in itself. It is only one part of the overall assessment and management process.

Diagnosing a "metabolic acidosis", for example, by itself, is often of little clinical use. What is really required is a more specific diagnosis of the metabolic acidosis cause (e.g. diabetic ketoacidosis, acute renal failure, lactic acidosis) to initiate the appropriate management. The acid-base analysis must be interpreted and managed in the context of the overall clinical picture.

METABOLIC ACIDOSIS

Metabolic acidosis is a common component of a critical illness. Evaluation of this component can aid in making diagnosis, assessing the severity (and the likely outcome) and allow the clinician to determine whether current treatment is adequate.

Metabolic acidosis (a low pH in the tissue) exists when there is an excess level of fixed or exogenous acids in the body. Fixed acids include hydrochloric acid, sulphuric acid, phosphoric acid, ketoacids and lactic acid. Examples of exogenous acids are salicylate and methanol.

Metabolic acidosis is accompanied by a drop in plasma bicarbonate concentration (relative to the bicarbonate concentration present prior to the onset of the acidosis). This drop in bicarbonate can either be caused by bicarbonate loss or by the presence of extra acid.

When evaluating a critically ill patient with a metabolic acidosis it is necessary to determine the type of acidosis to identify the cause of acidosis. To classify metabolic acidosis it is useful to calculate the anion gap and, if present, the size of the osmolar gap.

THE ROLE OF THE ANION GAP

The anion gap is defined as the concentration difference between the major measured cations (positively charged ions) and anions (negatively charged ions) within the plasma (normally from 12 to 18 mmol/l) (figure 2).

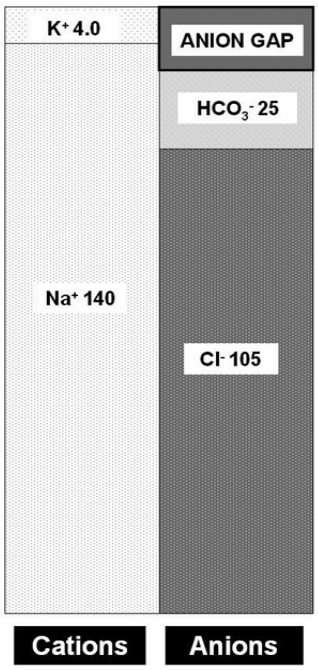

Fig. 2. Illustration of the anion gap (all figures are mmol/L^{-1})

Anionic proteins, phosphate, sulphate and low levels of organic acids, which are not measured, account for the difference (i.e. the "gap"). When examining the cause of a metabolic acidosis it is useful to calculate the anion gap.

Anion gap = $[Na^+ + K^+] – [HCO_3^- + Cl^-] = 15(\pm 3)$ mmol/L^{-1}.

A normal anion gap implies that acidosis occurs due to primary bicarbonate loss:

• Plasma bicarbonate is low (the hallmark of acidosis) and chloride concentration is raised.

• This bicarbonate loss may be:

– gastrointestinal (diarrhoea, fistula);

– renal (renal tubular acidosis, drug effect).

• Also occurs with rapid intravenous infusion of normal saline (excess chloride) or intravenous nutrition rich in cationic amino acids (e.g. arginine).

An increased anion gap implies that fixed acids are being retained or an abnormal organic acid is present.

• Plasma bicarbonate is low and chloride concentration is normal.

• Fixed acids may be retained in:
– uraemia;
– ketoacidosis (diabetic, alcoholic);
– lactic acidosis.
• If fixed acids are normal, exogenous acids should be considered:
– salicylate (aspirin) poisoning;
– methanol poisoning;
– ethylene glycol poisoning.

COMPENSATION FOR METABOLIC ACIDOSIS

When treating critically ill patients with metabolic acidosis, it is important to consider the adequacy of their ventilatory response to acidosis when deciding on treatment priorities. Buffering provides the main means of accommodating a metabolic acidosis.

As buffering capacity is exceeded, acidaemia develops. Once this rise in hydrogen ion concentration has reached the CSF, it is detected by chemoreceptors and compensation occurs by reducing carbon dioxide levels through hyperventilation (first described by Kussmaul).

Detection of low pH in CSF rather than blood explains the delay in this compensation; rapid onset acidosis (for example during convulsions) tends not to stimulate respiration in spite of a low blood pH. Even though respiratory compensation occurs relatively quickly, it can take up to twelve hours to reach maximal capacity.

Rule for a Metabolic Acidosis: the expected pCO2 (in mmHg) is calculated from the following formula:

$$\textbf{Expected } pCO_2 = 1.5 \times [HCO_3] + 8 \textbf{ (range: +/– 2)}$$

Comments:
– maximal compensation may take 12–24 hours to reach;
– the limit of compensation is a $PaCO_2$ of about 10 mmHg,
– hypoxia can increase the amount of peripheral chemoreceptor stimulation.

If the $PaCO_2$ is higher, then the compensation is at a very early stage or the patient has a superimposed respiratory acidosis. If this is the case then earlier intervention with respiratory support is indicated.

Metabolic Acidosis Correction. The treatment for a metabolic acidosis is judged largely on clinical grounds. Bicarbonate therapy is justified when metabolic acidosis accompanies difficulty in resuscitating an individual or in maintaining cardiovascular stability.

A typical dose of bicarbonate might be 1 mEq per kilogram of the body weight followed by a repeated blood gas analysis. The effect of a bicarbonate dose can be anticipated by calculating the dose required for complete correction. A lesser dose has a proportionately less effect.

$$\textbf{Dose (mEq)} = 0.3 \times \textbf{Wt (kg)} \times \textbf{BE (mEq/L)}$$

RESPIRATORY ACIDOSIS

The decision to ventilate a patient to reduce the $PaCO_2$ is a clinical decision and is based on exhaustion, prognosis, prospect of improvement from concurrent therapy, and in part on the $PaCO_2$ level. Once the decision is made, the $PaCO_2$ helps calculate the appropriate correction.

The Rule for Acute Respiratory Acidosis. The $[HCO_3]$ will increase by 1 mmol/l for every 10 mmHg elevation in pCO_2 above 40 mmHg.

Expected $[HCO_3]$ = 24 + {(Actual pCO_2 – 40) / 10}

Comment: the increase in CO_2 shifts the equilibrium between CO_2 and HCO3 to result in an acute increase in HCO_3. This is a simple physicochemical event and occurs almost immediately.

The Rule for Chronic Respiratory Acidosis. The $[HCO_3]$ will increase by 4 mmol/l for every 10 mmHg elevation in pCO_2 above 40 mmHg.

Expected $[HCO_3]$ = 24 + 4 {(Actual pCO_2 – 40)/10}

Comment: with chronic acidosis, the kidneys respond by retaining HCO_3, that is, renal compensation occurs. This takes a few days to reach its maximal value.

RESPIRATORY ALKALOSIS

The Rule for Acute Respiratory Alkalosis. The $[HCO_3]$ will decrease by 2 mmol/l for every 10 mmHg decrease in pCO_2 below 40 mmHg.

Expected [HCO3] = 24 – 2 {(40 – Actual pCO_2)/10}

Comment: in practice, this acute physicochemical change rarely results in a $[HCO_3]$ of less than about 18 mmol/l. (After all there is a limit to how low pCO_2 can fall as negative values are not possible!) So a $[HCO_3]$ of less than 18 mmol/l indicates a coexisting metabolic acidosis.

The Rule for a Chronic Respiratory Alkalosis. The $[HCO_3]$ will decrease by 5 mmol/l for every 10 mmHg decrease in pCO_2 below 40 mmHg.

Expected $[HCO_3]$ = 24 – 5 {(40 – Actual pCO_2) / 10} (range: +/– 2)

Comments: it takes 2 to 3 days to reach maximal renal compensation; the limit of compensation is a [HCO3] of about 12 to 15 mmol/l.

METABOLIC ALKALOSIS

A supranormal arterial blood pH with a base excess > 2 mmol/l caused either by loss of (non-carbonic) acid or gain of base. As the kidney is usually efficient at excreting large quantities of bicarbonate, persistence of a metabolic alkalosis usually depends on either chronic renal failure or a diminished extracellular fluid volume with severe depletion of K^+.

The patient is usually asymptomatic though, in case of spontaneous breathing he will hypoventilate. A metabolic alkalosis will cause a left shift of the oxyhaemoglobin curve, reducing oxygen availability to the tissues.

Causes. Loss of total body fluid, Na^+, Cl^+, K^+ usually due to:

– diuretics;

– large nasogastric aspirates, vomiting;

– secondary hyperaldosteronism with potassium depletion;

– use of haemofiltration replacement fluid containing excess buffer (e.g. lactate);

– renal compensation for chronic hypercapnia. This can develop within 1–2 weeks. Although more apparent when the patient hyperventilates, or is hyperventilated to normocapnia, an overcompensated metabolic alkalosis can occasionally be seen in the chronic state (i.e. a raised pH in an otherwise stable long term hypercapnic patient);

– excess administration of bicarbonate;

– excess administration of citrate (large blood transfusion);

– drugs, including laxative abuse, corticosteroids;

– Rarely, Cushing's, Conn's, Bartter's syndrome.

Management:

1. Replacement of fluid, sodium, chloride (i.e. give 0.9 % saline) and potassium losses are often sufficient to restore acid-base balance.

2. With distal renal causes related to hyperaldosteronism, addition of spironolactone (or potassium canrenoate) can be considered.

3. Active treatment is rarely necessary. If so, give ammonium chloride 5 g tds PO. Hydrochloric acid has been used on occasion of severe metabolic alkalosis (pH > 7.7). It should be given via a central vein in a concentration of 1 mmol HCl per ml water at a rate not exceeding 1 mmol/kg/h.

4. Compensation for a long-standing respiratory acidosis, followed by correction of that acidosis, e.g. with mechanical ventilation, will lead to an uncompensated metabolic alkalosis. To correct it, treatment with acetazolamide can be considered. Mechanical "hypoventilation", i.e. maintaining hypercapnia, can also be considered.

The Rule for a Metabolic Alkalosis. The expected pCO_2 (in mmHg) is calculated according to the following formula:

$$\textbf{Expected } pCO_2 = 0.7\,[HCO_3] + 20 \textbf{ (range: +/– 5)}$$

Comment: the variation in pCO_2 predicted by this equation is relatively large.

Remember that only primary processes are called acidosis or alkalosis. The compensatory processes are just that — compensation (figure 3). Phrases such as "secondary respiratory alkalosis" should not be used.

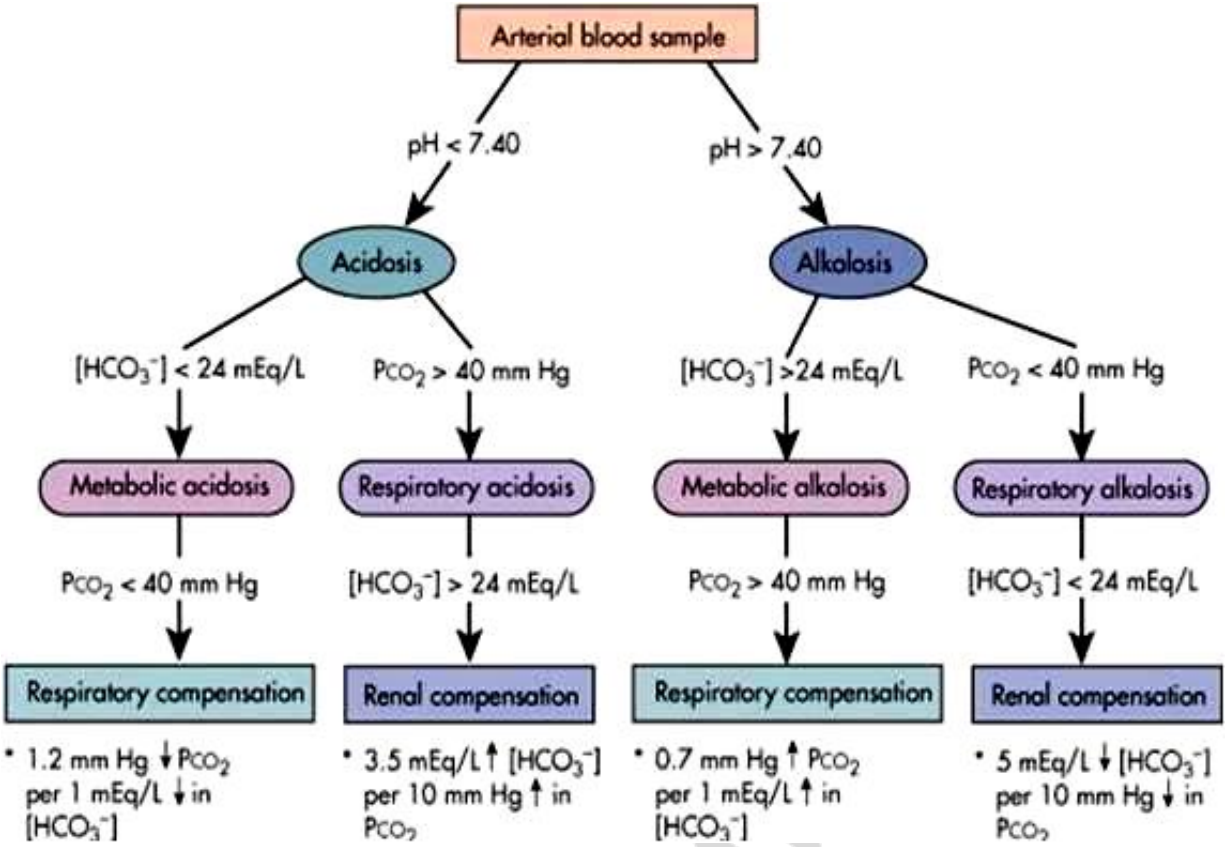

Fig. 3. Acide-base balance disturbances and their compensation

WATER AND ELECTROLYTE BALANCE DISORDERS

Disorders of Na^+ and K^+ homeostasis are very common problems, encountered in clinical practice on an almost daily basis. They are frequently mismanaged due to poor understanding of Na^+ and K^+ metabolism.

Surgical patients are frequently affected by electrolyte imbalance. They are often sedated or not allowed to eat and drink, and hence have intravenous fluid infusions prescribed for extended periods.

FLUID AND ELECTOLYTE PHYSIOLOGY

Fluids and electrolytes are present in a number of "compartments" in the body, according to their chemical composition.

Plasma is the fluid component of blood surrounding the red cells, intracellular fluid (ICF) is the fluid within the body's cells, and interstitial fluid (ISF) is the fluid found between the cells, outside blood vessels.

The intracellular and extracellular compartments are separated from one another by the plasma membrane of the cells. The extracellular compartments (interstitial/plasma/lymph) are separated by a layer of endothelial cells surrounded by a basement membrane; the capillaries.

To cross from the plasma to the cells or vice versa, substances must either cross both membranes of the endothelial cells or travel between the cells and then cross the basement membrane.

Capillaries act rather like a leaky hosepipe; although the bulk of the fluid flows along the pipe, the pressure forces some fluid out of the walls. The balance of hydrostatic and osmotic forces causing movement out and into the capillaries is known as Starling forces.

Water is present in plasma, ISF and ICF and passes freely between compartments under the influence of osmotic pressure gradients. The ISF and plasma together make up the extra cellular fluid (ECF).

Water accounts for 60 % of adult body weight (total body water (TBW) = 42 litres for a 70 kg adult).

TBW = 0.6 × Body Weight

Two thirds of this is ICF (28 litres) and one third is ECF (14 litres). The ECF can then be further subdivided into ISF (three quarters — 10.5 litres) and plasma (one quarter — 3.5 litres) (figure 4).

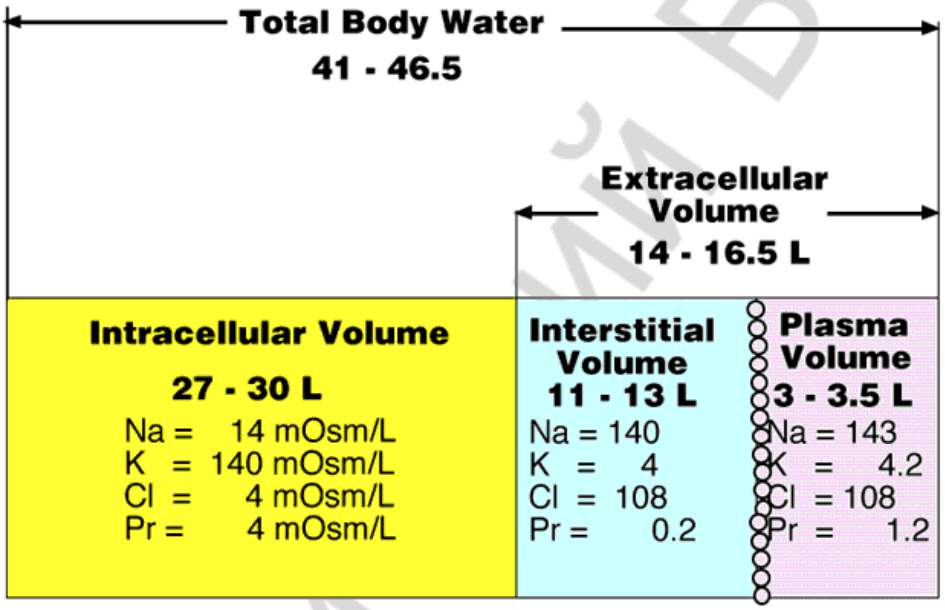

Fig. 4. Water compartments in the body

The ECF contains most of the sodium in the body, with equal sodium concentrations in the ISF and plasma. Sodium and water can pass freely through capillary membranes whilst albumin (the most important oncotically active constituent of the ECF)does not.

Albumin is unequally distributed in the intravascular and interstitial compartments (normal concentrations of 40 g/l^{-1} and 10 g/l^{-1} respectively) and is excluded from the intracellular compartment. This distribution helps to retain fluid within the plasma due to the osmotic effect of albumin.

Fluid replacement. Fluid replacement should address daily maintenance requirements and additional losses. Maintenance fluid, for patients who are unable take fluid enterally, should provide at least the minimal requirements of water, sodium and potassium. Remember that water and electrolyte requirements may increase in certain disease processes such as diarrhoea and vomiting.

TYPES OF INTRAVENOUS FLUID

Crystalloids are substances which contain relatively small molecules that dissociate into ions to form true solutions, and are therefore capable of passing through a semi-permeable membrane. Commonly used crystalloids include 0.9 % saline, glucose and Hartmann's (Ringer's lactate) solution.

On intravenous infusion, 0.9 % saline and Hartman's solution rapidly distribute into the entire ECF, leaving 1/4 of the infused volume in the IVS, i.e. 250 ml of a 1000 ml fluid bolus.

5 % glucose (the optical isomer 'dextrose' is now rarely found) loses all of its glucose at first pass through the liver and skeletal muscles.

The remaining water is distributed evenly throughout the entire TBW, leaving only 1/12 of the original volume in the intravascular space (IVS) (i.e. only 83 ml of a 1000 ml fluid bolus).

Colloids contain larger molecules that are dispersed throughout a solvent, i.e. they do not dissolve to form solutions. They cannot pass through semi-permeable membranes and consequently tend to remain in the IVS.

Gelatins (e.g. gelofusine, haemaccel). These colloids are polysaccharides, derived from gelatin, which are in turn derived from collagen and have an average molecular weight of 35,000 Daltons. (A Dalton or "atomic mass unit" is a unit of mass, equal to 1/12 the mass of carbon 12, which is assigned a mass of 12.)

Their half-life in the IVS is approximately 3 hours and they are renally excreted. Anaphylactic reactions have been reported with an incidence of 1 in 13,000. Gelatin solutions may interfere with platelet function and coagulation via a reduction in levels of the von Willebrand factor.

Dextrans (e.g. dextran 40, dextran 70). A dextran is a polysaccharide, derived from sucrose by the action of the bacterium Leuconostoc mesenteriodes. Dextran 40 has a molecular weight of 40,000 Daltons and dextran 70 a molecular weight of 70,000 Daltons.

The intravascular half-life increases with a molecule size, and ranges from 15 minutes to several days. The smaller molecular weight dextrans are predominantly excreted unchanged by the kidney (accounting for up to 70 % of Dextran 40), while the larger molecular weight dextrans are retained in the circulation for several days. Dextrans have an incidence of anaphylaxis of 1 in 4,500.

Dextrans are rarely used for fluid resuscitation, but they have a role in thrombo-embolic prophylaxis via volume expansion, reduction in viscosity, and lowering platelet and erythrocyte aggregation. Side effects include renal failure (due to tubular obstruction), interference with cross matching and coagulopathy.

Starches (e.g. hydroxyethyl starch (HES), Hetastarch). These synthetic colloids are of a similar structure as glycogen, consisting of glucose chain of molecules (> 90 % amylopectin).

They have molecules with a large range of molecular weights, with the smaller molecules (approximately 50,000 Daltons) excreted by the kidney and

the larger molecules slowly broken down by alpha-amylase hydrolysis of glycosidic bonds, yielding molecules small enough for renal clearance.

Anaphylactic reactions are rare with an incidence of 1 in 16,000. Slight prolongation of coagulation may occur after large infusions, and pruritis has also been reported. Total dose should not exceed 20 ml/kg^{-1} (1500 ml/day^{-1} for an average male).

Human albumin solutions are derived from human plasma by fractionation, and then they are heat sterilized to reduce the risk of infective transmission. They are presented as either 4.5 % (40–50 g/l^{-1}) or 20 % (150–200 g/l^{-1}) solutions in 0.9 % saline.

Traditionally albumin solutions were used as colloid in patients who were hypoalbuminaemic or in cases where high albumin loss was anticipated (e.g. burns), and also in the resuscitation of children.

DISTRIBUTION OF SODIUM AND POTASSIUM

The distribution of Na^+ and K^+ can be thought of as opposite — where one is found abundantly, the other is at low concentration. Sodium is the most prevalent cation in the ECF, with a normal level of about 140 mmol/l^{-1}, but with a typical intracellular concentration of around 10 mmol/l^{-1}.

