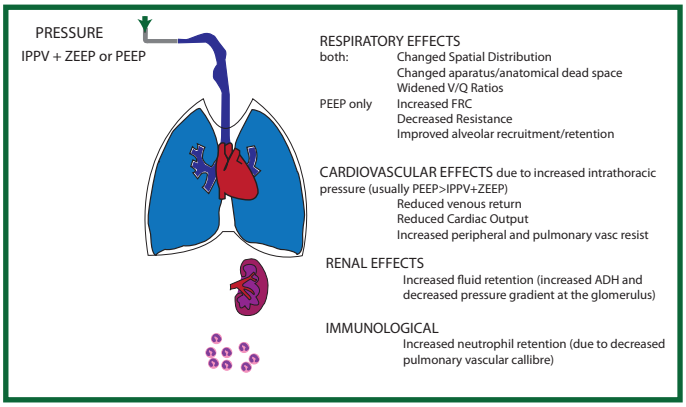
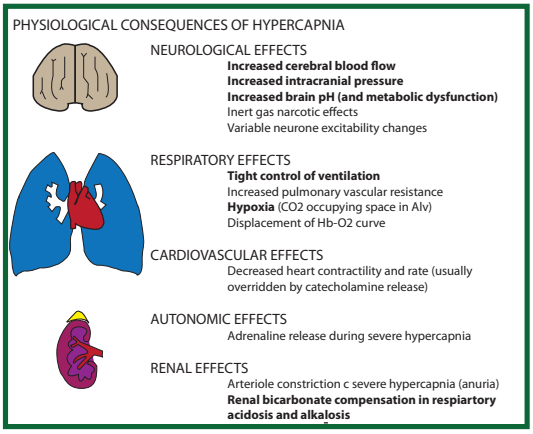
APPLIED RESPIRATORY PHYSIOLOGY

Intermittant Positive Pressure Ventilation (IPPV) and Positive End Expiratory Pressure (PEEP). IPPV ventilation can be delivered in many different techniques, often designed to correspond to patient initiated actions. During inspiration IPPV raises the pressure at the mouth above ambient levels and there is an inflow of air into the lungs. If the inspiration is prolonged then the ventilation will be dependent on the regional compliance of the lungs, if it is short then different time constants may result in preferential ventilation to regions of the lung with short time constants. During expiration two options exist. Firstly the pressure at the mouth drops to ambient resulting in Zero End Expiratory Pressure (ZEEP). There is no change to FRC. The alternative is PEEP which is used to increase the functional residual capacity (FRC), reduce airways resistance (wider calliber airways at higher FRC) and prevent or reverse lung collapse. Negative EEP is no longer used as a modality.

Physiological consequences of IPPV and PEEP. The physiological effects of IPPV with ZEEP or PEEP relate to the mean increase in intrathoracic pressure and as such PEEP has a more significant effect. Respiratory effects: IPPV results in minor changes in the spatial distribution of ventilation which is only relevant in patients with acute lung injury. PEEP increases lung volume, re-expands collapsed alveoli and therefore improves ventilation in these areas. Both delivery of IPPV and PEEP results in aparatus deadspace which may or may not influence the overall deadspace (sometimes it is cancelled by a reduction in anatomical deadspace). There is a slight worsening of V/Q ratios with IPPV but this is often not significant. As stated above PEEP increases FRC whilst IPPV with ZEEP does not. IPPV and PEEP do not change oxygenation in healthy patients but may have significant benefits is diseased patients, for the afore mentioned reasons, increasing the FRC above closing capacity, reducing airways resistance and improving recruitment and maintaining patency in alveolar units. The main deleterious effects of IPPV and especially PEEP is the cardiovascular effects. IPPV and PEEP cause a reduction in cardiac output by reducing venous return to the right atrium because of increased introathoracic pressure. With normal inspiration there is negative intrathoracic pressure which acts as a pump to draw blood into the chest from the major veins and this is abolished with postive intrathoracic pressure. The reduction in RV filing leads to less LV filling, which is exacerbated in hypovolaemic states. Furthermore the increased airway pressures lead to increased pulmonary vascular pressures and this increases RV strain. It is noted that whilst PEEP may improve PaO2 the decrease in CO may actually lead to decreased O2 delivery to the tissues (remember that DO = CO(sats x Hb + dissolved O2)). There is some increase in peripheral vascular resistance to counter the decreased CO but this is often inadequate. Interestingly, in heart failure patients the reduced RV filling may actually improve function by moving an overloaded RV to a more favourable position on the starling curve. Renal Effects: Prolonged IPPV causes increases in oedema, this is beleived to be from a combination of increased ADH and the reduced pressure gradient at the glomerulus caused by decreased arterial pressures and increased CVP. Immunological effects occur from increased neutrophil retention in the pulmonary vasculature due to their reduced calibre with IPPV and PEEP.





