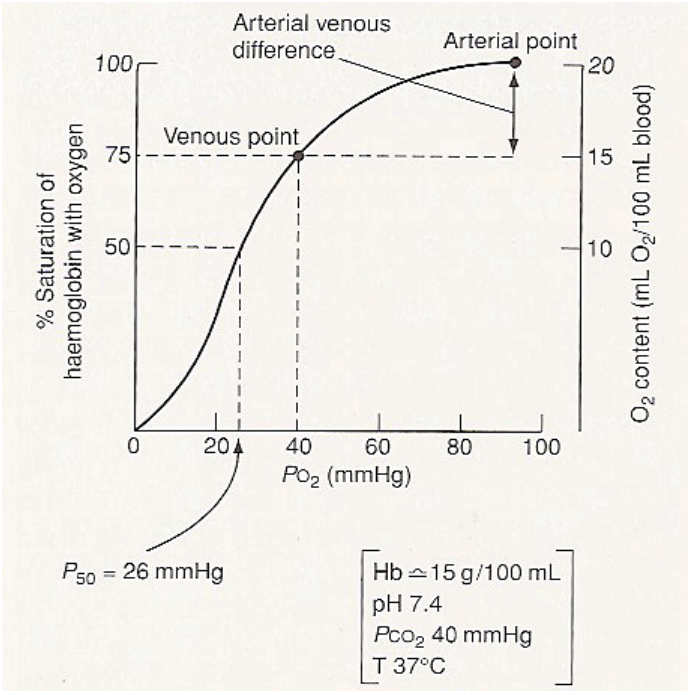
By Adam Hollingworth

Diagram or Die

Respiratory

Oxygen Curves

OHDC



OHDC with R & L shift

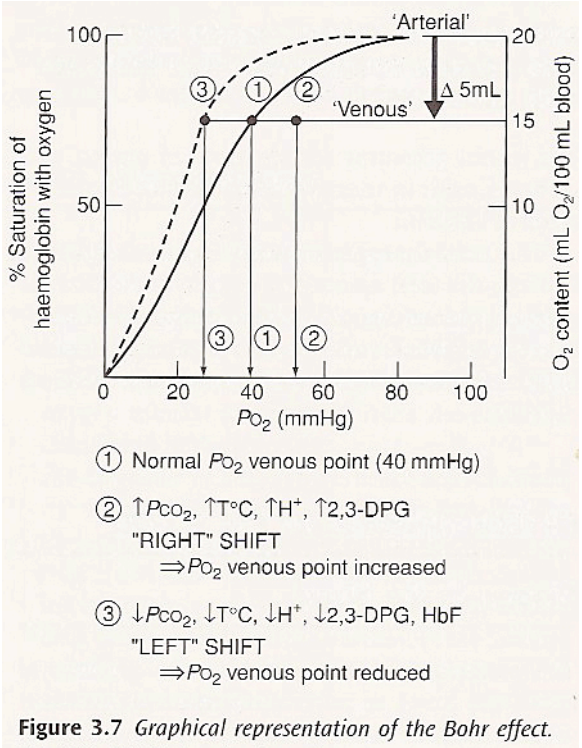
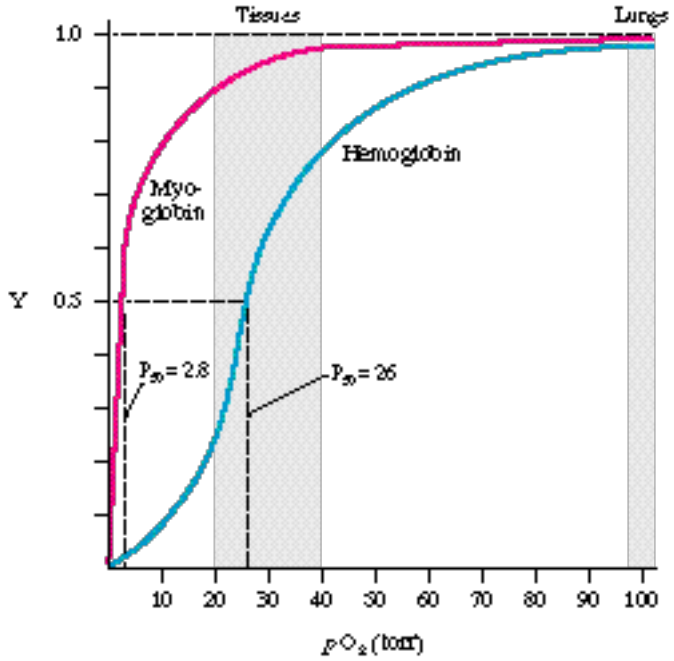


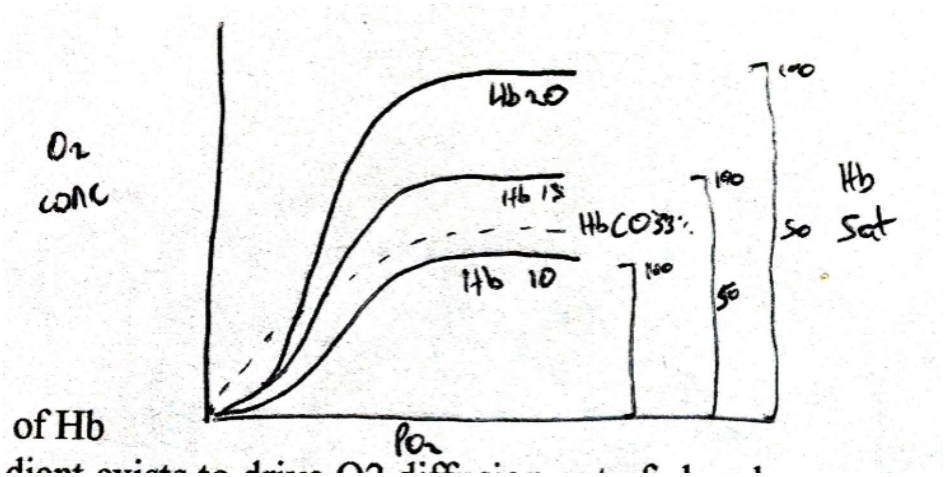
Figure 3.7 *Graphical representation of the Bohr effect.*

- foetal Hb p50 18

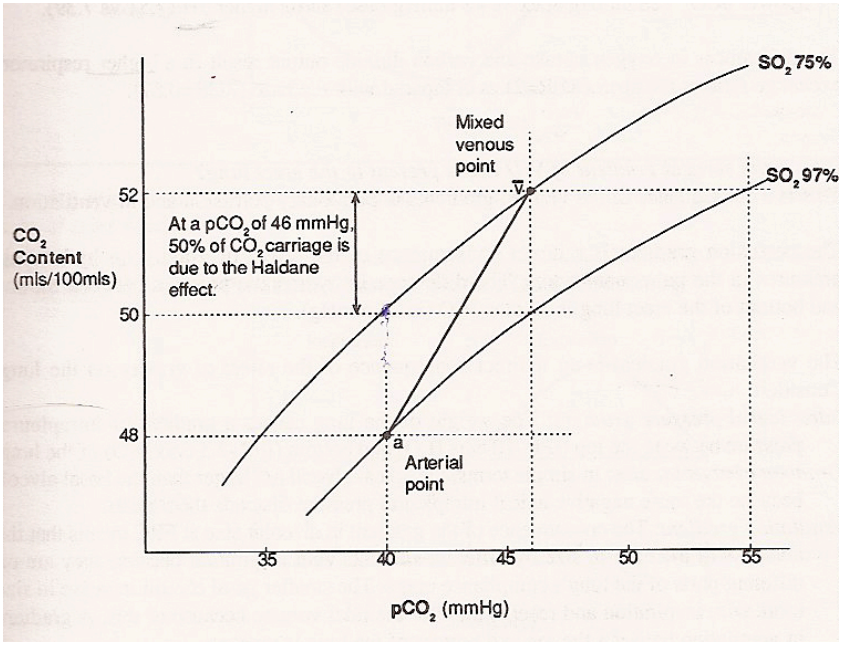
Hyperbolic Myoglobin Hb Curve



Anaemia



CO2 Dissociation Curve



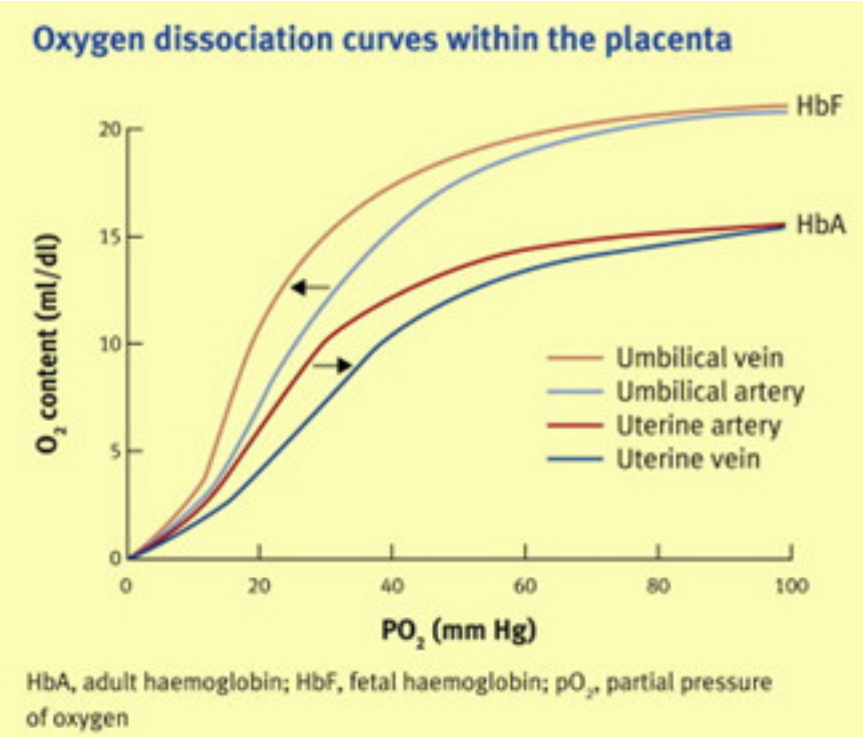
	pCO2	CaCO2
artery	40	48
vein	46	52

Maternal Resp Physiology

Normal Values

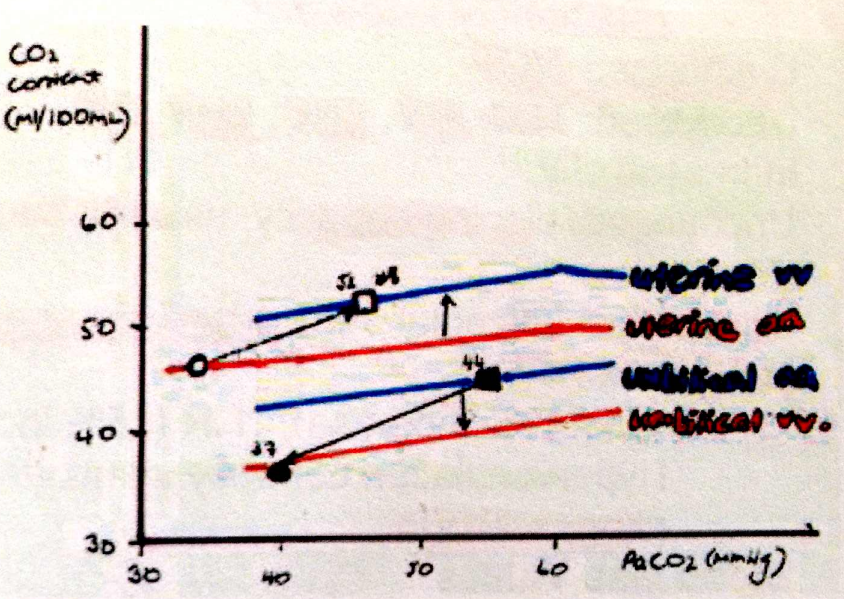
	Uterine A.	Uterine V.	Umbilical A.	Umbilical V.
PaO2	100	40	15	30
PaCO2	30	45	55	40
SO2	98	75	40	80
p50	26			18
CaO2	16	12	10	16
CaCO2	48	52	44	37

Double Bohr Effect



HbA, adult haemoglobin; HbF, fetal haemoglobin; pO_2, partial pressure of oxygen

Double Haldane Effect



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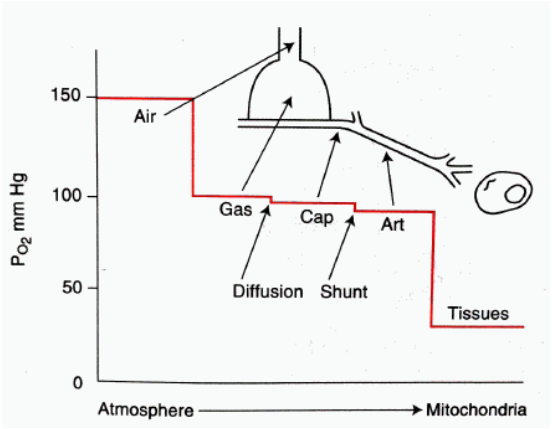
O2 Cascade

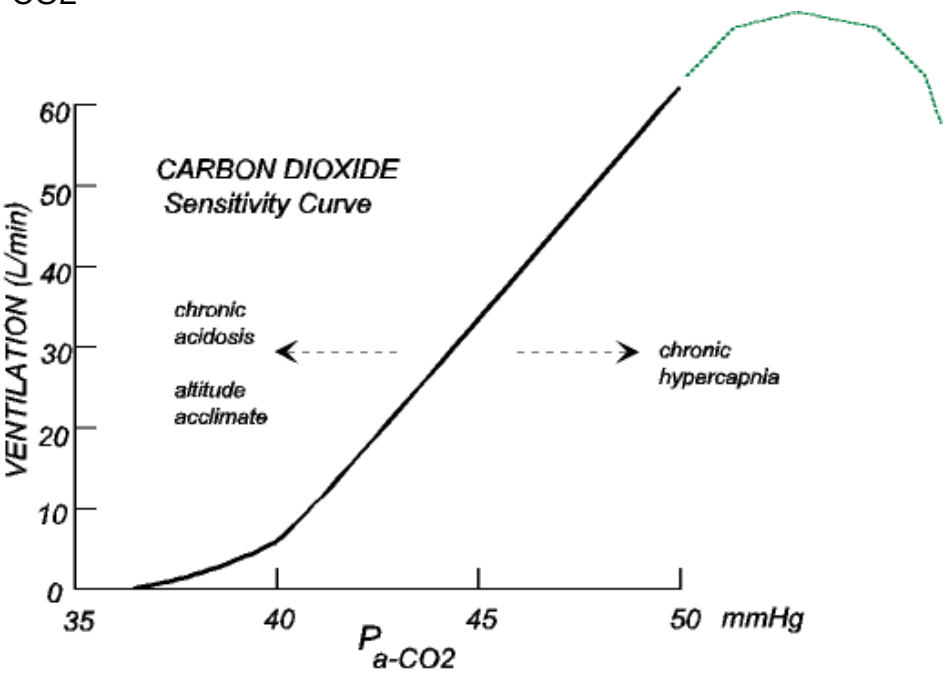
FiO2 = 0.21	FiO2 = 1
Dry room air = **159** mmHg	Dry room Air = **760**
↓ ← humidification of dry gas → ↓	
Saturated room air = **149**	Saturated room air = **711**
↓ ← gas exchange in alveoli (alv gas equation)→ ↓	
Alveolar gas = **100**	Alveolar Gas **661**
↓← Incomplete **diffusion** (immeasurably small)→↓	
End-capillary blood ~ **100**	End capillary blood ~ 661
↓ ← venous admixture (shunt, V/Q mismatch) → ↓	
Arterial blood = **97**	Arterial blood ~ **600**
↓ ← diffusion of O2 to cells → ↓	
End-tissue capillary blood = **40**	**End-tissue capillary blood ~48-50**[2]
↓ ← consumption in cells(mainly mitochondria)→ ↓	
Mitochondria = **4 – 22**	Mitochondria **~4-22**

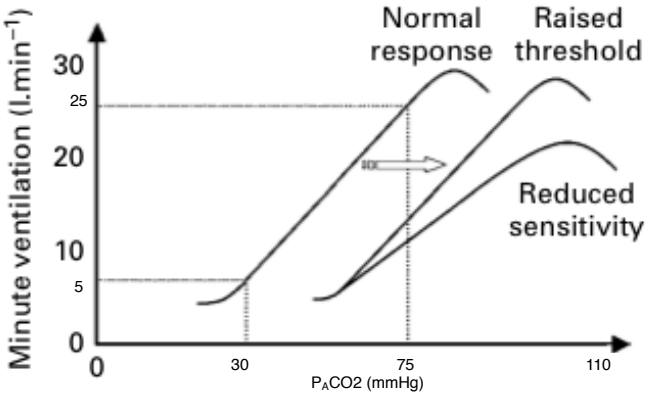
	CaO2 art	CaO2 central venous	Sats art	Sats central venous
FiO2 0.21	20	15	98	75
FiO2 1	21.3	16.3	100	



Ventilatory Responses

CO2





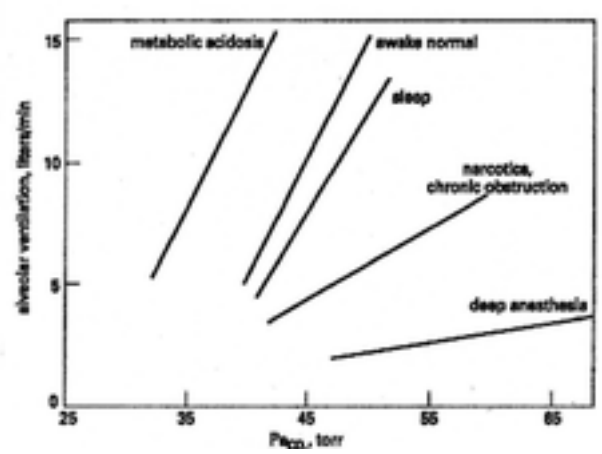
Normal Draw and label the axes as shown. Plot a normal P_{ACO_2} (5 kPa) at a normal MV (6 l.min^{-1}). If the P_{ACO_2} is doubled, the MV increases four-fold in a linear fashion. Therefore, join the two points with a straight line. Above 10–11 kPa, the line should fall away, representing depression of respiration with very high P_{ACO_2}. At the lower end of the line, the curve also flattens out and does not reach zero on either axis.

Raised threshold Plot a second parallel curve to the right of the first. This represents the resetting of the respiratory centre such that a higher P_{ACO_2} is required at any stage in order to achieve the same MV. This is seen with opiates.

Reduced sensitivity Plot a third curve with a shallower gradient. This represents decreased sensitivity such that a greater increment in P_{ACO_2} is required in order to achieve the same increment in MV. Also seen with opiates.

CO2 Response to Narcotics, Anaesthesia

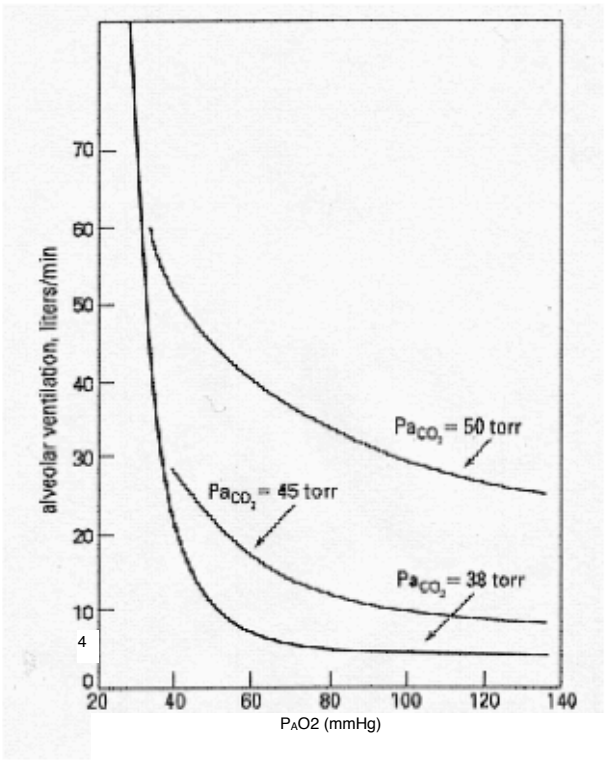
R SHIFT: (decreased sensitivity to CO2)
- Metabolic alkalosis
- Denervation of peripheral chemoreceptors
- Normal sleep
- Drugs
- Hypothermia



R SHIFT & DOWN:
- High dose opioids
- Anesthetics (enflurane > halothane > isoflurane)
- Neuromuscular blocker

L SHIFT: (increased sensitivity to CO2)
- Hypoxemia
- Metabolic acidosis
- Central (increased ICP, anxiety)
- Analeptics

O2 & CO2



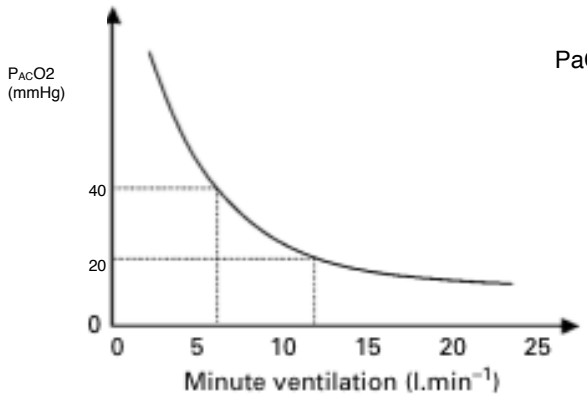
4

At P_{ACO_2} of 5 kPa The line should demonstrate that, under normal conditions, the minute volume (MV) remains relatively constant around 6 $l.min^{-1}$ until the P_{AO_2} falls below 8 kPa. Show that the rise in MV following this is extremely steep. This illustrates the hypoxic drive, which is so often talked about in the setting of COPD.

