# Respiration Module

## Session 4 – Chemical control

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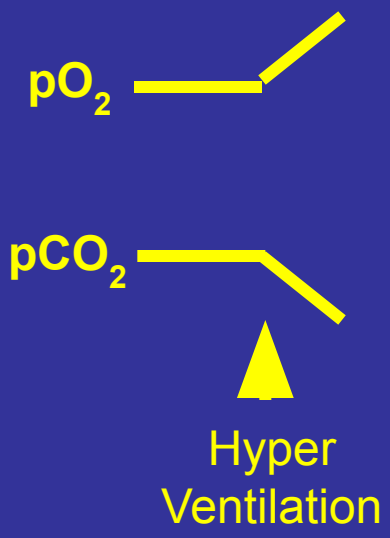
# Chemical control of breathing

- alveolar $pO_2$ and $pCO_2$ need to be kept constant
- rises in $pCO_2$ called *hypercapnia*
- falls in $pCO_2$ called *hypocapnia*
- falls in $pO_2$ called *hypoxia*

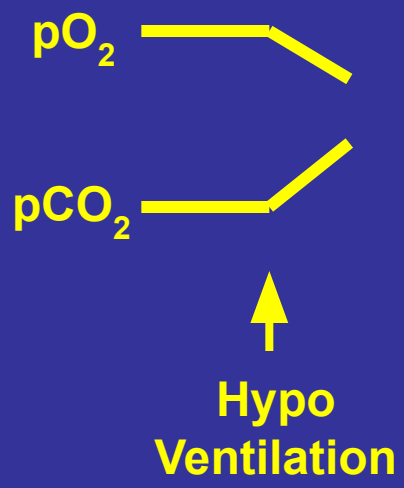
# Ventilation and alveolar partial pressures

- if ventilation *increases* with no change in metabolism - *hyperventilation*
  - $pCO_2$ will fall
  - $pO_2$ will rise



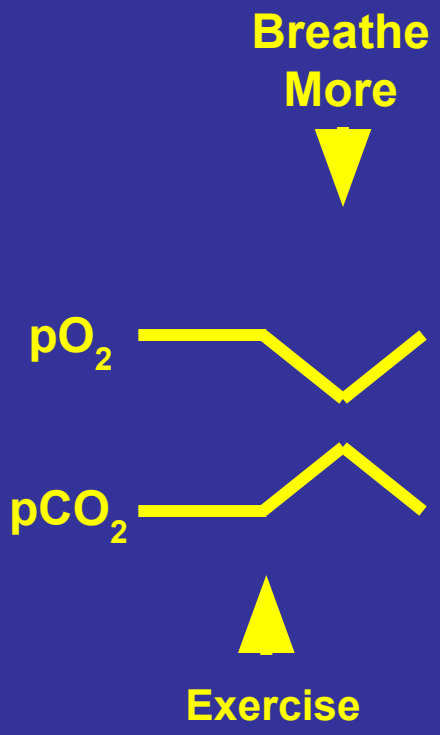
# Ventilation and alveolar partial pressures

- if ventilation *decreases* with no change in metabolism - *hypoventilation*
  - $pCO_2$ will rise
  - $pO_2$ will fall