In contrast, potassium is the most prevalent cation in the ICF, with a concentration around 150 mmol/l^{-1}. The intracellular space is the largest fluid compartment in the body, and this makes it the most abundant cation overall. Only about 1 % of the total body K^+ is found in the plasma with the levels kept between 3.5 and 4.5 mmol/l^{-1}.

The cell membrane acts as the barrier between the potassium-rich ICF and the sodium-rich ECF. While it allows free passage of water and non-polar, hydrophobic molecules, it is impermeable to large molecules or charged particles. Hence Na^+ and K^+ can only cross where specific carrier proteins allow them to do so.

In vivo, the membrane remains relatively impermeable to both Na^+ and K^+. Excitable cells can change their permeability to allow the influx and efflux of ions that constitute an action potential.

At rest, large concentration gradients for Na^+ and K^+ are maintained by the action of Na^+/K^+-ATPase, a transmembrane protein which pumps out 3 Na^+ for each 2 K^+ it pumps in. This also maintains the net negative resting membrane potential since it involves a net transfer of one positive charge out of the cell on each cycle.

Although the Na^+/K^+-ATPase maintains the concentration gradients across the cell membrane, other mechanisms are in overall control of total body Na^+ and K^+ levels.

SODIUM HOMEOSTASIS

The volume of circulating plasma is vitally important to the body, since an adequate plasma amount is required for normal tissue perfusion. The plasma

volume is proportional to the ECF volume, and since Na^+ is the major cation of the ECF, total body Na^+ content is proportional to ECF volume.

In healthy individuals, the kidney strives to achieve Na^+ balance — that is, to have Na^+ excretion equal to Na^+ ingestion. Long-term control of blood pressure is achieved by the excretion or retention of Na^+ (and hence plasma volume) in the kidney.

The vast majority (99–99.5 %) of Na^+ filtered by the kidney is reabsorbed in the proximal tubule and the loop of Henle. This reabsorption seems to be largely fixed, even in sodium overload. There is much greater control over the 0.5 % of filtered Na^+ reabsorbed in the distal tubule and collecting ducts.

It is this proportionately a tiny amount, that allows the body to either retain sodium and water or excrete them when necessary. Various hormones influence this balance of retention and excretion.

POTASSIUM HOMEOSTASIS

Small increases in the serum potassium concentration can quickly become life-threatening. The kidneys cannot excrete potassium quickly enough to contain surges due to oral potassium loads, and hence intracellular buffering plays an important role in homeostasis.

As the kidneys excrete the excess of potassium and its serum concentration falls, K^+ is released again from the cells. In the normal state 90 % of daily potassium intake is excreted via the kidneys and the rest via the colon. About 90 % of the filtered potassium load is reabsorbed by the start of the distal tubule, and this figure is largely constant through a wide range of potassium intake. The overall urinary excretion of K^+ is therefore controlled by the distal tubule and collecting ducts.

Water and electrolyte requirements for adults:

– water — 30–40 ml/kg^{-1};
– Na^+ — 1.0–2.0 mmol/kg^{-1};
– K^+ — 0.7–1.0 mmol/kg^{-1};
– Ca_2^+ — 0.1 mmol/kg^{-1};
– Mg_2^+ — 0.1 mmol/kg^{-1};
– Cl^- — 1.0–2.0 mmol/kg^{-1}.

ROUTINE INTRAOPERATIVE ADMINISTRATION

The goals of intraoperative fluid administration are to maintain adequate oxygen delivery, normal electrolyte concentrations and normoglycemia.

The total fluid requirement is composed of compensatory intravascular volume expansion (CVE), deficit replacement, maintenance fluids, restoration of losses and substitution of fluid redistribution (3rd space fluids):

Rate = CVE + deficit + maintenance + loss + third space

Deficits. The fluid deficit is equal to the maintenance fluid requirement multiplied by the hours since the last intake plus unreplaced preoperative external

and third space losses. When hypovolemia is present, it is necessary to infuse sufficient fluid to restore MAP, heart rate, and filling pressures to neally normal values prior to induction.

Losses. External losses (e.g., blood, ascites) should be replaced to maintain normal blood volume and normal composition of the ECFV. Blood loss is replaced initially with either 3 ml of balanced salt solution or 0.9 percent NaCl for each milliliter of blood loss.

For each milliliter of blood loss, 1 ml of colloid solution should be used, when crystalloid replacement provides only transient improvement of filling pressures, arterial blood pressure and heart rate despite full calculated infusion rates. Packed RBC infusions are used roughly 1 ml for each 2 ml of the lost blood plus either crystalloid or colloid as described above.

Evaporation from exposed viscera is entirely water, but the electrolyte is left behind, leading to a need of free water. The amount evaporated is directly proportional to temperature, exposed surface area and inversely proportional to relative humidity.

Redistribution. Redistribution, or so-called the 3rd-space losses, occurs primarily due to tissue edema and transcellular fluid displacement. Functionally this fluid is not available to the vascular space. Colloid enters the injured tissue at a more rapid rate than normally, but at a slower rate than electrolyte.

For example, bowel wall edema is lessened by utilizing colloid containing fluids compared with crystalloid fluids. The composition of the third-space losses is the equivalent to the ECFV electrolyte concentration plus a smaller amount of protein. Therefore, balanced salt solution is the most appropriate replacement fluid.

The redistributed volume correlates roughly with the degree of tissue manipulation. Intra-abdominal procedures with small incisions (e.g., hysterectomy) may require an additional 2 ml/kg/h, while a major bowel resection will require an additional 4 to 6 ml/kg/h.

Dehydration. Dehydration is the pathological loss of fluids (and usually accompanying electrolytes). It may be the primary issue, or merely a manifestation of some other processes.

History. In addition to the usual history, pay particular attention to “ins and outs”. Determine what fluids the patient has, see if there is a history of poor intake, or if the patient has been drinking excessive amounts of fluids. Ask which fluids and food the patient has been consuming.

On the output side, get a quantitative sense of what fluids have been lost. Has the patient been vomiting, had diarrhoea, lost blood, had an NG tube present to remove gastric secretions, sweated excessively? How frequently and how much did the patient urinate? Place all this information in a time frame.

CAUSES OF HYPONATRAEMIA

Osmolality and osmolarity differ according to whether the number of osmotically active particles is dissolved in a kilogram or a liter of solvent respectively.

Osmolality is measured in the laboratory with an osmometer that either assesses the depression of a sample's freezing point or the depression of its vapour pressure. It is preferablly to use the former as any volatile alcohols in the sample will evaporate as the sample is heated and the results from this method use will be inaccurate. Osmolarity can be calculated using various formulae including the following:

Calculated osmolarity = 2 [Na^+] + urea + glucose

The overall osmolarity of all three compartments is identical to about 280–300 mOsmol/l.

Consideration of the osmotic state of the patient is essential in the evaluation of hyponatraemia:

Normal osmolarity — pseudohyponatraemia:

– Due to a measurement error which can result when the solid phase of plasma (that due to lipid and protein) is increased.

– Typically caused by hypertriglyceridaemia or paraproteinaemia.

High osmolarity — translocational hyponatraemia:

– Occurs when an osmotically active solute that cannot cross the cell membrane is present in the plasma.

– Most solutes such as urea or ethanol can enter the cells, and cause hypertonicity without cell dehydration.

– However, in case of the insulinopenic diabetic patient, glucose cannot enter cells and hence water is displaced across the cell membrane, dehydrating the cells and 'diluting' the sodium in the serum.

– This is also the cause of hyponatraemia seen in the TURP syndrome, in which glycine is inadvertently infused to achieve the same effect.

Low osmolarity — true hyponatraemia. True hyponatraemia is always a hypo-osmolar condition. The next stage is to consider the volume status of the patient:

Hypovolaemic hyponatraemia:

– Loss of both sodium and water, but proportionately more sodium.

– Caused by solute and water losses from either a renal or gastrointestinal source.

– Usually these patients are consuming water or hypotonic fluid, although not in quantities sufficient to restore normovolaemia.

– An estimation of the urinary sodium level can be helpful: a level below 30 mmol/l^{-1} suggests an extrarenal cause, while a level above 30 mmol/l^{-1} suggests a primary renal problem.

Euvolaemic hyponatraemia:

– The most common form seen in hospitalized patients.

– May have a slight increase or decrease in volume, but it is not clinically evident, and they do not have oedema.

– The most common cause is the inappropriate administration of hypotonic fluid.

– The syndrome of inappropriate ADH secretion (SIADH) also causes euvolaemic hyponatraemia; in order to make this diagnosis one must first exclude renal, pituitary, adrenal or thyroid dysfunction, and the patient must not be taking diuretics.

Hypervolaemic hyponatraemia:

– Characterised by both sodium and water retention, with proportionately more water.

– Therefore has an increased amount of total body sodium.

– Causes are all characterised by disordered water excretion, and are usually easy to diagnose.

Effects and treatment of hyponatraemia. The normal range of serum sodium is usually quoted as being approx. 135–145 mmol/l^{-1}; however, levels between 125 mmol/l^{-1} and 150 mmol/l^{-1} are often asymptomatic.

Outside this range there is an increasing frequency of nausea, lethargy, weakness and confusion, and levels above 160 mmol/l^{-1} or below 110 mmol/l^{-1} are strongly associated with seizures, coma and death. As serum sodium and osmolarity fall, water tends to enter the cells causing them to swell. Clinically this is the most important for the brain.

Several factors put patients at increased risk of complications of hyponatraemia or its treatment:

– Postoperative patients, premenopausal women, elderly women taking thiazides, children, and patients who are hypoxaemic are all at increased risk of acute hyponatraemic cerebral oedema.

– Malnourished patients, alcoholics, those with burns or hypokalaemia are all at increased risk of osmotic myelinolysis due to overly rapid correction of hyponatraemia.

A recent review of the literature has pointed out that there is as yet no consensus on the optimum treatment of dysnatraemia. However, all authorities stress the importance of distinguishing between hyponatraemia that has developed acutely (usually it takes less than 48 hours) and chronic hyponatraemia. This is because of important differences in the management between the two groups.

Most authors suggest that hyponatraemia that has developed acutely (for instance, in the immediate postoperative period) can be safely treated with rapid correction. Rapid correction should only be undertaken in patients who are symptomatic, and the aim of treatment is to correct the level until the symptoms resolve.

Some sources have suggested that correction by up to 2 mmol/l^{-1}/h^{-1} is safe in the initial treatment of acute hyponatraemic states. Correction to a serum Na^+ of > 135 mmol/l^{-1} may be safe in this situation, but it is not necessary to correct rapidly once the symptoms have resolved.

Methods of rapid correction might include the administration of furosemide and/or hypertonic saline; however management should be by a specialist in an appropriate setting, with hourly monitoring of serum Na^+ levels.

Determine the Sodium Deficit

Na deficit (mEq) = (135 – Na (current) × Bode weight (kg) ×0.6

This formula is based on the assumption that the desired [Na^+] is 135 mEq/L, and that total body water is about 60 % of body weight (although this varies with age).

The treatment of chronic hyponatraemia is also determined by the presence or absence of symptoms. In the presence of symptoms, a rapid correction of up to 10 mmol/l^{-1} may be permissible.

Following this, however, the rate of reversal should be limited to 1.5 mmol/l^{-1}/h^{-1} and to no more than 8 mmol/l^{-1} over 24 hrs. Some sources suggest that a rate of 12 mmol/l^{-1} in 24 hrs is safe.

Fluid restriction is the mainstay of treatment in these patients, who need to have regular neurological assessment and rechecking of serum electrolytes at least every 12 hours.

In the long-term, treatment is aimed at identifying and dealing with the underlying cause. Future advances in the shape of selective ADH (AVP) antagonists (so-called aquaretics) contribute to the improvement in the long-term management of chronic hyponatraemia.

In all cases, hypovolaemia, if present, must be corrected first with 0.9 % saline. This removes the ADH response that is accentuating the sodium/water imbalance.

In hypervolaemic patients the treatment is aimed at fluid and salt restriction and application of loop diuretics. Aquaretics may also be useful for these patients. While evidence is lacking that chronic hyponatraemia is associated with worse surgical outcomes, asymptomatic hyponatraemia should be regarded as a relative contraindication to elective surgery.

CAUSES OF HYPERNATRAEMIA

Hypernatraemia is either caused by excessive salt intake, or (much more frequently) inadequate water intake. As with hyponatraemia, consideration of the volume status of the patient is essential.

Hypovolaemic hypernatraemia:

– Loss of both sodium and water, but relatively more water.

– An estimation of the urinary sodium level can be helpful: a level below 30 mmol/l^{-1} suggests an extrarenal cause, while a level above 30 mmol/l^{-1} suggests a primary renal problem.

– These patients are either not able to take in adequate fluid to replace their losses, or are prevented from doing so.

Euvolaemic hypernatraemia:

– Occurs when body water losses are partially replaced.

– May be due to a lack of available water, or due to a blunting of the normal thirst response seen in the extremes of age.

Hypervolaemic hypernatraemia:

– Seen where sodium retention is not matched by increased fluid intake.

– More uncommon than the other two types of hypernatraemia.

Treatment of hypernatraemia. Firstly any volume deficit should be corrected with 0.9 % saline until the hypovolaemia, as measured by orthostatic hypotension, improves.

The water deficit is calculated as:

Water deficit = TBW × (Na current – Na desired) / Na current

The cause of fluid loss should also be investigated and treated. The total body water deficit can be calculated based on the serum sodium and the assumption that 60 % of the body is water — this deficit should then be corrected with 5 % dextrose, with half given in the first 12–24 hours, and the rest over the next 24–36 hours.

In case of hypervolaemic hypernatraemia, the removal of excess sodium is the aim, and loop diuretics or dialysis may achieve this if the patient has renal dysfunction.

CAUSES OF HYPOKALAEMIA

Hypokalaemia is caused by a shift of potassium into cells, or more commonly by a total body potassium deficit. Occasionally the two situations may co-exist.

Intracellular potassium shifting:

– Excess insulin (exogenous or endogenous).

– β-adrenoceptor agonists (such as endogenous catecholamines or exogenous salbutamol).

– Theophylline toxicity.

– Acute rise in plasma pH.

Total body potassium deficit:

– May result from either decreased intake or increased losses.

– Diet must be severely deficient in K^+ over a long period in order to reach a position of clinical hypokalaemia; hence seen most commonly in alcoholics.

– Excessive losses may be either renal or extrarenal.

Renal causes include:

– Diuretics.

– Mineralocorticoid excess.

– Glucocorticoid excess.

– Renal tubular acidosis Type I and II.

– Diabetic ketoacidosis — glucose causes an osmotic diuresis, washing out potassium.

– Vomiting — which is not caused by a loss of K^+ in the vomit, it is rather caused by a loss of H^+ and water leading to metabolic alkalosis and increased aldosterone.

– Ureterosigmoidostomy.

– Rare inherited conditions such as Bartter's and Gitelman's Syndromes.

Extrarenal causes include:

– Inadequate intake.

– Excessive perspiration.

– Chronic diarrhoea.

– Gastrointestinal fistulae.

Effects of hypokalaemia. The effects of hypokalaemia depend upon the serum level. A normal value of 3.5–4.5 mmol/l^{-1} is generally accepted, but levels of 3.0–3.5 mmol/l^{-1} are usually asymptomatic. Below 3.0 mmol/l^{-1} general symptoms of weakness, lassitude and constipation are common.

Below 2.5 mmol/l^{-1} muscle necrosis has been described (probably due to an inability to increase blood flow during exercise), and below 2.0 mmol/l^{-1} an ascending paralysis may be seen, eventually leading to respiratory compromise.

Patients without underlying cardiac disease are unlikely to suffer myocardial effects, even at levels below 3.0 mmol/l^{-1}. However, those with ischaemic heart disease, heart failure or left ventricular dysfunction are at risk of arrhythmias with only mild or moderate hypokalaemia. Initially U-waves are seen on the ECG, with gradual sagging of the ST segment and flattening of the T-wave.

Slight widening of the QRS complex and PR elongation may be seen, and there is a predisposition to both ventricular and supraventricular ectopic rhythms, especially in a patient taking digoxin.

Renal effects of hypokalaemia include metabolic acidosis, increased ammoniagenesis and numerous structural changes in the kidney if the condition persists.

As with sodium, the rapidity of the change in K^+ level has a large influence on the severity of the symptoms.

Treatment of hypokalaemia. Once intracellular K^+ shifts have been excluded (theophylline toxicity, hyperinsulinaemia) the treatment of hypokalaemia is aimed at replacement of potassium. Ideally, this should be oral supplementation, but if the shifts are severe the initial replacement is best given intravenously, through a central vein within a critical care facility.

Careless administration of intravenous potassium is the commonest cause of hyperkalaemia in hospitalized patients, so appropriate consideration should be given to this decision. In any case, the rate of administration should not exceed 20 mmol/h^{-1}, and the patient should have continuous cardiac monitoring.

In the absence of factors causing potassium shifting into cells, the serum potassium is a good guide to the total body potassium deficit.

A fall from 3.5 to 3.0 mmol/l^{-1} suggests a deficit in the order of 5 % (around 175 mmol); a decline from 3.0 to 2.0 mmol/l^{-1} suggests a further 200–400 mmol deficit.

Magnesium deficiency is very commonly associated with hypokalaemia and levels should be checked and magnesium replaced if appropriate.

Prophylactic administration of potassium to postoperative patients at risk of cardiac abnormalities is common practice. There is evidence that minor elevation

of K^+ (within the normal range) can reduce the incidence of electrocardiac abnormalities such as U-waves, bifid T-waves and signs of digitalis toxicity.

Additionally, potassium supplementation may benefit patients with abnormal repolarisation in the context of congestive cardiac failure.

However, the practice of artificially augmenting the potassium level to abolish single ventricular ectopic beats or as a routine treatment for all postoperative patients is no longer considered best practice.

CAUSES OF HYPERKALAEMIA

Hyperkalaemia may be due to either an overall increase in total body potassium, or an acute shift of potassium from the intracellular to the extracellular compartment.

Extracellular potassium shifts occur in case of:

– Acidosis — H^+ is taken into the cell in exchange for K^+.

– Insulin deficiency, with hyperglycaemia — note that this is often found coexistent with a profound total body potassium deficit.

– Digitalis toxicity — due to inhibition of the Na^+/K^+-ATPase.

– β-blockers — typically cause only a mild elevation in K^+.

– Exercise — potassium efflux from skeletal muscle as a result of muscular contraction

– Suxamethonium administration.

Fasciculations lead to an efflux of potassium from the skeletal muscle, similar to the effect of exercise but more pronounced and more acute. A single 100 mg dose may cause serum potassium to rise by up to 1.0 mmol/l^{-1}. If the patient already has elevated serum potassium, this may be enough to cause a fatal arrhythmia.

In patients with a denervated muscle, the usual mechanisms keeping the acetylcholine receptors in the synaptic cleft are disturbed, and they spread out to cover the whole of the muscle fibre (extrajunctional receptors). Suxamethonium administration is contraindicated in these patients as it causes a much bigger potassium efflux and often leads to dangerous hyperkalaemia.

Excessive potassium input occurs in case of:

– Cellular lysis, as seen in haemolysis, rhabdomyolysis or tumour lysis syndrome.

– Inappropriate prescription of K^+-containing IV fluids or supplements is a very important cause in hospitalized patients.

Impaired renal excretion occurs in case of:

– Decreased GFR — renal failure is the commonest cause of hyperkalaemia.

– Mineralocorticoid insufficiency — this may be due to primary adrenal failure, hyporeninaemic hypoaldosteronism (Renal tubular acidosis type IV), or due to drugs similar to ACE inhibitors, Angiotensin-II receptor antagonists or spironolactone.

– Potassium sparing diuretics.

Primary renal insults (such as interstitial nephritis) causing decreased potassium excretion in the distal tubules and collecting ducts.

Pseudohyperkalaemia:

– A common cause of spuriously elevated potassium levels.

– The most common causes are in vitro haemolysis, or leaving the tourniquet on for an extended period prior to blood sampling.

– It is also seen in patients with highly elevated white cell or platelet counts, due to secretion of potassium from these cells prior to laboratory analysis.

Effects of hyperkalaemia. The most important effects of hyperkalaemia are on the heart. Levels below 6.0 mmol/l^{-1} rarely cause any clinical symptoms. As the serum K^+ level increases, ECG changes are noted: firstly peaking of the T waves, then broadening of the P-waves and QRS-complex when the level is > 7.0 mmol/l^{-1}.

Finally the ECG takes on a sinusoidal pattern, which is a precursor to cardiac arrest. Terminal ECG changes may develop very quickly, and even with mildly elevated potassium levels any sign of ECG involvement should prompt immediate treatment.

As with other electrolyte disturbances, the speed of hyperkalaemia onset is very important. A relatively small increase, if it occurs over a short time, can precipitate a fatal arrhythmia where a much higher level may be tolerated (for instance, in the insidious onset of renal failure) if it has developed over a longer period.

Other sequelae of hyperkalaemia include paraesthesiae, weakness, paralysis, a decreased renal production of ammonia, an increased renal retention of H^+ and a subsequent metabolic acidosis, natriuresis, and elevated levels of aldosterone and insulin.

Treatment of hyperkalaemia. The various therapies commonly used to reduce the K^+ level acutely may be divided into two groups: those that seek to transiently move the potassium to the intracellular compartment, and those that seek to remove an overall surplus of potassium from the body.

While the former group may be used in the vast majority of hyperkalaemic patients, not all hyperkalaemic patients have the excessed total body potassium.

The classic example is an acidotic patient with diabetic ketoacidosis, who has elevated serum potassium due to cellular impermeability in the absence of insulin, but who is often profoundly depleted in potassium levels overall.

Such patients require emergency management to lower the high potassium levels, but as treatment commences and their cells rapidly become permeable to potassium. Caution must be taken to avoid them developing a rebound hypokalaemia.

The therapies most often suggested for acute potassium lowering are infusions of glucose and insulin, β_2-adrenoceptor agonists, either nebulised or inhaled, and IV sodium bicarbonate.