At P_{ACO_2} of 10 kPa This line is plotted above and to the right of the first and demonstrates the effect of a coexisting hypercarbia on hypoxic ventilatory drive.

Carbon Dioxide vs Minute Ventilation

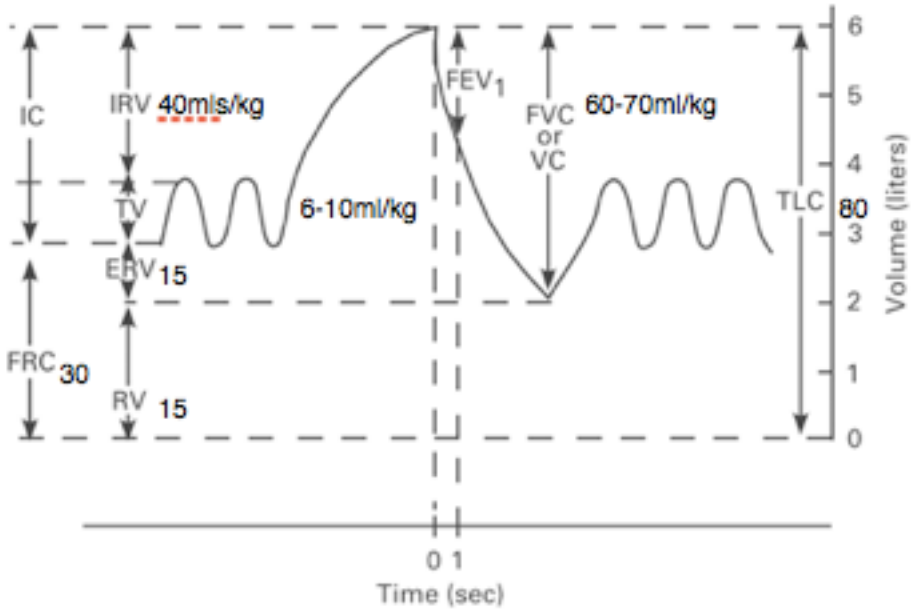
Alveolar carbon dioxide partial pressure versus minute ventilation



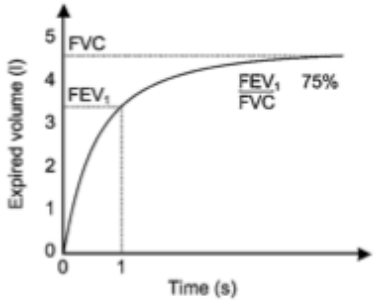
$$PaCO2 = \frac{VCO2}{MV} \times 760$$

Draw and label the axes as shown. This graph demonstrates the effect that ventilation has on P_{ACO_2} rather than the control of ventilatory drive by CO_2 itself. As MV doubles, so the P_{ACO_2} halves. The curve is, therefore, a rectangular hyperbola. Begin by plotting a normal P_{ACO_2} (5 kPa) at a normal MV (6 l.min^{-1}). Draw one or two more points at which MV has doubled (or quadrupled) and P_{ACO_2} has halved (or quartered). Finish by drawing a smooth curve through all the points you have drawn.

Spirometry



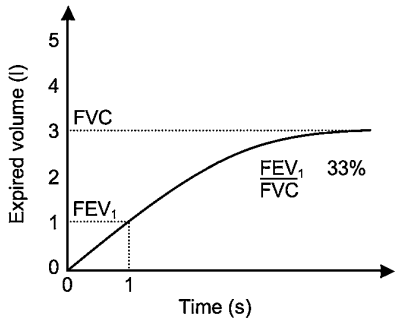
Normal spirometry



	FEV1	FVC	Ratio
N	3.5	4.5	75%
R	3.5	4	85%
O	1	3	33%

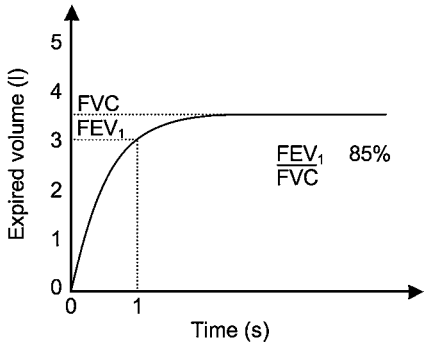
Draw and label the axes as shown. Next draw a horizontal line at the level of the forced vital capacity (FVC; 4500 ml) to act as a target point for where the curve must end. Normal physiology allows for 75% of the FVC to be forcibly expired in 1 s (FEV_1) . The normal FEV_1 should, therefore, be 3375 ml. Mark this volume at a time of 1 s. Construct the curve by drawing a smooth arc passing through the FEV_1 point and coming into alignment with the FVC line at the other end.

Obstructive pattern



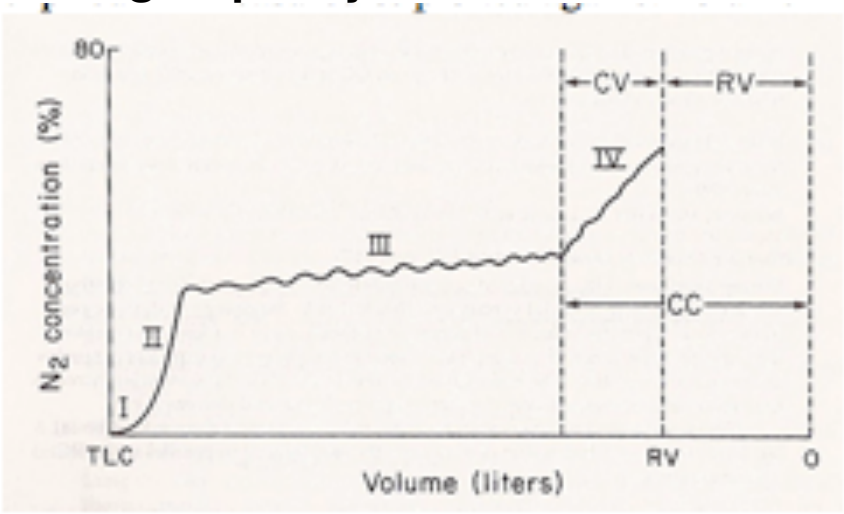
On the same axes, draw a horizontal line at a lower FVC to act as a target end point. Obstructive airway diseases limit the volume of gas that can be forcibly expired in 1 s and, therefore, the FEV_1/FVC ratio will be lower. In the graph above, the ratio is 33% giving a FEV_1 of 1000 ml for a FVC of 3000 ml. Construct the curve in the same way as before.

Restrictive pattern



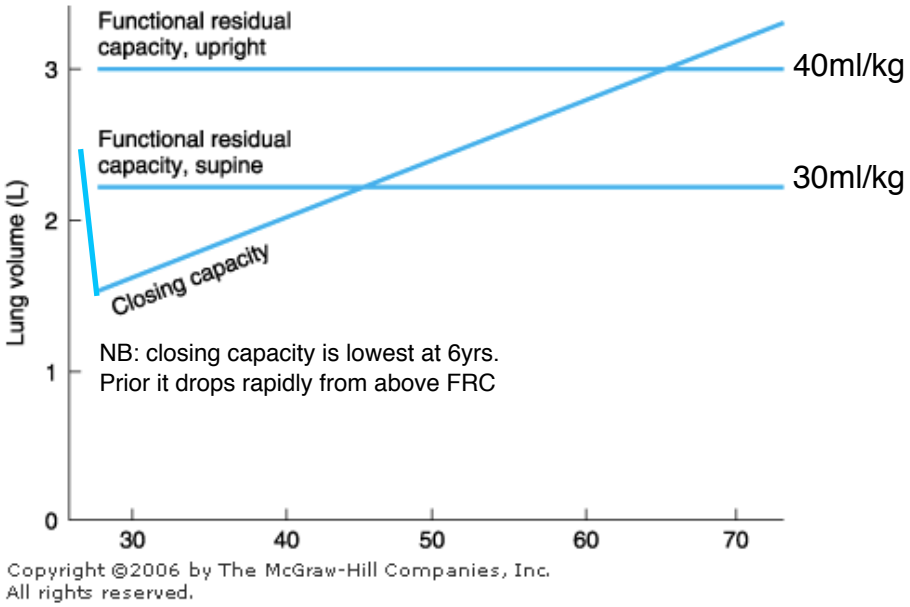
On the same axes, draw a horizontal line at a lower FVC than normal to act as a target end point. Restrictive lung disease curtails the FVC but generally does not affect early expiration. For this reason, the FEV_1/FVC ratio is normal or high. In the graph above, the ratio is 85%, giving a FEV_1 of 3000 ml for a FVC of 3500 ml. Construct the curve in the same way as before.

Closing Capacity & FRC



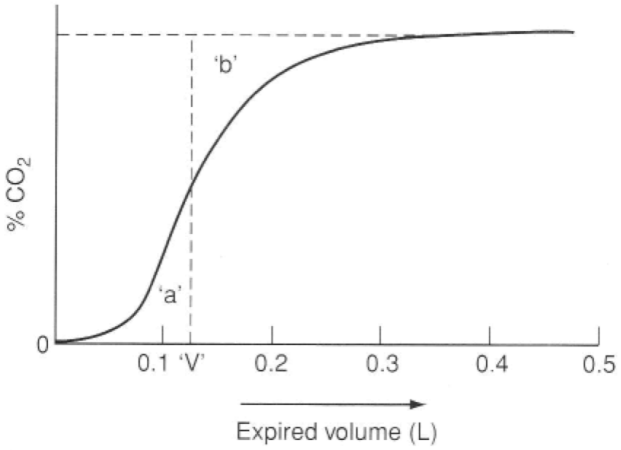
Phase 1 Pure dead space gas so no value on the *y* axis.
Phase 2 A mixture of dead space gas and alveolar gas. The curve rises steeply to a plateau. Demonstrate a vertical line that intercepts this curve such that area A equals area B. The anatomical dead space is taken as the volume expired at this point.
Phase 3 Plateau as alveolar gas with a steady N_2 content is exhaled. Note the curve is not completely horizontal during this stage.
Phase 4 Draw a final upstroke. This occurs at the closing volume. Note that the volume on the *x* axis at this point is not the value for the closing volume itself but rather the volume exhaled so far in the test. The closing volume represents the volume remaining within the lung at this point.

FRC & Age



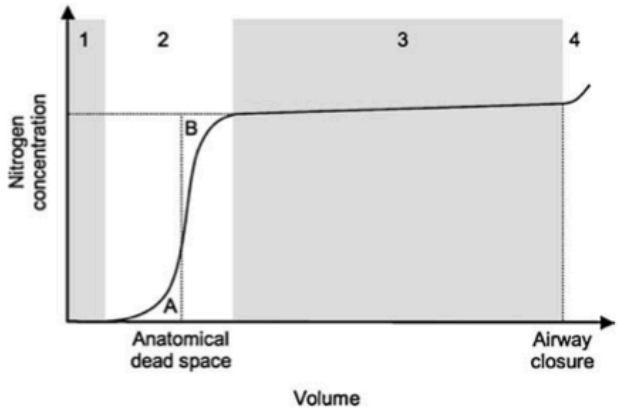
- CC = residual lung volume at which dependent small airways **start** closing
- CV = volume able to expire after onset of dep small airway closure, before RV
  - ↳ ie portion of VC which can be exhaled (with max effort) after onset of airway closure

Single Breath N2 washout (Fowlers)



- Tidal breath 100% O2,
- then expire measuring volume out of N2 or CO2

If area 'a' = area 'b'
Then 'V' = anatomical dead space



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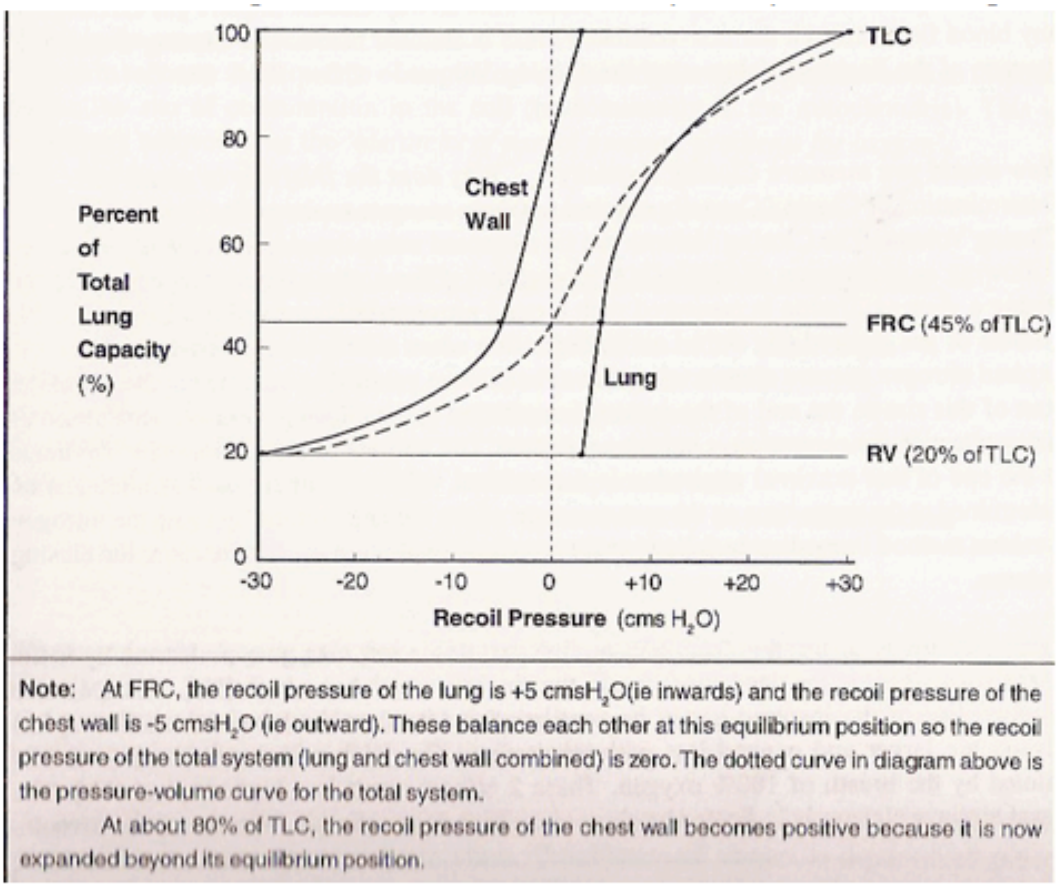
Phase 4 Draw a final upstroke. This occurs at the closing volume. Note that the volume on the *x* axis at this point is not the value for the closing volume itself but rather the volume exhaled so far in the test. The closing volume represents the volume remaining within the lung at this point.

Pressure Volume Curve

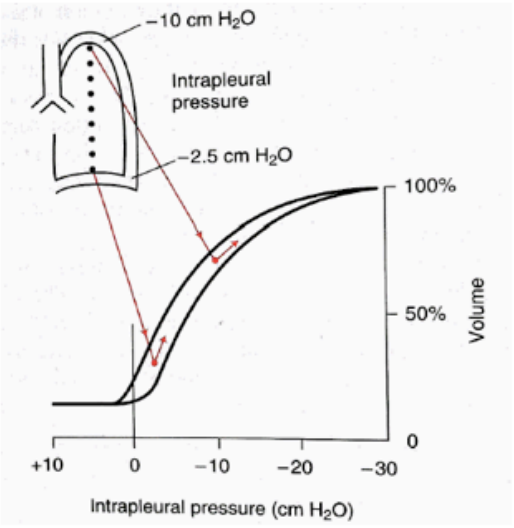


Note: At FRC, the recoil pressure of the lung is +5 cmsH_2O (ie inwards) and the recoil pressure of the chest wall is -5 cmsH_2O (ie outward). These balance each other at this equilibrium position so the recoil pressure of the total system (lung and chest wall combined) is zero. The dotted curve in diagram above is the pressure-volume curve for the total system.

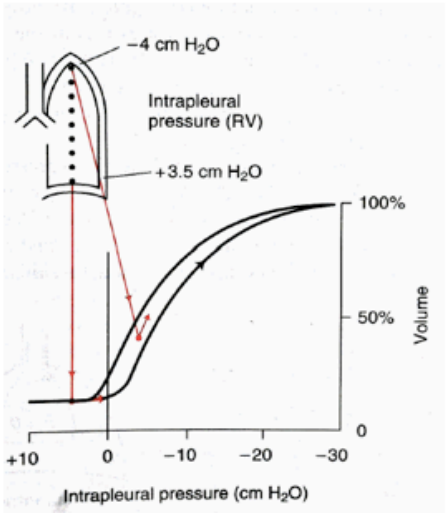
At about 80% of TLC, the recoil pressure of the chest wall becomes positive because it is now expanded beyond its equilibrium position.

alveolar pressure – ambient pressure = (alveolar P – IPP) + (IPP – ambient P)

Compliance Curve

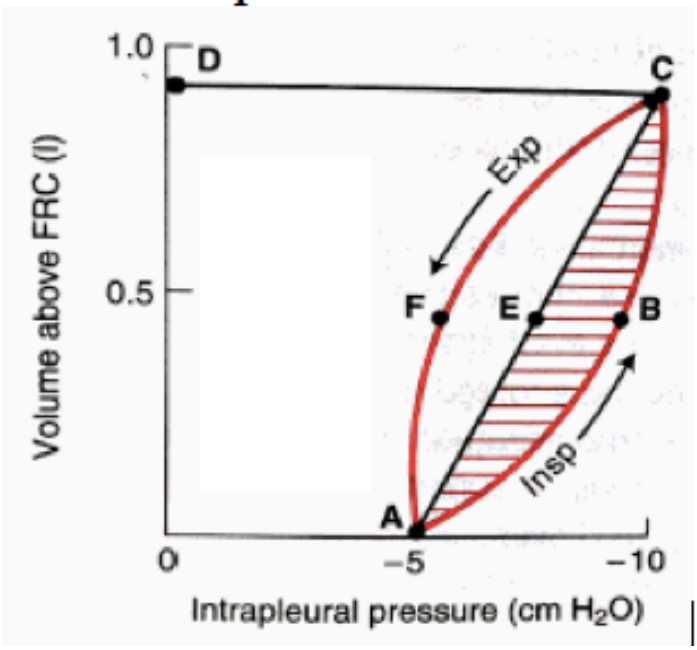


normal lung volume



low volume; residual volume (after forced expiration)

Work of Breathing (Pressure - Volume Loops)

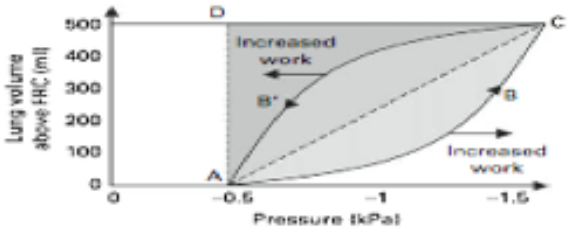


Work of breathing

In normal circumstances, the work done on expiration utilizes energy stored within the elastic tissues on inspiration. Expiration is, therefore, said to be passive unless the energy required to overcome airway resistance exceeds that which is stored.

Work of breathing graph

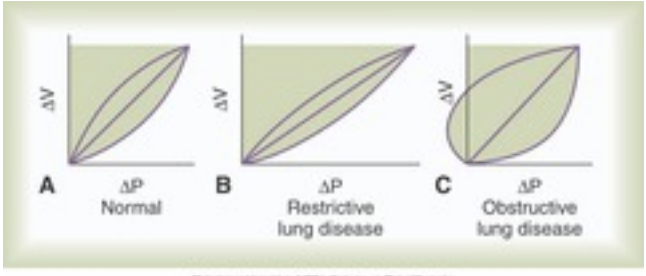
The purpose of the graph is to demonstrate the effect of airway and tissue resistance on the pressure–volume relationship within the chest.



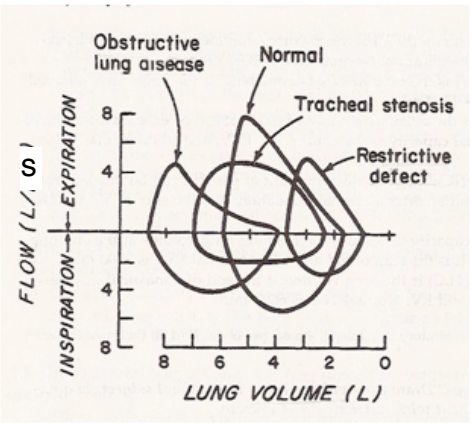
Draw and label the axes as shown. Remember the curve should only start to rise from −0.5 kPa on the *x* axis as the intrapleural pressure within the lung remains negative at tidal volumes. If there were no resistance to breathing, each tidal breath would increase its volume along the theoretical line AC and back again on expiration along the line CA.

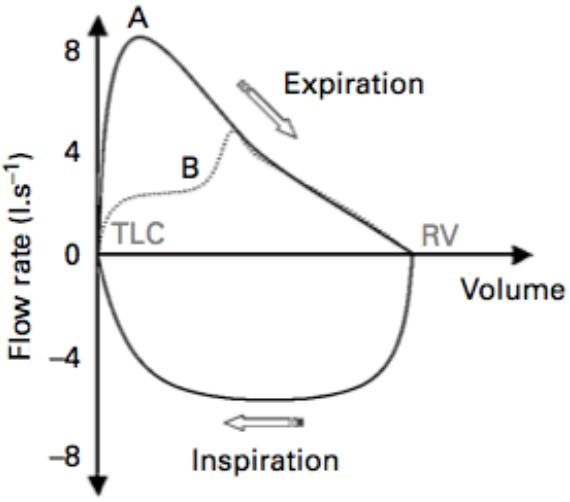
Inspiration The line ABC is the physiological line traced on inspiration. The area ACDA represents work to overcome elastic tissues resistance. The extra area enclosed by ABCA represents the work done in overcoming viscous resistance and friction on inspiration. If this resistance increases, the curve bows to the right as shown.