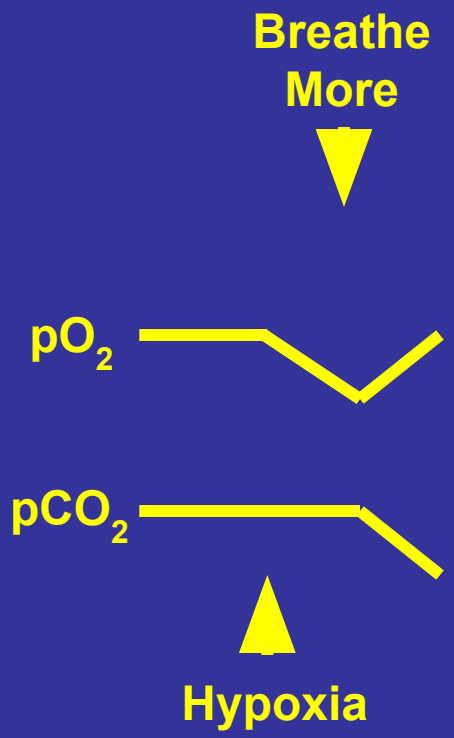
# The problem

- if $pO_2$ falls and $pCO_2$ rises then can correct both by breathing more
- cannot always control both partial pressures by changing ventilation rate



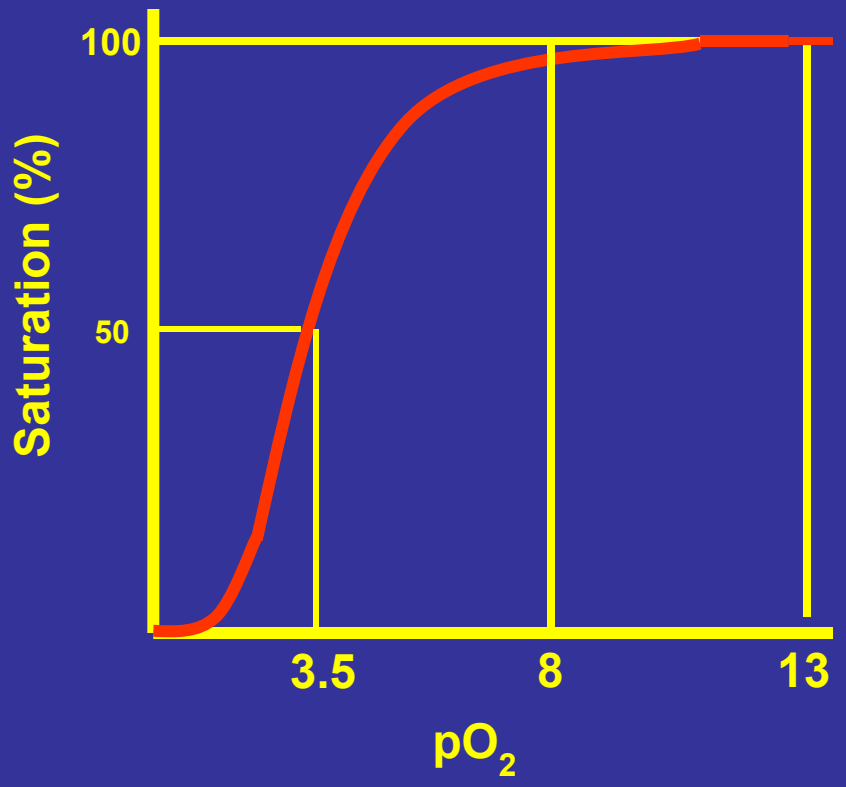
# The problem

- but, if $pO_2$ falls with no change in $pCO_2$ correcting the hypoxia will produce hypocapnia
- sometimes the system must choose which to control



# Hypoxia

- $pO_2$ can fall to about 8kPa before the saturation of Hb is significantly reduced
- but further falls lead to large reductions in oxygen transport
- system just needs to protect against marked hypoxia



# Hypercapnia and hypocapnia

- $pCO_2$ affects plasma pH
- $pH = pK + \log([HCO_3^-]/(pCO_2 \times 0.23))$
- at constant $[HCO_3^-]$
  - if $pCO_2$ rises pH falls
  - if $pCO_2$ falls pH rises
- small changes in $pCO_2$ lead to large changes in pH

# Effects of acid and alkaline blood

- if plasma pH falls below 7.0 enzymes lethally denatured
- if plasma pH rises above 7.6, free calcium concentration falls enough to produce fatal *tetany*

# Ventilation and acid base balance

- hypoventilation leads to hypercapnia
- hypercapnia causes plasma pH to fall
- this is *respiratory acidosis*