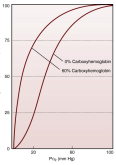
Physiological effects of hypercapnia and hypocapnia. Hypocapnia is always due to increased alveolar ventilation, and this may be due to hypoxaemia (which drives increased ventilation at altitude), metabolic acidosis compensation and neurological disorders (such as head injuries) and emotional states such as fear. Hypercapnia is due to four different causes; increased inspired concentration of CO2, increased CO2 production, hypoventilation and increased dead space. Carbon dioxide has at least five major effects on the brain, it is the main factor governing cerebral blood flow, it influences ICP the through changes in blood flow, it is the main factor influencing the brain pH, it has inert narcotic effects like NO, and it influences the excitability of certain neurons especially those in the reticuloactivating system. It is the pH and to a lesser extent the inert gas narcotic effects which have the most clinical obvious influence which is on levels of consciousness. Raised ICP is also very significant in regards to clincial effects and deliberate hypocapnia was often an aim in head injury although this is now out of vogue. In severe hypercapnia (<100 mmHg) increased catecholamines are released especially adrenaline which leads to autonomic responses (organs may be less responsive however due to the low pH). From a respiratory perspective ventilation responses to a change in CO2 is very sensitive as previously discussed. When patients are hypercapnic there is noted pulmonary vasoconstriction which may cause V/Q changes, raised CO2 in the alveolar units displaces O2 and leads to hypoxia and there is a displacement of the O2-Hb curve to the right, improving O2 delivery at the tissues. Cardiovascular changes are complex, in isolation hypercapnia leads to decreased contractility and rate but increased catecholamines often overwhelm this response. Renal blood flow in unchanged in normal ranges but during severe hypercapnia there is arteriole constriction and subsequent anuria. Prolonged hypercapnia leads to increased HCO3 absorption and a compensatory metabolic alkalosis, in prolonged hypocapnia HCO3 is dumped leading to a metabolic acidosis compensation. In addition to these electrolyte changes hypercapnia causes K to leak out of cells leading to an increase in plasma K levels.

Physiological consequences of Hypoxia Hypoxia refers to inadequate tissue PO2 to ensure ongoing oxidative phosphorylation. This is the PO2 at the end of the oxygen cascade which may equate to a gradient at the mitochondria of as little as 2mmHg. There is no defined safe level however of arterial PO2 which will ensure adequate tissue PO2 due to other variables such as perfusion, O2 consumption and Hb concentration. When tissue is hypoxic the body reverts to anerobic pathways which result in energy production some 19 times less efficient that oxidative phosphorylation. Furthermore the byproducts of anerobic energy production, H+ and lactate ions are transported away in the peripheral tissues, but do not cross the BBB and therefore much of the damage in cerebral hypoxia is related to the damage caused by intracellular acidosis rather than the depletion of energy stores. At a cellular level in addition to the production of lactate and H+ ions, there is a leaking of K+ and an influx of Ca++, this leads to failure of the Na/K pump and eventual cell death. On a systemic level hypoxia leads intially to hyperventilation (but only when the aterial PO2 is below 55), hypoxic pulmonary vasoconstriction, increased organ perfusion, especially the brain, increased cardiac output, decreased pH due to lactate production and right shift of the Hb-O2 curve due to DPG production. Long term hypoxia leads to polycythemia as seen in chronic lung disease and aclimitisation.

TISSUE LEVEL
- Impaired oxidative phosphorylation
- Increased anerobic energy production→ lactate & H^+
- Localised acidosis (worse in the brain due to the BBB)
- K^+leakage → Ca^{2+} into cell → Na^+/K^+pumps failure → rapid depolaristation → cell death

SYSTEMICAL LEVEL
- Hyperventilation when PaO2 is below 55 mmHg
- Hypoxic pulmonary vasoconstriction
- Increased cardiac output
- Preferential organ perfusion (especially brain)
- Acidosis and Hb-O2 curve right shift

LONG TERM
- Increased haemaglobin levels



Carbon Monoxide Poisoning usually due to inhalation but may be due to ingestion of methylene chloride which is metabolised in the liver to CO. CO binds to heme with an affinity 240 times that of O2. It causes an allosteric change in which greatly inhibits the three other heme binding sites from offloading O2. The result is a shift of the O2 dissociation curve to the left. CO also inhibits oxidative phosphorylation like cyanide but to a less extent which exacerbates the hypoxia. The mechanism of the delayed neurological sequelae is not well understood but may be related to toxic oxygen species generated by xanthine oxidase. Treatment is via high flow O2 and HBOT may be indicated.

As patients age several changes occur in the respiratory system, most of which lead to a gradual worsening of function. Compliance bucks the trend and has no measurable difference as patients age. As patients age they have more variable patterns when sleeping with more apnoeic periods, variations in upper airways resistance and episodes of transient hypoxaemia down as low as 75%. Anatomical dead space is increased in infants due to their large head and neck, with on average of 3.3ml/kg. This reduces down to 2 ml/kg as a young adult and then gradually increases by roughly a ml per year. The diffusing capacity of the lung gradual worsens throughout life in a linear fashion. Functional residual capacity gradual increases throughout life, and may increase markedly in disease states such as COPD. The closing capacity increases more rapidly then FRC and as a result will equal FRC in a supine patient (gravity decreases FRC) at the age of 44 and an erect patient in their seventies. This leads to a worsening of V/Q ratios with age as gas trapped by a CC>FRC constitutes a shunt. The end result is that arterial PO2 values gradually decline with age.