Expiration The line CB′A is the physiological line traced on expiration. The area enclosed by CB′AC is the work done on expiration against airway resistance. As this area is enclosed within the area ACDA, the energy required can be supplied from the stored energy in the elastic tissues. If this resistance increases, the curve bows to the left, as shown. The difference in area between ACB′A and ACDA represents the energy lost as heat.



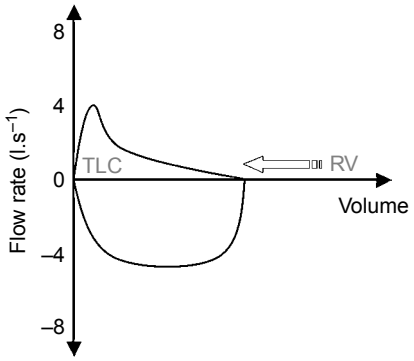
Flow Volume Loop





Draw and label the axes as shown; the *x* axis need not display numerical values but a note should be made of the TLC and RV. Note that the highest volume (TLC) is on the left of the *x* axis. The units on the *y* axis are litres per second as opposed to litres per minute. Positive deflection occurs during expiration and negative deflection during inspiration. The patient takes a VC breath before starting the test with a forced expiration. The loop is drawn in a clockwise direction starting from TLC. The normal loop (A) rises rapidly to a flow rate of 8–10 l.s^{-1} at the start of forced expiration. The flow rate then decreases steadily as expiration continues in a left to right direction so that a relatively straight curve is produced with a slight concavity at its centre. An important point to demonstrate is the phenomenon of dynamic compression of the airways. The curve traced by the normal loop represents the maximum possible flow rate at each lung volume. Even if patients 'holds back' their maximal effort by expiring slowly at first (B), they will be unable to cross this maximal flow line. This is because the airways are compressed by a rise in intrathoracic pressure, thus limiting flow. The more effort that is put into expiration, the more these airways are compressed and so total flow remains the same. The inspiratory limb has a much squarer shape to it and a maximum flow of 4–6 l.s^{-1} is usually achieved. Inspiration occurs from RV to TLC in a right to left direction as shown.

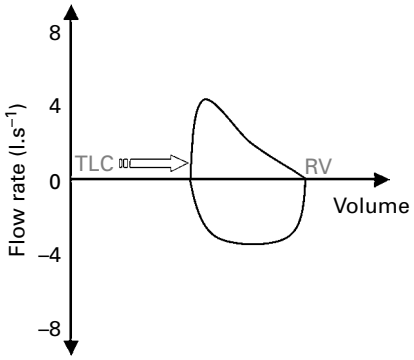
Obstructive disease



- ↑TLC - due to ↓AWR & optimise compliance
- ↓gradient upstroke: due to ↓caliber airways
- ↓peak flow: due to ↑AWR & ↓recoil pressure
- ↓gradient downslope: due to:
  - ↓caliber airways
  - earlier onset dynamic airways compression
- ↑RV - due to gas trapping

Obstructive disease reduces peak expiratory flow rate (PEFR) and increases RV via gas trapping. The TLC may also be higher although this is difficult to demonstrate without values on the *x* axis. The important point to demonstrate is reduced flow rates during all of expiration, with increased concavity of the expiratory limb owing to airway obstruction. The inspiratory limb is less affected and can be drawn as for the normal curve but with slightly lower flow rates.

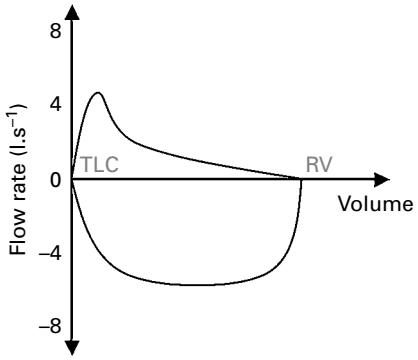
Restrictive disease



- ↓TLC - due to ↓compliance
- N gradient upstroke
- ↓peak flow: due to start at lower lung volume
- ↑gradient downslope: due to:
  - fibrotic interstitium provides traction limiting dynamic compression
- ↓RV - due to later closing capacity

In contrast to obstructive disease, restrictive disease markedly reduces TLC while preserving RV. The PEFR is generally reduced. Demonstrate these points by drawing a curve that is similar in shape to the normal curve but in which the flow rates are reduced. In addition, the left-hand side of the curve is shifted to the right, demonstrating a fall in TLC.

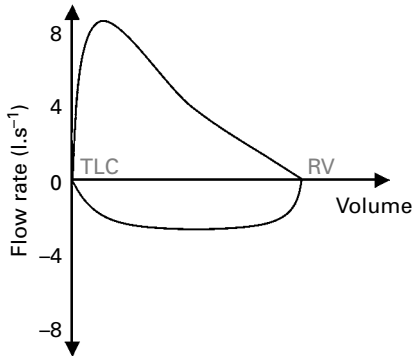
Variable intrathoracic obstruction



NB: pattern reversed in +ve PV

An intrathoracic obstruction is more likely to allow gas flow during inspiration as the negative intrathoracic pressure generated helps to pull the airways open. As such, the inspiratory limb of the curve may be near normal. In contrast, the positive pressure generated during forced expiration serves only to exacerbate the obstruction, and as such the expiratory limb appears similar to that seen in obstructive disease. Both TLC and RV are generally unaffected.

Variable extrathoracic obstruction

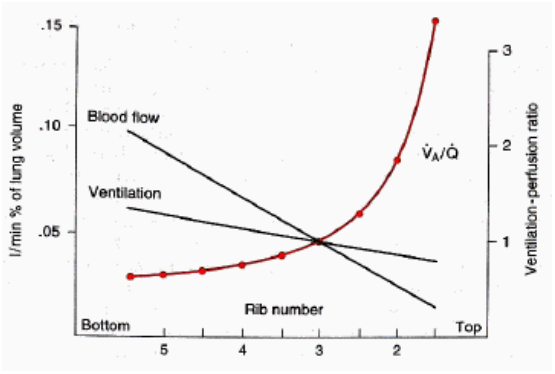


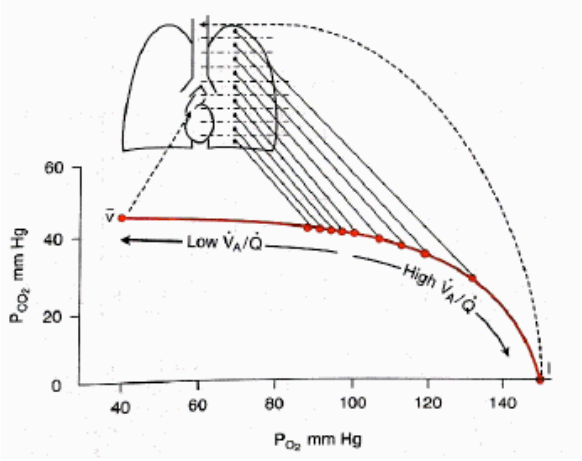
NB: pattern reversed in +ve PV

An extrathoracic obstruction is more likely to allow gas flow during expiration as the positive pressure generated during this phase acts to force the airway open. As such, the expiratory limb may be near normal. In contrast, the negative pressure generated in the airway during inspiration serves to collapse the airway further and the inspiratory limb will show markedly reduced flow rates at all volumes while retaining its square shape. Both TLC and RV are generally unaffected.

This curve is seen where a large airway has a fixed orifice through which gas is able to flow, such as may be seen in patients with tracheal stenosis. The peak inspiratory and expiratory flow rates are, therefore, dependent on the diameter of the orifice rather than effort. The curves should be drawn almost symmetrical as above, with both limbs demonstrating markedly reduced flow. The TLC and RV are generally unaffected.

Regional Vent & Blood Flow

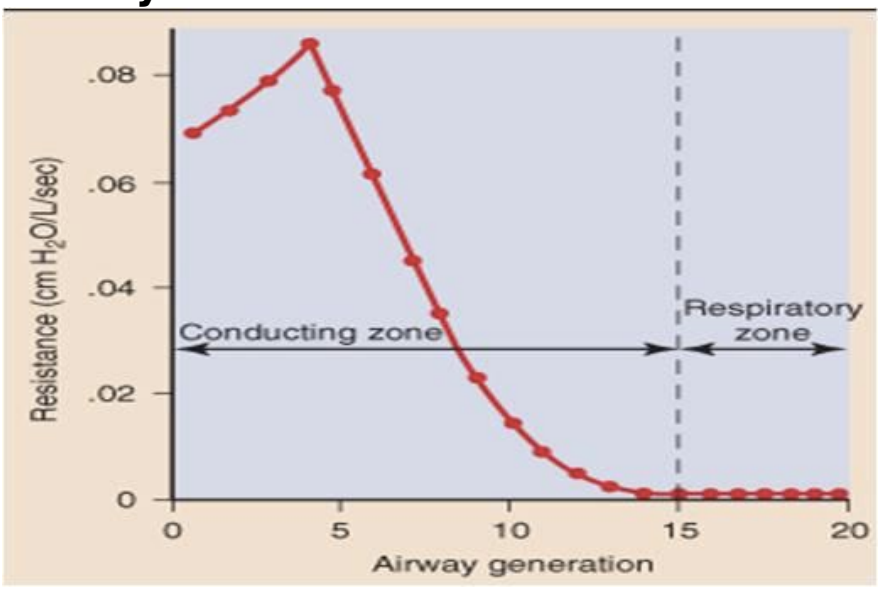




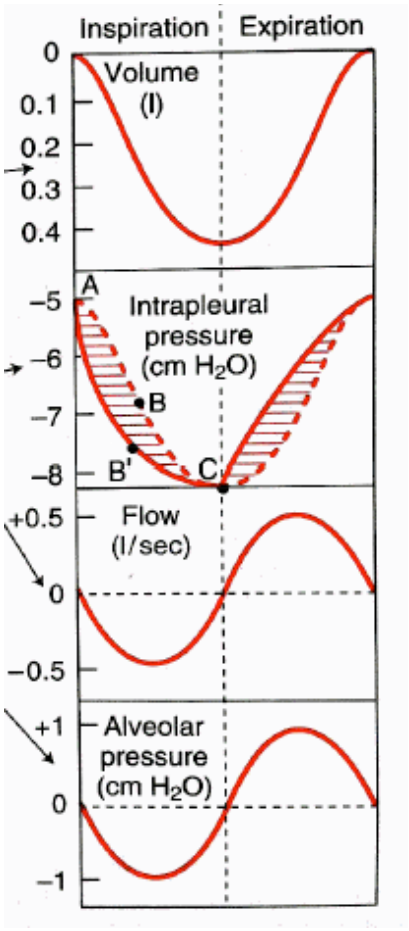
The graph can be drawn with either one or two *y* axes. The example above has two, flow and $\dot{V}/\dot{Q}$ ratio, and gives a slightly more complete picture. The *x* axis should be arranged from the bottom to the top regions of lung in a left to right direction as shown. Both ventilation and perfusion decrease linearly from bottom to top. Perfusion starts at a higher flow but decreases more rapidly than ventilation so that the lines cross approximately one third of the way down the lung. At this point the $\dot{V}/\dot{Q}$ ratio must be equal to 1. Using this point and a maximum $\dot{V}/\dot{Q}$ ratio of around 3, draw a smooth curve passing through both of these as it rises from left to right. The graph demonstrates that higher lung regions tend towards being ventilated but not perfused (dead space, $\dot{V}/\dot{Q} \approx \infty$) and lower regions tend towards being perfused but not ventilated (shunt, $\dot{V}/\dot{Q} \approx 0$).

Lung	PO2	PCO2	V/Q
apex	130	28	3
base	90	43	0.63

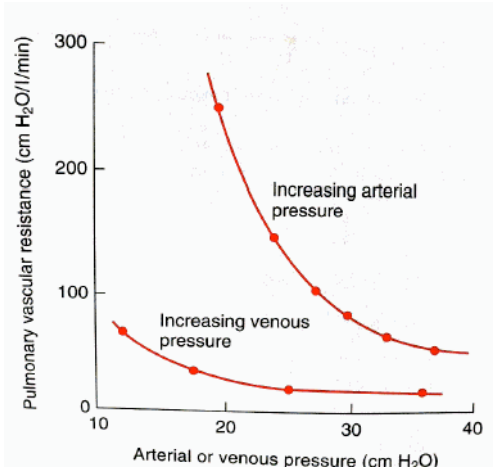
Airway Resistance

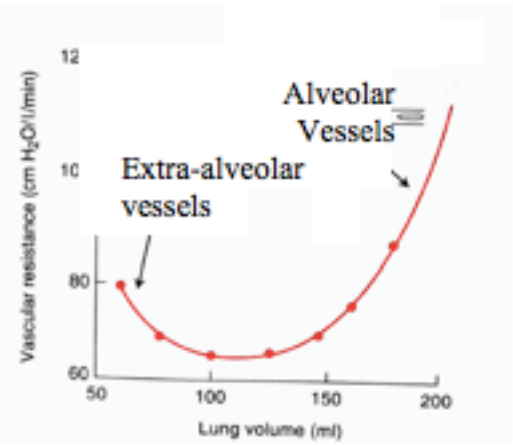


Pressures In Breath Cycle



PVR - Venous Pressure & Lung Volume





Iso Shunt Diagrams

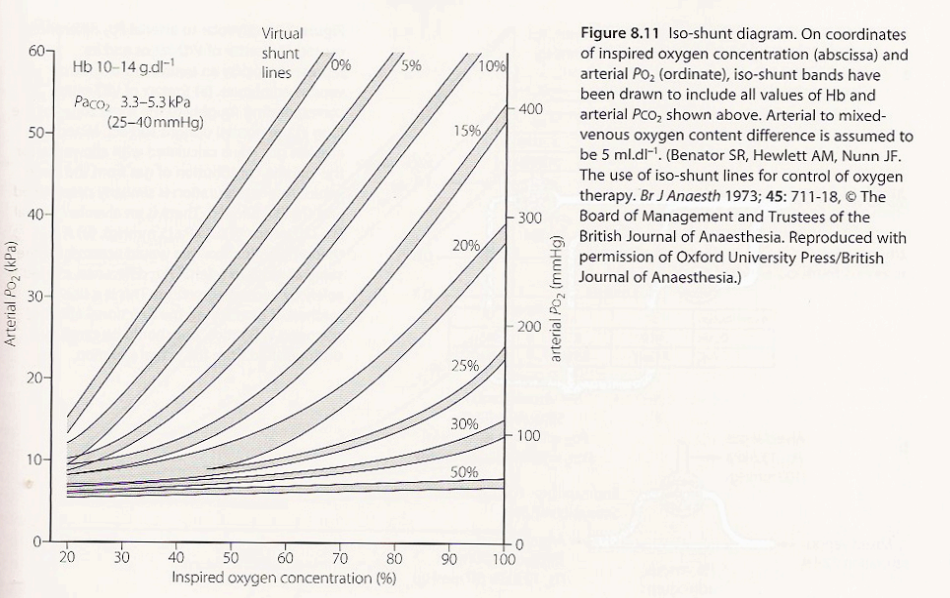
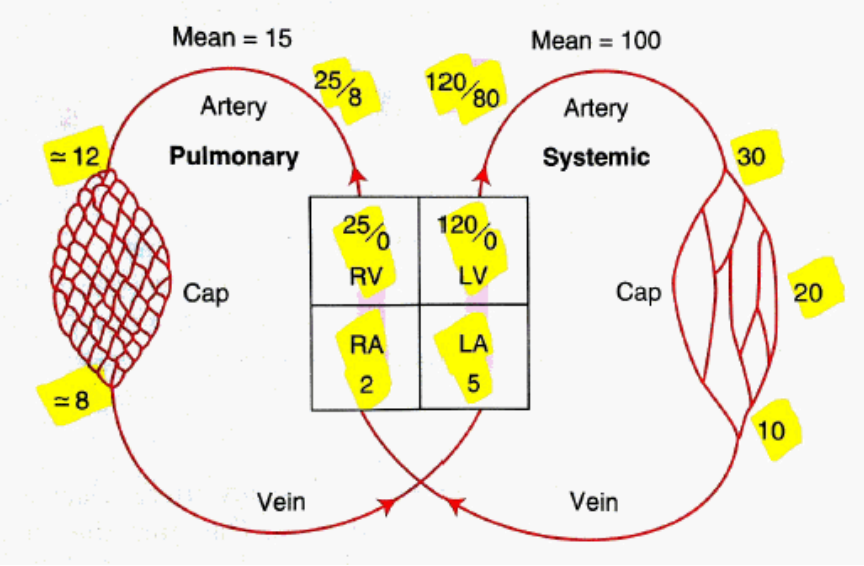


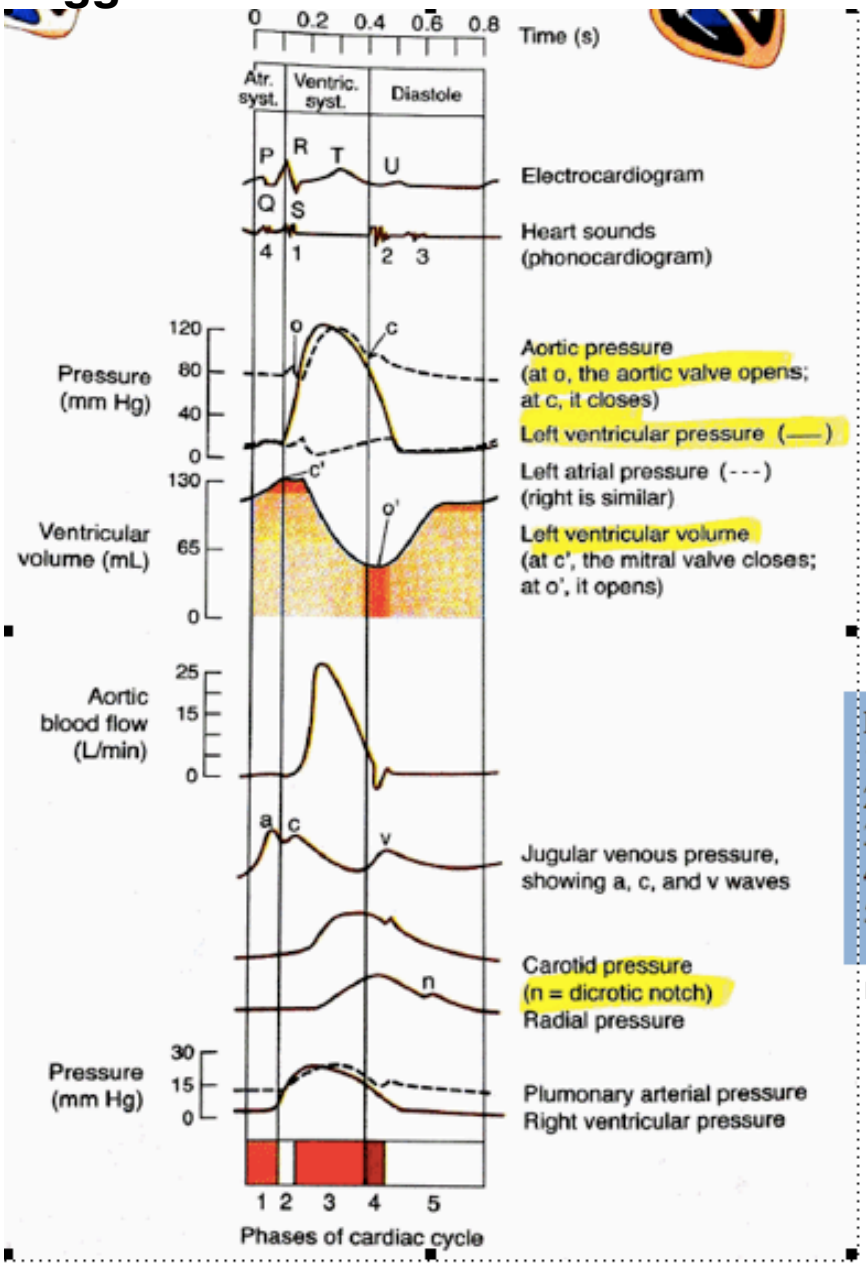
Figure 8.11 Iso-shunt diagram. On coordinates of inspired oxygen concentration (abscissa) and arterial P_{O_2} (ordinate), iso-shunt bands have been drawn to include all values of Hb and arterial P_{CO_2} shown above. Arterial to mixed-venous oxygen content difference is assumed to be 5 ml.dl^{-1}. (Benator SR, Hewlett AM, Nunn JF. The use of iso-shunt lines for control of oxygen therapy. *Br J Anaesth* 1973; **45:** 711-18, © The Board of Management and Trustees of the British Journal of Anaesthesia. Reproduced with permission of Oxford University Press/British Journal of Anaesthesia.)

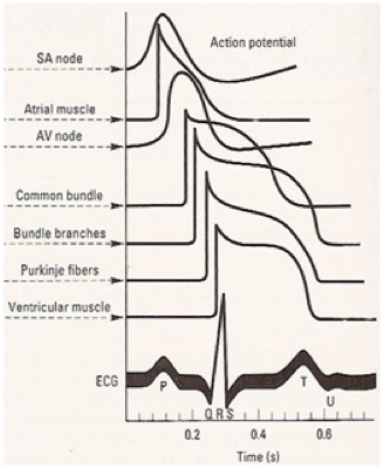
Pulmonary Pressures



Cardiovascular

Wiggers





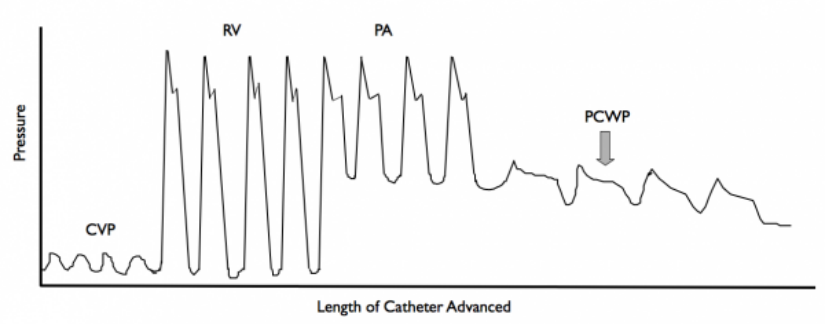
Phases:
1. atrial systole
2. isovolumetric contraction
3. vent ejection
4. isovolumetric relaxation
5. vent filling

NB isovolumetric contraction lasts 0.05sec

Heart Sounds

- S1 = closure of AV valves = start of systole
- S2 =
  - closure of aortic & pulmon valves = end of systole
  - inspiration ⇒ physiological splitting of S2 by late closure of pulmon valve due to incr preload
- S3 =
  - rapid vent filling 1/3 through diastole
  - can be normal
- S4 =
  - Filling of stiff ventricle following atrial contraction
  - Just before S1
  - Always pathological

PA Catheter Pressure Changes



Right atrium (RA) The pressure waveform is identical to the CVP. The normal pressure is 0–5 mmHg.