Of these, glucose-insulin and beta-agonists both seem to be effective, and a combination seems more effective than either being used in isolation.

The same review investigated two methods for removing excess potassium from the system: K^+-absorbing styramine resins, and dialysis. Of these, the evidence was that resins were not effective at 4hrs after administration, but longer-term studies have not been done. Dialysis was effective at decreasing total body potassium over the same period.

In addition, the administration of calcium (as either calcium gluconate or calcium chloride) is recommended as a means of rapidly reversing the repolarisation abnormalities seen in severe hyperkalaemia. Furthermore, it must always be remembered that a cornerstone of treatment is to diagnose the underlying cause of hyperkalaemia and take steps to reverse this.

NUTRITION

The main goal in initiating nutritional therapy is to prevent or treat malnutrition/undernutrition among patients unable to sustain sufficient oral intake.

The patients who are likely to benefit most are those who are already malnourished, who would otherwise undergo a long period of starvation, and who are therefore less able to tolerate further catabolism.

For some conditions, there are disease specific formulae to optimize the patient's nutritional status by managing nutrients, fluid and electrolytes, adjusted to the specific pathophysiological processes.

A careful balance of macronutrients (protein, lipid and carbohydrate) provides energy requirements, while micronutrients (vitamins and minerals) are required in very small amounts to maintain health but not to provide energy.

The variability in resting energy expenditure makes it very difficult to predict caloric requirements. Both underfeeding and overfeeding can be harmful.

Resting energy expenditure (REE) can be measured using indirect calorimetry and calculated using the Oxford equation, which has now largely replaced the abbreviated Weir equation and the Harris Benedict equation.

These equations estimate BMR in afebrile healthy individuals and therefore need to be modified in the following circumstances:

– Fever Increase by 10 % for each 1 °C above 37 °C (up to max of 40 °C).

– Sepsis Increase by 9 % regardless of temperature Surgery Increase by 6 % if patient has had surgery or trauma

– Burns Increase by 100 % if any size over 30 % (or use Toronto formula).

These factors are additive, so the energy requirements for a 33-year old man (height 1.80 m, weight 75 kg), admitted after a laparotomy for a ruptured appendix and sepsis (temperature 39 °C), work out to approximately 2460 kcal/kg^{-1}/day^{-1} as follows: 25 kcal/kg^{-1}/day^{-1} is generally recommended for most acutely ill patients.

BMR = (13.75 × 75 kg) + (5 × 180 cm) – (6.78 × 33 years) + 66 = = 1773.5 kcal/day^{-1}.

REE = 1773.5 × 1.2 (add 20 % for temperature) × 1.09 (for sepsis) × 1.06 (surgery) = 2458.9 kcal/day^{-1} (i.e. roughly 2460 kcal/day^{-1}).

The Harris–Benedict equation is an empirically derived equation with variables that reflect the relative contributions to overall heat production per square meter body surface area of activity, age, sex, and body size:

For males:

BEE = 66.47 + 13.75 × BW (kg) + 5 × H (cm) – 6.74 × Age (years).

For females:

BEE = 655 + 9.6 × BW (kg) + 1.85 × H (cm) – 4.68 × Age (years).

BEE equals basal energy expenditure in kilocalories per day.

To apply this equation to nutritional requirements the BEE is multiplied by time activity and injury factors to arrive at a daily nutrition requirement in kilocalories per day, or TEE.

Activity factors vary from 1 for bed rest to 1.3 for ambulatory patient. Injury factors vary from 1 to 1.2 for minor surgery to 1.8 for major sepsis. For each degree above 37.2 °C the daily nutrition requirement is multiplied by 1.07.

Protein requirements are determined and the remaining calories are divided between glucose and lipid (table 4). During recovery the aim should be to provide values of 25–30 kcal/kg^{-1}/day^{-1} to support the process of anabolic reconstitution.

Table 4

Protein, glucose and lipid requirements

Protein	Provides 4 kcal/g^{-1} Around **1.5 g/kg^{-1}/day^{-1}** (range 1.2 to 2 g/kg^{-1}/day^{-1} for ICU patients) Use **2 g/kg^{-1}/day^{-1}** if severely catabolic e.g. severe sepsis, burns or trauma Should be a mixture of essential and non essential amino acids
Lipid	Provides 9.3 kcal/g^{-1} Calories from lipid should be limited to 40 % of total calories
Carbohydrate	Provides 3.75 kcal/g^{-1} in vivo **3 to 4 g/kg^{-1}/day^{-1}** Give the remaining energy requirements as carbohydrate

Failure to deliver at least 25 % of calculated requirements is associated with worse outcome, however it is better to underfeed rather than attempt to match a calculated energy requirement, particular in sepsis and trauma.

The National Institute for Clinical Excellence (UK) has recommended that parenteral nutrition should be limited to a maximum of 50 % or the calculated requirements for the first 48 hours after initiation.

Predictive equations should be used with caution, as they provide a less accurate measure of energy requirement then indirect calorimetry.

They are even more problematic in the obese patients. For all classes of obesity (BMI above 30), the goal of an enteral nutrition regime should not exceed 60–70 % of target energy requirement or 11–14 kcal/kg^{-1} actual body weight per day (or 22–25 % kcal/kg^{-1} ideal body weight per day).

The proportion of a feed made up by protein is sometimes expressed as a calorie: nitrogen ratio. 6.25 g of protein contains 1 g of nitrogen.

Then calories (kcal) are divided by nitrogen (g). Recommended calorie: nitrogen ratios are around 100:1 which will be achieved using the above figures. The optimal ratio for lipid/carbohydrate is not known.

Oral feeding is the optimal route of nutritional support. However most ICU patients are incapable or intolerant of oral diet and are therefore fed enterally or parenterally.

Enteral nutrition is recommended over parenteral nutrition by practice guidelines in Europe and North America. This is based on numerous trials involving a variety of critically ill patients, including trauma, burns, head injury, major surgery and acute pancreatitis.

Parenteral nutrition is indicated where enteral nutrition is not recommended, for example in intestinal obstruction/perforation, non-functioning gut, gastrointestinal fistula, prolonged ileus, oesophageal/gastric surgery, perforation or malignancy.

Micronutrients. Vitamins are organic compounds that usually act as cofactors for enzymes involved in metabolic pathways. Trace elements are ions that act as cofactors for enzymes or as structurally integral parts of enzymes and are often involved in electron transfer.

Types of nutritional support.

***Food fortification*.** This is the process of adding micronutrients to food.

Enteral nutrition can be either oral or tube feeding (Nasogastric, Orogastric, Enterostomy (gastrostomy or jejunostomy), post-pyloric feeding (nasojejunal or jejunostomy)).

Parenteral nutrition (via either peripheral or central vein):

– *Peripheral access*: low osmolarity fluids only (< 850 mOsm/L^{-1}).

Limited by large volumes needed to provide calories.

– *Central access*: solutions usually hypertonic.

ENTERAL NUTRITION

Enteral nutrition should be started within the first 24–48 hours of admission. It is also important to achieve the estimated caloric target within 48–72 hours. The use of enteral feeding protocols increases the overall percentage of provided goal calories, since they allow doctors to avoid slow initiation and premature cessation of feed.

If caloric and protein needs cannot be met by enteral feeding alone, parenteral feeding or a combination of both needs to be considered.

The important steps to ensure adequate enteral nutrition:

1. Confirm the tube position (clinically and radiographically).

2. Secure the tube well and check the site regularly for potential tube dislodgment.

3. Start feeding early.

4. Aspirate regularly (4 hourly) and accept gastric residual volumes of 200–250 ml. Adjust feeding rates accordingly. Once feeding is established this can be stopped.

5. Minimise aspiration risk via the following:

– patient should be head-up tilt at least 30°;

– avoid bolus feeds;

– use prokinetics early: metoclopramide 10 mg IV 8 hourly +/– erythromycin 75 mg IV 6 hourly;

– consider switch to post-pyloric tube feed.

6. Diarrhea associated with tube feeding, needs further evaluation.

PARENTERAL NUTRITION

Parenteral feeding is the intravenous administration of nutrients. This may be supplemental to oral or tube feeding, or it may provide the only the source of nutrition as total parenteral nutrition (TPN).

The only absolute indication for parenteral nutrition (PN) is gastrointestinal failure. All efforts to improve tolerance of enteral feeding such as use of pro-kinetic agents and/or a post-pyloric feeding tube should be used before starting PN.

Patients receiving less than 25 % of their predicted needs are at the increased risk of sepsis and those who are intolerant of enteral nutrition, despite all attempts to improve this, should be considered for parenteral supplementation.

During acute illness, the aim is to provide energy as close as possible to estimated or measured energy expenditure in order to decrease the negative energy balance. In the absence of indirect calorimetry, ICU patients should receive 25 $kcal/kg^{-1}/day^{-1}$ increasing to target levels over the next 2–3 days.

PN can be given as separate components but is more commonly given as a sterile emulsion of water, protein, lipid, carbohydrate, electrolytes, vitamins and trace elements according to the recommendations discussed earlier regarding nutritional requirements.

Standard formulations require thorough mixing before infusion. The electrolyte concentration can be altered for each patient and additional trace elements and vitamins may be added.

Protein is given as amino acids and includes essential amino acids. It should also ideally include most of the non-essential amino acids.

Critical illness results in a relative deficiency of glutamine. In a number of small studies IV glutamine improves survival and infection rates in patients on PN, particularly with traumas and burns. Glutamine supplementation is likely to be beneficial for patients receiving TPN for more than 10 days.

Lipid is commonly given as Intralipid®; it is emulsion made of soya with chylomicron-sized particles. It provides a source of essential fatty acids, (linolenic acid, an omega-3 fatty acid and linoleic acid, an omega-6 fatty acid) and is a vehicle to deliver fat-soluble vitamins.

Because lipid preparations are expensive, it is possible to give parenteral nutrition with low levels of lipid thus giving 6 % of total energy requirement as lipid is enough to avoid essential fatty acid deficiency.

If no parenteral lipid is given, vegetable oil should be massaged into the patient's limbs once a day; lipid is absorbed through the skin and may prevent or delay essential fatty acid deficiency, although requirements in critical illnesses may be too high for this to be sufficient.

Watch for signs of deficiency: dry, scaly skin, with or without hair loss, and abnormal liver function tests. Most vegetable oils can be used (safflower, corn, soya, groundnut or sunflower) but not palm oil, as it contains virtually no linolenic acid. Fat-soluble vitamins will need to be given separately.

Carbohydrate is given as glucose. The minimal amount of carbohydrate required is about 2 g/kg^{-1} glucose per day. It should provide approx. 60 % of non-protein calories.

Electrolytes and micronutrients. Critically ill patients are prone to fluid and sodium overload, and renal dysfunction is frequent. The exact electrolyte requirement needs to be determined by close plasma electrolyte monitoring and should not be a fixed element of parenteral nutrition prescription.

Patients with sepsis may have large amount of vitamin A losses in their urine, burn patients lose selenium, zinc and copper via their exudates and trauma patients lose selenium and zinc through their drains.

Selenium impairs the role of glutathione peroxidase as a free radical scavenger and selenium supplementation may be helpful in general ICU patients.

INTENSIVE THERAPY OF ACUTE CIRCULATORY DISORDERS

SHOCK

Shock is a condition of inadequate tissue perfusion or insufficient delivery of oxygenated blood and nutrients. Shock is a progressive disorder that, if uncorrected, leads to death.

Phases of shock. For hypovolemic and cardiogenic shock, however, the pathways to death are reasonably well understood. Unless the insult is massive and rapidly lethal (e.g., a massive haemorrhage from a ruptured aortic aneurysm), shock in those settings tends to evolve through three general (though somewhat artificial) phases:

– An initial ***nonprogressive phase*** during which reflex compensatory mechanisms are activated and perfusion of vital organs is maintained.

– A ***progressive stage*** characterized by tissue hypoperfusion and onset of worsening circulatory and metabolic imbalances, including acidosis.

– An ***irreversible stage*** in case when cellular and tissue injury is so severe that even if the hemodynamic defects are corrected, survival is not possible.

Shock can be classified into 4 major types. Further there are the parameters and examples to differentiate between the types of shock:

Hypovolemic — associated with decreased preload.

Cardiogenic — results from heart pump dysfunction (more commonly left-sided) causing a decrease in cardiac output in the setting of increased preload.

Obstructive — secondary to obstruction of the cardiac flow or filling.

Distributive — associated with significant vasodilation in the setting of relative hypovolemia and decreased SVR. The classic description of distributive shock includes an elevated cardiac output.

Parameters to evaluate shock. The usual parameters of BP, heart rate, and urine output, which have been traditionally used as indicators of global perfusion since the 1960s, have given way to a new definition of shock, based on the demand and supply of oxygen at the tissue level; thus, measures of regional perfusion have replaced global vital signs. Normal BP does not necessarily mean normal perfusion, as adequate pressure does not equate to adequate cardiac output (CO).

Cardiac output (CO) is the product of heart rate (HR) and stroke volume (SV): CO = HR × SV.

Stroke volume is determined by three main factors: preload, afterload and contractility.

Indicators of regional perfusion, such as blood lactate and base deficit, are important because early hemodynamic assessment based on vital signs and central venous pressure (CVP) does not detect persistent global hypoxia.

Clinical criteria, including vital signs, level of consciousness and assessments of peripheral perfusion (core-periphery temperature gradient, capillary return time) are mandatory.

Hemodynamic monitoring such as mean arterial pressure (MAP), systolic BP, and diastolic BP can be done continuously with an arterial line and confirmed with hourly noninvasive BP monitoring.

– MAP may be calculated by adding the diastolic pressure to one third of the difference between the systolic and diastolic pressures.

Shock Index (the ratio of heart rate to systolic BP has been described as the shock index). A ratio of < 1 is associated with decreased response to volume loading, but if > 1, it usually indicates a variable response to fluid administration. Its use is mostly confined to hypovolemic shock and may be unreliable in septic and cardiogenic shock, when heart rate may increase in response to other factors.

– Urine output of < 0.5 mL/kg/hour, change in mental status, and tachypnea indicate decreased organ perfusion. Urine output is usually recorded each hour.

Serum markers of tissue metabolism:

– Lactate levels > 4 mmol/L have been associated with greater mortality in shock. Early lactate clearance is associated with better prognosis. This can be measured from an arterial or venous gas sample 2 or 3 times a day, or more often if required, to monitor response to treatment.

– Base deficit, negative base excess, also correlates with outcome in shock. Initial base deficit does not correlate well with initial blood lactate because there are numerous causes of an elevated lactate (e.g., metformin, beta-2 agonists) other than hypoperfusion.

The base excess is defined as the amount of hydrogen ions that would be required to return the pH of the blood to 7.35 if the $PaCO_2$ levels were adjusted to normal.

Measuring the preload. ***Preload*** is the ventricular volume at the end of diastole. An increased preload leads to an increased stroke volume. Preload is mainly dependent on the return of venous blood from the body and is influenced by changes in position, intra-thoracic pressure, blood volume and the balance of constriction and dilatation (tone) in the venous system.

The relationship between ventricular end-diastolic volume and stroke volume is known as **"Starling's law"**, which states that the energy of contraction of the muscle is related/proportional to the initial length of the muscle fiber. This can be graphically illustrated by a series of 'Starling curves' (figure 5).

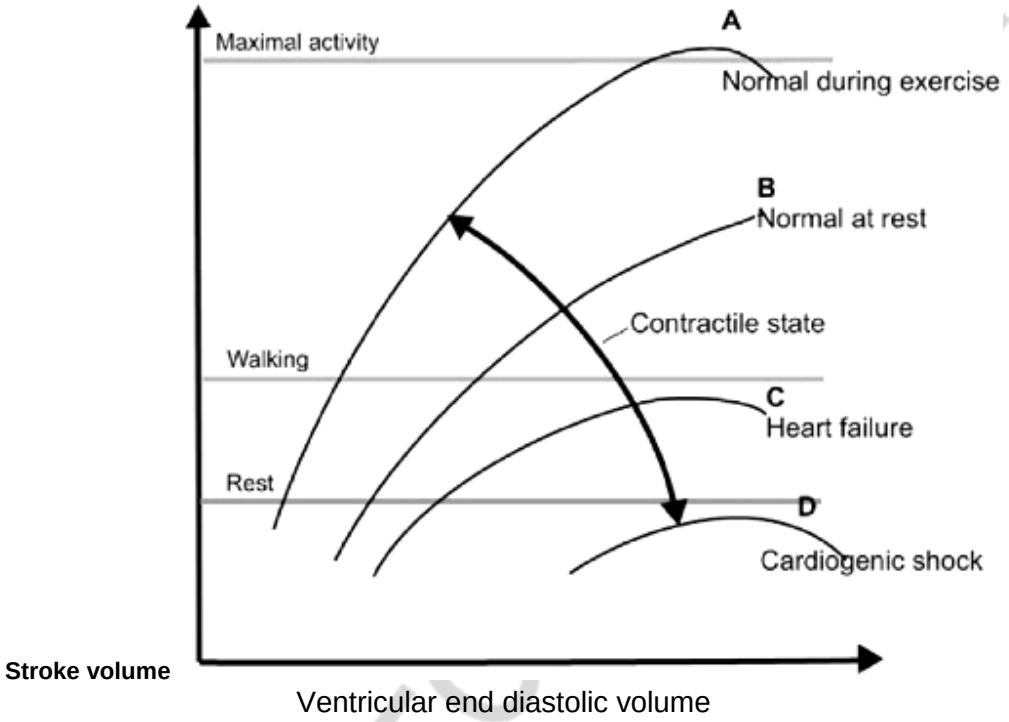

Fig. 5. Starling's Law

The curves show how the heart performs at different states of contractility, ranging from the normal heart to one in cardiogenic shock. This is a condition where the cardiac output is insufficient to maintain tissue perfusion. There is also the curve for an increasing level of physical activity, which requires a corresponding increase in cardiac output.

Preload is measured by dynamic response of the CVP to a fluid challenge (e.g., 125 mL of crystalloid or colloid). Alternatively, in some centres other methods are used, including echocardiography and various methods of determining CO (e.g., pulse-induced continuous cardio-output monitoring). In most developed health care systems pulmonary artery catheters have been replaced by these techniques.

Measuring preload responsiveness. Measures of preload responsiveness can guide fluid administration. There are various methods of doing this, including stroke volume variation, systolic pressure variation, pulse pressure variation, plethysmographic variation, and passive leg rising.

Typically an increase in CO of 10 % to 12 % after a fluid bolus of 300 to 500 mL of crystalloids is taken as a positive response. Passive leg rising is frequently used as a simple mechanical manoeuvre to optimize the preload.

Measuring contractility and afterload. CO is the output of left ventricle/right ventricle per minute. There are various methods of calculating CO, but an ideal standard has not been established. Methods include dilution and thermodilution using a pulmonary artery catheter.

These use the Fick principle, and the rate at which the indicator substance is diluted or temperature falls is proportional to the CO. Alternative noninvasive methods include Doppler ultrasound and measurements of pulse pressure, although the latter is a function of both CO and arterial function. As CO is affected by the phase of respiration, it needs to be measured at the same point in the respiratory cycle each time to enable comparison.

The ratio of the CO (stroke volume × heart rate) to the body surface area in meters squared is the cardiac index. Normal values of the cardiac index range from 2.2 to 2.5 L/minute/m^2. In cardiogenic shock the cardiac index is typically < 1.8 without inotropes and < 2.0 to 2.2 with inotropes.

Systemic vascular resistance (SVR): this is a measure of afterload derived from the CO, MAP, and CVP.

Measures of tissue perfusion. Oxygen delivery (DO_2): the amount of oxygen delivered to the tissue is calculated as the product of CO, oxygen saturation, and the haemoglobin level in the blood. A DO_2 of > 600 has been associated with better outcomes.

$$DO_2 = CO \times \text{oxygen saturation} \times \text{hemoglobin level g/L (1.36)} \times 100.$$

Mixed venous oxygen saturations: means saturation of oxygen in the pulmonary artery and is the standard for defining global adequacy of tissue perfusion. Normal venous saturations are between 65 % and 75 %.

Superior vena cava oxygen saturation is usually higher by about 8 % as compared to inferior vena cava oxygen saturation, but they parallel each other in shock. A sustained elevation of > 80 % in the presence of low oxygen delivery carries a poor prognosis, as it indicates tissue inability to utilize oxygen, and is usually seen after cardiac arrest resuscitation.

Oxygen debt is due to an imbalance between supply and demand, which is associated with increased organ dysfunction. Early correction of venous saturations to > 70 % is associated with better outcomes. Venous saturations of < 70 % are an independent predictor of mortality.

Lactate levels are a measure of tissue perfusion. Levels > 4 mmol/L are associated with greater mortality in shock. Base excess levels can be misleading and are generally not used.

Shock management: General measures

– Remember the ABC resuscitation!

– Check the airway and give high-flow oxygen by face mask to optimize O_2 saturation.

– If a conscious level is impaired (GCS < 8), airway is unprotected, and/or breathing is inadequate, consider intubation.

– Place the patient flat and raise the feet to restore BP.

– Insert 2 large-bore intravenous cannulae and start crystalloid infusion.

– Send blood for U&Es, glucose, FBC, X-match and blood cultures.

– Insert central venous line to monitor CVP, and to provide inotrope infusions if necessary. Insert arterial line for more accurate assessment of BP.

– Catheterize the bladder to monitor urine output.

– Titrate fluid replacement according to BP, CVP, and urine output. Overdosage of fluid in patients with cardiac pump failure will precipitate pulmonary oedema with little gain or fall in stroke volume or cardiac output.

– Persistent hypotension in spite of adequate filling is an indication for inotropic support. The choice of first-line agent varies to some extent depending on the diagnosis.

– Treat the underlying condition and enlist specialist help as early as possible.

Drugs. The choice of first-line agent varies to some extent depending on the underlying diagnosis (table 5).

