Intermittent 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 calibers 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 apneustic dead space which may or may not influence the overall dead space (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 differences is diseases patients, for the aforesaid 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 intrathoracic 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 positive intrathoracic pressure. The reduction in RV filling 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 IPPV may improve PaO₂ the decrease in CO may actually lead to decreased O₂ delivery to the tissues (remember that DO = CO(sxs Hb + dissolved O₂)). There is some increase in peripheral vascular resistance to counter the decreased CO but this is often not significant. 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 beieved 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. Hypcapnia is due to four different causes; increased inspired concentration of CO₂, increased CO₂ production, hyperventilation 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 inerts narcotic effects which have the most clinical obvious influence which is on levels of consciousness. Raised ICP is also very significant in regards to clinical 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 vascular constriction 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 to other variables such as perfusion, O₂ consumption and Hb concentration. When tissue is hypoxic the body reverts to anaerobic pathways which result in energy production some 19 times less efficient than oxidative phosphorylation. Furthermore the byproducts of anaerobic 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 initially to hyperventilation (but only when the arterial 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 acclimatisation.

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 hems with an affinity 240 times that of O₂. It causes an allosteric change in which greatly inhibits the three other heme binding sites from displacement of Hb-O₂ curve

APPLIED RESPIRATORY PHYSIOLOGY

PHYSIOLOGICAL CONSEQUENCES OF HYPERCAPNIA

NEUROLOGICAL EFFECTS
Increased intracranial pressure
Increased brain pH (and metabolic dysfunction)
Insert gas-narctotic effects
Variable nerve excitability changes

RESPIRATORY EFFECTS
Tight control of ventilation
Inhaled gases increase arterial CO₂ tension
Hypoxia (CO₂ occupying space in Ar) Displacement of Hb-O₂ curve

CARDIOVASCULAR EFFECTS
Decreased heart contractility and rate (usually reversible by catecholamines release)

AUTONOMIC EFFECTS
Adrenaline release during severe hypoxia

RENAL EFFECTS
Anoxic-constriction c severe hypoxia (anuria)
Bicarbonate compensation in respiratory acidosis and alkalosis

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

SYSTEMIC LEVEL
Hyperventilation when PaO₂ is below 55 mmHg
Hypoxic pulmonary vasoconstriction
Increase PaO₂ with FIO₂
Preferential organ perfusion (especially brain)
Acidosis and Hb-O₂ curve right shift

LONG TERM
Increased haemoglobin levels

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 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.