# Hyperventilation

- causes $pCO_2$ to fall
- so pH rises - *respiratory alkalosis*
- can cause lethal tetany

# Role of the kidneys

- plasma pH depends on the *ratio* of [$HCO_3^-$] to $pCO_2$, not on their absolute values
- changes in $pCO_2$ can be compensated by changes in [$HCO_3^-$]
- the kidney controls [$HCO_3^-$]
- respiratory acidosis is *compensated* by the kidneys increasing [$HCO_3^-$]
- respiratory alkalosis is *compensated* by the kidneys decreasing [$HCO_3^-$]
- this takes 2-3 days

# Metabolic acid

- if the tissues produce *acid*, this reacts with $HCO_3^-$
- the fall in [$HCO_3^-$] leads to a fall in pH
- *metabolic acidosis*
- this can be compensated by changing ventilation
- increased ventilation lowers $pCO_2$
- restores pH towards normal

# Metabolic alkali

- if plasma [$HCO_3^-$] rises (e.g. after vomiting)
- plasma pH rises
- *metabolic alkalosis*
- can be compensated to a degree by decreasing ventilation

# Therefore

- Plasma pH depends on the ratio of [$HCO_3^-$] to $pCO_2$
- Respiratory driven changes in pH compensated by the kidney
- Metabolic changes in pH compensated by breathing

# Control of ventilation

- do not need to control $pO_2$ precisely, but must keep it above 8kPa
- need to control $pCO_2$ precisely to avoid acid base problems,
- but sometimes change ventilation to correct metabolic disturbances of pH

# Responses to hypoxia

- alveolar $pO_2$ must fall a lot to stimulate breathing
- arterial $pO_2$ monitored by *peripheral chemoreceptors*
- in the *carotid bodies* and *aortic bodies*
- large falls in $pO_2$ stimulate
  - increased breathing
  - changes in heart rate
  - diversion of blood flow to brain

# Responses to $pCO_2$

- peripheral chemoreceptors will detect changes but are rather insensitive
- *central chemoreceptors* in the *medulla* of the brain are much more sensitive

# Central chemoreceptors

- detect changes in arterial $pCO_2$
- small rises in $pCO_2$ increase ventilation
- small falls in $pCO_2$ decrease ventilation
- the basis of negative feedback control of breathing