Table 5

Drugs for inotropic support

Drug	Dose	Cardiac Output	Blood Pressure	Systemic Vascular Resistance
Dopamine*	2.5–20 mcg/kg/min	+	+	+
Norepinephrine†	0.05–2 mcg/kg/min	+	++	++
Epinephrine	0.05–2 mcg/kg/min	++	++	+
Phenylephrine	2–10 mcg/kg/min	-	++	++
Dobutamine‡	2.5–10 mcg/kg/min	+	+/-	-

HYPOVOLEMIC SHOCK

Hypovolemic shock refers to a medical or surgical condition in which rapid fluid loss results in multiple organ failure due to inadequate perfusion. Most often, hypovolemic shock is secondary to rapid blood loss (hemorrhagic shock).

The human body responds to acute haemorrhage by activating 4 major physiologic systems: the hematologic, cardiovascular, renal, and neuroendocrine systems.

The hematologic system responds to an acute severe blood loss by activating the coagulation cascade and contracting the bleeding vessels.

The cardiovascular system initially responds to hypovolemic shock by increasing the heart rate, myocardial contractility, and constricting peripheral blood vessels. This response occurs secondary to an increased release of norepinephrine and decreased baseline vagal tone (regulated by the baroreceptors in the carotid arch, aortic arch, left atrium, and pulmonary vessels). The cardiovascular system also responds by redistributing blood to the brain, heart, and kidneys and away from skin, muscle, and GI tract.

The renal system responds to hemorrhagic shock by stimulating an increase in renin secretion from the juxtaglomerular apparatus. Renin converts angiotensinogen to angiotensin I, which subsequently is converted to angiotensin II by the lungs and liver. Angiotensin II has 2 main effects, both of which help to reverse hemorrhagic shock, vasoconstriction of arteriolar smooth muscle, and stimulation of aldosterone secretion by the adrenal cortex. Aldosterone is responsible for active sodium reabsorption and subsequent water conservation.

The neuroendocrine system responds to hemorrhagic shock by causing an increase in circulating antidiuretic hormone (ADH). ADH indirectly leads to an increased reabsorption of water and salt (NaCl) by the distal tubule, collecting ducts, and the loop of Henle.

Review of blood volume loss. The physical examination should always begin with an assessment of the airway, breathing, and circulation. Do not to rely on systolic BP as the main indicator of shock. Compensatory mechanisms prevent a significant decrease in systolic BP until the patient has lost 30 % of the blood volume. More attention should be paid to the pulse, respiratory rate, and skin perfusion.

Haemorrhage may be classified according to the actual amount of blood loss, or as a percentage of the circulating blood volume. Classes of haemorrhage have been defined, based on the percentage of blood volume loss.

Total blood volume in males is approximately 69 ml of blood per kg of body weight. Females have approximately 65 ml of blood per kg of body weight.

Class I haemorrhage (loss of 0–15 %):

– In the absence of complications, only minimal tachycardia is seen.

– Usually, no changes in BP, pulse pressure, or respiratory rate occur.

A delay in capillary refill of longer than 3 seconds corresponds to a volume loss of approximately 10 %.

Class II haemorrhage (loss of 15–30 %):

– Clinical symptoms include tachycardia (rate > 100 beats per minute), tachypnea, decrease in pulse pressure, cool clammy skin, delayed capillary refill, and slight anxiety.

Class III haemorrhage (loss of 30–40 %):

– By this point, patients usually have marked tachypnea and tachycardia, decreased systolic BP, oliguria, and significant changes in mental status, such as confusion or agitation.

– Most of such patients require blood transfusions, but the decision to administer blood should be based on the initial response to fluids.

Class IV haemorrhage (loss of > 40 %). Symptoms include the following: marked tachycardia, decreased systolic BP, narrowed pulse pressure (or immeasurable diastolic pressure), markedly decreased (or no) urinary output, depressed mental status (or loss of consciousness), and cold and pale skin. This amount of haemorrhage is immediately life threatening.

Lab studies. When the history is taken and the physical examination performed, further workup depends on both the probable cause of the hypovolemia, and stability of the patient's condition.

– Initial laboratory studies should include analysis of the CBC, electrolyte levels (e.g. Na, K, Cl, HCO_3, BUN, creatinine, glucose levels), prothrombin time, activated partial thromboplastin time, ABGs, and urinalysis (in patients with trauma).

– Blood should be typed.

Imaging Studies. Patients with marked hypotension and/or unstable conditions must first be resuscitated adequately.

The atraumatic patient with hypovolemic shock requires ultrasonographic examination in the ED if an abdominal aortic aneurysm is suspected. If GI bleeding is suspected, a nasogastric tube should be placed, and gastric lavage should be performed. Endoscopy can be performed (usually after the patient has been admitted) to further delineate the source of bleeding.

If abdominal injury is suspected, diagnostic peritoneal lavage may be performed in unstable patients, or CT scanning in stable patients. If long-bone fractures are suspected, radiographs should be obtained.

***Management of haemorrhagic shock*:**

– Remember the ABC of resuscitation.

– Check and correct any problems with the airway and breathing.

– Give oxygen in a high inspired concentration by face mask. Intubate patients who are unconscious.

– Control external haemorrhage by elevating the limb and by direct firm pressure with a clean pad over the bleeding site.

– Insert a large cannula (14 gauge) into a suitable vein, use two when shock is worse than class one. When it is difficult to find veins, cannulate the external jugular or femoral vein or perform a cut down at the ankle or antecubital fossa.

– In small children the intra-osseus route has been used with success. Do not use leg veins when intra-abdominal haemorrhage is suspected, or cannulate veins in an injured arm or shoulder.

– Once IV access is obtained, initial fluid resuscitation is performed with an isotonic crystalloid, such as lactated Ringer solution or normal saline. An initial bolus of 1–2 L is given in an adult (20 mL/kg in a pediatric patient), and the patient's response is assessed.

Choice of intravenous fluids. The choice of fluids will often be determined by what is available. There are 3 types of intravenous fluid: crystalloid, colloid and blood. Dextrose 5 % is not effective in the treatment of shock as it leaves the circulation rapidly. It should only be used as a last resort.

Crystalloids are distributed rapidly between the circulation and the extracellular (interstitial) fluid. When treating shock give three times the estimated blood loss (i.e. when replacing 1000 mls blood loss give 3000 mls of crystalloid).

Colloids remain within the circulation for a longer time (typically 4–8 hours) and should be administered in an equal volume to the blood loss.

Blood transfusion is required in previously healthy patients when estimated blood loss is more than 30 % of the circulating blood volume (1500 ml in an adult). In previously anaemic patients transfusion is required with less severe haemorrhage. After blood transfusions of 8 units or more coagulation factors may become deficient requiring fresh frozen plasma (if available).

All transfused fluids should be warmed because hypothermia increases the risk of DIC and infection. Prolonged hypovolaemic shock carries a high mortality rate because of progression to organ failure and disseminated intravascular coagulation (DIC).

The first priority in treatment of major blood loss is the restoration of blood volume to maintain tissue perfusion and oxygenation. Fluid resuscitation must be started when early signs and symptoms of blood loss are suspected, but not when blood pressure is falling or absent. Initial fluid resuscitation should be made by rapid infusion of warmed isotonic crystalloid (Hartmann's/Ringer's lactate or 0.9 % saline) via large bore cannulae. The initial dose is 1 to 2 litres for adults and 20 ml/kg^{-1} for children. Volume replacement should be guided by the patient's response to initial therapy by repeated reevaluation of ABC (table 6).

The guidelines in this table are based on the 3:1 rule. Most patients in hemorrhagic shock require as much as 300 ml of electrolyte solution for each 100 ml of blood loss.

Table 6

Evaluation of fluid resuscitation and organ perfusion

	Rapid response	**Transient response**	**Minimal or no response**
Vital Signs	Return to normal	Transient improvement, recurrence of decreased blood pressure and increased heart rate	Remain abnormal
Estimated blood loss	Minimal (10–20 %)	Moderate and ongoing (20–40 %)	Severe (> 40 %)
Need for more crystalloid	Low	High	High
Need for blood	Low	Moderate to high	Immediate
Blood preparation	Type and crossmatch	Type-specific	Emergency blood release
Need for operative intervention	Possibly	Likely	Highly likely
Early presence of surgeon	Yes	Yes	Yes

American College of Surgeons, Advanced Trauma Life Support (ATLS) responses to initial fluid resuscitation. * For a 70-kg man.

CARDIOGENIC SHOCK

Cardiogenic shock is characterized by a decreased pumping ability of the heart that causes inadequate perfusion to the tissues. It most commonly occurs in association with, and as a direct result of, acute ischemic damage to the myocardium. The most common initiating event in cardiogenic shock is acute myocardial infarction (AMI). Dead myocardium does not contract, and once more than 40 % of the myocardium is involved, cardiogenic shock may result.

History. Most patients with cardiogenic shock have an AMI and, therefore, with the constellation of symptoms of acute cardiac ischemia (e.g. chest pain, shortness of breath, diaphoresis, nausea and vomiting). Patients experiencing cardiogenic shock may also have pulmonary oedema and presyncopal or syncopal symptoms.

Physical: physical examination often reveals that the patient is in the middle of an AMI. Patients are in frank distress, are profoundly diaphoretic, and have severe shortness of breath and chest pain.

– Clinical assessment begins with paying attention to the ABCs and vital signs.

– Breathing may be laboured, with audible coarse crackles or wheezing.

– Patients with marked tachycardia, cool and clammy extremities, poor peripheral pulses, and varying degrees of end-organ dysfunction (e.g., decreased mental function and urinary output).

– Neck examination may reveal jugular venous distention, which may be prominent. This finding is evidence of right ventricular failure.

– Careful cardiac examination may reveal mechanical causes of cardiogenic shock.

Causes: the vast majority of cardiogenic shock cases are due to acute myocardial ischemia. Other related causes include the following:

– Infectious and/or inflammatory processes (e.g., acute myocarditis);

– Pharmacologic agents (e.g., beta-blockers, calcium-channel blockers);

– Mechanical causes (e.g., valvular dysfunction, tamponade, cardiomyopathy).

Lab studies. In most cases, the usual workup includes tests, which usually are assessed in cases of suspected cardiac ischemia:

– cardiac enzymes (e.g., creatine kinase, troponin, myoglobin);

– electrolytes;

– coagulation profile (e.g., prothrombin time, activated partial thromboplastin time);

– an ABG test may be useful to evaluate acid-base balance, because acidosis can have a particularly deleterious effect on the myocardial function.

Other tests. An ECG is helpful if it reveals an acute injury pattern consistent with an AMI. A normal ECG, however, does not rule out the possibility. ECGs are often most helpful when they can be compared with previous tracings.

Emergency department care:

– Treatment begins with the ABC assessment.

– Once the ABCs are managed, an early focus of treatment should be reversed to the underlying cause and in most cases means revascularization. If a catheterization laboratory is readily available, percutaneous transluminal coronary angioplasty with or without stent placement may be performed to achieve a better outcome. If no catheterization laboratory is available, the next best option is thrombolytic therapy, if no contraindications are present.

– Supportive care and the prevention of further ischemia have various implications in these patients. They require oxygen, intravenous fluids, and close cardiac and hemodynamic monitoring. Providing high-flow oxygen, decreasing myocardial oxygen consumption, and increasing perfusion of the ischemic myocardium may reduce ischemia. Extreme heart rates should be avoided because they may increase myocardial oxygen consumption and infarct size thus impairing the pumping ability of the heart.

– Pharmacologic interventions may be advisable, depending on the circumstances.

– Nitrates and/or morphine are advised for the management of pain; however, they must be used with caution because such patients are in shock, and excessive use of either of these agents can produce profound hypotension.

– Dopamine may provide vasopressor support. With higher doses, it has the disadvantage of increasing heart rate and myocardial oxygen consumption.

– Dobutamine, amrinone, or milrinone may provide inotropic support.

DISTRIBUTIVE SHOCK

Distributive shock is characterized by hypotension (systolic blood pressure < 90 mm Hg) due to a severe reduction in systemic vascular resistance (SVR), with normal or elevated cardiac output in most instances.

Septic shock is the most commonly encountered form of distributive shock.

Other causes of distributive shock include systemic inflammatory response syndrome (SIRS) due to noninfectious inflammatory conditions; toxic shock syndrome (TSS); anaphylaxis; drug or toxin reactions, including insect bites, transfusion reaction, and heavy metal poisoning; addisonian crisis; hepatic insufficiency; and neurogenic shock due to brain or spinal cord injury.

Pathophysiology. Decreased tissue perfusion in distributive shock results primarily from arterial hypotension caused by a reduction in SVR. In addition, a reduction in effective circulating plasma volume often occurs due to a decrease in venous tone and subsequent pooling of blood in venous capacitance vessels, and loss of intravascular volume into the interstitium due to increased capillary permeability also occurs. Finally, primary myocardial dysfunction is often manifested with ventricular dilatation, decreased ejection fraction (despite normal stroke volume and cardiac output), and depressed ventricular function curves.

In anaphylaxis, decreased SVR occurs due to primarily massive histamine release from mast cells after their activation by antigen-bound immunoglobulin E (IgE), increased synthesis and release of prostaglandins.

History. Patients with septic shock or SIRS may have prior complaints suggesting infection or inflammation of the respiratory or urinary tract, or abdominal cavity.

Patients with anaphylaxis commonly have recent iatrogenic (drug) or accidental (i.e., bee sting) exposure to an allergen and coexisting respiratory complaints (wheezing and dyspnoea) and/or pruritus.

Shock due to adrenal insufficiency may be observed in patients with chronic adrenal insufficiency and recent physiologic stress or in new-onset adrenal insufficiency. Adrenal insufficiency as a cause of shock should be considered in any patients with hypotension without signs of infection, cardiovascular disease, or hypovolemia.

ANAPHYLACTIC SHOCK

Anaphylaxis is an acute systemic reaction caused by the release of mediators from mast cells and basophils. More than one organ system should be involved for the reaction to be considered anaphylaxis. The most common organ systems involved include the cutaneous, respiratory, cardiovascular, and gastrointestinal systems.

Patients often initially describe a sense of impending doom, accompanied by pruritus and flushing. This can evolve rapidly into the following symptoms, broken down by organ system:

– cutaneous/ocular — urticaria, angioedema, conjunctival pruritus, and swelling;

– respiratory — nasal congestion, rhinorrhea, throat tightness, shortness of breath, cough, hoarseness;

– cardiovascular — dizziness, weakness, syncope, chest pain, palpitations;

– gastrointestinal — nausea, vomiting, diarrhoea, bloating, cramps;

– neurologic — headache (rare, except in exercise-induced anaphylaxis) and seizure (very rare).

Symptoms usually begin within 5–30 minutes from the time the antigen is injected. If the antigen is ingested, symptoms usually occur within 2 hours, although they often occur much faster, as with severe food allergy. In rare cases, symptoms can be delayed in onset for several hours.

Physical. The first priority should be to assess the patient’s respiratory and cardiac status. Respiratory:

– Severe angioedema of the tongue and lips may obstruct airflow.

– Laryngeal edema may manifest as stridor or severe air hunger.

– Loss of voice may also be observed.

– Bronchospasm, airway edema, and mucus hypersecretion may manifest as wheezing.

– Hypoxia can cause altered mental status.

Cardiovascular:

– Tachycardia is present in one fourth of patients, usually as a compensatory measure for intravascular volume loss.

– Bradycardia is more suggestive of a vasovagal reaction, although it has been observed in true anaphylaxis.

– Hypotension (and resultant loss of consciousness) may be observed secondary to capillary leak, vasodilation, and hypoxic myocardial depression.

– Cardiovascular collapse with shock can occur immediately, without any other findings.

Cutaneous:

– Urticaria (hives) can occur anywhere on the body, often localizing on the palms, soles, and inner thighs. The lesions are erythematous, raised, highly pruritic, and of variable size.

– Angioedema is also commonly observed. These lesions involve the deeper dermal layers of skin and are usually nonpruritic and nonpitting. Common areas of involvement are larynx, lips, eyelids, hands, feet, and genitals.

– Isolated whole-body erythematous flushing is also occasionally observed.

– Gastrointestinal: Vomiting, diarrhoea, and abdominal distention are observed frequently.

Medical care. Anaphylaxis is a medical emergency requiring immediate recognition and intervention. Basic equipment and medication should be readily available in the physician's office.

– For the initial assessment, check the airway closely and secure as needed. Assess the level of consciousness and obtain blood pressure, pulse, and oximetry values.

– Place the patient in the supine position, and begin supplemental oxygen.

– Remove the source of the antigen if possible (e.g., stinger after bee sting).

– A tourniquet applied to the extremity with the antigen source can retard antigen exposure to the systemic circulation. Release the tourniquet every 5 minutes, and do not leave it in place for longer than 30 minutes.

– Administer intramuscular or subcutaneous epinephrine into a different extremity immediately. Epinephrine (adrenaline) is the most effective drug in most cases of anaphylaxis and should be given as early as possible. The α-agonist activity of epinephrine is able to reverse vasodilatation and oedema. In addition, epinephrine is a valuable α-agonist which has a positive inotropic action, dilates bronchial smooth muscle, and reduces the release of inflammatory mediators, such as leukotrienes and histamine. Epinephrine maintains the blood pressure, antagonizes the effects of the released mediators, and inhibits further release of mediators from mast cells and basophils. Anaphylactic deaths correlate with a delay in the administration of epinephrine. The initial dose can be repeated as necessary, depending on the response. Intramuscular administration of epinephrine results in higher and more rapid maximum plasma concentrations of epinephrine compared with the subcutaneous route.

– Maintaining proper blood pressure is important in the treatment of anaphylactic reactions. Hypotension is often the most difficult manifestation of anaphylaxis to treat. Establish intravenous access for the administration of adjunctive medications and the administration of intravenous fluids to maintain

blood pressure, if needed. Fluid therapy is important to counteract the large fluid shifts associated with vasodilatation and capillary leakage. Rapidly restore the vascular volume with isotonic crystalloid and consider us e of a col loid when the volume of crystalloid exceeds 30 ml/kg^{-1}. Avoid administering the substances that are suspected to be the cause of the reaction. The exact amount should be individualized, based on blood pressure recovery and urine output. In severe cases, invasive monitoring of central venous pressure and cardiac output may be required.

– Pressors also may be needed to support blood pressure. Intravenous epinephrine (1:10,000 preparation) can be administered as a continuous infusion, especially when the response to intramuscular or subcutaneous epinephrine (1:1000) is poor. For patients who are refractory to epinephrine, consider other vasoconstrictor drugs such as norepinephrine (starting with 0.1 mcg/kg^{-1}/min^{-1}) 11 or vasopressin.

– If appropriate, start cardiopulmonary resuscitation immediately, following the usual resuscitation measures for cardiocirculatory insufficiency.

– Antihistamines and corticosteroids have a place as secondary treatment for anaphylaxis and help to prevent oedema, cutaneous symptoms and relapse of the anaphylactic reaction as seen in biphasic or protracted anaphylaxis. Hydrocortisone is the preferred steroid because it has a fast onset. Administer both an H1 and an H2 blocker because studies have shown the combination to be superior to an H1 blocker alone in relieving the histamine-mediated symptoms. Diphenhydramine and ranitidine are an appropriate combination.

– Respiratory compromise in the acute setting (ie, respiratory failure) mandates endotracheal intubation. If the endotracheal tube cannot be passed because of severe laryngeal edema, tracheotomy is required.

– In cases of bronchospasm without arterial hypotension, a β_2-adrenergic agonist (such as salbutamol, 2.5–5 mg) can be administered through an inhalation chamber adapted to the ventilatory circuit. If this treatment is resistant, consider the intravenous route: administer a 100 to 200 mcg bolus of salbutamol, followed by continuous perfusion of this drug (5 to 25 mcg/min^{-1}).

Serum tryptase is a mast cell protease increased in cases of anaphylaxis, signaling an immune-mediated mechanism. Tryptase concentrations can be measured in serum (or plasma) 30 minutes after onset of symptoms and reach a peak between 15 minutes and one hour. 23 The half-life of tryptase is about 120 minutes and the levels gradually decrease over time.

SEPSIS AND SEPTIC SHOCK

Sepsis, a syndrome of physiologic, pathologic, and biochemical abnormalities induced by infection, is a major public health concern, accounting for more than $ 20 billion (5.2 %) of total US hospital costs in 2011. A 1991 consensus conference developed initial definitions focused on the then-prevailing view that sepsis resulted from a host's systemic inflammatory response syndrome (SIRS) to infection.

The **Systemic Inflammatory Response Syndrome** (SIRS) is an immune response to a variety of severe insults including infection, burns, pancreatitis, and trauma. It affects many organ systems. It includes two or more signs: temperature > 38 °C or < 36 °C; heart rate > 90/min; respiratory rate > 20/min or $PaCO_2$ < 32 mmHg (4.3 kPa); white blood cell count > 12 000/mm^3 or < 4000/mm3 or > 10 % immature bands (from Bone et al.).

Key concepts of sepsis:

– Sepsis is the primary cause of death from infection, especially if not recognized and treated promptly. Its recognition mandates urgent attention.

– Sepsis is a syndrome shaped by pathogen factors and host factors (e.g., sex, race and other genetic determinants, age, comorbidities, environment) with characteristics that evolve over time. What differentiates sepsis from infection is an aberrant or dysregulated host response and the presence of organ dysfunction.

– Sepsis-induced organ dysfunction may be occult; therefore, its presence should be considered in any patient presenting with infection. Conversely, unrecognized infection may be the cause of new-onset organ dysfunction. Any unexplained organ dysfunction should thus raise the possibility of underlying infection.

– The clinical and biological phenotype of sepsis can be modified by preexisting acute illness, long-standing comorbidities, medication, and interventions.

– Specific infections may result in local organ dysfunction without generating a dysregulated systemic host response.

New terms and definitions.

Sepsis is defined as life-threatening organ dysfunction caused by a dysregulated host response to infection. Organ dysfunction can be identified as an acute change in total SOFA score ≥ 2 points consequent to the infection (table 7).