Right ventricle (RV) The RV pressure waveform should oscillate between 0–5 mmHg and 20–25 mmHg.

Pulmonary atery (PA) As the catheter moves into the PA, the diastolic pressure will increase owing to the presence of the pulmonary valve. Normal PA systolic pressure is the same as the RV systolic pressure but the diastolic pressure rises to 10–15 mmHg.

PAOP This must be lower than the PA diastolic pressure to ensure forward flow. It is drawn as an undulating waveform similar to the CVP trace. The normal value is 6–12 mmHg. The values vary with the respiratory cycle and are read at the end of expiration. In spontaneously ventilating patients, this will be the highest reading and in mechanically ventilated patients, it will be the lowest. The PAOP is found at an insertion length of around 45 cm.

ECG

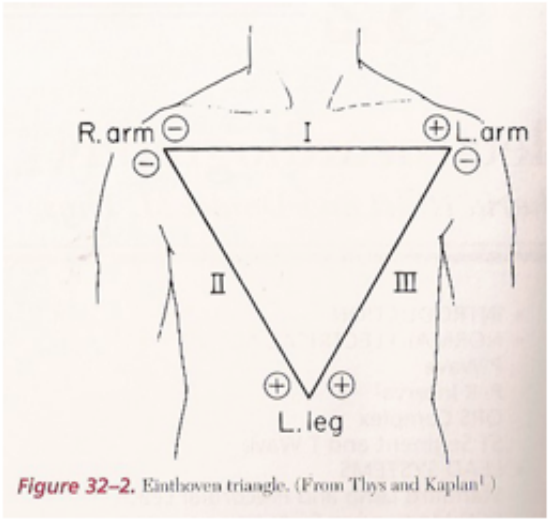
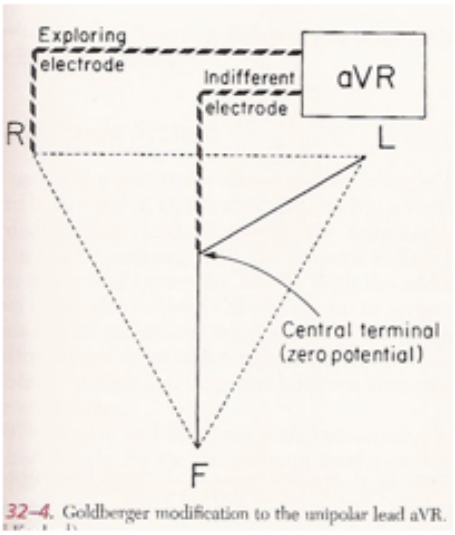
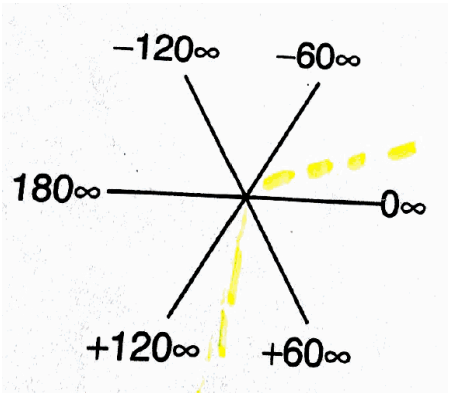
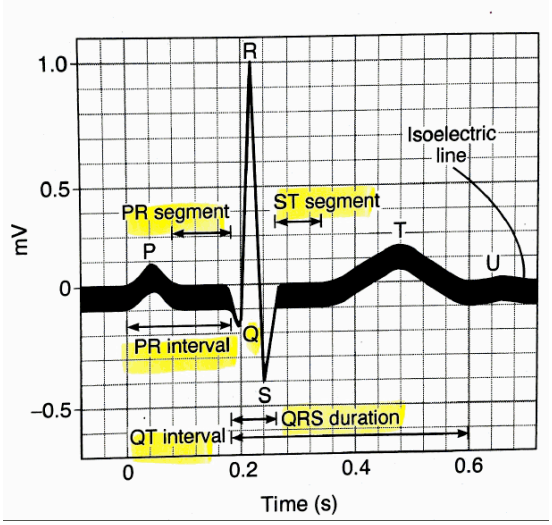


Figure 32–2. Einthoven triangle. (From Thys and Kaplan[1])



32–4. Goldberger modification to the unipolar lead aVR.

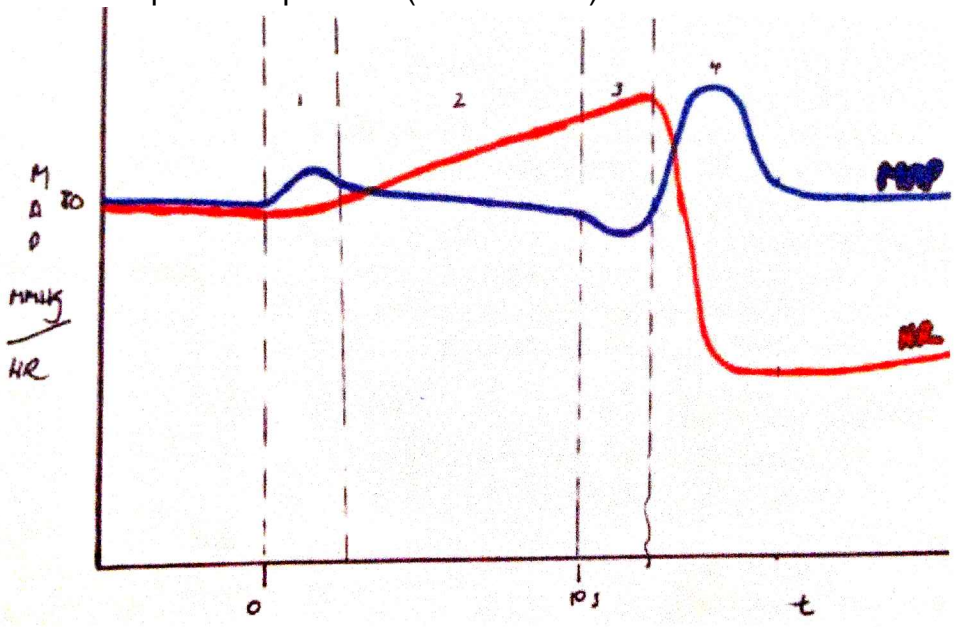




Norm axis = -30 ⟹ +110 deg

Valsalva

- max HR phase 2: phase 4 (>1.5 = norm)



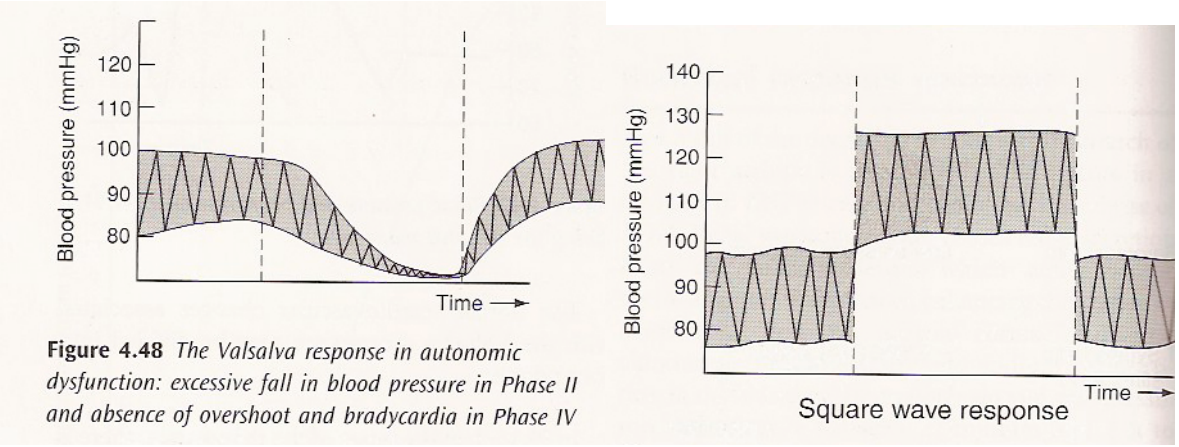
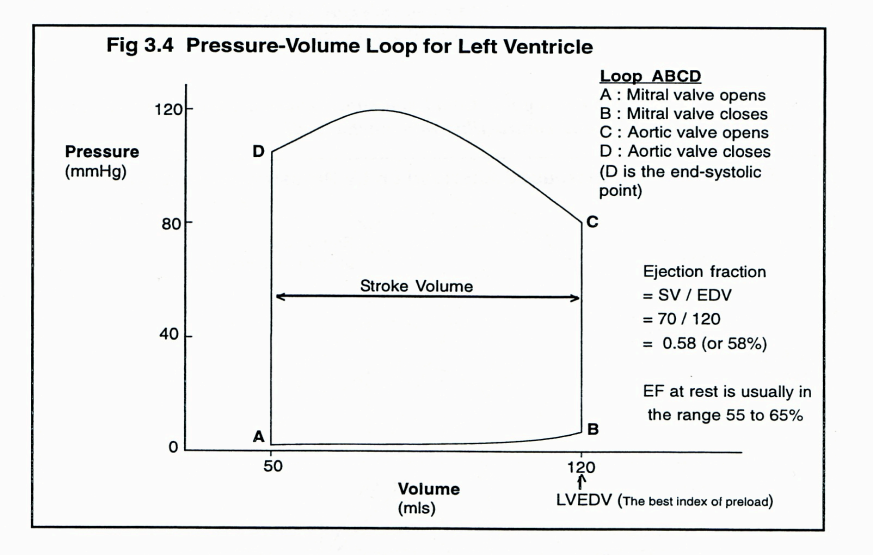


Figure 4.48 *The Valsalva response in autonomic dysfunction: excessive fall in blood pressure in Phase II and absence of overshoot and bradycardia in Phase IV*

Pathological patterns

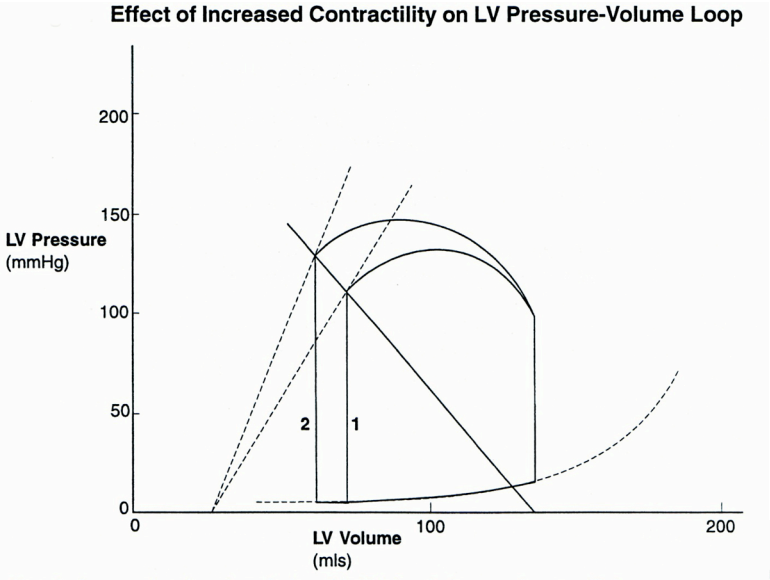
- **Square Wave Response**
  - see in heart failure
  - chars:
    - elevated bp throughout phase 2
    - no reactive ↑bp in phase 3
    - HR remains constant
  - Caused by ↑ed pulmon blood volume acts as reservoir that maintains LV filling during phase 2
- ß block response:
  - smaller phase 4 bp overshoot
  - due to ↓HR at start of phase 4
- α block response:
  - ↓bp phase 2
  - ↑overshoot phase 4 - due to ↑ed HR start of phase 4

LV P-V Loops



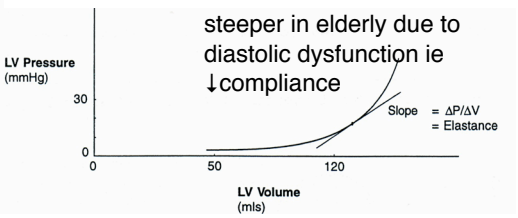
- All the information obtained from Vent P-V loop (favourite exam topic):
  - EF
  - LVEDV – Note: this is number on x axis – NOT point B
  - Indices for afterload = Ea line
  - Indices for ventricular compliance (EDVP Line)
  - Contractility = Ees line
  - Stroke work (PxV = Joules) = area within loop
  - B-A = diastolic filling
  - C-B=isolvolumetric contraction
  - D-C = volume ejected
  - D-A= isovolumetric relaxation

Effect of ↑ed Contractility

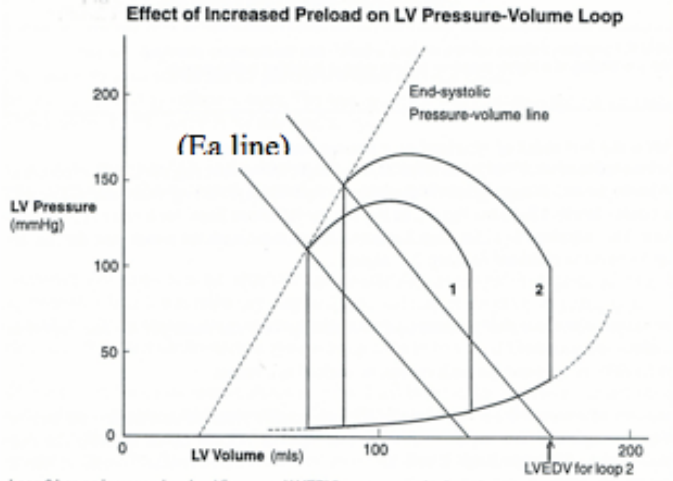


Note the increased stroke volume for loop 2 (which has the increased contractility).

- The increased slope of the end-systolic pressure-volume line is an index of the increased contractility.
- The end-systolic points of both loops lie on the same 'afterload line' so there afterload is the same for the 2 loops.
- The LVEDV is the same for the 2 loops so the pre-load is the same.



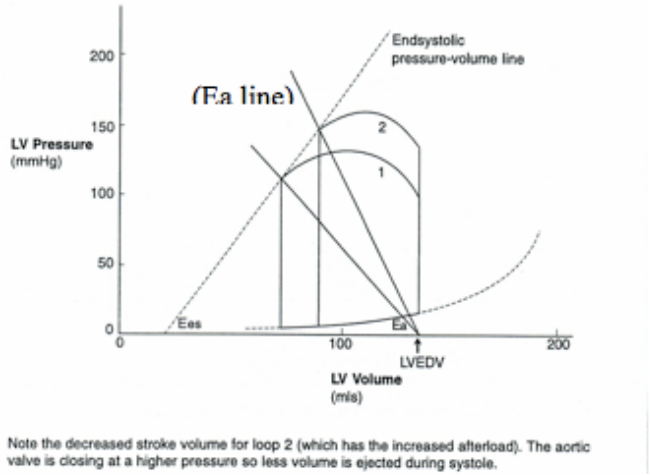
Effect of ↑ed Preload



Loop 2 has an increased preload (increased LVEDV) as compared to loop 1
Note: Loop 2 has a larger stroke volume than loop 1.

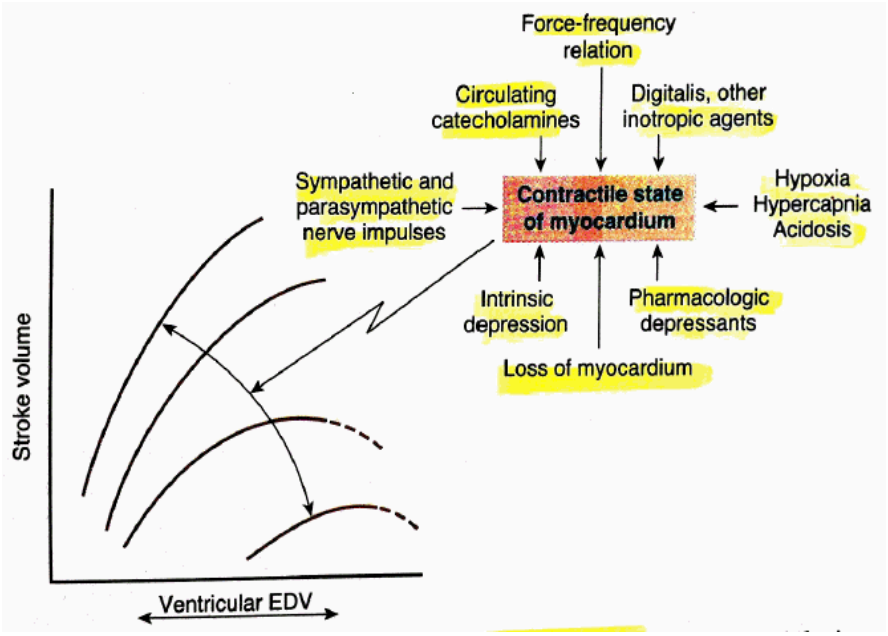
The afterload & contractility have remained constant. The afterload lines for the 2 loops are parallel so they have the same afterload . Both end-systolic points are on the same contractility line so the 2 loops have the same contractility.

Effect of Increased Afterload:



Note the decreased stroke volume for loop 2 (which has the increased afterload). The aortic valve is closing at a higher pressure so less volume is ejected during systole.

Starling Curve



Coronary Blood Flow

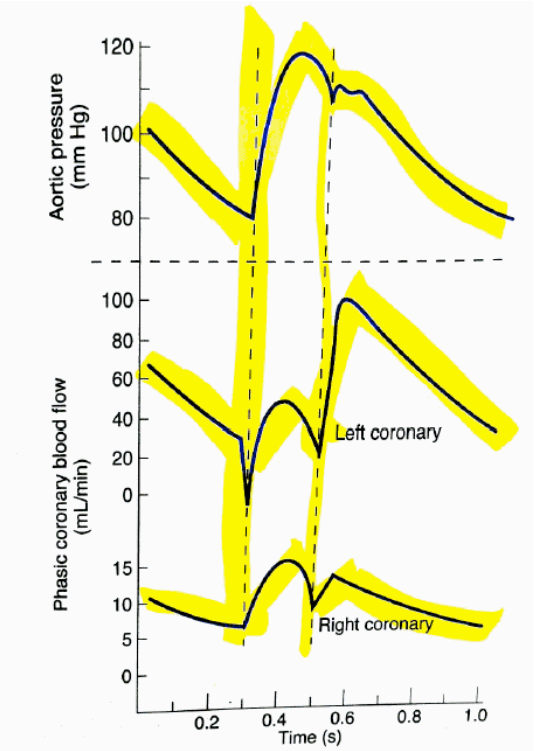
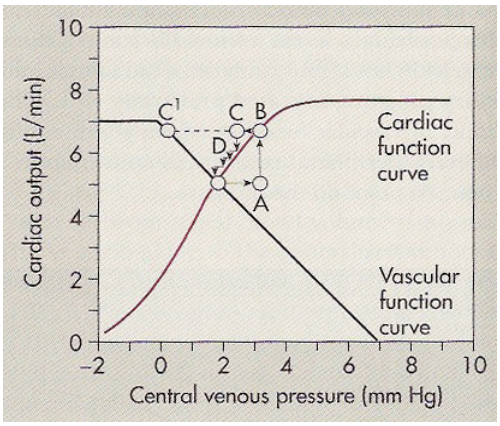


FIGURE 34–13 Blood flow in the left and right coronary arteries during various phases of the cardiac cycle. *Systole occurs* between the two vertical dashed lines. (Reproduced with permission from Berne RM, Levy MN: *Physiology,* 2nd ed. Mosby, 1988.)

By Adam Hollingworth

Vascular Function Curves

normal:



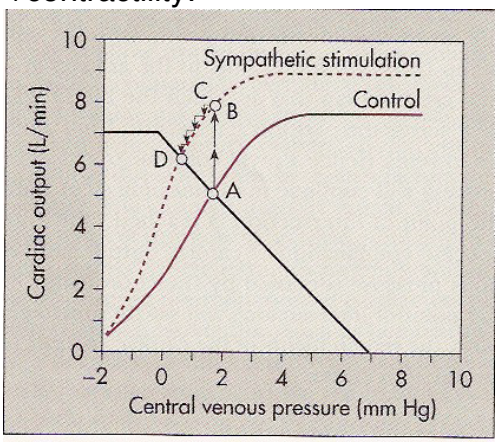
Venous return

Venous return will depend on pressure relations:

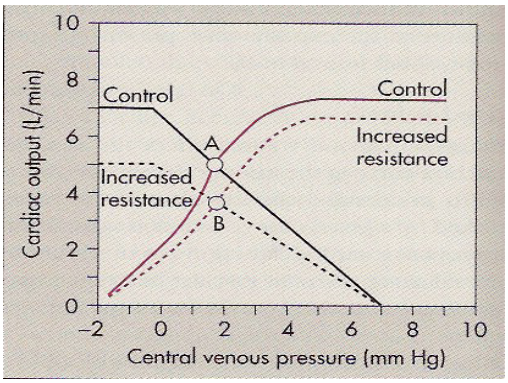
$$VR = \frac{(MSFP - RAP)}{R_{ven}} \times 80$$

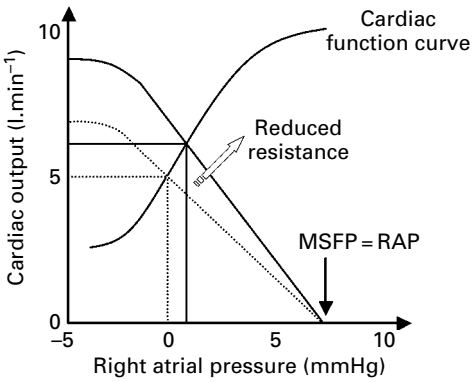
where VR is venous return, MSFP is mean systemic filling pressure, RAP is right atrial pressure and R_{ven} is venous resistance.