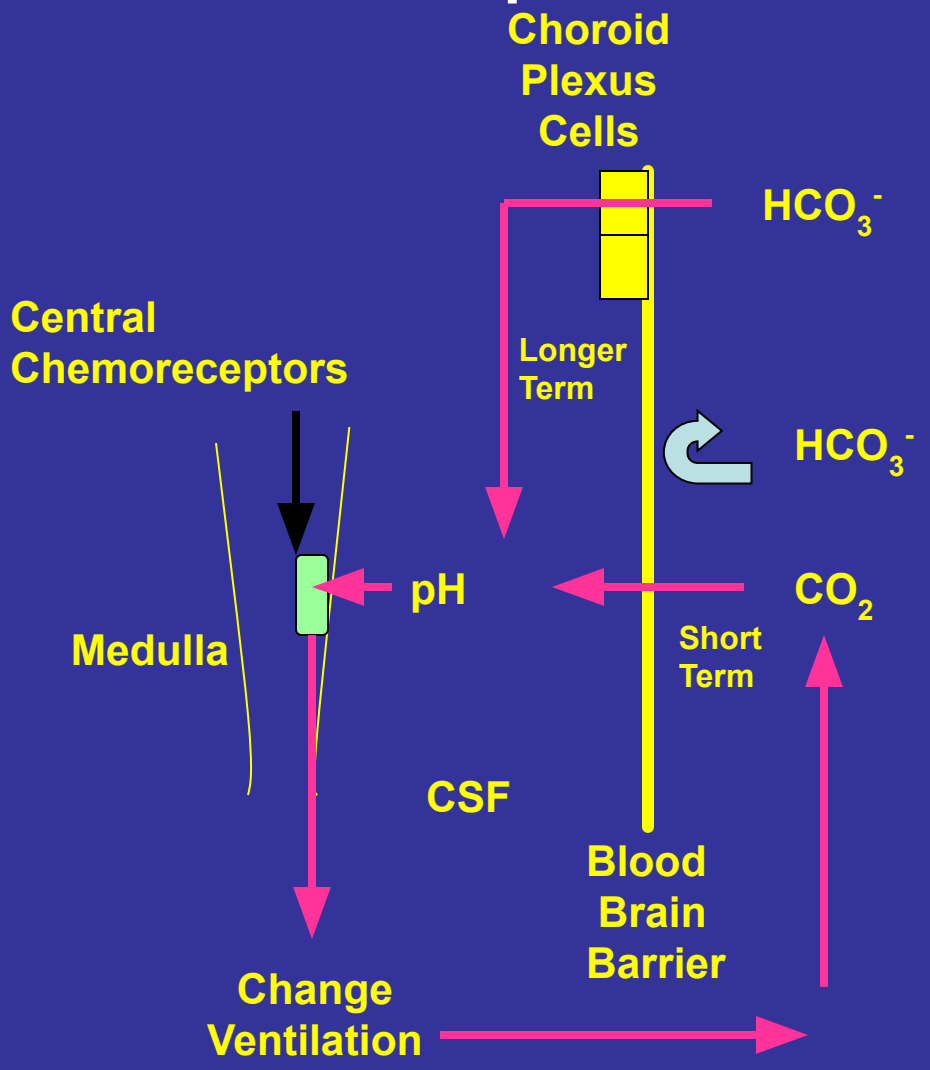
# Negative feedback control

- if $pCO_2$ rises, central chemoreceptors stimulate breathing
- which blows off $CO_2$,
- and returns $pCO_2$ to normal
- and vice-versa

# Central chemoreceptors

- actually respond to changes in the pH of cerebro-spinal fluid (CSF)
- CSF separated from blood by the blood-brain barrier
- CSF [$HCO_3^-$] controlled by choroid plexus cells
- CSF $pCO_2$ determined by arterial $pCO_2$