The baseline SOFA score can be assumed to be zero in patients not known to have preexisting organ dysfunction. A SOFA score ≥ 2 reflects an overall mortality risk of approximately 10 % in a general hospital population with suspected infection. Even patients presenting withmodest dysfunction can deteriorate further, emphasizing the seriousness of this condition and the need for prompt and appropriate intervention, if not already being instituted.

Sepsis is a life-threatening condition that arises when the body’s response to an infection injures its own tissues and organs.

Patients with suspected infection who are likely to have a prolonged ICU stay or to die in the hospital can be promptly identified at the bedside with qSOFA, i.e. alteration in mental status, systolic blood pressure ≤ 100 mmHg, or respiratory rate ≥ 22/min.

Septic shock is a subset of sepsis in which underlying circulatory and cellular/metabolic abnormalities are profound enough to substantially increase mortality.

Patients with septic shock can be identified with a clinical construct of sepsis with persisting hypotension requiring vasopressors to maintain MAP ≥ 65 mm Hg and having a serum lactate level > 2 mmol/L (18 mg/dL) despite adequate volume resuscitation. With these criteria, hospital mortality is in excess of 40 %.

Table 7

Sequential [Sepsis-Related] Organ Failure Assessment Score

System	Score				
	0	**1**	**2**	**3**	**4**
Respiration PaO_2/FIO_2, mmHg (kPa)	≥ 400 (53.3)	< 400 (53.3)	< 300 (40)	< 200 (26.7) with respiratory support	< 100 (13.3) with respiratory support
Coagulation Platelets, ×103/μL	≥ 150	< 150	< 100	<50	< 20
Liver Bilirubin, mg/dL (μmol/L)	< 1.2 (20)	1.2–1.9 (20–32)	2.0–5.9 (33–101)	6.0–11.9 (102–204)	> 12.0 (204)
Cardiovascular	MAP ≥ 70 mm Hg	MAP < 70 mm Hg	Dopamine < 5 or dobutamine (any dose)	Dopamine 5.1–15 or epinephrine ≤ 0.1 or norepinephrine ≤ 0.1 μg/kg/min	Dopamine > 15 or epinephrine > 0.1 or norepinephrine > 0.1 μg/kg/min
Central nervous system Glasgow Coma Scale score	15	13–14	10–12	6–9	< 6
Renal Creatinine, mg/dL (μmol/L) Urine output, mL/d	< 1.2 (110)	1.2–1.9 (110–170)	2.0–3.4 (171–299)	3.5–4.9 (300–440) < 500	> 5.0 (440) < 200

The new measure, termed ***qSOFA*** (for quick SOFA) and incorporating altered mentation, systolic blood pressure of 100 mm Hg or less, and respiratory rate of 22/min or greater, provides simple bedside criteria to identify adult patients with suspected infection who are likely to have poor outcomes.

In sepsis, failure of the circulatory system to maintain organ perfusion results from hypovolaemia, myocardial depression and abnormal regulation of vascular tone. This, together with increased metabolic rate, causes an imbalance between tissue oxygen supply and demand,leading to global tissue hypoxia.

Initial management. The key early interventions in sepsis are assessment and management of airway, breathing and circulation to optimise oxygen delivery. Intravenous antibiotics should be started within the first hour.

Airway:

– Give oxygen.

– A patient with an obstructed airway should be managed immediately with simple airway manoeuvres and an oro- or nasopharyngeal airway if necessary. Patients with a reduced conscious level should be nursed in the recovery position.

– Where facilities exist, intubation and ventilation is indicated for airway obstruction or failure to localise pain because of a low conscious level. Some of these patients may respond to fluid resuscitation with conscious level improvement, and a fluid challenge is a sensible initial step prior to giving any anaesthetic drugs.

Breathing. All septic patients should be given as much oxygen as possible. Higher concentrations of oxygen can be achieved with two oxygen concentrators connected into to a non-rebreathing mask with a reservoir bag, or one connected to a mask and one to nasal cannulae.

Respiratory failure may require intubation and ventilation. Signs of respiratory failure include tachypnoea, dyspnoea, use of accessory muscles, poor chest expansion, poor air entry, cyanosis, low oxygen saturation and hypoxia and/or hypercapnia on arterial blood gases,if these are available.

Hypercapnia may be evident clinically, causing drowsiness or a flapping tremor of the hands. Breathing may also be helped by sitting the patient up, deep breathing, coughing and chest physiotherapy.

If available, some patients may benefit from continuous positive airway pressure (CPAP) or noninvasive ventilation (NIV). In the short term (e.g. while preparing to intubation), assisting breathing with a bag-valve-mask or Ambubag® (with a PEEP valve if possible) can be helpful. Remember that unless you are assisting breathing, patients find it difficult to breathe through an Ambu-valve and a simple mask with reservoir bag will achieve more effective oxygenation.

Intubating critically ill patients has significant risks. They have little oxygen reserve and, despite full preoxygenation, will desaturate quickly.

Fluid resuscitation should be started while preparing to intubate, but expect the blood pressure to drop significantly and have a vasopressor agent drawn up. Ketamine may cause less hypotension than otherinduction agents. Patients who are moribund and have a depressed level of consciousness may not tolerate any sort of intravenous agent. Occasionally such patients can be intubated without sedation, using local anaesthetic agent sprayed through a cannula onto the larynx under direct laryngoscopy.

Circulation. ***Fluid resuscitation*****.** Septic patients need a lot of fluid. An initial fluid bolus of 20–30 ml/kg^{-1} of crystalloid (e.g. Hartmann's solution) is appropriate — i.e. around 2 litres for a 70 kg adult. Further fluid boluses can be given, assessing the response to each. In Rivers' study patients received on average 5 litres of fluid in the first 6 hours and there was no increase in the need for ventilation.

The choice of fluid does not seem to be important. Hartmann's solution has some advantages over 0.9 % saline, but either is acceptable. Hartmann's is more similar in composition to extracellular fluid than saline and less likely to cause a hyperchloraemic metabolic acidosis. Dextrose (glucose) is useless for resuscitation.

Colloids theoretically stay in the intravascular space longer than crystalloids, however capillary permeability is increased in sepsis.

INTENSIVE THERAPY OF ACUTE RESPIRATORY FAILURE (ARF)

The main function of the lungs is to provide continuous gas exchange between inspired air and the blood in the pulmonary circulation, supplying oxygen and removing carbon dioxide, which is then cleared from the lungs by subsequent expiration.

Respiratory failure is a syndrome in which the respiratory system fails in one or both of its gas exchange functions: oxygenation and carbon dioxide elimination in the normal work of breathing.

In practice, respiratory failure is defined as a PaO_2 value of less than 60 mm Hg while breathing air or a $PaCO_2$ of more than 50 or less than 30 mm Hg. Respiratory failure may be acute or chronic.

The problems are as follows: central — a problem of respiratory drive, peripheral — a problem of the respiratory pump, large airway — a problem of gas transfer, or alveolar — a problem of gas exchange.

1. Central ventilation: the neurologic system does not activate respiration in response to an increase in arterial CO_2 tension.

2. Peripheral ventilation: the thoracic pump (chest and diaphragm) is not effective in guaranteeing adequate minute ventilation.

3. Gas Transfer: air does not pass effectively from the upper to the lower airway due, for example, to increased airway resistance.

4. Gas Exchange:

a) Gas does not pass effectively from alveoli to capillaries due to a pathologic process in the interstitial space (diffusion defect);

b) Wasted Ventilation — alveoli are being ventilated but not perfused: dead space ventilation or more air than blood can utilize (high ventilation/perfusion (V/Q) ratio as the extreme version of dead space ventilation);

c) Blood flow is inadequately utilized. Blood is passing through the lungs without coming into the contact with aerated alveoli: perfused but not ventilated — shunt or ventilation falls behind blood flow (low V/Q ratio the extreme version of right to left shunt).

The ventilator pump is composed of the chest cage, the ventilator muscles, and the nervous system elements involved in respiration. The pump primarily affects carbon dioxide excretion (CO_2). The lung involves the elements that allow inspired gas to exchange with pulmonary blood flow and primarily affects blood oxygenation (O_2). The large arrow from lung to pump shows that lung disease often increases the work of the pump.

Types of Respiratory Failure:

– ***Hypoxemic respiratory failure (type I)*** is characterized by a PaO_2 of less than 60 mm Hg with a normal or low (less than 30 mm Hg) $PaCO_2$.

– ***Hypercapnic respiratory failure (type II)*** is characterized by a $PaCO_2$ of more than 50 mm Hg. Actually the process of CO_2 elimination is called ventilation.

Pathophysiological mechanisms of Hypoxemic respiratory failure (type I) include the following:

– Ventilation/Perfusion Mismatch;

– Diffusion abnormality.

PATHOPHYSIOLOGICAL MECHANISMS OF VENTILATION/PERFUSION MISMATCH

Shunting is a form of ventilation-perfusion mismatch when the alveoli are not ventilated (due to collapse or pus or oedema fluid) but are still perfused. As a result blood traversing the alveoli is not oxygenated.

– Shunting is relatively resistant to oxygen therapy. The increase in the inspired oxygen concentration has little effect because it can not reach alveoli where shunting occurs while blood leaving normal alveoli is already 100 % saturated.

– the most common cause of hypoxaemic respiratory failure in critically ill patients;

– hypoxic pulmonary vasoconstriction reduces the blood flow to non-ventilated alveoli and reduces the severity of the hypoxaemia.

Causes of shunting: pneumonia, pulmonary oedema, atelectasis, collapse, pulmonary haemorrhage, pulmonary contusion.

Ventilation without perfusion is the opposite extreme of ventilation-perfusion mismatch. Gas passes in and out of the alveoli but no gas exchange occurs because the alveoli are not perfused and the ventilation is ineffective. In this respect these alveoli behave like other ventilated parts of the lung but do not participate in gas exchange (e.g. the major airways) and these alveoli therefore make up a physiologically dead space.

Ventilation without perfusion causes include low cardiac output, high intra-alveolar pressure leading to compression or stretching of alveolar capillary (mechanically ventilated patients).

Diffusion abnormality may be due to the alveolar membrane abnormality or a reduction in the number of alveoli resulting in a reduction in alveolar surface area. The causes include Acute Respiratory Distress Syndrome (ARDS), fibrotic lung disease.

HYPERCAPNIC RESPIRATORY FAILURE (TYPE II) VENTILATION FAILURE

Failure to ventilate is the most common cause of acute respiratory distress in the recovery room. It is characterized by reduced alveolar ventilation manifested as an increase in the $PaCO_2$ > 50 mmHg (6.5 kPa).

Causes of hypoventilation:

• **Neurological:**

– central: loss of ventilatory drive due to general anaesthetic agents, benzodiazepines, stroke or brain injury;

– spinal: spinal or epidural anaesthesia; spinal cord injury, cervical — loss of diaphragmatic function, thoracic — loss of intercostals.

– peripheral: phrenic nerve injury in neck or thoracic surgery.

– muscular: persistent neuromuscular blockade; diaphragmatic trauma; myopathic disorders — myasthenia gravis (in patients after thymectomy).

• **Anatomical:**

– chest wall — flail chest; intra-abdominal hypertension (abdominal packs placed);

– pleura — pleural effusions, pneumothorax (patient after thoracic or retroperitoneal surgery: nephrectomy, abdominal aortic aneurysm, esophagectomy);

– airways — airway obstruction: laryngeal edema, inhalation of a foreign object (tooth or throat pack), bronchospasm.

Oxygen delivery. When considering the adequacy of oxygen delivery to the tissues, three factors need to be taken into account: haemoglobin concentration, cardiac output and oxygenation.

The quantity of oxygen made available to the body in one minute is known as the oxygen delivery:

$$\textbf{Oxygen delivery } (\text{ml } O_2/\text{min}^{-1}) = \textbf{Cardiac output } (\text{l}/\text{min}^{-1}) \times$$
$$\times \textbf{ Hb concentration } (\text{g}/\text{l}^{-1}) \times 1.34 \text{ (ml } O_2/\text{gHb}^{-1}) \times \textbf{ \% saturation}$$

TYPES OF HYPOXIA AND THEIR CAUSES

Hypotonic (Hypoxic) hypoxia. The most frequent cause of hypotonic hypoxia is alveolar ventilation-perfusion mismatch caused by chronic bronchitis with emphysema (COLD) in smokers. The mixed venous oxygen tension is low. Hypotonic or hypobaric hypoxia is caused by insufficient oxygen uptake into the blood from the lungs.

Insufficient oxygen uptake also occurs in space, during flying or diving. Hypotonic hypoxia is defined as a PaO_2 of less than 7.3 kPa (55 mmHg). Below this threshold the ventilation starts to increase.

Anaemic hypoxia. The disorder is due to an insufficient oxygen carrying capacity of the haemoglobin. Anaemic hypoxia is a common phenomenon (ex.: anaemia and cyanosis; methaemoglobinaemia; cherry-red skin colour in case of CO-haemoglobinaemia).

Ischaemic or stagnant hypoxia is caused by the insufficient bloodflow (cardiac insufficiency or local ischaemia). Stenosis of the coronary arteries leads to chest pain or angina pectoris.

Arteriosclerosis and stenosis of the leg arteries causes claudication (intermittent walking due to hypoxic pain). The poor circulation in shock conditions is a generalised hypoxic ischemia.

Histotoxic hypoxia is caused by insufficient capacity for oxygen utility, caused by blockade of the mitochondrial metabolism as in cyanide poisoning or by blockade of the ATP-production following supramaximal exercises, where the oxygen utility is excessive.

Diagnosis of respiratory failure includes the following:

– history;
– physical examination;
– pulse oximetry;
– ABG analysis;
– chest radiograph;
– electrocardiogram (ECG).

The **clinical** signs of respiratory failure are signs of respiratory compensation (tachypnoea, use of accessory muscles, nasal flaring, intercostal, suprasternal or supraclavicular recession), increased sympathetic tone (tachycardia, hypertension, end-organ hypoxia, sweating), signs of end-organ hypoxia (altered mental status, bradycardia and hypotension (late signs)) and haemoglobin desaturation (cyanosis).

Pulse oximetry estimates arterial saturation using absorption of two different wavelengths of infrared light. Relationship between saturation and PaO_2 is described by the oxyhaemoglobin dissociation curve. Pulse oximetry saturation (SpO_2) ~90 % is a critical threshold. Below this level a small fall in PaO_2 produces a sharp decrease in SpO_2.

ABG analysis is a golden standard of diagnosis of acute respiratory failure (ARF) (**normal levels:** PaO_2 — 90–100 mm Hg; $PaCO_2$ — 35–45 mm Hg; SaO_2 — 95–100 %).

Chest radiography and **electrocardiogram** (ECG) should be made to all patients with respiratory failure**,** because cardiovascular disease can cause respiratory failure; the former because it gives insight into the anatomy of the lungs and chest wall. Frequently, the chest radiography reveals an unexpected cause of respiratory failure.

Management of acute respiratory failure:

1. The assessment of the patient with acute respiratory distress involves taking a history, examining the patient and quantifying the degree of respiratory injury.

2. This involves determining the problem, whether it is failure to ventilate, failure to oxygenate or failure to maintain the airway.

3. Failure to maintain the airway leads to failure of gas flow and ultimately hypoxemia and hypercarbia. The problem is either central loss of airway patency or mechanical airway obstruction.

4. Failure to oxygenate is caused by ventilation perfusion mismatch: the patient typically has a rapid shallow breathing pattern.

5. Failure to ventilate is caused by a problem in the central nervous system or a problem with the thoracic pump: the patient typically has a slow shallow breathing pattern.

6. Failure to ventilate is an ominous sign.

7. Look for an immediately reversible cause of failure to ventilate — such as narcosis, deep sedation or persistent neuromuscular blockade.

8. In the absence of a reversible cause, positive pressure ventilation is required.

If a patient is in ARF, you have to take a history, examine the patient and make a blood gas test to identify whether it is hypoxemia or hypercarbia. If it is hypoxemia it may be due to oxygenation failure. If it is hypercapnia it may be due to ventilation failure.

In case of mild or moderate hypoxemia you have to provide oxygen therapy and look for cause. In case of progressive hypoxemia you should provide intubation and mechanical ventilation. While in severe hypoxemia you should provide intubation, mechanical ventilation and define the cause.

ARF management includes:

– emergency therapy;
– diagnosis;
– planned therapy;
– elimination of ARF pathological mechanisms;
– causal treatment;
– elimination of other system pathology.

ARF emergency therapy includes:

– airway opening;
– oxygen therapy;
– normalization of sputum drainage;
– mechanical ventilation/noninvasive ventilation.

Airway opening. The so-called "**Safar triple method**" to provide straight open airway includes:

– ***tilting the victim's head*** (do not overtilt, the position is supposed to be as if one is "scenting the morning air";
– ***lifting the victim's mandible***;
– ***opening the victim's mouth***.

Additional devices (adjuncts) to basic airway techniques:

– oropharyngeal airways;
– nasopharyngeal airways;
– tracheal tube;
– laryngeal mask airway (LMA);
– conicotomy, trachestomy.

OXYGEN THERAPY

Giving patients supplemental O_2 to breathe is one of the most common therapeutic manoeuvres. The risks of O_2 therapy are small, and O_2 should be given as an emergency procedure to all patients in respiratory distress. Simultaneously, PaO_2 and $PaCO_2$ should be measured, so that subsequent O_2 therapy can be applied rationally to raise PaO_2, and to prevent or reverse severe tissue hypoxia.

Hudson-type masks do not give precise FIO_2 and should only be used when hypoxemia is not a major concern. But Hudson-type masks do allow delivery of humidified gas.

Masks fitted with a Venturi valve deliver a reasonably accurate FIO2 (0.24, 0.28, 0.35, 0.40, 0.60) except for the patients with very high inspiratory flow rates.

A tight-fitting anaesthetic mask and reservoir bag allows 100 % oxygen to be delivered.

In case of O_2 therapy application there are essentially two risks: O_2 toxicity and CO_2 narcosis. Parenchymal lung damage from oxygen occurs with $FiO_2 > 60$ % for more than 48 hours without intermittent periods of breathing air.

Methods of sputum drainage normalization include:

– intravenous rehydration therapy;
– medication inhalation;
– vibration percussion, vacuum massage;
– postural drainage;
– cough stimulation and imitation;
– sputum aspiration;
– tracheobronchial lavage/bronchoscopy.

NONINVASIVE POSITIVE PRESSURE VENTILATION

Many patients with ventilatory failure can be successfully treated with noninvasive positive pressure ventilation (NIPPV). NIPPV improves gas exchange, reduces the work of breathing, and relieves dyspnoea. Patients who most likely benefit include those with acute hypercapnic exacerbations of chronic obstructive pulmonary disease (COPD) or with hypercapnic forms of acute cardiogenic pulmonary edema. In selected patients with acute hypoxemic nonhypercapnic respiratory failure, NIPPV may obviate the need for endotracheal intubation. Selection may require exclusion of patients with hemodynamic instability, central neurologic dysfunction, or an inability to protect the upper airway.

Clinical criteria for mechanical ventilation:

– apnea or bradypnea less than 10;
– tachypnoea more than 40;
– respiratory distress with altered mentation;
– coma;
– clinically apparent increased work of breathing;
– obtundation and need for airway protection;
– controlled hyperventilation (e.g. in head injury);
– severe circulatory shock.

Laboratory criteria for mechanical ventilation:

– $PaO_2 < 55$ mm Hg;
  $PaCO_2 > 50$ mm Hg ;
– PH < 7.32.

Pulmonary function tests for mechanical ventilation:

– vital capacity < 10 mL/kg;
  Negative inspiratory force < 25 cm H_2O;
– FEV1 < 10 mL/kg.

CONTINUOUS POSITIVE AIRWAYS PRESSURE

Continuous positive airways pressure (CPAP) provides a constant positive pressure throughout the respiratory cycle. It acts to open collapsing alveoli which may be full of fluid (or a collapsing upper airway in obstructive sleep apnoea). It also increases functional residual capacity (FRC) and compliance, so that the work of breathing is reduced and gas exchange is improved. It allows a higher administration of FiO_2, than in standard oxygen delivery masks.

Positive end expiratory pressure (PEEP). PEEP is a preset pressure added to the end of expiration only, to:

– maintain the lung volume,

– prevent airway or alveolar collapse,

– open up atelectic or fluid-filled lung (e.g. in ARDS or cardiogenic pulmonary oedema).

PEEP improves oxygenation by:

– recruiting collapsed alveoli,

– redistributing lung water,

– decreasing A–V mismatch

– increasing FRC.

Indications:

– hypoxaemia requiring high FIO_2;

– optimisation of pressure-volume curve in severe respiratory failure;

– hypoxaemia secondary to left heart failure;

– improvement of cardiac output in left heart failure;

– reduced work of breathing during weaning in patients with high PEEP;

– neurogenic pulmonary oedema.

Types of support. Most ventilators can be set to apply the delivered tidal volume in control or support mode.

***Control mode*.** In control mode, the ventilator delivers the present tidal volume once it is triggered regardless of patient effort. If the patient is apneic or possesses limited respiratory drive, control mode can assure delivery of appropriate minute ventilation.

***Support mode*.** In support mode, the ventilator provides inspiratory assistance through the use of an assist pressure. The ventilator detects inspiration and supplies an assist pressure during inspiration; it terminates the assist pressure upon detecting the onset of the expiratory phase. Support mode requires adequate respiratory drive.

Two basic types of ventilators:

1. ***Pressure cycled ventilators*** deliver gas into the lungs until a prescribed pressure is reached, when inspiratory flow stops and, after a short pause, expiration occurs by passive recoil.

This has the advantage of reducing the peak airway pressures without impairing cardiac performance in situations such as ARDS. However, if the airway pressures increase or compliance decreases the tidal volume falls, so patients need to be monitored closely to avoid hypoventilation.

2. **Volume cycled ventilators** deliver a preset tidal volume into the lungs over a predetermined inspiratory time (usually ~30 % of the breathing cycle), hold the breath in the lungs (for ~10 % of the cycle), and then allow passive expiration as the lungs recoil.