↑contractility:

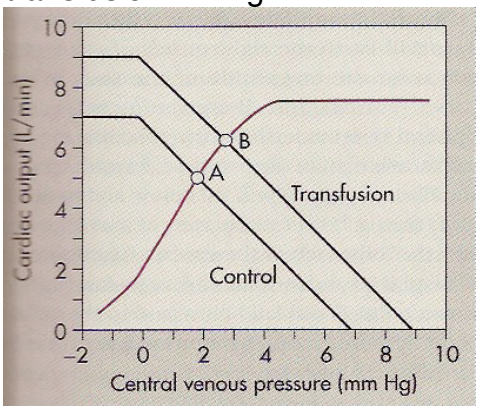


↑afterload:

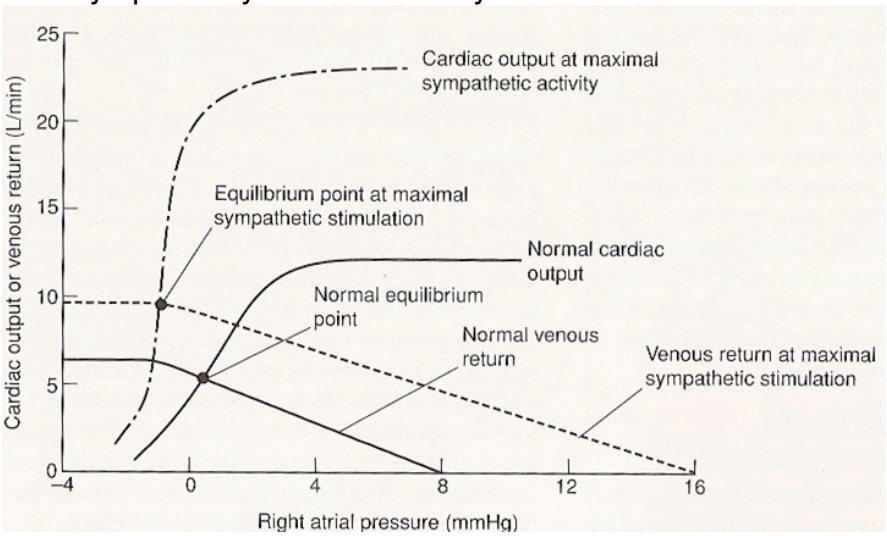




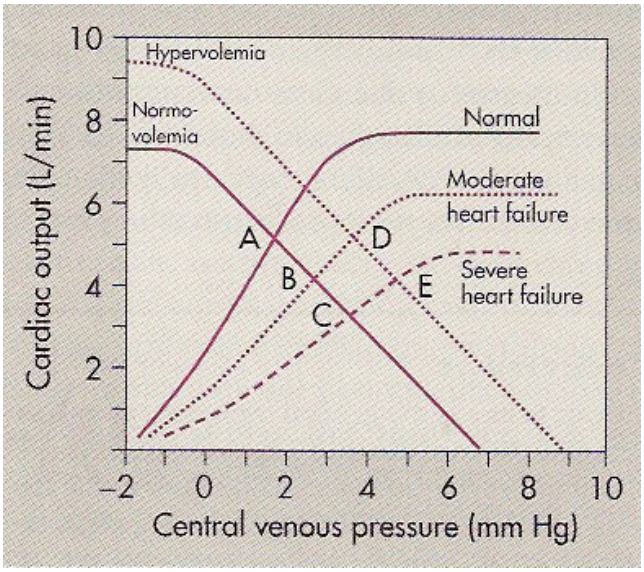
transfusion/↑filling:



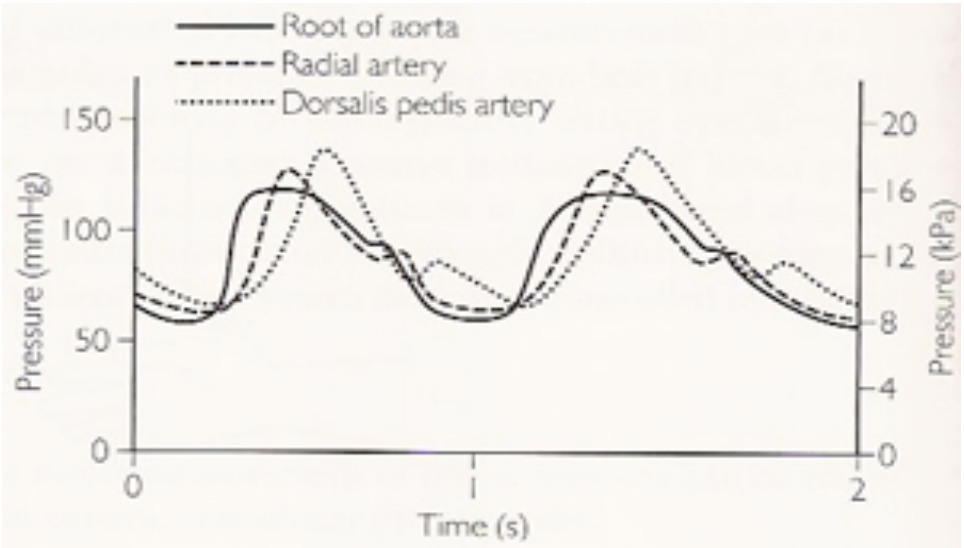
Max symp activity: ie ↑contractility & venoconstriction ⟹ ↑VR



heart failure:



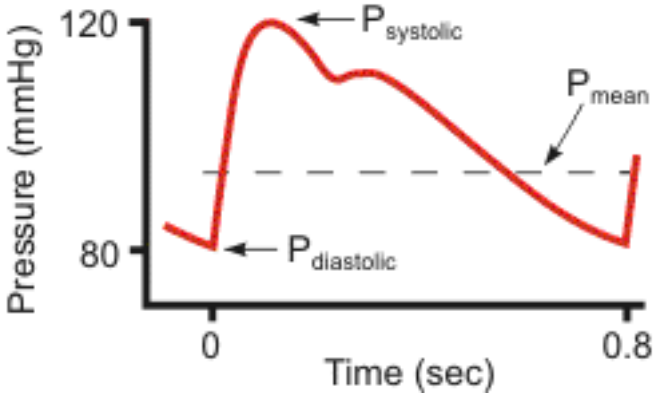
Aortic & Radial Artery Pressure Traces



- Comparing radial vs aortic curve:
  - Delayed:
    - due to time taken to travel down the arterial tree.
      - Faster if low compliance, eg elderly, atherosclerotic disease
  - Distorted shape: due to
    - reflection
    - resonance
    - damping
    - different conduction speeds of the different pressure components
      ↳ high pressure components travel faster.
  - Taller: due to lower compliance, ⇒ resulting in higher systolic P
  - Narrower at its peak: due to higher velocity of the higher pressure peak.
  - Diastolic hump instead of an incisura:
    - loss of incisura due to damping of high pressure components
    - Resonance and reflection in the arterial tree causes the diastolic hump
  - slight drop in MAP - radial MAP 5% lower than aoritc
  - diastolic pressure tends to ↓ towards periphery
  - ↑pulse pressure towards periphery - radial pulse pressure 40% higher than aorta

- In elderly radial trace will look less different to aortic: = due to lower vascular compliance which causes the pressure wave to travel faster and be less distorted.
- Changes to **Aortic** contour with ageing:
  - slower upstroke (decreased contractility)
  - Higher peak due to lower aortic compliance

A Line Trace

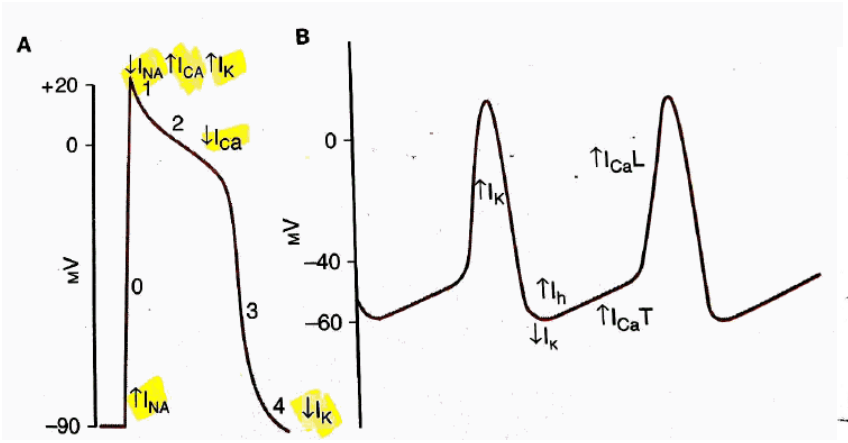


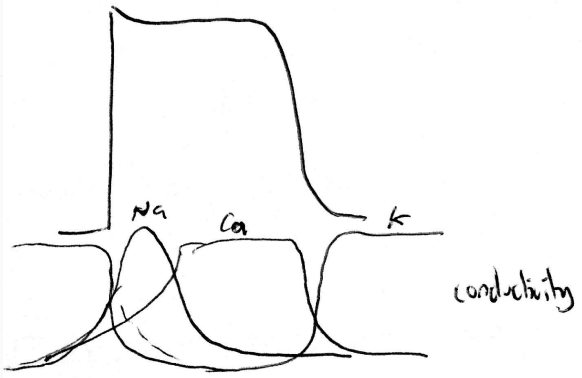
- myocardial contractility = The slope of the upstroke (dp/dt) ie steep upstroke = strong LV
- Stroke volume:
  - by measuring the area from start of upstroke up to incisura
  - (if multiply SV with HR, an estimate of CO can be derived)
- SVR = The slope of downstroke
  - steeper the slope= the faster the arterial run-off (ie low SVR)
  - Position of incisura/dicrotic notch (diastolic hump in peripheral artery) on the down slope:
    - Sitting high up = high SVR vs
    - sitting low down = low SVR
- haemodynamic significance of arrhythmias - bp & pulse contour following abnormal beats indicate degree of impairment of cardiac pumping
- index of myocardial demand (tension time index, TTI) = Area under systolic part
- index of O2 supply to heart (diastolic P time index, DPTI) = Area under diastolic part

- ∴ Endocardial viability ratio (EVR) = DPTI / TTI
- high ratio = ↑ed O2 supply to heart

- Vascular volume status (preload):
  - In ventilated pts see "arterial swing" (change in systolic peaks):
    - during single cycle of +ve pressure vent ⟹
      - inspiration: 1st +/- 2nd beat see ↑ SV **then** following beats see ↓SV
        ↳ due to superadded ↑ITP
      - expiration: ↑ing SV due to ↓ITP allowing ↑preload
    - during spont vent: see complete opposite
  - **delta down** = ↓SV in inspiration during +ve pressure vent
    - rate of decline during inspiration can be calculated by software averaging.
    - = a good indicator of LV preload: better than PCWP
  - delta up = ↑SV in expiration during +ve pressure vent
    - gives an indication of afterload
      ↳ although less accurate than what delta down is for preload
- Pressure:
  - Systolic,
  - diastolic,
  - MAP - calculated by
    - integrating pressure signal over pulse duration.
    - MAP = integral divided by time
- High peak (high systolic) may be due to low arterial compliance.
- Rate, rhythm

Cardiac AP





- Phases:
  - 0 = rapid depolarisation towards threshold
    - Na influx via fast voltage gated Na channel opening in response to AP
    - Overshoot seen briefly as Na channels self inactivating
  - 1 = rapid repolarisation –
    - Na channels close
    - Ca open – Ca start to flow in
    - K channels open – K flow out
  - 2 = plateau –
    - Ca influx in which maintains depolarisation (via L type channel)
    - Na channel closing continues which contines to repolarisation
  - 3 = repolarisation –

- rapid K channel
- slow K channel

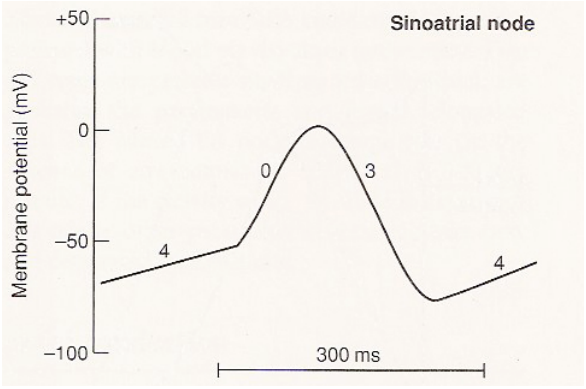
↳ both show K out

- Na & Ca channels return to baseline state
- Ion channels & electrogenic pumps return membrane to resting potential

○ 4 = return to resting membrane potential –

- K channels return to baseline state
- Na/K/ATPase electrogenic pump

Pacemaker Potential



- phases:
  - **prepotential** (4) ⇒ slow drive to threshold
    - fall in membrane K permeability
    - I_f = inward slow positive current displayed: (for "funny" current)
      - opening of transient Ca (T type) ⇒ Ca influx

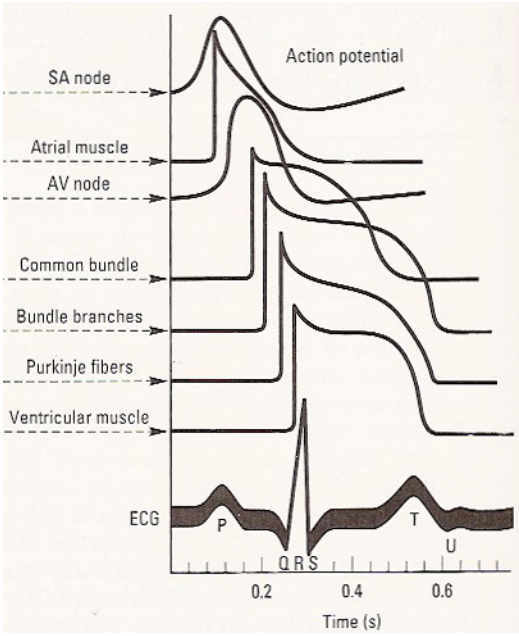
        ↳ not effecting by catecholamines

        ↳only found in cells which lack a T tubule system ie pacemaker cells & vasc smmoth mm (not ventricular myocardium)
      - ↑activity of electrogenic 3Na-2Ca exchange system

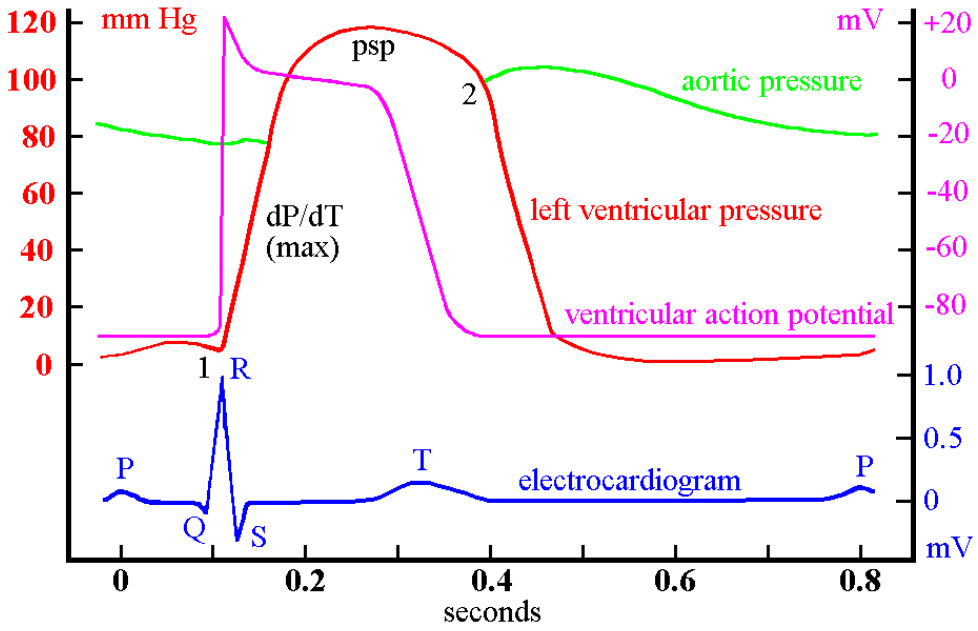
        ↳ driven by inward movement of Ca
  - **depolarisation** (0)– opening long lasting Ca channel ⇒ Ca influx
    - (L type) long lasting Ca channel
    - produce long lasting current relative to Na
    - the most predominant Ca type
    - start opening during initial upstroke
    - verapamil block them
    - catecholamines activate them
  - **repolarisatrion** (3) – K channel opening ⇒ K efflux
  - **hyperpolarisation** (4)– closing of K channel, opening of H channel

    ↳passes Na & K

ECG in Different Parts of Heart

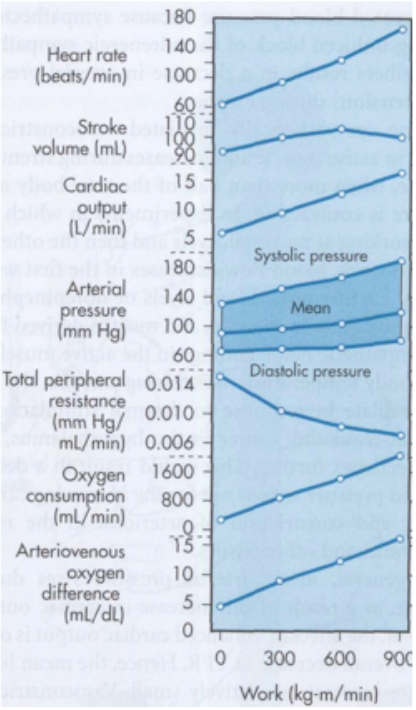


Physical Contraction vs ECG & Cardiac AP

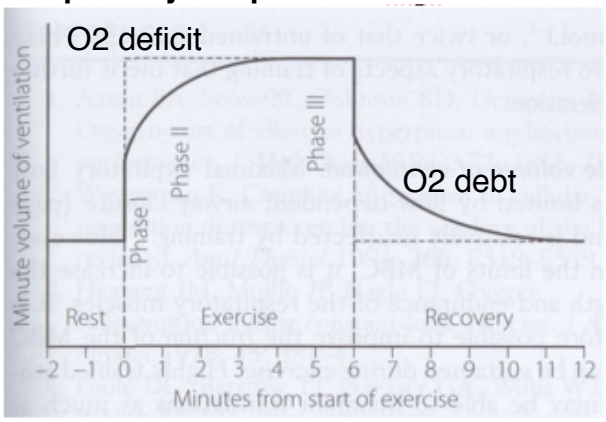


Exercise

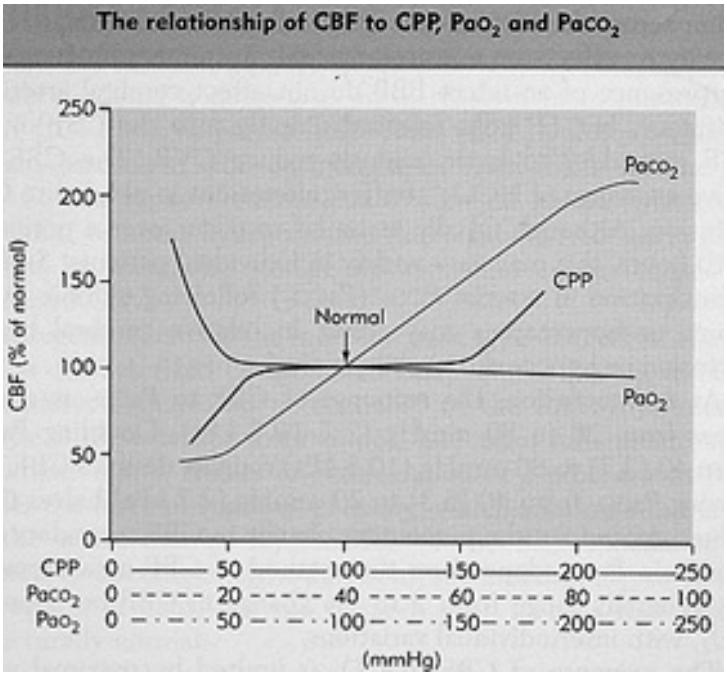
CVS Response



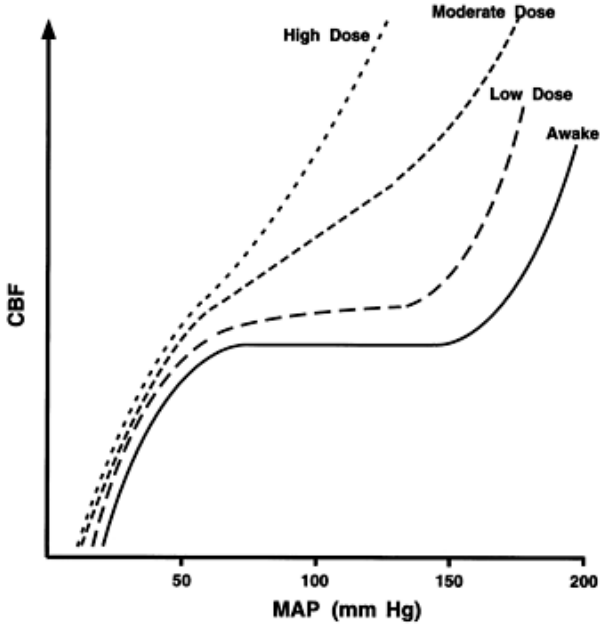
Respiratory Response



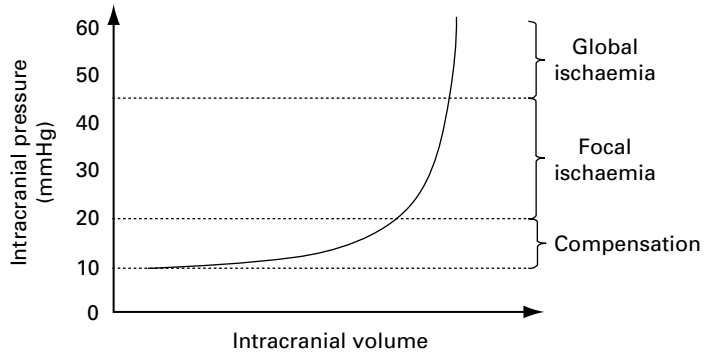
Neurophysiology
CBF, PO2, PCO2



Changes with Anaesthesia

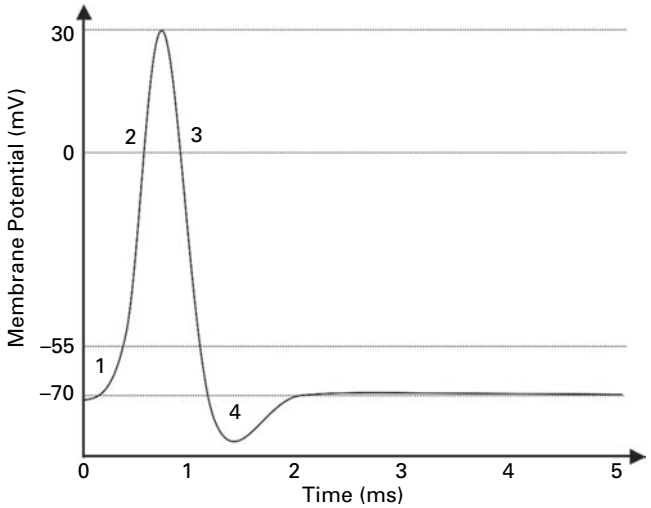


Intracranial Elastance Curve



Draw and label the axes as shown. Note that the *x* axis is usually drawn without any numerical markers. Normal intracranial volume is assumed to be at the left side of the curve and should be in keeping with an ICP of 5–10 mmHg. Draw a curve similar in shape to a positive tear-away exponential. Demonstrate on your curve that compensation for a rise in the volume of one intracranial component maintains the ICP < 20 mmHg. However, when these limited compensatory mechanisms are exhausted, ICP rises rapidly, causing focal ischaemia (ICP 20–45 mmHg) followed by global ischaemia (ICP > 45 mmHg).