# Central Chemo receptors

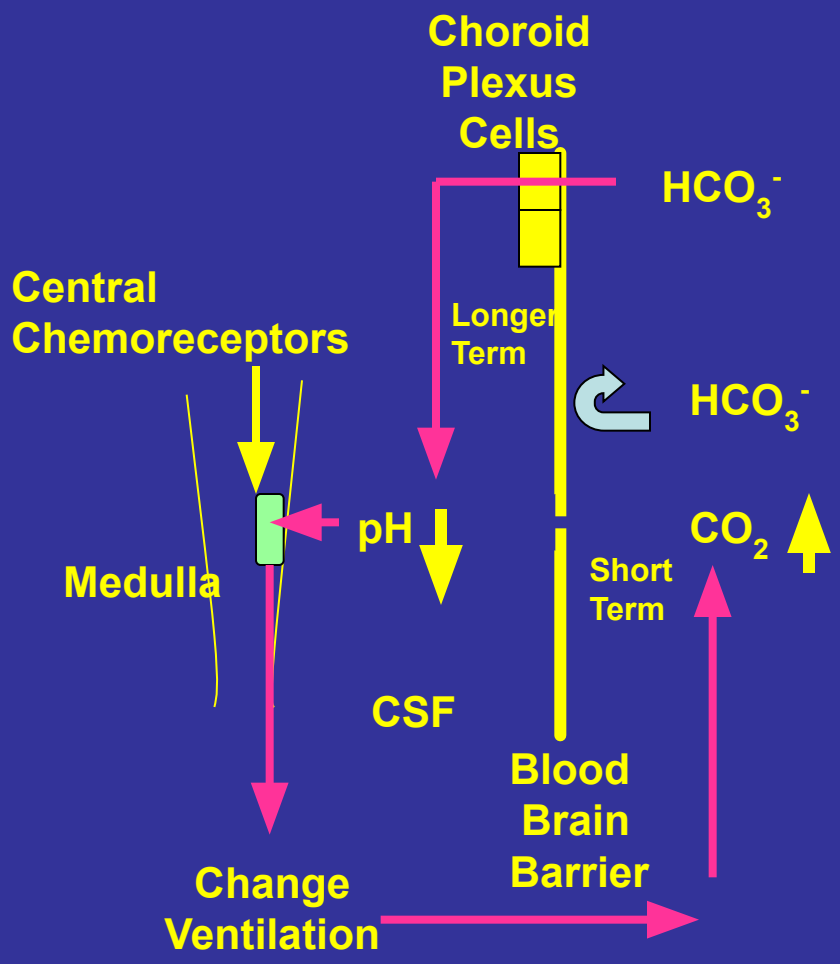


# Cerebro-spinal fluid pH

- determined by ratio of $[HCO_3^-]$ to $pCO_2$
- $[HCO_3^-]$ fixed in short term
- so falls in $pCO_2$ lead to rises in CSF pH
- rises in $pCO_2$ lead to falls in CSF pH
- but persisting changes in pH corrected by choroid plexus cells which change $[HCO_3^-]$

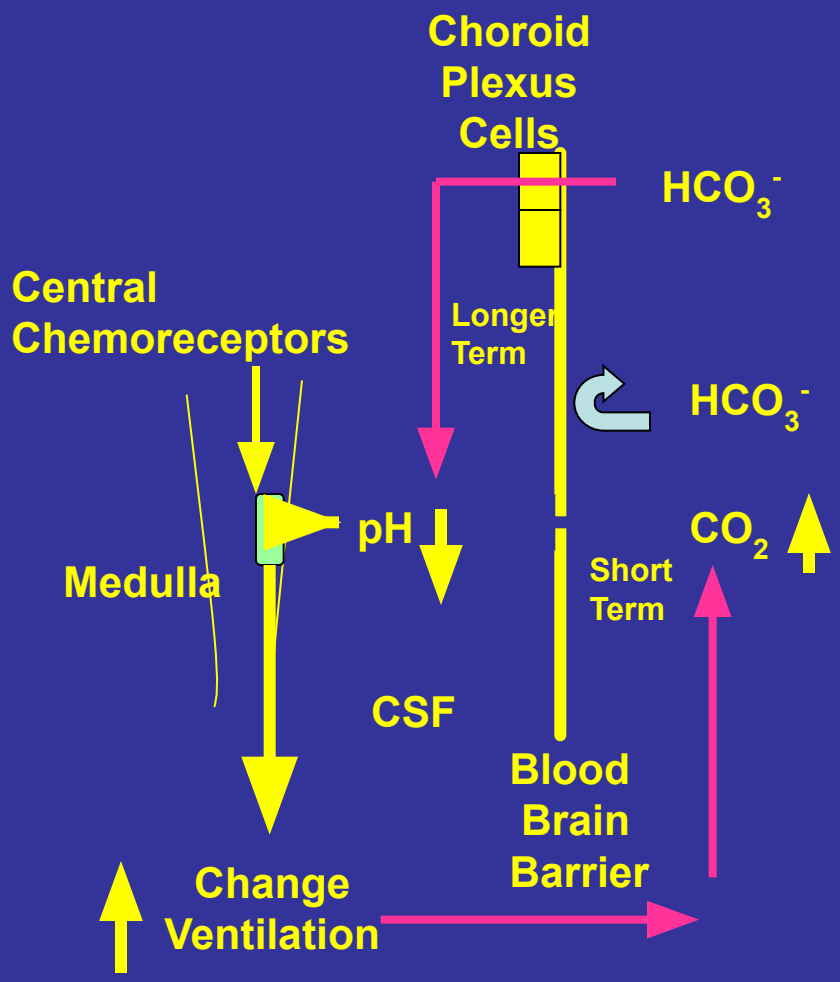
# Feedback control

- Elevated pCO2 drives CO2 into CSF across blood brain barrier
- CSF [$HCO_3^-$] initially constant
- So CSF pH falls