HYPERBARIC OXYGENATION THERAPY

The word "hyperbaric" is from the Greek root "hyper" meaning "*over, above*" and "baro" meaning "*weight*". Therefore, hyperbaric is "above the (normal) weight" of the atmosphere.

Hyperbaric Oxygenation Therapy (HBOT) is the treatment method of using hyper-pressurized oxygen. The principles of such treatment are based on physical laws, which regulate gas dissolution in body fluids and gas propagation in tissues.

Oxygen in blood is chemically linked with hemoglobin (19.1 volume percents), as well as dissolved in plasma (0.3 volume percents). Normally it is the hemoglobin of red blood cells that delivers oxygen to tissues, while dissolved fraction plays only a regulatory function in this process.

Diseases, associated with impairment of oxygen delivery to organs and tissues, lead to hypoxia (oxygen deprivation). Vital organs (head, brain, kidneys, liver) are extremely sensitive to the lack of oxygen and are not able to function normally under oxygen deficit conditions.

Hypoxia can have various causes, such as disruption of vascular permeability, damage of blood-supplying organs (atherosclerosis, inflammation, edema, etc.), low hemoglobin contents and many other reasons, related to respiratory pathology, cardiac abnormalities, etc.

Such conditions can be treated not only with medication, but also with oxygenation therapy. However, under normal atmospheric pressure even pure oxygen respiration cannot solve the hypoxia problem at the level of cells and tissues. The sole solution is to increase the contents of oxygen, transferred by blood.

HBOT sessions are conducted in a special pressure chamber (hyperbaric apparatus), where high oxygen pressure is created under hermetic conditions. Modern hyperbaric apparatuses, manufactured by Russian and international producers, provide wellness and comfort during treatment sessions. The patient can either seat or lie in a free pose, inhaling the flow of curing oxygen. He or she can even sleep during the session.

Every patient passes thorough pre-HOT medical check with laboratory tests, diagnosis and is prescribed an individual treatment plan, which may include various forms of therapy apart from HOT, if necessary.

Duration and number of HOT sessions is determined individually, depending on the diagnosis and indications. Usually the whole treatment program takes from 5 to 12 sessions, depending on particular pathology, of 45–60 minutes each.

The patient's condition is constantly monitored by his/her attending physician. Usually patients feel good during HOT sessions. Constant control guarantees absence of any advers effects.

In case of Hyperbaric Oxygen Therapy the patient's entire body is exposed to pure oxygen at above-atmospheric pressures.

Hyperbaric Oxygen Therapy speeds healing in patients with problem wounds, decreases swelling in the tissues and contributes to the acceptance of skin grafts. HBO benefits patients by:

– increasing oxygen levels in the blood stream;

– helping new blood vessels form in injured tissue;

– helping the body more effectively fight infection and kill bacteria;

– helping reverse the toxic effects of poisons, such as carbon monoxide;

– decreasing the size of air bubbles and allow more blood and oxygen to reach your tissues.

ASTHMA

Pathophysiology: acute asthma is a condition characterized by paroxysmal spasmodic narrowing of the bronchial airways due to inflammation of the bronchi and contraction of the bronchial smooth muscle.

The inflammatory component is central to the pathogenesis of symptoms: bronchoconstriction and airway hyperresponsiveness lead to dyspnoea and wheezing.

An additional important mechanism underlying acute asthma involves antigen-antibody interactions, which activate membrane phospholipase and result in production of arachidonic acid.

Causes:

– respiratory infections;

– allergens, particularly cats;

– exercise;

– weather, including cold and dry air, weather changes, significant increases in humidity;

– air pollution;

– aspirin ingestion;

– chemical irritants (i.e., toluene diisocyanate) may be related to nocturnal asthma.

– high serum histamine levels.

Emergency department care. The mainstay of therapy for acute asthma is inhaled beta2-agonists. The most effective particle sizes are 1–5 microns. Larger particles are ineffective because they are deposited in the mouth and central airways.

Standard delivery systems and routes are as follows:

– albuterol, salbutamol;

– metabolic effects include a slight tendency toward tachycardia.

Many patients who present with tachycardia and acute asthma actually decrease their heart rate with inhaled beta-agonist therapy. Also, inhaled beta-agonists decrease potassium by an average of 0.4 mEq/L.

Patients who respond poorly or not at all to an inhaled beta-agonist regimen usually respond to parenteral beta2-agonists, such as 0.25 mg terbutaline or 0.3 mg of 1:1000 concentration of epinephrine administered subcutaneously.

This is the best treatment choice if bronchospasm does not improve after 2–3 treatments with inhaled beta-2 agonists.

For severe asthma, magnesium has been shown to be beneficial with 2 g over 30 min often recommended.

The goals of therapy are to maintain SaO_2 greater than 92 % and treat dehydration if it is clinically apparent.

Antibiotics should be administered only if bacterial sinusitis, bronchitis, or pneumonia is suspected clinically. Asthma exacerbation severity and therapeutic choices instituted should be evaluated according to the percent of predicted FEV1 or PEFR.

Drug Category: *Glucocorticoids* — these anti-inflammatory agents restore the beta2-agonist receptors in the bronchial smooth muscles and, therefore, restore the response to beta2-agonists. Glucocorticoids are indicated if response to the first or second beta2-agonist inhaler treatment is incomplete.

The onset of steroids effects occurs approximately in 4 hours in children and 6 hours in adults. Bioavailability of orally and parenterally administered steroids is not different.

Severe life-threatening asthma.

First-line therapy:

– oxygen 4 L/min O_2 (SpO_2 > 90 %);
– inhaled B2 agonists such as albuterol or salbutamol;
– infusion therapy;
– systemic corticosteroids;
– methylxanthines (aminophylline);
– ipratropium bromide;
– magnesium sulphate;
– epinephrine or terbutaline.

Indications to tracheal intubation for life-threatening asthma:

– violation of consciousness;
– progression of ARF, despite adequate therapy;
– severe cardiac arrhythmia;
– progressive acidosis (pH < 7.2);
– progressive hypoxemia;
– hypercapnia;
– respiratory depression, respiratory muscle fatigue.

When the patient is sitting upright, using accessory muscles in neck and chest to breathe he is at risk of sudden respiratory failure.

When the patient is in the state of somnolence, confusion, or exhausted — it may indicate that he has impending respiratory arrest.

PULMONARY EMBOLISM

Pulmonary embolism (PE) is an extremely common and highly lethal condition and a leading cause of death in all age groups. Deep vein thrombosis (DVT) and PE are much more common than usually realized. Most patients with DVT develop PE and the majority of cases are unrecognized clinically.

Pathophysiology: pulmonary thromboembolism is not a disease. Rather, it is an often fatal complication of underlying venous thrombosis. Under normal conditions, microthrombi (tiny aggregates of red cells, platelets, and fibrin) are formed and lysed continually within the venous circulatory system.

Under pathological conditions, microthrombi may escape the normal fibrinolytic system to grow and propagate. PE occurs when these propagating clots break loose and embolize to block pulmonary blood vessels.

History. PE is so common and so lethal that the diagnosis should be sought actively in every patient with any chest symptoms that cannot be proven to have another cause.

Symptoms that should provoke a suspicion of PE must include chest pain, chest wall tenderness, back pain, shoulder pain, upper abdominal pain, syncope, hemoptysis, shortness of breath, painful respiration, new onset of wheezing, any new cardiac arrhythmia, or any other unexplained symptom referable to the thorax.

The classic triad of signs and symptoms of PE (hemoptysis, dyspnea, chest pain) are neither sensitive nor specific. They occur in fewer than 20 % of patients with the diagnosis of PE, and most patients with such symptoms are found to have some aetiology other than PE.

Patients with PE often present with primary or isolated complaints of seizure, syncope, abdominal pain, high fever, productive cough, new onset of reactive airway disease (“adult-onset asthma”), or hiccoughs. They may also have new-onset atrial fibrillation, disseminated intravascular coagulation.

Physical. Massive PE causes hypotension due to acute cor pulmonale, but the physical examination findings early in submassive PE may be completely normal. Initially, abnormal physical findings are absent in most patients with PE.

After 24–72 hours, loss of pulmonary surfactant often causes atelectasis and alveolar infiltrates that are indistinguishable from pneumonia on clinical examination and by x-ray. New wheezing may be appreciated. If pleural lung surfaces are affected, pulmonary rub may be heard.

Emergency department care. Fibrinolytic therapy has been the standard of care for all patients with massive or unstable PE since the 1970s. Unless overwhelming contraindications are evident, a rapidly acting fibrinolytic agent should be administered immediately to every patient who has suffered any degree of hypotension or is significantly hypoxemic from PE.

Heparin reduces the mortality rate of PE because it slows or prevents clot progression and reduces the risk of further embolism. Heparin does nothing to dissolve clot that has developed already, but it is still the single most important

treatment that can be provided, because the greatest contribution to the mortality rate is the ongoing embolization of new thrombi.

Oxygen should be administered to every patient with suspected PE, even when the arterial PO_2 is perfectly normal, because increased alveolar oxygen may help to promote pulmonary vascular dilatation.

General management of pulmonary embolism:

1. Give oxygen with FIO_2 0.6–1. 1.0 to maintain $SaO_2 \geq 90–95$ %.
2. Place a patient in a flat position; improvement often follows increased venous return.
3. Provide fluid replasement to optimise right heart filling.
4. Give epinephrine infusion if circulation still compromised.
5. Provide mechanical ventilation if the patient is tired or cannot maintain adequate oxygenation. Gas exchange may worsen due to loss of preferential shunting and decrease in cardiac output.
6. Provide anti-coagulation
7. Consider pulmonary embolectomy.

PULMONARY OEDEMA

Pulmonary oedema is an emergency state caused by filtration of fluid out of the pulmonary capillaries into the interstitial space (interstitial oedema), and eventually in the alveolar spaces (alveolar oedema).

The amount of fluid filtered out of the pulmonary capillaries is determined by the Starling equation. The capillary hydrostatic pressure is the main outward force, and this pressure is larger at the base than at the apex of the upright lung.

The main inward force is the colloid osmotic pressure of the blood proteins. Normally, the alveoli are kept free of fluid, because a net outflux of fluid from the vasculature is balanced by a small lymph flow to the hilar lymph nodes.

Pulmonary oedema has at least 3 causes:

1. Increased pressure. Patients with left cardiac failure (acute myocardial infarct, chronic myocardial failure, mitral stenosis, aortic stenosis, and hypertension) can drown in their own plasma transudates.

The increased venous backpressure distends all pulmonary vessels (lung congestion), and as soon as the pulmonary capillary pressure is higher than the colloid osmotic pressure (normally 3.3 kPa or 25 mmHg), there is a filtration of plasma water into the pulmonary interstitial tissues and into the alveoli.

The pulmonary vascular pressure rises in the supine position causing attacks of lung oedema to occur at night.

2. Increased capillary permeability. Pulmonary oedema can be caused by capillary damage with war gas, toxins, pneumonia etc.
3. Reduced concentration of plasma proteins increases net filtration at the arteriolar end of the lung capillary and reduces net reabsorption of filtered fluid at the venular end.

Oedema is particularly serious in the lungs, because it widens the diffusion distance between the alveolar air and the erythrocytes. There is not enough time

for oxygen to travel from the air to the individual erythrocyte. Thus, the blood leaving the lungs is only partially oxygenated. Both the VC and the compliance are reduced.

Increased pulmonary capillary pressure is caused by any type of left ventricular failure (acute myocardial infarction or chronic heart failure) and by mitral valve stenosis. A pressure above 2.6 kPa (20 mmHg) causes interstitial oedema, and as the pressure rises above 4 kPa, alveolar oedema develops. Interstitial oedema may not be recognised, but alveolar oedema is dramatic.

The patient is severely dyspnoeic, with tachypnoea, tachycardia, and coughing up a frothy pink sputum containing red cells. There is basal crepitation by auscultation and often whistling bronchi.

Since the fluid-filled alveoli are not ventilated with air, any blood passing them does not participate in gas exchange. The effect is a functional veno-arterial shunt with hypoxaemia, although hypoxic vasoconstriction tends to reduce its size.

Initially, the non-affected alveoli are overventilated and $PACO_2$ is low. Hypercapnia is a late complication when the gas exchange is severely compromised.

Other causes of pulmonary oedema include decreased colloid osmotic pressure (hypoproteinaemia, overtransfusion), increased capillary permeability (pulmonary oxygen toxicity, radiation damage), and high-altitude oedema.

Therapy key points:

– Primarily, it is important to find the cause of pulmonary oedema, such as left cardiac failure, and correct the disorder.

– Patients with chronic cardiac failure have reduced contractility, which improved by positive inotropic agents such as digoxin.

– Patients with lung oedema must sit down in bed and calm down. This reduces venous return and cardiac output and the effective filtration pressure.

– Breathing of the air enriched with oxygen reduces hypoxia and dilatates the lung vessels. The filtration pressure is reduced.

– Effective diuretics increase the excretion of Na^+ and water via the kidneys. The loss of fluid also implies oedema fluid.

– Positive pressure breathing is thought to minimise the difference between the central and the peripheral venous pressure, so the venous return and cardiac output are reduced. The blockade of lung capillary bloodflow in the overpressure-phase, and the fear of the patient (increases cardiac output) do not make this treatment the best of choice.

First-line actions:

– oxygen and intubation as needed;
– nitroglycerine;
– furosemide IV 0.5–1.0 mg/kg;
– morphine IV 2 to 4 mg;
– if the patient’s BP is adequate, sitting upright position;
– monitor O_2 saturation with pulse oximeter.

ACUTE RESPIRATORY DISTRESS SYNDROME

Acute respiratory distress syndrome (ARDS) is a process of hypoxaemic respiratory failure associated with noncardiogenic pulmonary oedema. It is the result of diffuse inflammatory damage to the alveoli and pulmonary capillaries from a range of local or systemic insults. ARDS is often associated with multiple organ dysfunctions and carries a high mortality and financial cost.

Criteria for ARDS diagnosis:

– acute onset within 1 week of a known clinical insult or new/worsening respiratory symptoms;

– PaO_2/FiO_2 201–300 mmHg with PEEP/CPAP ≥ 5 cm H_2O;

– respiratory failure not fully explained by cardiac failure or fluid overload;

– bilateral opacities.

Acute lung injury (ALI), a less severe form of ARDS in which the PaO_2/FiO_2 ratio is ≤ 300 mm Hg (40 kPa) is now termed mild ARDS.

Precipitants for ARDS can be classified as direct or indirect.

Direct:

– pneumonia;
– lung contusion;
– aspiration of gastric contents;
– fat embolism;
– toxic inhalation;
– near drowning;
– reperfusion injury.

Indirect:

– multiple trauma;
– massive transfusion;
– sepsis;
– pancreatitis;
– cardiopulmonary bypass;
– burns;
– bone marrow transplant;
– drugs and toxins.

History. Shortness of breath is universal, but other symptoms are related to the predisposing condition.

Examination. Findings are similar to those of pulmonary oedema due to other causes:

– *respiratory* — laboured breathing, tachypnoea, diffuse crackles, cyanosis;
– *cardiovascular* — sweating, tachycardia;
– *CNS* — agitation, leading to lethargy and decreased level of consciousness.

In addition there may be features of the underlying condition.

Investigations.

Arterial blood gases:

– PaO_2/FiO_2 ratio of ≤ 300 mm Hg (40 kPa);

– hypocarbia may be seen, although hypercarbia develops later, as respiratory failure progresses.

Radiology. Chest X-ray shows diffuse bilateral fluffy shadows (although initially they may be less widespread or unilateral) and may show other pulmonary signs if there is a direct pulmonary predisposing condition.

Management — supportive measures. There are no established treatments for ARDS, but treating the underlying condition (for example eradicating infection with antibiotics or surgery) and providing support for each system are paramount.

Management of patients with ARDS:

– search and treat the underlying cause;

– provide supportive therapy;

– ventilatory management (ventilate at low tidal volume, apply generous PEEP);

– rescue therapies (maintain a low hydrostatic pressure in the lungs (avoid fluid overload));

– non-ventilatory management (the prone position in severe cases, consider steroids in persistent ARDS).

SEVERE COMMUNITY-ACQUIRED PNEUMONIA

Pneumonia is an acute infectious disease, mainly of bacterial aetiology, characterized by focal lesions of the lungs and presence of intraalveolar exudation.

Causes of hypoxia in pneumonia mainly include the venous shunt in the inflammatory foci where ventilation is reduced and perfusion is increased, violations of gases diffusion through the alveolar-capillary membrane because of its oedema.

Criteria of severe community-acquired pneumonia (CAP):

1. Respiratory frequency > 30 breaths min at admission.
2. Severe respiratory failure defined by a PaO_2/FlO_2 ratio < 250.
3. Requirement for mechanical ventilation.
4. Chest radiograph showing:
   a) bilateral involvement;
   b) involvement of multiple lobes;
   c) increase in the size of the opacity by 50 % within 48 h of admission.
5. Shock (SBP < 90 mm Hg or DBP < 60 mm Hg).
6. Requirement for vasopressors for more than 4 h.
7. Urine output < 20 ml/h or acute renal failure requiring dialysis.

Treatment of CAP. General:

– *antimicrobials (empirical antibiotics).* Antibiotic therapy should cover community-acquired pathogens. Antibiotics should be administered intravenously and only stepped down to oral administration in patients with a good clinical response;

– oxygen;

– mechanical ventilation;

– fluid to correct dehydration and provide maintenance requirements;
– organ support.

INTENSIVE THERAPY OF COMATOSE STATES

CLINICAL PHYSIOLOGY OF THE BRAIN CEREBRAL BLOOD FLOW

The brain is unusual in that it is only able to withstand very short periods of lack of blood supply (ischaemia). This is because neurones produce energy (ATP) almost entirely by oxidative metabolism of substrates including glucose and ketone bodies, with very limited capacity for anaerobic metabolism. Without oxygen, energydependent processes cease, leading to irreversible cellular injury if blood flow is not re-established rapidly (3 to 8 minutes under most circumstances). Therefore, adequate cerebral blood flow must be maintained to ensure a constant delivery of oxygen and substrates, and to remove the waste products of metabolism.

Cerebral blood flow (CBF) is dependent on a number of factors that can broadly be divided into:

1) those affecting cerebral perfusion pressure;

2) those affecting the radius of cerebral blood vessels.

This relationship can be described by the Hagen-Poiseuille equation which describes the laminar flow of an incompressible uniformly viscous fluid (so called Newtonian fluid) through a cylindrical tube with constant circular cross-section. Although blood does not meet all of these criteria, it tends to flow in a laminar manner at the level of capillaries.

The Hagen-Poiseuille equation:

$$\text{Cerebral Blood Flow} = \Delta P\ \pi\ R4/8\ \eta\ l,$$

where ΔP = cerebral perfusion pressure; R = radius of the blood vessels; η = viscosity of the fluid (blood); l = length of the tube (blood vessels); π = constant, 3.14.

Some facts and figures:

– CBF averages 50 ml/100 g^{-1}/min^{-1} (ranging from 20 ml/100 g^{-1}/min^{-1} in white matter t o 70 ml/100 g^{-1}/min^{-1} in grey matter).

– The adult brain weighs 1400 g or 2 % of the total body weight. Therefore it can be seen that CBF is 700 ml/min^{-1} or 15 % of the resting cardiac output. This reflects the high oxygen consumption of the brain of 3.3 ml/100 g^{-1}/min^{-1} (50 ml/min^{-1} in total) which is 20 % of the total body consumption. This is often referred to as the cerebral metabolic rate for oxygen or $CMRO_2$. This is higher in the cortical grey matter and generally parallels cortical electrical activity.

Perfusion of the brain is dependent on the pressure gradient between the arteries and the veins and this is termed the cerebral perfusion pressure (CPP). This is the difference between the mean arterial blood pressure (MAP) and the mean cerebral venous pressure. The latter is difficult to measure and approximates to the more easily measured intracranial pressure (ICP).

CPP = MAP – ICP

MAP can be estimated as equal to: diastolic blood pressure + 1/3 pulse pressure (difference between systolic and diastolic pressures) and is usually around 90 mm Hg. ICP is much lower and is normally less than 13 mm Hg.

CPP is normally about 80 mm Hg. Clearly, CPP will be affected by anything that changes the MAP or ICP. Blood loss causing hypotension will reduce MAP and CPP (hence the reduced level of consciousness seen in severely shocked patients), while an intracerebral haematoma will increase ICP, with the same effect (see below for more details).

If both co-exist, the effect is a catastrophic fall in CPP and the risk of brain ischaemia. An increase in CPP is usually the result of an increase in MAP, the contribution made by reducing ICP is minimal, except in pathological states when ICP is very high. In a normal brain, despite the potential for changes in MAP (sleep, exercise etc), CBF remains constant over a wide range of CPPs. This is achieved by a process called autoregulation.

Cerebral arterial blood vessel caliber is regulated by four primary factors:

– cerebral metabolism;

– carbon dioxide and oxygen levels;

– autoregulation;

– neurohumeral factors.

The radius of the arterial vessels is particularly important because, due to its effect on CBF, an increased radius (vasodilatation) leads to an increase in cerebral blood volume which in turn increases ICP and reduces CPP, so a balance must be reached.

Changes in CBF and metabolism tend to follow each other; local or global increases in metabolic demand are met rapidly by an increase in CBF and substrate delivery and vice versa. These changes are thought to be controlled by several vasoactive metabolic mediators including hydrogen ions, potassium, CO_2, adenosine, glycolytic intermediates, phospholipid metabolites and more recently, nitric oxide (NO).

At normotension, the relationship between partial pressure of carbon dioxide in arterial blood ($PaCO_2$) and CBF is almost linear and at a $PaCO_2$ of 10.6 kPa (80 mm Hg) CBF is approximately doubled. No further increase in flow is possible at this point as the arterioles are maximally dilated. Conversely at 2.7 kPa (20 mm Hg) flow is almost halved and again cannot fall further as the arterioles are maximally vasoconstricted. These effects are regulated by a complex and interrelated system of mediators. The initial stimulus is a decrease in brain extracellular pH brought about by an increase in $PaCO_2$, further mediated by nitric oxide, prostanoids, cyclic nucleotides, potassium channels, and a decrease in intracellular calcium concentration as a final common mediator.