Nerve Action Potential



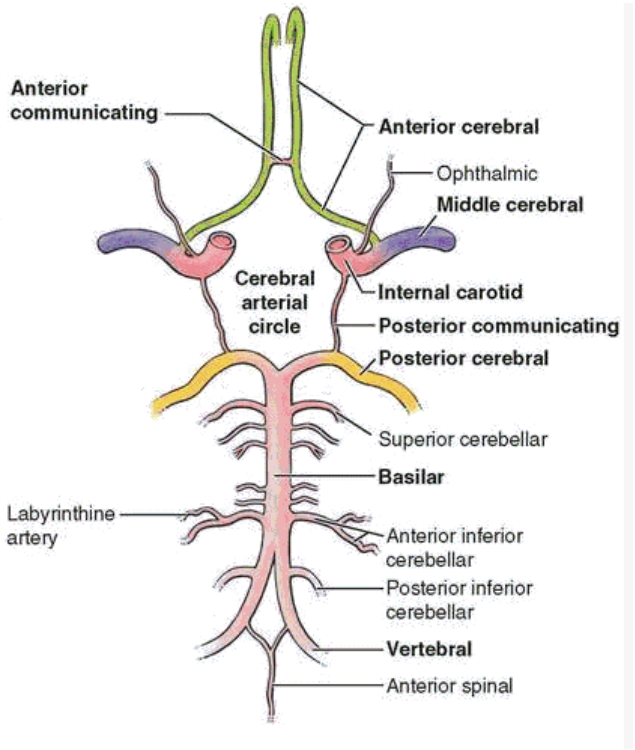
Draw and label the axes as shown.

Phase 1 The curve should cross the *y* axis at approximately -70 mV and should be shown to rapidly rise towards the threshold potential of -55 mV.

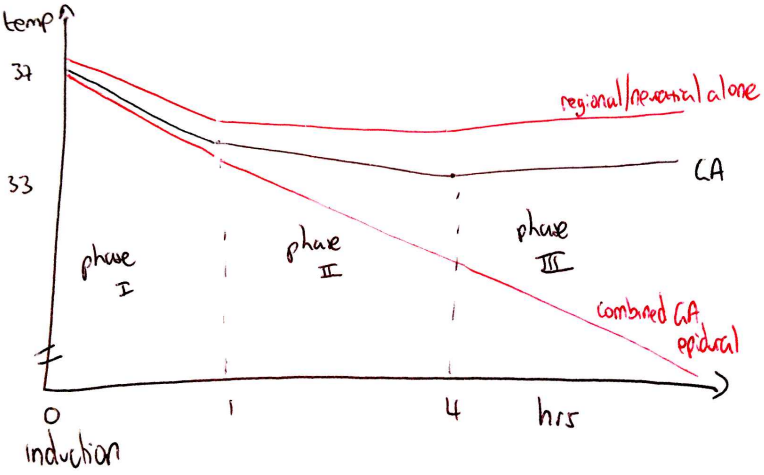
Phase 2 This portion of the curve demonstrates the rapid rise in membrane potential to a peak of $+30$ mV as voltage-gated Na^+ channels allow rapid Na^+ entry into the cell.

Phase 3 This phase shows rapid repolarization as Na^+ channels close and K^+ channels open, allowing K^+ efflux. The slope of the downward curve is almost as steep as that seen in phase 2.

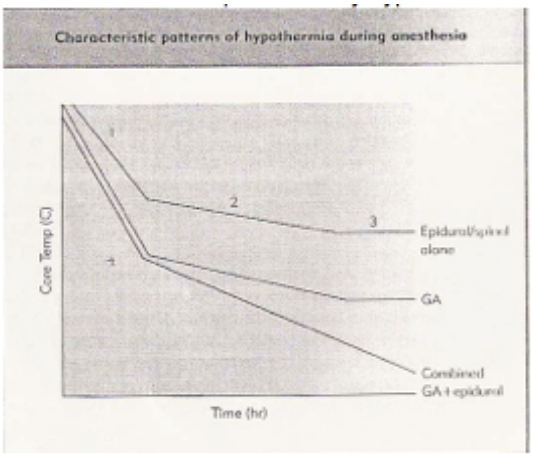
Phase 4 Show that the membrane potential 'overshoots' in a process known as hyperpolarization as the Na^+/K^+ pump lags behind in restoring the normal ion balance.



Thermoregulation in Surgery

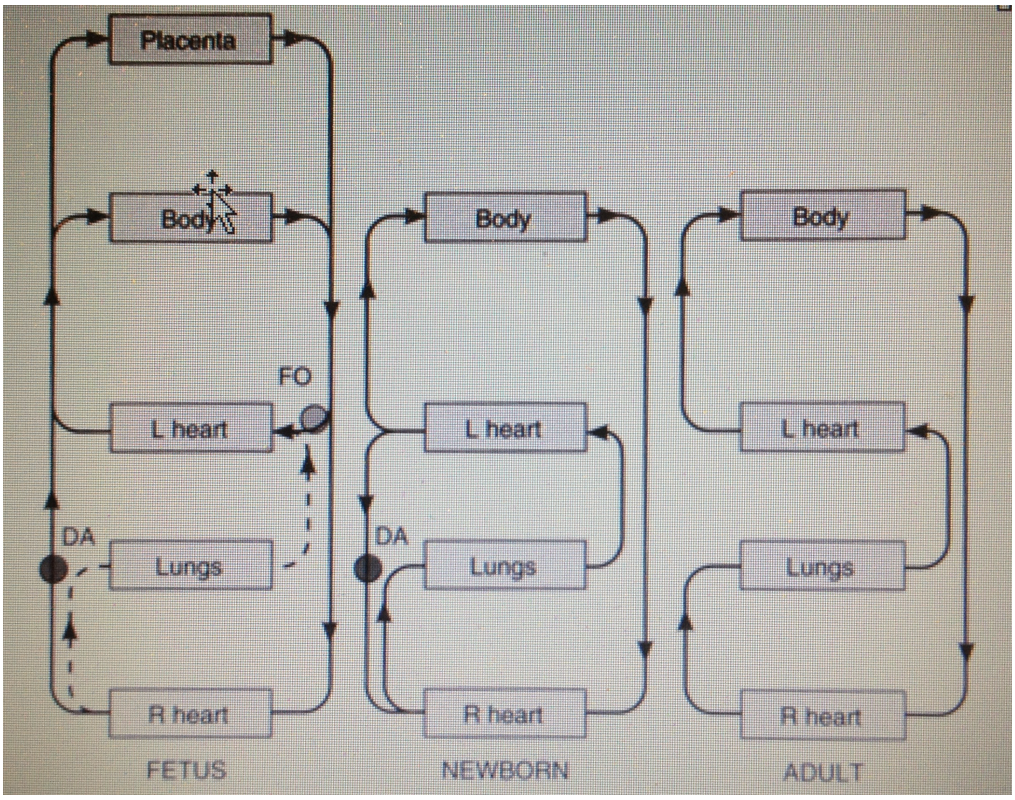


- Phase 1 = vasoD (lose 1-1.5C over 1hr
- Phase 2 = Ongoing heat loss>production (lose 1C over 1-4hrs
- Phase 3 = VasoC as reached threshold response



Foetal Physiology

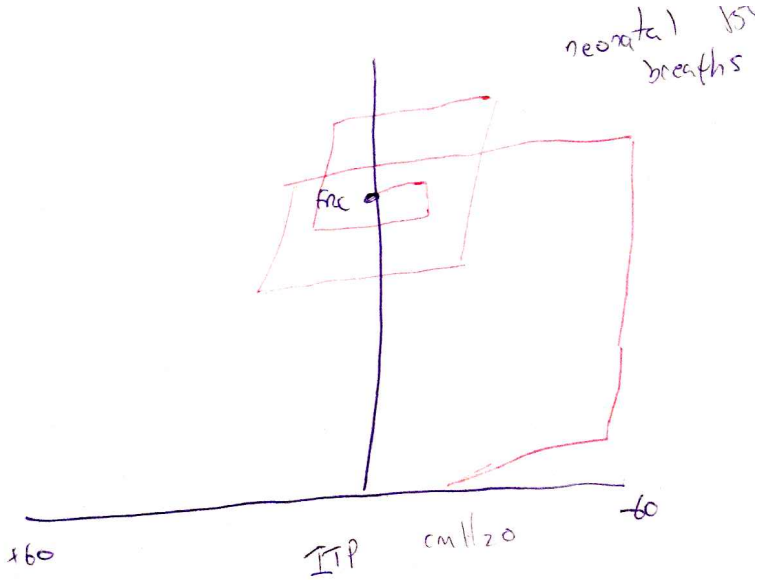
Foetal Circulation



Foetal Circulation Sats

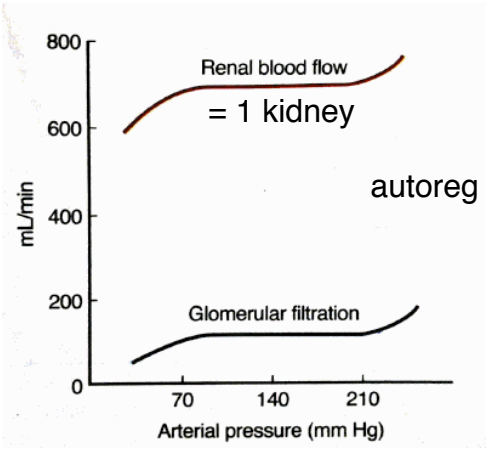
DV = 80%
IVC = 67%
systemic = 67%
SVC = 32%
RV = 50%

Neonatal 1st Breaths



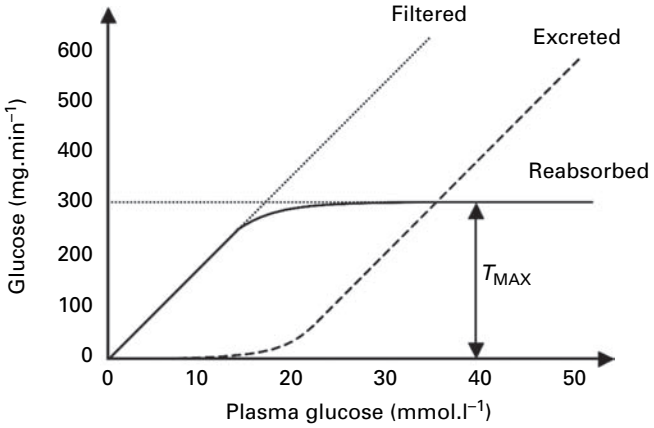
Renal

Renal Blood Flow Autoregulation



autoreg 75 - 175mmHg

Glucose Handling



Filtered After drawing and labelling the axes, draw a line passing through origin, rising at an angle of approximately 45°. This demonstrates that the amount of glucose filtered by the kidney is directly proportional to the plasma glucose concentration.

Reabsorbed This line also passes through the origin. It matches the 'filtered' line until 11 mmol.l^{-1} and then starts to flatten out as it approaches maximal tubular reabsorption (T_{MAX}). Demonstrate that this value is 300 mg.min^{-1} on the y axis.

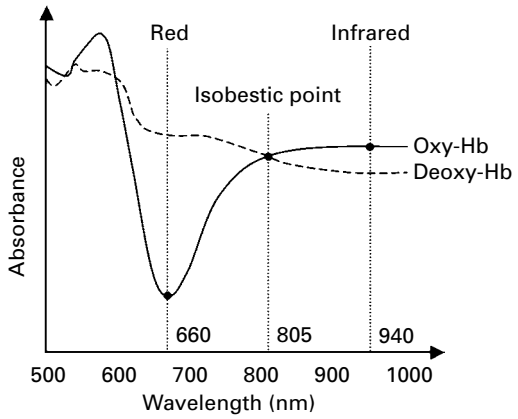
Excreted Glucose can only appear in the urine when the two lines drawn so far begin to separate so that less is reabsorbed than is filtered. This happens at 11 mmol.l^{-1} plasma glucose concentration. The line then rises parallel to the 'filtered' line as plasma glucose continues to rise.

Measurement

Saturations

Haemoglobin absorption spectra

R = 660 / 940

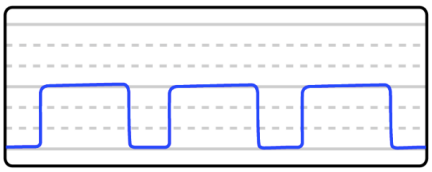


Phases of Capnograph

- notes:
  - early expiration - trace remains at baseline - as no CO2 in resp deadspace
  - rapid upstroke: = transition from dead space gas to alveolar gas
  - plateau - ongoing expiration
  - downstroke = inspiration: start of inspiration of O2. represents washing out of CO2 from sample chamber
  - trough = ongoing inspiration
  - x axis defines length of phases:
  - I:E ratio usually 1:2

Sample Waveforms

normal:

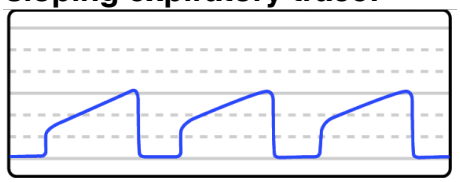


straight line:

- causes:
  - equipment failure - should have checked preop!

- complete obstruction of lungs - severe bronchospasm
- complete obstruction of airway eg tracheal tube obstruction
- complete obstruction of sample tubing
- resp arrest
- cardiac arrest - no CO_2 being delivered to lungs
- oesophageal intubation - although often initially see some $ETCO_2$

sloping expiratory trace:



- causes:
  - partial obstruction of lungs eg brochospasm, COPD
  - partial obstruction of airway eg tracheal tube secretions, kinking

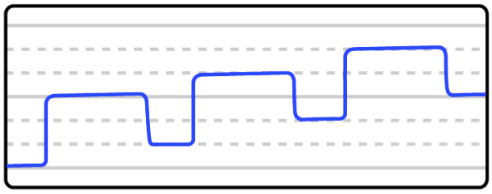
high exp tracing:

- causes:
  - inadequate ventilation - lung has to 'pack' more CO_2 into each breath
  - ↑ed CO_2 production:
    - MH

low exp trace:

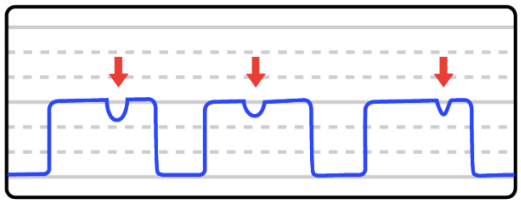
- causes:
  - hyperventilation

re-breathing:



- causes:
  - failing CO_2 scrubbing

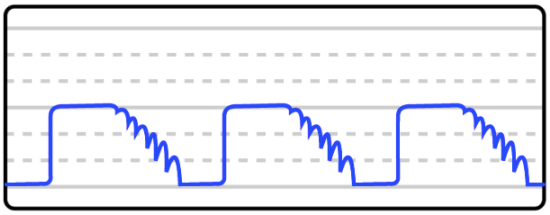
relaxant notches:



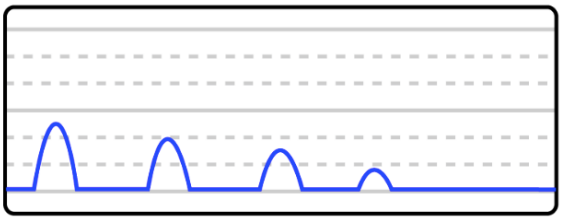
- aka curare cleft
- causes:
  - mm relaxants wearing off ⟹ diaphragm spont active during expiration

- surgeons pushing on diaphragm/chest wall

cardiac notches:

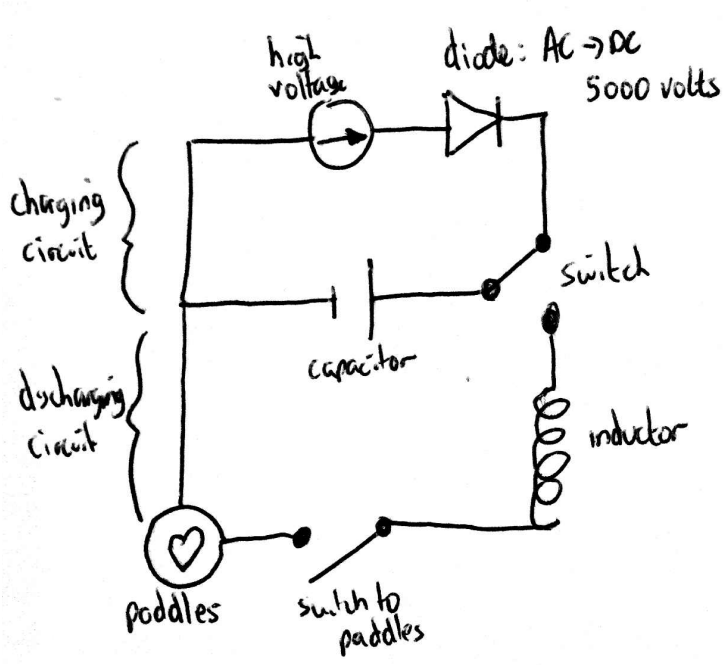


oesophageal intubation:



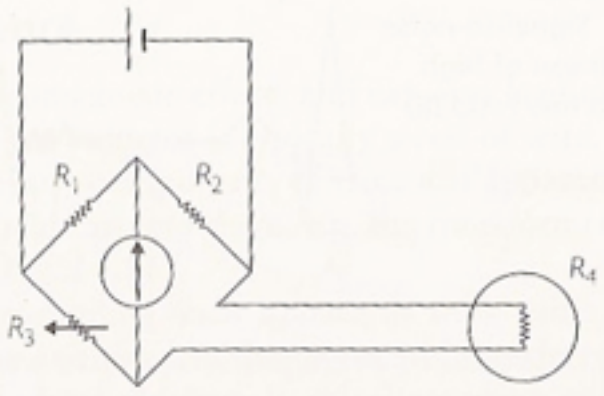
• dont be fooled by initial CO2!!

Defibrillator



Wheatstone Bridge

Figure 14.14 Wheatstone bridge circuit; R_4 is a strain gauge transducer or resistance thermometer and R_3 is a variable resistance which is adjusted until there is a null deflection on the galvanometer



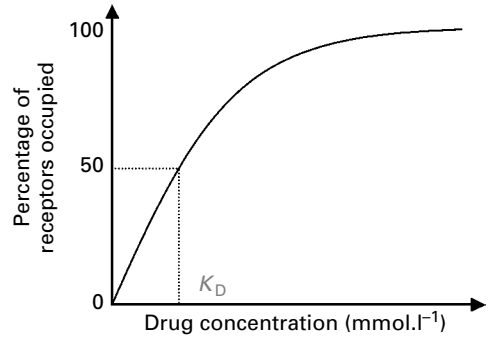
Pharmacology

Affinity

Affinity

A measure of how avidly a drug binds to a receptor.

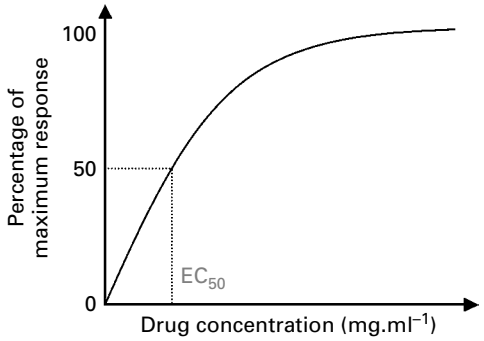
In the laboratory, affinity can be measured as the concentration of a drug that occupies 50% of the available receptors, as suggested by the definition of K_D.