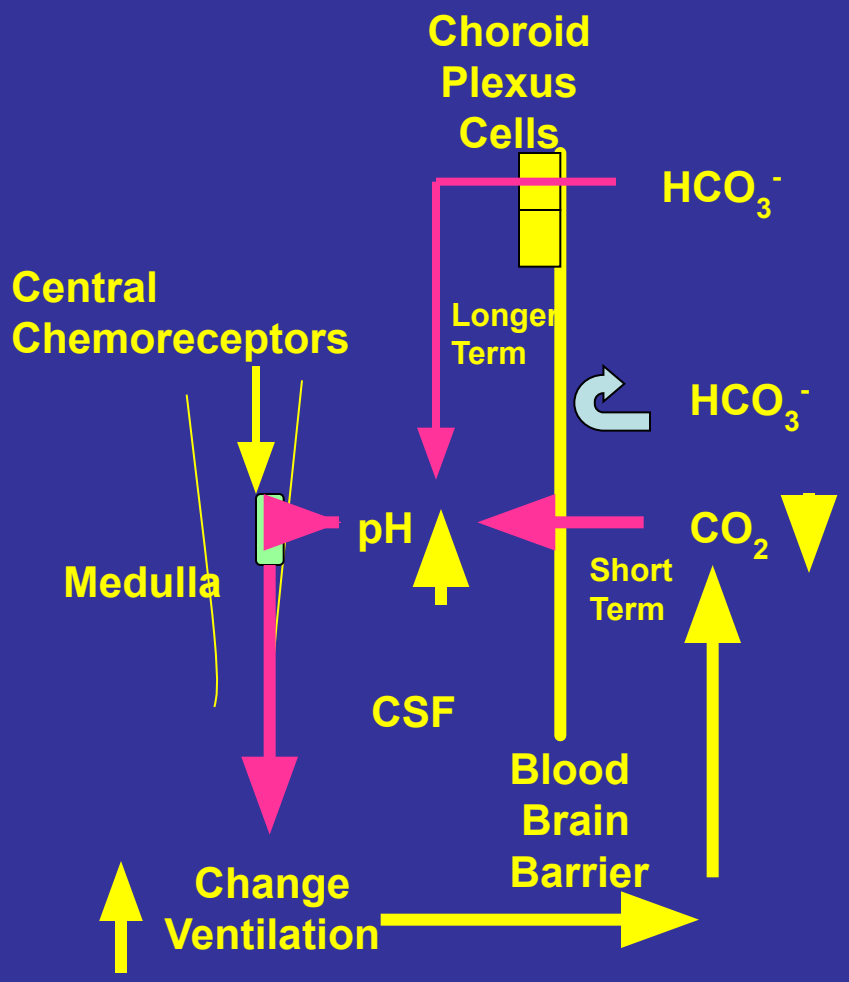
# Feedback control

- Fall in CSF pH detected by central chemoreceptors
- Drives increased ventilation



# Feedback control

- Increased ventilation
- Lowers $pCO_2$
- and restores CSF pH



# Role of Choroid Plexus

- CSF [$HCO_3^-$] determines which $pCO_2$ is associated with ‘normal’ CSF pH
- CSF [$HCO_3^-$] therefore ‘sets’ the control system to a particular $pCO_2$
- It can be ‘reset’ by changing CSF [$HCO_3^-$]

# Long term changes

- Persisting hypercapnia
- Persisting hypoxia