Arteriolar tone has an important influence on how $PaCO_2$ affects CBF. Moderate hypotension impairs the response of the cerebral circulation to changes in $PaCO_2$, and severe hypotension abolishes it altogether.

The response of the cerebral vessels to CO_2 can be utilised to help manage patients with raised intracranial pressure, for example aftertraumatic brain injury. Hyperventilation reduces the $PaCO_2$ and causes vasoconstriction of the cerebral vessels (reduces their radius) and therefore reduces cerebral blood volume and ICP. However if $PaCO_2$ is reduced too much, the resulting vasoconstriction can reduce CBF to the point of causing or worsening cerebral ischaemia.

Clearly hypercapnia and the resulting vasodilatation and increase in ICP must also be avoided. $PaCO_2$ is therefore best maintained at low-normal levels to prevent raising ICP (35–40 mm Hg, 4.7–5.3 kPa). This CO_2 reactivity may be lost in areas of the brain that are injured. Furthermore, impaired cerebral CO_2 vasoreactivity is associated with a poor outcome in patients with severe head injury. CO_2 reactivity is generally preserved during inhalation anaesthesia (up to about 1 MAC of volatile) and can therefore be utilised to help control ICP and brain swelling during surgery.

CBF increases once PaO_2 drops below about 6.7 kPa so that cerebral oxygen delivery remains constant. Hypoxia acts directly on cerebral tissue to promote the release of adenosine, and in some cases prostanoids that contribute significantly to cerebral vasodilatation.

Hypoxia also directly effects the cerebrovascular smooth muscle to produce hyperpolarisation and reduce calcium uptake, both mechanisms enhancing vasodilatation. The brain requires a constant flow of blood over a range of pressures and this is achieved by the process of autoregulation. The stimulus to autoregulation is CPP, not MAP. In adults, under normal circumstances (ICP < 10 mm Hg), CPP and MAP are very similar and CBF remains constant with a CPP of 60–160 mm Hg.

The higher the ICP the more CPP deviates from MAP and must be calculated. The autoregulation curve is shifted to the right in chronic hypertensive patients and to the left in neonates and younger children, gradually moving to adult values as they get older.

Autoregulation is thought to be a myogenic mechanism, whereby vascular smooth muscle constricts in response to an increase in wall tension and to relax to a decrease in wall tension. At the lower limit of autoregulation, cerebral vasodilation is maximal, and below this level the vessels collapse and CBF falls passively with falls in MAP.

At the upper limit, vasoconstriction is maximal and beyond this the elevated intraluminal pressure may force the vessels to dilate, leading to an increase in CBF and damage to the blood-brain-barrier. Metabolic mediators, such as adenosine, may also be involved in the low-pressure range of autoregulation. As with all the other mechanisms that affect the radius of the blood vessels, autoregulation will also change the cerebral blood volume and may affect ICP.

Pressure autoregulation can be impaired in many pathological conditions including patients with a brain tumour, subarachnoid haemorrhage, stroke, or head injury. A loss of CBF regulatory capacity can be attributed either to damage of the control system (e.g. cerebral vessels) or of the feedback mechanisms involved

in the brain's haemodynamic control. At this time, CBF becomes pressure dependent and thus small changes in MAP can have profound changes on CBF and cerebral blood volume.

A major difference between other systemic circulations and the cerebral circulation is the relative lack of humoral and autonomic control on normal cerebrovascular tone. The main effect of the sympathetic nerves is vasoconstriction that protects the brain by shifting the autoregulation curve to the right in hypertension. The parasympathetic nerves contribute to vasodilatation and may play a part in hypotension and reperfusion injury (for example after cardiac arrest).

Blood viscosity is directly related to haematocrit. As viscosity falls, CBF increases (see Hagen-Poiseuille equation). However, there will also be a reduction in oxygen-carrying capacity of the blood. The optimal haematocrit is where there is a balance between flow and capacity, usually about 30 %.

$CMRO_2$ decreases by 7 % for each 1 °C fall in body temperature and is paralleled by a similar reduction in CBF. At 27 °C, CBF is approximately 50 % of normal. By 20 °C, CBF is about 10 % of normal. The reduction in $CMRO_2$ is the factor that allows cold patients to withstand prolonged periods of reduced CBF without ischaemic damage, for example during cardiopulmonary bypass.

Again, because of vasoconstriction, cerebral blood volume and ICP are reduced. Although this has been tried to help control high ICP, clinical trials have been disappointingly ineffective in showing an improved outcome.

Intracranial pressure (ICP) is important as it affects cerebral perfusion pressure and cerebral blood flow. Normal ICP is between 5 and 13 mm Hg. Because it is very dependant on posture, the external auditory meatus is usually used as the zero point.

Some facts and figures:

– Constituents within the skull include the brain (80 %, 1400 ml), blood (10 %, 150 ml) and cerebrospinal fluid (CSF 10 %, 150 ml).

– The skull is a rigid box, so if one of the three components increases in volume then there must be compensation by a decrease in the volume of one or more of the remaining components otherwise the ICP will increase. The term compliance is often used to describe this relationship, but it is more accurately elastance, the reciprocal of compliance (change in pressure for unit change in volume).

– Compensatory mechanisms include movement of CSF into the spinal sac, increased reuptake of CSF and compression of venous sinuses. These mechanisms reduce the liquid volume of the intracranial contents.

CSF is a specialised extracellular fluid in the ventricles and subarachnoid space which has a multitude of functions:

Mechanical protection by buoyancy.

– CSF provides a constant chemical environment for neuronal activity.

– CSF is important for acid-base regulation to control of respiration.

– CSF provides a medium for nutrients after they are transported actively across the blood-brain-barrier.

– CSF is produced at a rate of 0.3–0.4 ml/min^{-1} (500 ml/day^{-1}) by the choroid plexus in the lateral, third and fourth ventricles.

CSF is produced by the filtration of plasma through fenestrated capillaries followed by active transport of water and dissolved substances through the epithelial cells of the blood-CSF barrier. This is distinct from the blood-brain-barrier which consists of endothelial cells linked by tight junctions whose function is to protect the brain from chemicals in the blood stream. CSF formation is dependent on the CPP and when this falls below 70 mm Hg, CSF production also falls because of the reduction in the cerebral and choroid plexus blood flow.

Following production, CSF then circulates through the ventricular system and the subarachnoid spaces, aided by ciliary movements of the ependymal cells. Resorption takes place mostly in the arachnoid villi and granulations into the circulation: the mechanism behind the resorption is the difference between the CSF pressure and the venous pressure. An obstruction in CSF circulation, overproduction of CSF or inadequate resorption results in hydrocephalus.

PATHOLOGICAL CONDITIONS CAUSING A RISE IN VOLUME OF INTRACRANIAL CONSTITUENTS

Any of the three intracranial constituents (tissue, blood or CSF) can increase in size and volume. As ICP rises, CPP falls eventually to a point when there is no cerebral blood flow, no cerebral perfusion and brain death. Prior to this, brain structures begin to herniate (protrude through an opening). Physiological compensatory mechanisms occur to try and maintain cerebral blood flow:

– **Temporal lobe herniation** beneath the tentorium cerebelli (uncal herniation) — causes cranial nerve III palsy (dilatation of pupil on the same side as lesion (ipsilateral) followed by movement of eye down and out).

Herniation of cerebellar peduncles through the foramen magnum (tonsillar herniation). Pressure on the brainstem causes the Cushing reflex — hypertension, bradycardia and Cheyne-Stokes respiration (periodic breathing).

– **Subfalcine herniation** occurs when the cingulate gyrus on the medial aspect of the frontal lobe is displaced across the midline under the free edge of the falx cerebri and may compress the anterior cerebral artery.

– **Upward or cerebellar herniation** occurs with either a large mass or increased pressure in the posterior fossa. The cerebellum is displaced in an upward direction through the tentorial opening and causes significant upper brainstem compression.

Primary brain damage occurs at the time of the head injury and is unavoidable except through preventative measures. Following this the aim of management is to reduce secondary brain damage which is caused by a reduction in oxygen delivery due to hypoxaemia (low arterial PaO_2) or anaemia, a reduction in cerebral blood flow due to hypotension or reduced cardiac output, and factors which cause raised ICP and reduced CPP.

The most important management strategy ensures A (Airway and C spine protection in trauma), B (Breathing and adequate oxygenation) and C (blood pressure and CPP). Following this, further strategies to reduce ICP and preserve cerebral perfusion are required. Techniques that can be employed to reduce ICP are aimed at reducing the volume of one or more of the skull contents.

Often, blood pressure needs to be augmented with drugs that produce arterial vasoconstriction such as metaraminol or norepinephrine (which requires central venous access). Following a head injury when autoregulation is impaired, if there is a drop in MAP from drugs or blood loss, the resulting cerebral vasodilatation increases cerebral blood volume, which in turn raises ICP and further drops CPP. This starts a vicious cycle. So by raising MAP, ICP can often be reduced.

ICP is traditionally measured by use of a ventriculostomy or external ventricular drain (EVD), which involves a catheter placed through a small hole in the skull (burr hole) into the lateral ventricle.

ICP is then measured by transducing the pressure in a fluid column. Ventriculostomies also allow drainage of CSF, which can be effective in decreasing the ICP. More commonly ICP is now measured by placing some form of measuring device (for example a minature transducer) within the brain tissue (intraparenchymal monitor). An epidural monitor can also be used but becomes increasingly unreliable at extremes of pressure. If ICP is not measured directly, we can estimate it and therefore make changes in MAP to maintain CPP:

Patient is drowsy and confused (GCS 9–13) ICP = 20 mm Hg; GCS < 9, ICP = 30 mm Hg.

COMA

Altered Mental Status (AMS) is an alteration of a patient's level of cognitive (knowledge-related) ability, appearance, emotional mood, and speech and thought patterns. The level of consciousness relates to one's level of awareness and responsiveness to his or her surroundings.

Lethargy is generally referred to when one is suffering from a mild to moderate depression of the level of consciousness. It implies an abnormal state of drowsiness or sleepiness in which it may be difficult to arouse the patient.

Stupor is a more profound depression of one's level of consciousness. One might say that stupor is an extreme form of lethargy requiring a greater stimulus to produce a lesser degree of arousal.

Coma is an abnormal state of deep unconsciousness from which a patient cannot be awakened.

Definition. *Coma* (from the Greek *komas*, or deep sleep) is a state of unresponsiveness in which the patient is incapable of arousing to external or internal stimuli (lack of alertness). **Coma is a clinical syndrome characterized mainly by the decreased or absent consciousness and protective reflexes**.

The degree of coma can vary from lighter stages with observed changes in autonomic function or brief moaning to strong stimulation, to the deepest stage

with absence of any brain stem responses (e.g., pupillary and corneal reflexes), cyclic autonomic activity, and motor tone.

Causes of altered mental status include the following (**AEIOU TIPS**):

A: Alcohol, other toxins, drugs.

E: Endocrine, electrolytes.

I: Insulin (diabetes).

O: Oxygen, opiates.

U: Uremia (renal, including hypertension).

T: Trauma, temperature.

I: Infection.

P: Psychiatric, porphyria.

S: Subarachnoid hemorrhage, space-occupying lesion.

Key points:

– The neuroanatomy of coma can be divided into three major categories: diffuse brain dysfunction or bithalamic injury, primary brain stem disorders, and secondary brain stem compression from supratentorial and infratentorial mass lesions.

– Most cases of coma are due to metabolic disorders or exogenous drug intoxication.

– Patient's evaluation must follow an orderly sequence, beginning with vital signs, general physical examination, and neurologic examination.

– The most important single sign distinguishing toxic-metabolic coma from primary brain disease is presence of pupillary light responses.

– The neurologic examination of the patient in coma is brief and focuses on: 1) the level of consciousness, 2) pupils, 3) eye movements, 4) motor responses, 5) a respiratory pattern.

– Computed tomographic (CT) scanning of the brain is the most valuable acute test to rule out structural causes of coma.

– Hypoxic-ischemic encephalopathy after cardiopulmonary arrest or shock states may be ameliorated by aggressive measures to increase cerebral blood flow after resuscitation.

– Serial neurologic examination over the first 72 hours is most helpful to determine the prognosis for patients with atraumatic coma; for anoxic brain injury, failure to recover pupillary responses or corneal reflexes in the first 24 hours is a poor prognostic sign.

– As therapies aimed at cerebral resuscitation and preservation following acute injury are developed and proved their effectiveness, prior guidelines for determining prognosis will require redefinition and reconfirmation.

– The Uniform Determination of Death Act states that "an individual who has sustained either: 1) irreversible cessation of circulatory and respiratory functions, 2) irreversible cessation of all functions of the entire brain, including the brain stem, is dead".

– The determination of death by brain criteria is based on clinical examination, and in most cases does not require confirmatory tests. However,

the cause of coma must be known, and the cause must be sufficient to explain irreversible cessation of whole brain function.

DIAGNOSIS OF COMA

Coma: clues from examination.

History. If available, the assessment may be made easier. Even if the history is not extensive, a witness may help to establish whether coma commenced suddenly (suggestive of a vascular event) or whether there was a gradual decline in the level of consciousness over hours or even days. Individuals known to suffer from specific diseases may be wearing a Medicalert bracelet or carrying their regular medication. An enormous amount may be learned from a rapid but thorough examination.

General examination. This should establish the following.

Core temperature. A fever usually indicates infection but sometimes results from diencephalic lesions. Hypothermia is often forgotten as a cause for coma; the possibility of myxoedema should be considered.

Heart rate and rhythm. May indicate a dysrhythmia as the reason for poor cerebral perfusion.

Blood pressure. Prolonged hypotension of any cause will lead to anoxia and ischaemia. Apart from a cardiac cause, occult bleeding, a cause of sepsis, and drug intoxication need to be considered.

Respiratory pattern. Shallow, slow breathing should alert the examiner to the possibility of drug intoxication, e.g. opiates. Deep, rapid Kussmaul breathing suggests acidosis. Brainstem compromise can cause distinctive patterns of breathing.

Breath. Alcohol, ketones, hepatic, or uraemic factor.

Skin. There may be signs of head trauma. Bruising over the scalp or mastoids, blood in the nostrils, or external auditory meatus raises the possibility of a basal skull fracture. A rash suggests the possibility of meningitis. Look for signs of chronic liver disease or sallow discoloration of uraemia. Intravenous drug abuse may be suggested by needle tracks.

Heart. Occasionally bacterial endocarditis or vasculitides associated with heart murmurs present with coma.

Abdomen. Look for enlargement of organs which may give clues to the cause of coma. It is important not to miss an acute intra-abdominal event such as perforation of a viscus or a leaking aortic aneurysm.

Fundi. Papilloedema indicates raised intracranial pressure but its absence does not exclude that possibility. Subhyaloid haemorrhages are pathognomonic of subarachnoid haemorrhage but are rare. Changes of diabetic or hypertensive retinopathy suggest the possibility of encephalopathy secondary to these conditions.

Is there meningism? Neck stiffness should be assessed only if it is certain that there has been no trauma to the cervical spine. Increased stiffness suggests

meningeal irritation, either because of inflammation or infiltrative processes affecting the meninges, or because of the blood presence. Meningism raises the possibility of meningitis, encephalitis, or subarachnoid haemorrhage. Start antibiotics immediately if meningitis is suspected.

Assess the the Glasgow Coma Scale (GCS). The GCS is the globally accepted method of quantifying and recording the neurological status of the head-injured patient. It is also useful in determining any improvement or deterioration in neurological function and facilitates accurate communication between health professionals. The scale is made up of three sections, with a minimum score of 3 and a maximum of 15. The components of GCS are:

***Eye opening*:**
– spontaneously — 4;
– to speech — 3;
– to pain — 2;
– none — 1.

***Verbal response*:**
– orientated — 5;
– confused — 4;
– inappropriate — 3;
– incomprehensible sounds — 2;
– none — 1.

***Motor response*:**
– obeys commands (for movement) — 6;
– purposeful movement to painful stimuli (“localises”) — 5;
– withdrawal from painful stimuli — 4;
– abnormal (spastic) flexion, decorticate posture — 3;
– extensor (rigid) response, decerebrate posture — 2;
– none — 1.

The standard painful stimulus applied to the patient should allow the differentiation of purposeful movement (“localising”), from withdrawal and abnormal flexion. Strictly speaking true localisation or purposeful movement should follow a stimulus from one site to another. Squeezing/pinching the trapezius muscle and supra-orbital pressure are preferred stimuli.

Nail bed pressure and sternal rub are less reliable and not of use in patients with spinal injury. Care must also be taken when assessing motor response in those with a suspected cervical spine injury, as any response may cause the patient make attempts to move his head. This may reveal brainstem dysfunction or lateralizing signs. When testing the motor response decorticate or decerebrate posturing may become evident. If there is a change in these signs, it may indicate brain shift.

For evidence of brainstem dysfunction test and observe:
– pupillary response;
– corneal reflex;
– resting position of eyes;

– spontaneous eye movements;
– oculocephalic response/Doll's head manoeuvre (if no C-spine injury);
– oculovestibular response/caloric stimulation;
– swallowing;
– respiratory pattern.

If there appears to be diffuse brainstem dysfunction, it may not be easy to distinguish between structural and metabolic aetiologies. The most important clue is that in metabolic coma, irrespective of its size, the pupils continue to react except in very few exceptional cases (atropine, scopolamine, or glutethimide intoxication will depress brainstem function and produce pupillary abnormalities).

Testing of brainstem reflexes, assessing the GCS, and general examination may reveal facial asymmetry, and differences in muscle tone, reflexes, and plantar responses between the two sides. All these features point toward the possibility of a structural lesion, although occasionally metabolic coma is associated with focal neurological signs.

COMA: IMMEDIATE MANAGEMENT

Priorities:

– Stabilize the patient (airway, breathing, circulation). Give oxygen.
– Consider giving thiamine, dextrose, naloxone, or flumazenil.
– Examine the patient. Is there meningism? Establish Glasgow Coma Scale score. Is there evidence of brainstem failure? Are there focal or lateralizing signs?
– Plan for further investigations.
– Observe for signs of deterioration and attempt to reverse them.

Stabilize the patient:

– **Open the airway** by lying the patient on his side. Note the pattern of breathing. If there is apnoea or laboured or disturbed breathing, intubation and ventilation should be considered. Measure arterial blood gases.

– **Support the circulation.** Correct hypotension with colloid and/or inotropes. If prolonged therapy is required, it is necessary to provide careful and frequent monitoring of central venous pressure and/or pulmonary artery wedge pressure. Search for any occult source of bleeding, e.g. intra-abdominal.

– Treat seizures with usual drugs but beware of over-sedation and hypotension.

– Take blood for glucose, U&Es, calcium, liver enzymes, albumin, clotting screen, FBC, toxicology (including urgent paracetamol and salicylate levels). Urine should be saved for toxicology screen.

Give thiamine, dextrose, naloxone, or flumazenil. Check BM stix. There is a good argument for giving 50 ml of 50 % dextrose immediately for presumed hypoglycaemia because this usually will not cause any harm.

– The only concern is that glucose may precipitate Wernicke's encephalopathy in malnourished individuals. Some clinicians therefore favour giving a bolus of thiamine 100–200 mg iv beforehand.

– **Naloxone** should only be given if opiate intoxication is suspected (small pupils) and the patient is in coma or has a markedly reduced respiratory rate. In adults naloxone 0.8–2.0 mg iv should be given at the intervals of 2–3 minutes to a maximum of 10 mg.

– **Flumazenil** should only be administered if benzodiazepine intoxication is suspected; it is contraindicated in epileptics who have received prolonged benzodiazepine therapy. In adults flumazenil 200 Bμg should be given over 15 seconds; further 100 Bμg boluses may be given at 1-minute intervals (a usual dose is 300–600 Bμg, maximum total dose outside the intensive care setting is 1 mg).

– Both naloxone and flumazenil may be given intravenously, if drowsiness recurs, but intensive care monitoring is advisable.

COMA: MANAGEMENT

Plan for further investigations. The history, physical examination and/or laboratory studies may help make the diagnosis. Often, however, a diagnosis cannot be reached so rapidly. The practical approach is to divide patients according to the below scheme:

Brainstem function intact. Urgent CT head scan. This will reveal one of the following:

– Operable lesions (e.g. subdural haematoma, subarachnoid or intracerebral haemorrhage); refer as appropriate.

– Inoperable lesions (e.g. bilateral cortical infarcts); supportive treatment is recommended.

– Normal: a lumbar puncture should be performed. CSF analysis may suggest an infective process (e.g. meningitis, encephalitis). If the CSF is normal, the most probable diagnosis is metabolic coma.

The brainstem function not intact:

– Consider whether there are signs of brain shift.

– If a herniation syndrome appears to be progressing rapidly, mannitol should be given, hyperventilation commenced, and a surgeon should be contacted urgently.

– If the tempo of events is not so rapid, mannitol may be given and an urgent CT scan arranged.

– Even if the brainstem signs appear to be non-progressive, a CT scan should be made to exclude the possibility of an operable posterior fossa mass or haemorrhage (e.g. cerebellar haemorrhage).

– If the CT is normal, a lumbar puncture should be performed to exclude infection. If it is without pathology, then the possible diagnosis is metabolic coma, or possibly infection, e.g. encephalitis, without leukocytic response.

– MRI is more sensitive in detecting intrinsic brainstem pathology.

– Lumbar puncture should be repeated on the next day if there is no improvement in the patient's condition. Supportive treatment is recommended.

Monitoring progress:

– This requires regular observations of vital signs and a neurological state (including GCS score).

– An important cause of deterioration in structural brain lesions is brain shift leading to herniation syndromes.