The curve should be drawn as a rectangular hyperbola passing through the origin. K_D is shown and in this situation is a marker of affinity (see text). In practice, drug potency is of more interest, which encompasses both affinity and intrinsic activity. To compare potencies of drugs, the EC_{50} and ED_{50} values (see below) are used.

Dose-Response

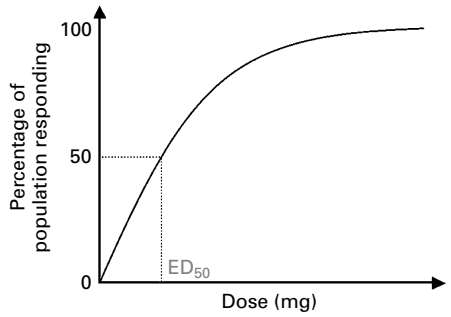
Dose–response curves



The curve is identical to the first but the axes are labelled differently with percentage of maximum response on the *y* axis. This graph will have been produced from a functional assay in the laboratory on a single subject and is concerned with drug potency. Demonstrate that the EC_{50} is as shown.

Quantal Dose Response

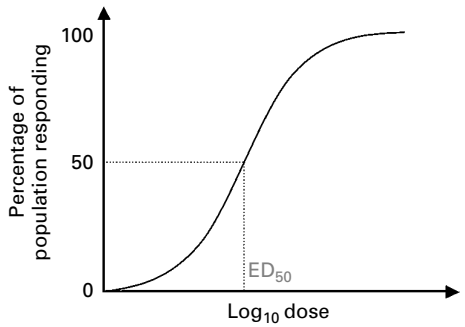
Quantal dose–response curves



The curve is again identical in shape but this time a population has been studied and the frequency of response recorded at various drug doses. It is, therefore, known as a quantal dose–response curve. The marker of potency is now the ED_{50} and the *y* axis should be correctly labelled as shown. This is the 'typical' dose–response curve that is tested in the examination.

Log Dose Response

Log dose–response curve

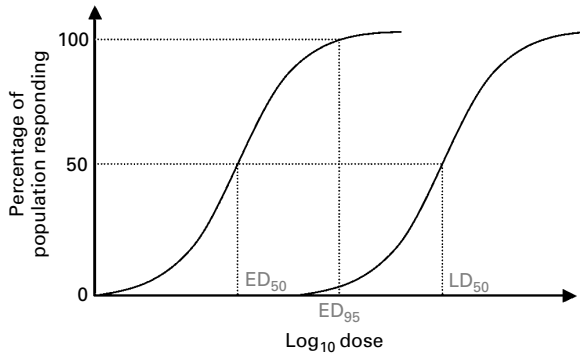


The curve is sigmoid as the *x* axis is now logarithmic. Ensure the middle third of the curve is linear and demonstrate the ED_{50} as shown. Make this your reference curve for a full agonist and use it to compare with other drugs as described below.

Therapeutic index

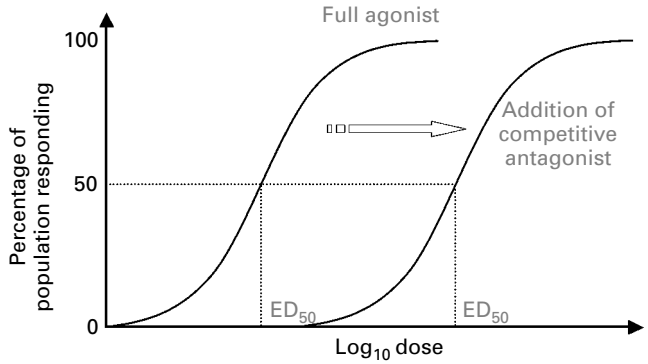
The therapeutic index of a drug reflects the balance between its useful effects and its toxic effects. It is often defined as

LD_{50}/ED_{50}

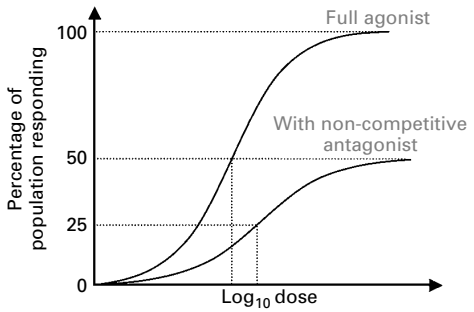


Both curves are sigmoid as before, The curve on the left represents a normal dosing regimen aiming to achieve the desired effect. Label the ED_{50} on it as before. The curve to the right represents a higher dosing regimen at which fatalities begin to occur in the test population. The LD_{50} should be at its midpoint. The ED_{95} is also marked on this graph; this is the point at which 95% of the population will have shown the desired response to dosing. However, note that by this stage some fatalities have already started to occur and the curves overlap. You can draw the curves more widely separated if you wish to avoid this but it is useful to demonstrate that a dose that is safe for one individual in a population may cause serious side effects to another.

Reversible Competitive Antagonist



Non Competitive Antagonist



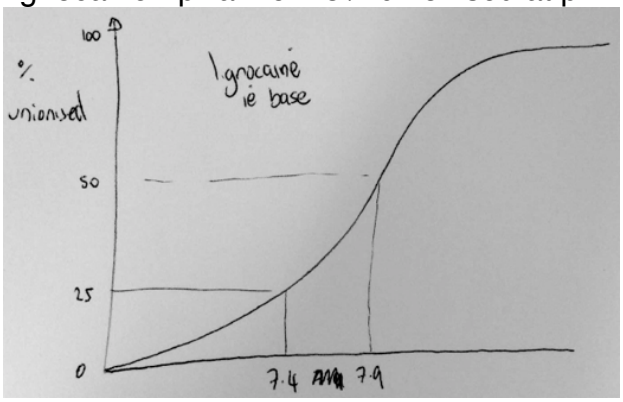
Because a non-competitive antagonist alters the shape of the receptor, the agonist cannot bind at all. The usual sigmoid curve is displaced down and to the right in a similar manner to the graph of agonist versus partial agonist drawn above. Increasing the dose of agonist does not improve response as receptor sites are no longer available for binding.

pKa

Unionised up Y axis, pH along bottom

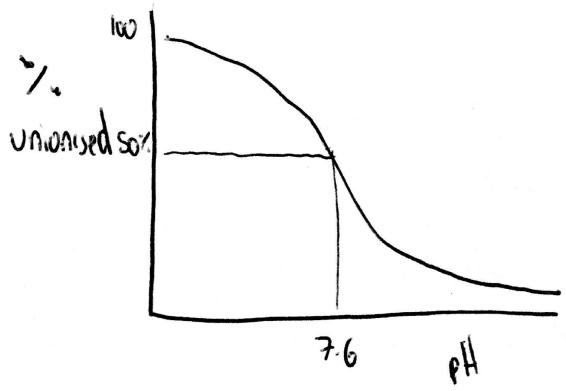
Basic Drug

fentanyl - pKa 8.4; 10% unionised at pH 7.4
alfentanil - pKa 6.5: 90% unionised at pH 7.4
lignocaine - pKa 7.9: 25% unionised at pH 7.4



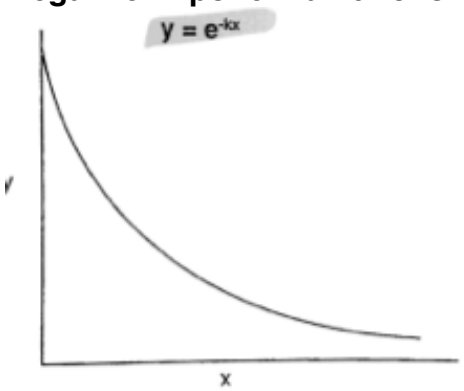
Acid Drug

STP - pKa 7.6: 60% unionised at pH 7.4

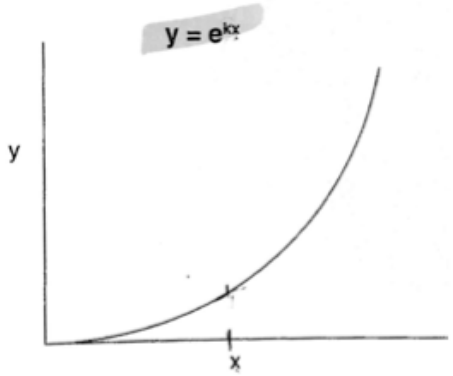


Exponential Functions

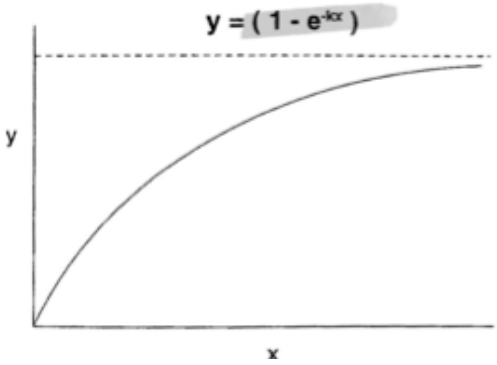
Negative Exponential function / Washout Curve



Positive Exponential Function / Runaway Curve

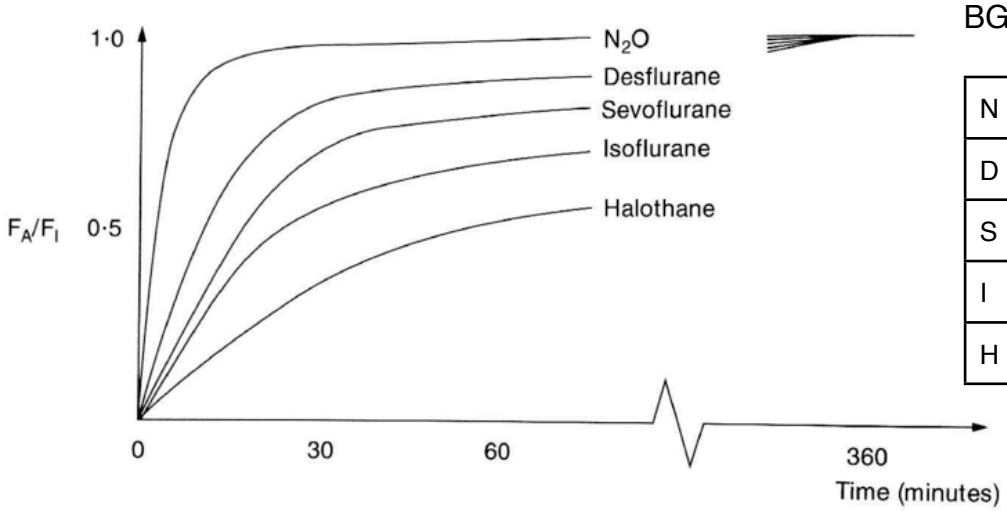


Build up Exponential function / Wash in curve



Wash in Curve Volatiles

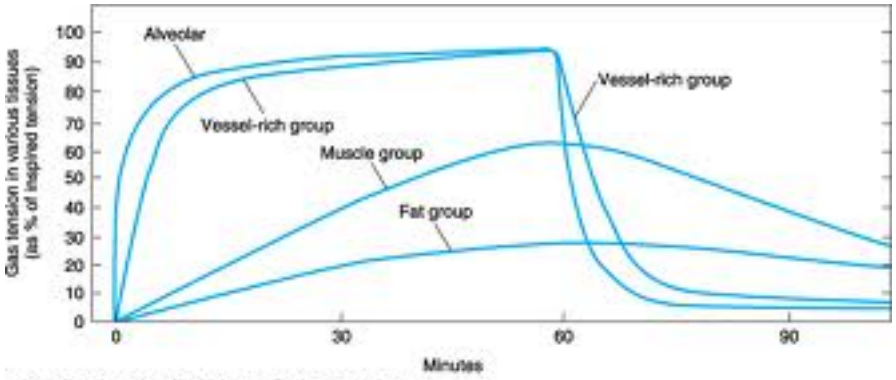
<FRC>< vessel rich >< mm >< fat >< bone >



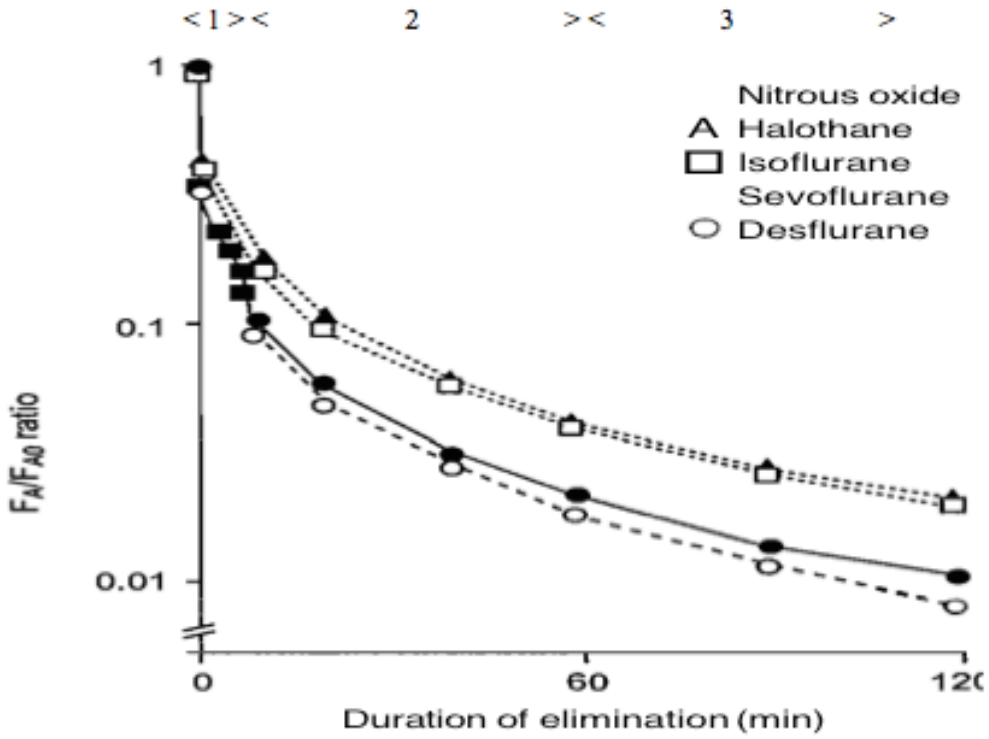
BG Ratios:

N	0.47
D	0.42
S	0.58
I	1.4
H	2.4

Figure 8.7. Different agents approach a F_A/F_I ratio of 1 at different rates. Agents with a low blood:gas partition coefficient reach equilibrium more rapidly. (F_A/F_I represents the ratio of alveolar concentration to inspired concentration.)



Wash Out Curves

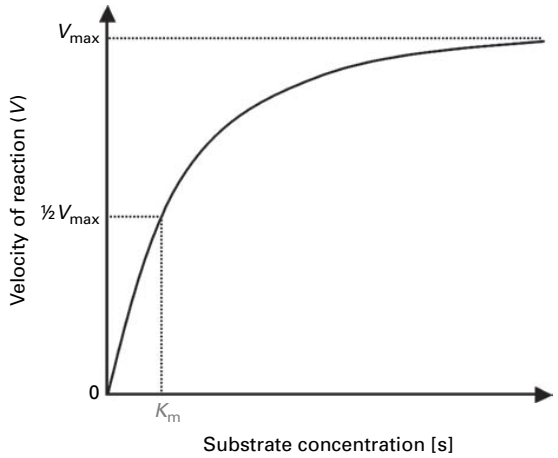


- 1 =
  - circuit
  - FRC
  - V1
- 2 =
  - V2
  - V3
- 3 =
  - elimination phase

Fig. 5. Elimination of sevoflurane and other inhalational thetics over 120 minutes. F_A/F_{A0} is the ratio of end-tidal tration **(F_A)** to the F_A immediately before the begir elimination (F_{A0}) [from Yasuda et al.,[55] with permission

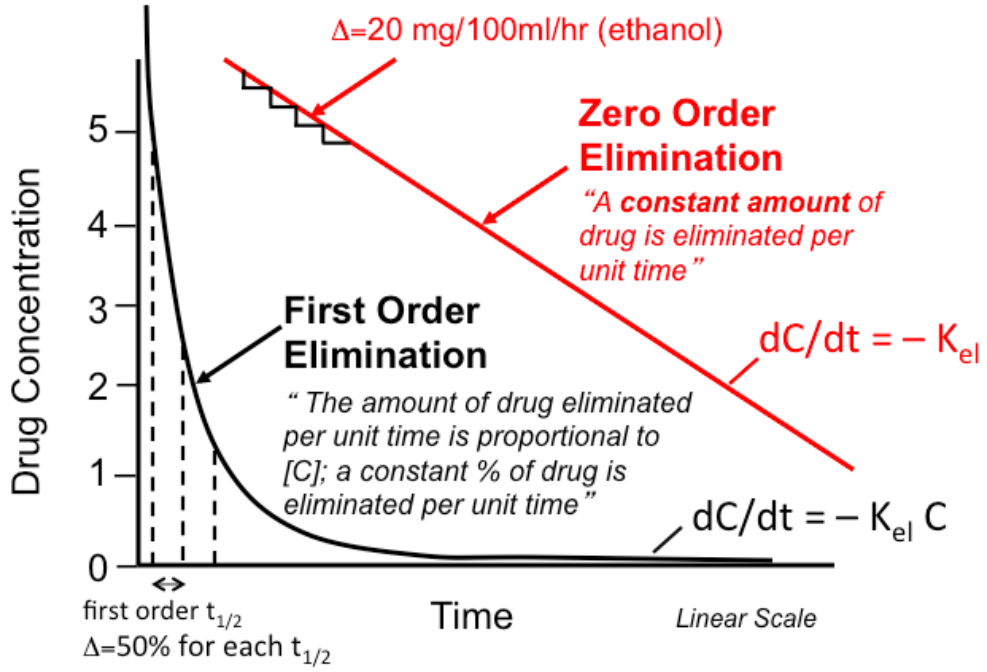
1st & Zero Order Kinetics

Michaelis–Menten graph



The shape of the curve is an inverted rectangular hyperbola approaching V_{max}. Ensure you mark K_m on the curve at the correct point. The portion of the curve below K_m on the x axis is where the reaction follows first-order kinetics, as shown by a fairly linear rise in the curve with increasing [S]. The portion of the curve to the far right is where the reaction will follow zero-order kinetics, as shown by the almost horizontal gradient. The portion in between these two extremes demonstrates a mixture of properties.

First order Kinetics After Bolus Dose



Plasma vs effect site Concentration

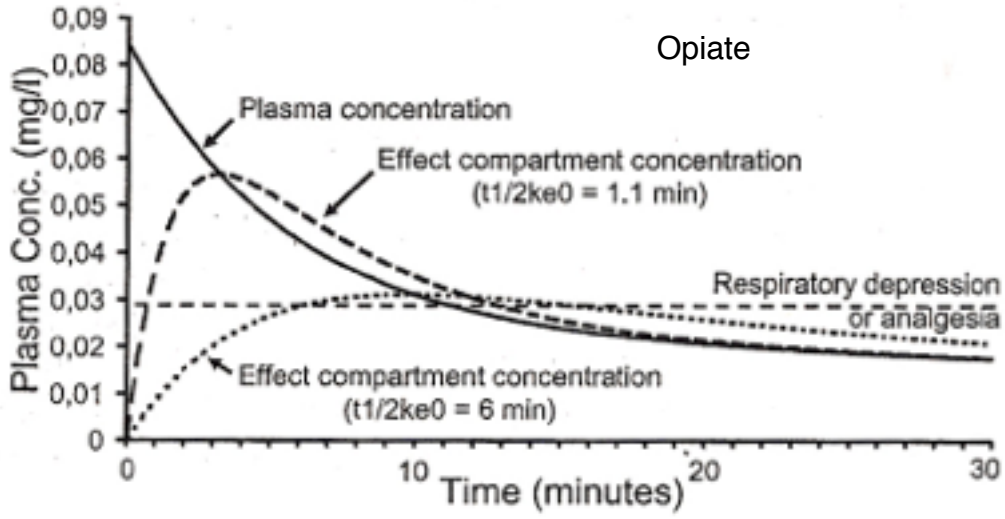
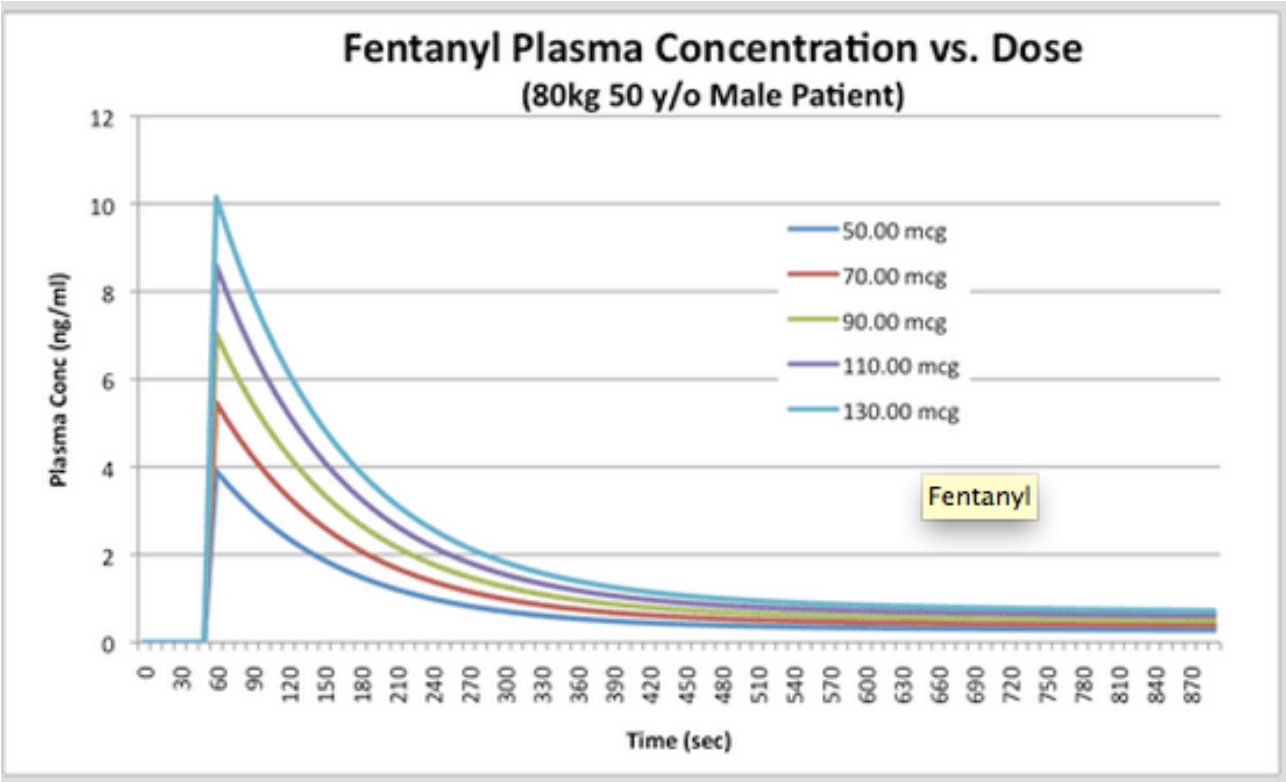