– Other reasons for deterioration are electrolyte or metabolic changes, hypovolaemia, or fluid overload. Plasma electrolytes and fluid balance need to be regularly assessed to avoid such problems.

Prognosis. In coma due to head injury, prognosis is clearly related to GCS score. Patients scoring 8 or less have a very poor prognosis. In non-traumatic coma, GCS alone is not a very good predictor. Patients with drug intoxications may have very low scores on admission but, in general, have good outcomes. Assessment of prognosis in non-traumatic coma is aided by simple features of the examination. For example, if after 24 hours it is still not possible to elicit pupillary responses, corneal reflexes, and oculovestibular response, survival is extremely unlikely.

Diabetic Emergencies. Patients with diabetes are susceptible to two major acute metabolic complications: *diabetic ketoacidosis* and *hyperosmolar, nonketotic coma* (HONC).

Hyperglycemia is most often due to insulin deficiency or to resistance or glucose overadministration. Hyperglycemia produces osmotic diuresis, exacerbation of brain, spinal cord, and renal damage by ischemia, delayed gastric emptying, hypophosphatemia, and delayed wound healing.

Even with supramaximal levels of insulin, adults can use only 3 to 5 mg/kg/min at rest (approximately 240 ml/h of 5 percent dextrose solutions). The maximum rate of disposition is less in stress states, more with the decreased metabolic rate.

In general, no more than 2 to 3 mg/kg/min (120 to 180 mg/kg/h, i.e., 10 g/h for a 70-kg person, which is supplied by 240 ml of a 5 percent dextrose solution/hour) should be administered. The maximum rate of glucose disposition in young children is 4 to 8 mg/kg/min, and the optimal rate is less than 5 mg/kg/min.

KETOACIDOSIS

Diabetic patients present to anaesthetists with ketoacidosis usually in the setting of trauma or sepsis, for surgical intervention.

Clinical picture:

– Ketoacidosis begins with anorexia, nausea, and vomiting, polyuria and polydipsia.

– Abdominal pain may be present.

– Subsequent progression to altered consciousness or frank coma may occur.

– The initial examination usually shows Kussmaul respiration (gasping for breath — which also smells of acetone) together with signs of dehydration.

– The body temperature is within the norm, fever suggests presence of infection.

– Initial potassium concentrations that are normal to high, a total-body potassium deficit of several hundred millimoles.

– Hypertriglyceridemia

– The serum amylase level may be elevated, and frank pancreatitis can occur.

These are the mainstays of treatment:

– Diabetic ketoacidosis cannot be reversed without insulin: insulin is administered until the acidosis has been reversed and the urine ketone negative.

– The patient is profoundly volume depleted (usually 3–8 litres) and requires aggressive volume resuscitation.

– The acidosis is more important than the hyperglycemia, more difficult to treat and lasts longer.

Plan:

1. ABC.

2. Intravenous access, blood sampling (FBC, renal, liver, bone profile, ABG, blood cultures), urine for ketones, glucose and microbiology, CXR.

3. Actrapid 10 to 20 iu iv stat.

4. Commence iv insulin infusion, using hourly sliding scale.

5. IV Fluid: 1 litre NaCl 0.9 % stat, then 1 L over 30 mins, 1 L over 1 hour, 1 L over 2 hours, 4 hours and then 8 hourly.

6. Add 10–20 mmol KCL or KPO4 to 2nd and subsequent litres of fluid.

7. When blood glucose < 15 mmol/l replace NaCL with Solution 5 %, as glucose is required to metabolise the ketone bodies.

8. Administer broad spectrum antimicrobial agents (e.g. augmentin).

9. Bicarbonate is not usually required for acidosis reversal.

The plasma glucose level invariably falls more rapidly than the plasma ketone level. Insulin administration should not be stopped because glucose concentrations approach the norm; rather, as mentioned, glucose should be infused and insulin continued until the ketosis has cleared.

Acute complications of ketoacidosis:

– Vascular thrombosis induced by volume depletion, hyperosmolality, increased viscosity of blood, and changes in clotting factors favoring.

– ARDS and sepsis syndrome.

– Acute gastric dilation/acute gastritis.

– Cerebral oedema.

– Myocardial infarction.

HYPOGLYCEMIA

History. Patients often have a history of diabetes mellitus. A history of insulin usage or ingestion of an oral hypoglycemic agent may be known, and possible toxic ingestion should be considered. Inquire if the patient is taking any new medications. Obtaining an accurate medical history may be difficult if the

patient's mental status is altered. The medical history may include diabetes mellitus, renal insufficiency/failure, alcoholism, hepatic cirrhosis/failure, other endocrine diseases, or recent surgery. The social history may include ethanol intake and nutritional deficiency. Look for other symptoms suggesting infection.

Physical. Physical findings are nonspecific in hypoglycemia and generally are related to the central and autonomic nervous systems. Assess vital signs for hypothermia, tachypnea, tachycardia, hypertension, and bradycardia (neonates).

The head, eyes, ears, nose, and throat (HEENT) examination may indicate blurred vision, pupils normal to fixed and dilated, icterus (usually cholestatic due to hepatic disease), and parotid pain (due to endocrine causes).

Cardiovascular disturbances may include tachycardia (bradycardia in neonates), hypertension or hypotension, and dysrhythmias. Respiratory disturbances may include dyspnea, tachypnea, and acute pulmonary edema. GI disturbances may include nausea and vomiting, dyspepsia, and abdominal cramping.

Skin may be diaphoretic and warm or show signs of dehydration with decrease in turgor.

Neurologic conditions include coma, confusion, fatigue, loss of coordination, combative or agitated disposition, stroke syndrome, tremors, convulsions, and diplopia.

Causes:

– Hypoglycemia may result from medication changes or overdoses, infection, diet changes, metabolic changes over time, or activity changes; however, no acute cause may be found.

– Drugs that may be related to hypoglycemia include the following: oral hypoglycemics, salicylates, haloperidol, ethanol, tricyclic antidepressants, propranolol plus ethanol, angiotensin converting enzyme (ACE) inhibitors, and lithium.

Lab studies. Serum glucose should be measured frequently and used to guide treatment, because clinical appearance alone may not reflect the sate severity. Hypoglycemia is defined according to the following serum glucose levels: < 50 mg/dL in men; < 45 mg/dL in women; < 40 mg/dL in infants and children.

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 index is elevated in insulinoma, normal or low with exogenous insulin, and increased with oral sulfonylureas.

Check liver function tests, serum insulin, and cortisol and thyroid levels.

Search for a source of infection. Studies should be considered to rule out the possibility of a concurrent occult infection contributing to the new hypoglycemic episode:

– complete physical examination;

– chest X-ray (CXR);

– urinalysis;

– blood cultures.

Imaging studies. Performing an abdominal CT scan or an ultrasound to rule out abdominal tumor may be appropriate in the patient with new-onset hypoglycemia and no clear etiology. In diabetic patients presenting with hypoglycemia, perform CXR to rule out infection.

Prehospital care: treatment of hypoglycemia consists of correcting the glucose deficiency and directing further treatment to the underlying cause.

Emergency department care. The initial approach should include the following: ABCs, intravenous (IV) access, oxygen, and monitoring. A hyperglycemic patient with an altered mental status may receive a bolus of glucose. This procedure is unlikely to harm the patient with high glucose; however, the delay in giving glucose to the hypoglycemic patient may be detrimental. Once the diagnosis of hypoglycemia is made, search carefully for the cause in the previously healthy patient. In the diabetic patient, search for the cause (e.g. medication changes, dietary changes, new metabolic changes, recent illness, occult infection) of the episode.

Consultations. Endocrinology, toxicology, or infectious disease subspecialists may be consulted, but, in general, an internal or family practice specialist can manage hypoglycemia and determine its underlying etiology.

Management of head injuries. Head injury is a major cause of long term disability and economic loss to society. Much of the neurological damage resulting from a head injury does not occur immediately, but in the minutes, hours and days that follow. It is for this reason that so much emphasis is placed on immediate management of head-injured patients. The primary injury is due to irreversible mechanical injury, but secondary injury which leads to cerebral ischaemia, results from raised intracranial pressure (ICP), hypotension, hypoxia, anaemia, seizures, hypoglycaemia and hyperthermia. Prevention and correct management of these complications improves outcome from head injuries.

The main aim of assessment and management of head-injured patients is to maintain adequate cerebral blood flow (CBF) and to avoid cerebral ischaemia and hypoxia.

In patients with a head injury, the normal auto-regulation of CBF is lost and CBF is proportional to cerebral perfusion pressure (CPP), which in turn is directly determined by both the mean arterial pressure (MAP) and the intracranial pressure (ICP):

$$\mathbf{CPP = MAP - ICP}$$

The cranium is a rigid structure with a fixed capacity, which contains 80 % brain, 10 % blood and 10 % CSF. These structures are all non-compressible, therefore an increase in the volume of any of these contents, unless coupled by a decrease in volume of another, results in an increase in ICP.

The main mechanisms of maintaining CPP are to ensure adequate MAP (by the use of fluids and vasopressors) and to prevent excessive rises in ICP.

In normal individuals the ICP is 0–10 mm Hg and this is largely determined by auto-regulation of CBF (i.e. the amount of blood in the cranium).

Vasoconstriction or vasodilatation of cerebral vessels occurs in response to changes in MAP, PaO_2, $PaCO_2$ and blood viscosity.

Although these responses may be obtunded in head injury, prevention of secondary brain injury involves manipulation of these variables.

An increase in $PaCO_2$ causes vasodilatation and an increase in CBF, which may increase ICP; a decrease in $PaCO_2$ causes vasoconstriction leading to decreased CBF and ICP. Thus inappropriate hyperventilation may cause ischaemia. A fall in PaO_2 causes vasodilatation with a consequent rise in ICP.

Initial assessment. Patients presenting with significant head injury may have multiple injuries. The history of the mechanism of injury is useful in determining the potential extent of the head injury and is also an indication of the likelihood of other injuries.

For example, the driver of a vehicle travelling at 60mph and not wearing a seatbelt raises the suspicion of both major head injury and significant extra-cranial injury.

Brain injury may be worsened by airway or circulatory compromise; use the **ABC approach** to identify and treat life-threatening injuries early.

Once the patient has a secure airway, he is adequately oxygenated and has a stable cardiovascular system, consideration should be given to transfer him to a neurosurgical unit (where available).

When discussing the case with the neurosurgeon, it is important to convey the mechanism of injury, any other injuries and the results of a brief neurological assessment. The surgeon will want to know the history, the Glasgow Coma Score (GCS) at the scene, on arrival at the hospital and the current GCS (especially the motor score), the pupillary size and reaction, and whether there are any signs suggesting a collection of blood on one side of the cranial cavity ("lateralising" signs).

Management. The main aims of management of any moderate or severe head injury are initial assessment and resuscitation, deciding whether ventilatory support is necessary and establishing a diagnosis, with a CT head scan if this is available. Early contact with a specialist of neurosurgical units is key; he will often advise on specific therapies. Early transfer, when indicated, is also important. The Association of Anaesthetists of Great Britain and Ireland suggest a maximum time of 4 hours between injury and surgery. Throughout this process management should be equal to that in an ICU, directed at maintaining the MAP and CPP and preventing rises in ICP.

Airway. The main concern is whether the patient is able to protect their airway and therefore whether intubation is necessary. Indications for intubation include:

– GCS $\leq$ 8;

– risk of raised ICP due to agitation (i.e. sedation required);

– inability to control/protect the airway or loss of protective laryngeal reflexes;

– a fall of 2 or more points in the motor component of the GCS;

– to optimise oxygenation and ventilation;
– seizures;
– bleeding into mouth/airway;
– bilateral fractured mandible.

This is not an exhaustive list and clinical judgement is important. If there is doubt, it is safest to intubate and consider early extubation rather than delay intubation and risk secondary brain injury from hypoxia.

Rapid sequence intubation is almost always required. Maintain cervical spine immobilisation during intubation, unless the cervical spine is clinically and radiologically cleared.

Propofol, etomidate, benzodiazepines and barbiturates all reduce ICP and are preferentially used. Ketamine produces a rise in ICP, but may be the only induction agent available in certain countries. Opioids and depolarising neuromuscular drugs do not increase ICP. The fasciculations caused by suxamethonium may cause a transient rise in ICP. Nitrous oxide may also cause a rise in ICP via increased blood flow.

All patients with head injury should have plain X-rays of the cervical spine and some may require a CT scan.

Breathing. Hypoxaemia is associated with a significant increase in mortality. A drop in PaO_2 below 8 kPa (about 60 mm Hg) causes an increase in CBF and ICP. Targets for gas exchange should be a PaO_2 greater than 13 kPa (100 mm Hg) and a $PaCO_2$ in the low normal range — usually 4.5–5.0 kPa (35–39 mm Hg).

Prolonged hyperventilation is not recommended since cerebral vasoconstriction and ischaemia may result, but short bursts of hyperventilation (a few minutes) may help to control episodes of high ICP.

Circulation. The loss of the autoregulation of CBF can result in a reduction in oxygen delivery. Maintenance of the MAP and CPP is essential; resuscitation and treatment of life-threatening circulatory instability should take precedence over neurosurgical interventions. This may include surgery for haemorrhage control.

Use fluids, and where necessary vasopressors to achieve a MAP greater than 80–90 mm Hg. This figure is recommended as a guide until ICP monitoring is established, and assumes that the ICP is 20 mm Hg and therefore ensures a CPP of at least 60–70 mm Hg (since CPP = MAP – ICP).

Once ICP monitoring is established then treatment is targeted at maintaining CPP 60–70 mm Hg. Aiming for higher CPP targets has been associated with adverse cardio-respiratory outcomes.

Ideally the MAP is measured using an arterial line. A central venous catheter may be useful for monitoring and the administration of vasopressors. A urinary catheter allows monitoring of urine output and fluid balance, especially if mannitol or other diuretics are used.

Some clinical signs are suggestive of raised ICP. These include:
– headache;
– dizziness;

– loss of consciousness;
– confusion;
– hypertension and bradycardia (Cushing's reflex);
– nausea;
– vomiting;
– focal weakness or paresis;
– other focal neurological signs;
– change or asymmetry pupils.

Management of raised ICP. Improving venous drainage from the brain:

– Elevation of the bed head to 30^{o}.

– Good neck alignment — head in the neutral position.

– Ensuring ties holding the endotracheal tube in place, do not compress the neck veins. Alternatively tape the tube using "trouserlegs".

– Where possible immobilise the patient's cervical spine with sandbags and tape rather than restrictive neck collars.

Reducing cerebral oedema:

– Use mannitol (an osmotic diuretic) 0.5–1 g/kg^{-1} (= 5–10 ml/kg^{-1} of 10 % or 2.5–5 ml/kg^{-1} of 20 % mannitol). Some units use small aliquots of hypertonic saline as an alternative.

– Use furosemide (a loop diuretic) 0.5–1 mg/kg^{-1}.

– Maintain serum Na^{+} in the range 140–145 $mmol/L^{-1}$.

Reduction of the cerebral metabolic rate for oxygen:

– Close temperature regulation. Avoid hyperthermia, but do not actively induce hypothermia.

– Use of sedation and anaesthetic drugs. Ensure that the patient is appropriately sedated and has received adequate analgesia.

– If the patient has a witnessed seizure loading with an anticonvulsant, usually phenytoin 18 mg/kg^{-1}, should be considered.

– In cases of intractable raised ICP, a thiopentone infusion can be used to reduce the cerebral metabolic rate to a basal level. This is identified on EEG monitoring as 'burst supression'.

Reducing intracranial blood volume:

– Consider whether the patient has suffered a new or worsening intracranial haemorrhage. Are there any new or lateralising signs? Is a repeated CT scan required?

– Hyperventilation can be used to reduce the PaCO2 as a temporary measure, but cerebral ischaemia may result if this is prolonged (for more than a few minutes).

– The final resort if ICP remains raised is to perform a decompressive craniectomy (part of the cranial bone is removed).

Reducing CSF volume. In a neurosurgical centre, use of an external ventricular drain (EVD) allows drainage of CSF to relieve raised ICP.

STROKE

Pathology: haemorrhage, embolus or thrombosis.

"Secondary" stroke may occur with meningitis, bacterial endocardi tis, subarachnoid haemorrhage and vascul itis.

Dissection and cerebral venous thrombosis need to be considered, as anticoagulation is indicated for both (unless a large infarct is establ ished, as there is an increased risk of bleeding).

Dissection should be suspected in younger patients, often presenting with severe headache or neck pain ± Horner's syndrome ± seizures after trauma or neck manipulation. Cerebral venous thrombosis may mimic stroke, tumour, subarachnoid haemorrhage or meningo-encephal itis and may present with headache, seizures, focal signs or obtundation.

Urgent CT scan is indicated when the diagnosis is in doubt, for continuing deterioration, suspicion of subarachnoid haemorrhage, hydrocephalus or trauma, or for patients who are anticoagulated or who have a bleeding tendency.

Aims of treatment. To protect the penumbra with close attention to oxygenation, hydration, glycaemic control, and avoidance of pyrexia. Blood pressure control is needed for severe hypertension (e.g. > 200/120 mm Hg) and hypotension.

Drug therapy including thrombolysis and aspirin. The evidence for anticoagulation remains contentious as there is an increased risk of bleeding and no consistent subgroup benefit has been shown. Early anticoagulation is probably beneficial for intracranial stenosis, a stroke-in-evolution, complete vessel occlusion with minimal deficit and in low risk patients with a high probability of recurrence (secondary prevention).

For thrombolysis the extent of reperfusion depends on the aetiology with basilar > middle cerebral artery > internal carotid, and embol ic > thrombotic. Pooled studies with rt-PA (0.9 mg/kg) given within 3 h of stroke onset (and tight blood pressure control) showed a favourable outcome. However, there was a 6-fold increase in haemorrhage (to 5.9 %), of whom 60 % died. This was more common in the elderly, and with more severe stroke.

Neurosurgical intervention may be considered for cerebel lar haematoma, cerebel lar infarction and the malignant middle cerebral artery syndrome (for massive infarction on the non-dominant side).

SUBARACHNOID HAEMORRHAGE

In 15 % no cause is found; of the remainder, 80 % are due to a ruptured aneurysm, 5 % to arteriovenous malformations and 15 % follow trauma. The anterior part of the Circle of Will is is affected in 85–90 % of cases while 10–15 % affect the vertebrobasilar system. There is a 30 % risk of rebleeding for which the mortal ity is 40 %. Those surviving a month have a 90 % chance of surviving a year. Cerebral vasospasm occurs in 40–70 % of patients at 4–12 days after the bleed. This is the most important cause of morbidity and mortality.

Hydrocephalus, seizures, hyponatraemia and inappropriate ADH secretion are recognised compl ications.

Clinical features. SAH may be preceded by a prodrome of headache, dizziness and vague neurological symptoms. Often there is rapid onset (minutes to hours) presentation including collapse, severe headache ± meningism. Cranial nerve palsies, drowsiness and hemiplegia may also occur.

Diagnosis. Diagnosis is usually made by CT scan; if there is no evidence of raised intracranial pressure, a lumbar puncture may be performed revealing blood-stained CSF wi th xanthochromia.

Management. Bed rest. Maintain adequate hydration, nutrition, analgesia, sedation. Cerebral vasospasm is prevented by nimodipine infusion and maintenance of a full intravascular volume.

Systemic hypertension should only be treated if severe (e.g. systolic pressure > 220–230 mm Hg) and prolonged.

Surgery — the timing is controversial with either early or delayed (7–10 days) intervention being advocated. The Regional Neurosurgical Centre should be consulted for local policy.

Antifibrinolytic therapy (e.g. tranexamic acid) reduces the incidence of rebleeding but has no beneficial effect on outcome.

GENERALISED SEIZURES

Control of seizures is necessary to prevent ischaemic brain damage, to reduce cerebral oxygen requirements and to reduce intracranial pressure. Where possible correct the cause and give specific treatment. A CT scan may be necessary to identify structural causes. Common causes include:

– hypoxaemia;
– hypoglycaemia;
– hypocalcaemia;
– space-occupying lesions;
– metabolic and toxic disorders;
– drug withdrawal, e.g. alcohol, benzodiazepines, anticonvulsants;
– infection, especially meningoencephalitis;
– trauma;
– idiopathic epilepsy.

Most seizures are self-limiting, requiring no more than protection from injury (coma position, protect head and do not force anything into the mouth).

Specific treatment. Hypoxaemia should be corrected with oxygen (FIO_2 0.6–1.0). Intubation and ventilation if the airway is unprotected or SpO_2 < 90 %. Blood glucose should be measured urgently and hypoglycaemia corrected with IV 50 ml 50 % glucose. Anticonvulsant levels should be corrected in known epi leptics. Cerebral oedema should be managed with sedation, induced hypothermia, control led hyperventilation and osmotic diuretics. In patients with a known tumour, arteritis or parasitic infection, high dose dexamethasone may be given.

Thiamine 100 mg IV should be given to alcoholics. Consider surgery for space-occupying lesions, e.g. blood clot, tumour.

Anticonvulsants. Anticonvulsants are necessary where there are repeated seizures, a single seizure lasts > 30 min or there is cyanosis.

A benzodiazepine (e.g. lorazepam, diazepam) is the usual first l ine treatment.

Phenytoin — a loading dose should be given intravenously if the patient has not previously received phenytoin. Phenytoin may not provide immediate control of seizures wi thin the first 24 h.

If seizures continue appropriate anticonvulsants include:

– Magnesium sulphate;

– Clonazepam, which is particularly useful for myoclonic seizures;

– Thiopental or propofol infusion in severe intractable epilepsy.

With all anticonvulsants care should be taken to avoid hypoventilation and respiratory failure. However, mechanical ventilation will certainly be required if thiopental is used, and probably to maintain oxygenation in cases of continued seizures.

Other supportive treatment. Muscle relaxants prevent muscular contraction during seizures but will not prevent continued seizures. They may be necessary to facilitate mechanical venti lation but continuous EEG monitoring should be used to judge seizure control. Correction of circulatory disturbance is required to maintain optimal cerebral blood flow.

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