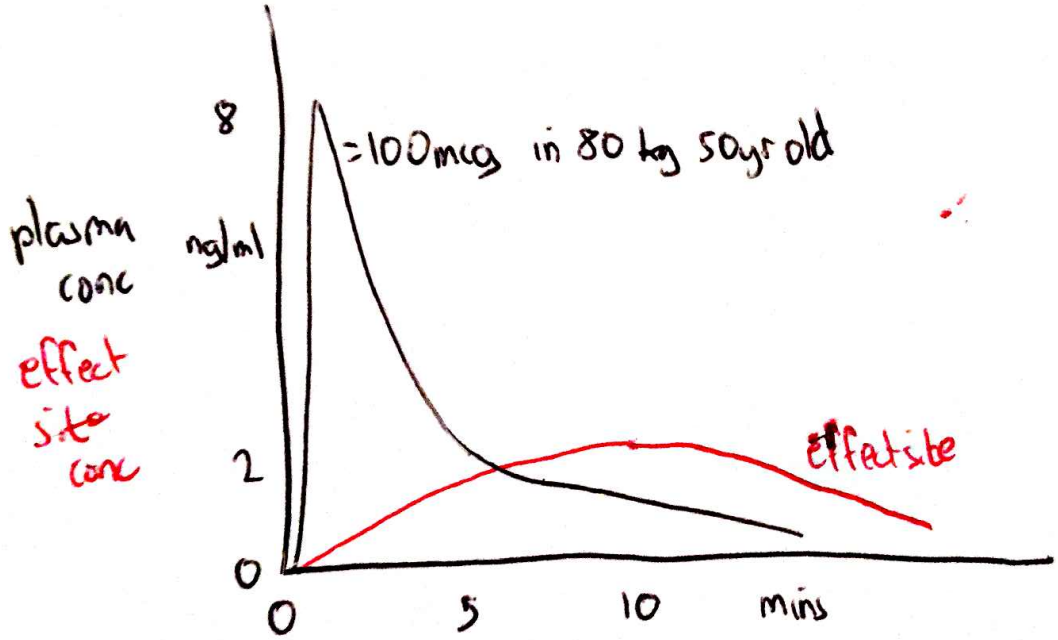
Figure 8.4

Plasma concentration-time curve of a single intravenous bolus dose of an opiate in relation to the effect compartment concentration associated with respiratory depression or analgesia for that opiate. Note the differences in effect compartment concentration curves, and hence differences in clinical effect resulting from a short versus a long $t_{1/2}k_{e0}$. Such differences in $t_{1/2}k_{e0}$ determine the clinical usage of drugs administered as intravenous boluses during anaesthesia.

Fentanyl Plasma & Effect Site Concentrations



Fentanyl Plasma vs effect site conc:



Fentanyl apnoeic threshold = 1.5-3ng/ml

CSHT

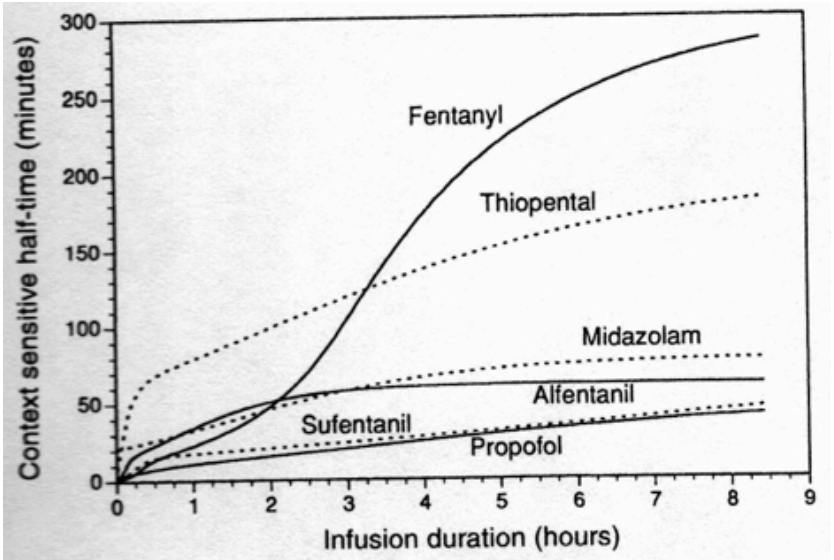


Figure 12–17 Context-sensitive half-times as a function of infusion duration (the "context") derived from pharmacokinetic models of fentanyl, sufentanil, alfentanil, propofol, midazolam, and thiopental. (From Hughes MA, Glass PSA, Jacobs JR: Context-sensitive half-time in multicompartment pharmacokinetic models for intravenous anesthetic drugs. Anesthesiology 76:334-341, 1992.)

Opiate Decrement Times

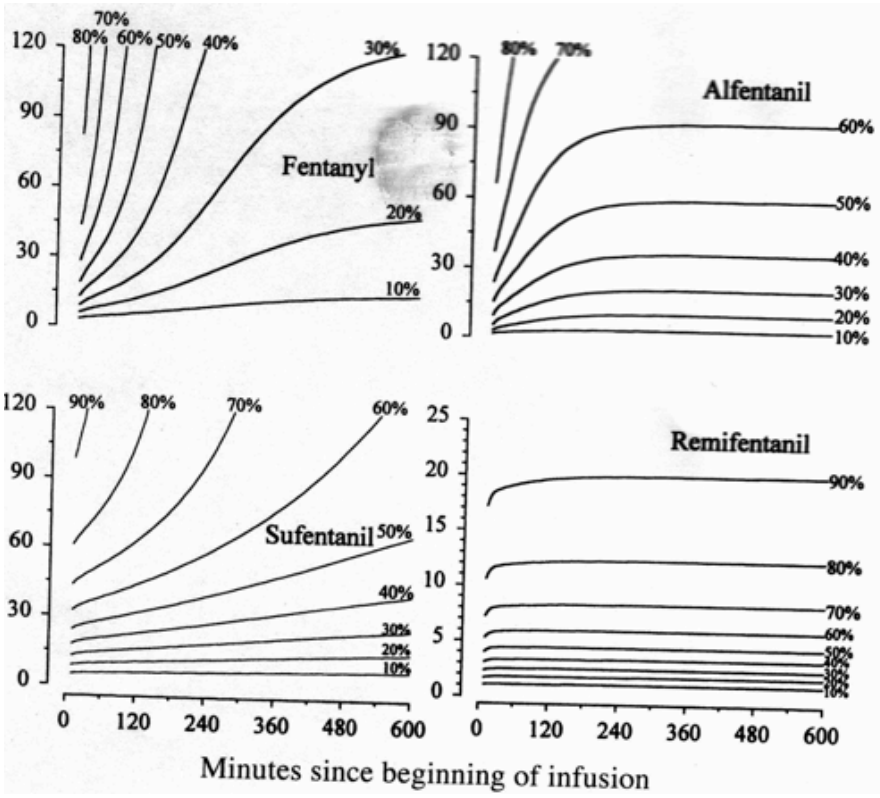


Figure 12–18 Context-sensitive effect-site decrement times for alfentanil, fentanyl, sufentanil, and remifentanil showing the time required for decreases in a given percentage (labeled for each curve) from the maintained effect-site concentration after termination of the infusion.

Propofol Plasma & Effect Site Times

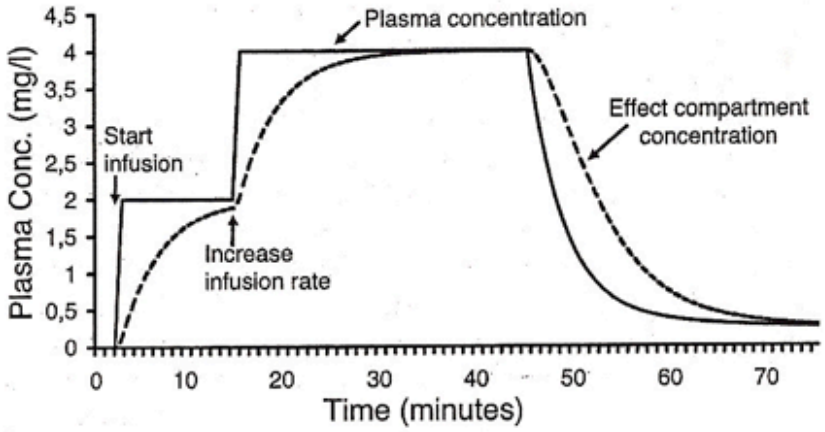
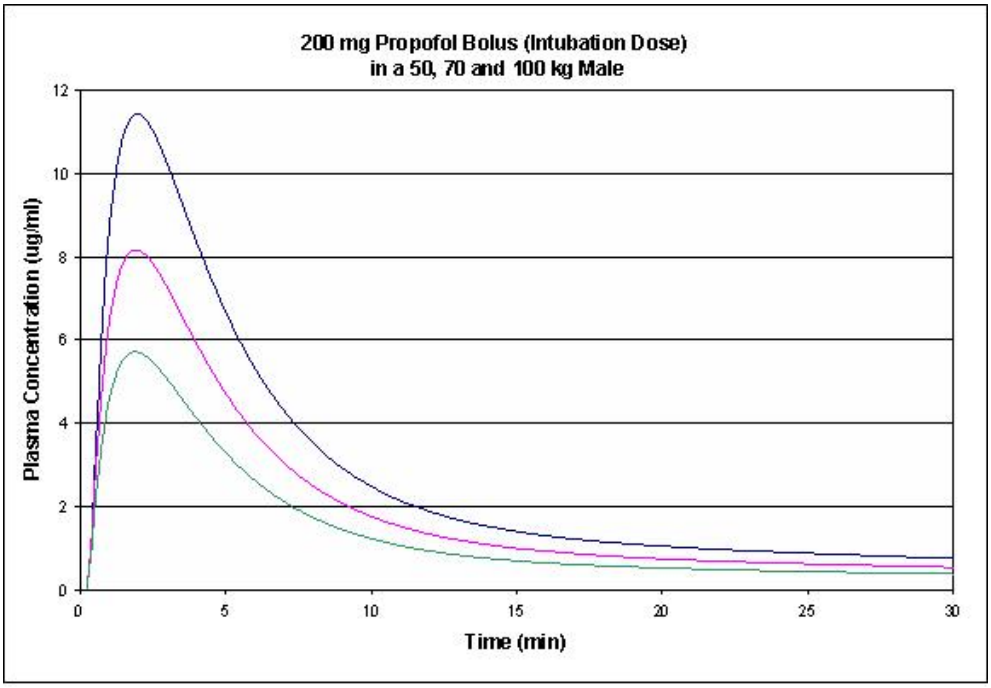


Figure 9.4

Theoretical possible plasma concentration-time curve for Propofol administered by a modern computer controlled TIVA pump with effect compartment steering. As can be seen, such modern TIVA pumps can administer step-wise increments in plasma drug concentrations, which are followed by changes in effect compartment concentrations. These are active processes controlled by the perfusor pump. However, reduction of plasma and effect compartment drug concentrations is a passive process set in action by reducing the infusion rate, or by stopping drug administration. Drug concentrations then decline due to plasma elimination, as well as exchange of drug between other compartments and the central compartment.



Multi-Compartment Model

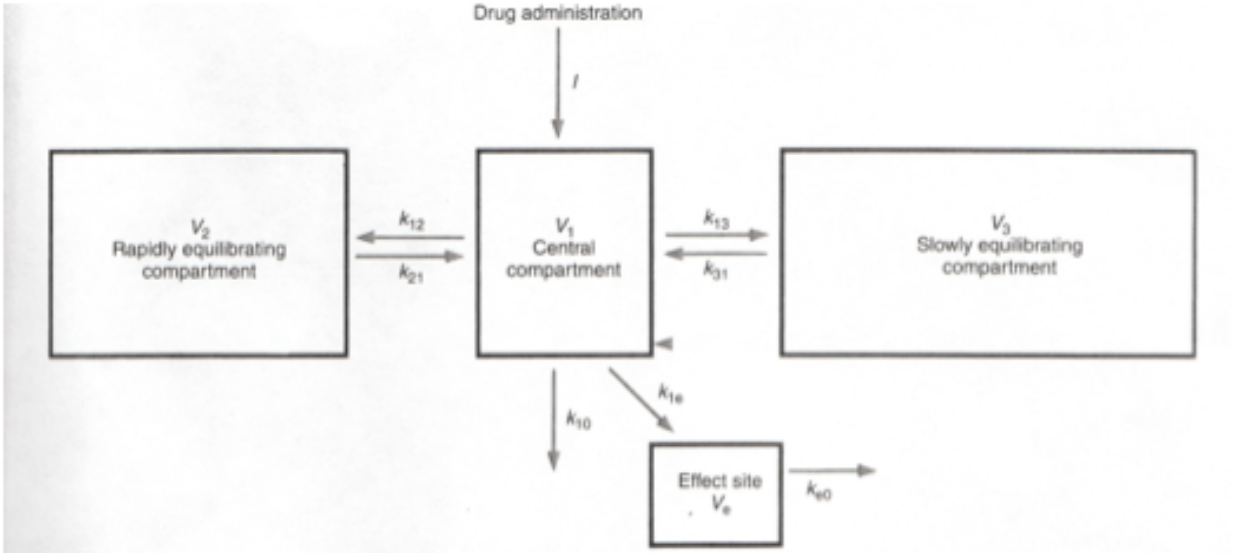


Figure 3–22 A three-compartment model with an added effect site to account for the equilibration delay between the rise and fall of arterial drug concentrations and the onset and offset of drug effect. The effect site is assumed to have a negligible volume.

Statistics

Sensitivity, Specificity, NPV, PPV

		Condition (as determined by "Gold standard")		
		Condition Positive	Condition Negative	
Test Outcome	Test Outcome Positive	**True Positive**	**False Positive** (Type I error)	**Positive predictive value** = Σ True Positive / Σ Test Outcome Positive
	Test Outcome Negative	**False Negative** (Type II error)	**True Negative**	Negative predictive value = Σ True Negative / Σ Test Outcome Negative
		Sensitivity = Σ True Positive / Σ Condition Positive	Specificity = Σ True Negative / Σ Condition Negative	

Drug Structures

Keto-Enol STP Structures

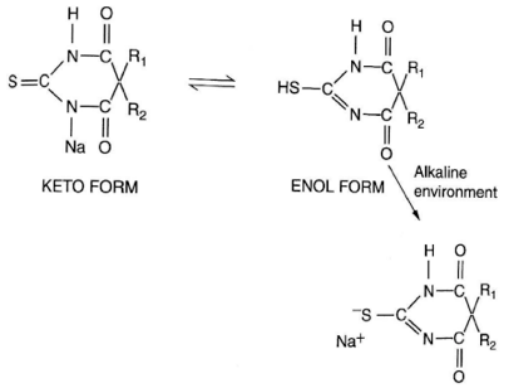
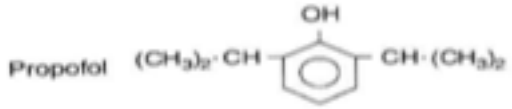
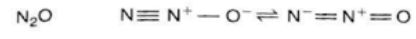


Figure 8.4. Keto-enol transformation of barbiturates – tautomerism. Alkaline solutions favour the water-soluble enol form.

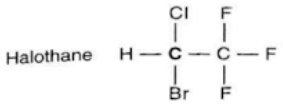
Propofol



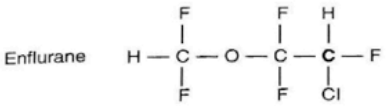
Volatiles



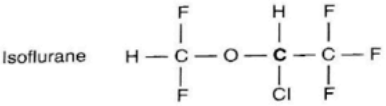
N_2O = simple inorganic molecule



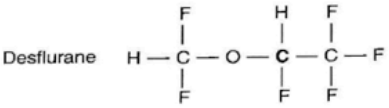
= halogenated hydrocarbon



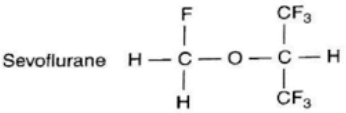
= halogenated methyl ether



= halogenated ethyl methyl ether



= fluorinated ethyl methyl ether



= polyfluorinated isopropyl methyl ether

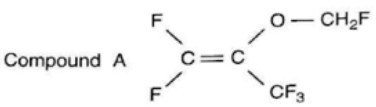
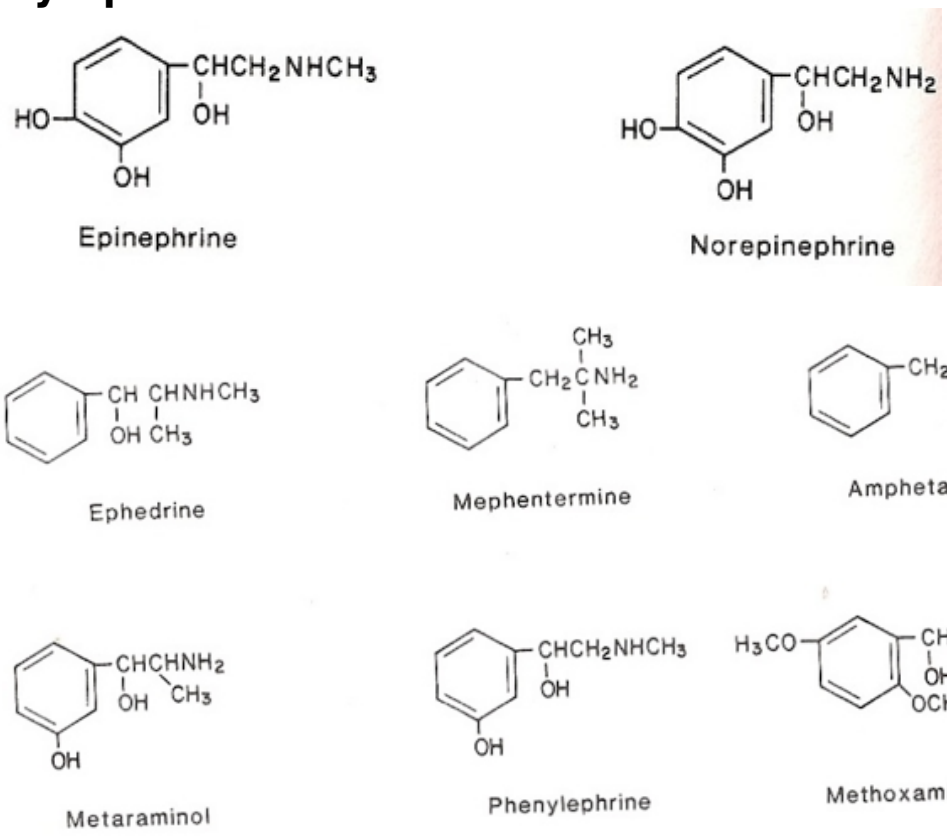


Figure 8.10. Structure of some inhaled anaesthetics and Compound A. **C** represents a chiral centre.

Sympathomimetics



Structural Isomer

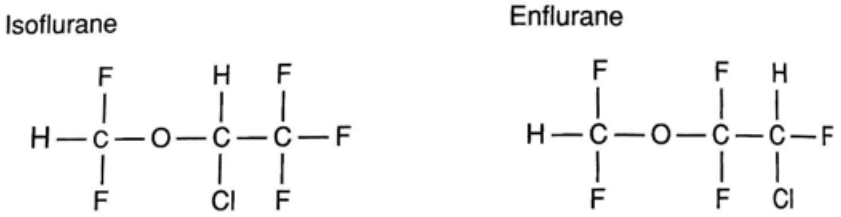


Figure 5.1. Structural isomers: (a) $C_{18}H_{23}NO_3$; (b) $C_3H_2ClF_5O$.

Stereolsomer

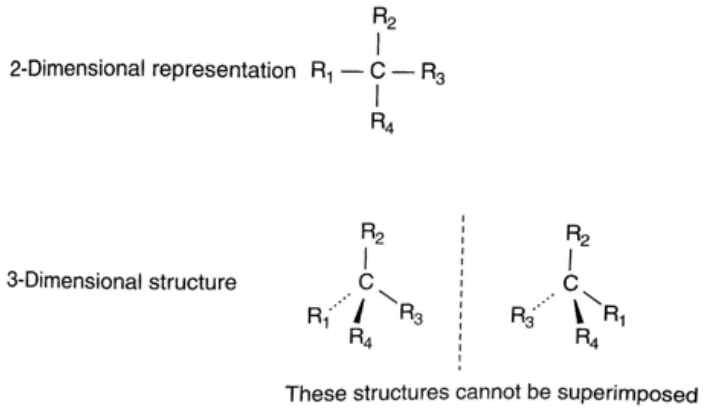


Figure 5.2. Chiral centres.