REGULATION OF RESPIRATION

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GMC

- The Respiratory system in human performs a critical task
- That is to regulate & respond to O_2 demands
- Maintaining a constant O_2 & CO_2 in the blood
- Therefore, regulation of respiration is critically important for Homeostasis

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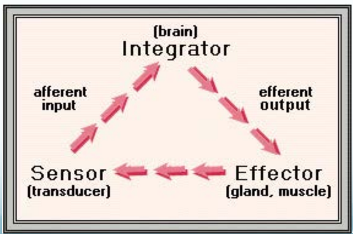
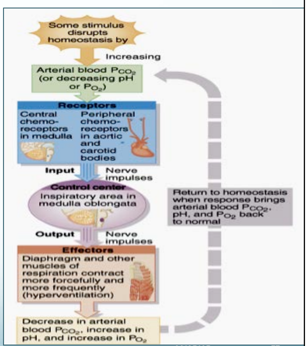
- Any physiological control system is composed of 3 interconnecting structures:
- Integrator (centre), Sensor & Effector



The Respiratory Control System

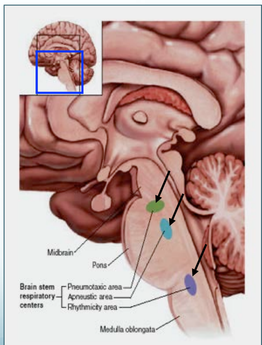
- Integrator (Centre) →
  neural network in brainstem
- Sensors →
  - The main are chemosensors sensing changes in CO_2, O_2 & pH
  - Other contributors: in the lungs, cardiovascular, skeletal muscles, tendons of respiratory muscles,
- Effector → respiratory muscles

Inspiration; diaphragm &external intercostals
Expiration; internal intercostals & abdominal recti



The Respiratory Centre

- Present in brain stem
- Medullary group of neurons (rhythmicty centre)
- Pontine:
  - Apneustic
  - Pneumotaxic



Medullary Respiratory Neurons (Rhythmicity Centre)

- 2 distinct groups of neurons;
- The Dorsal Respiratory Group (DRG)
- The Ventral Respiratory Group (VRG)
- The 2 groups are bilaterally paired
- There is cross communication between them
- responsible for initiation & regulation of breathing

Medullary Respiratory Neurons
Dorsal Respiratory Group (DRG)

- Inspiratory neurons that discharge during inspiration & stop discharging during expiration (Inspiratory Rhythm generator)
- They generate a Ramp Signal; they initiate inspiration with a weak burst of action potentials that gradually increase in amplitude, then ceases for the next 3 sec. until a new cycle begins
- This provides a gradual increase in lung volume during inspiration

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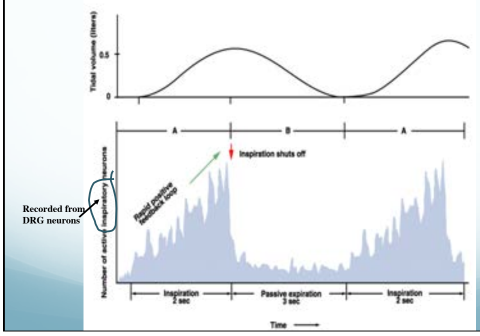
Basic rhythmic breathing and Inspiratory Neuronal Activity

The basis of rhythmic breathing. During inspiration the activity of inspiratory neurons increases steadily (ramps up). At the end of inspiration, the activity shuts off abruptly and expiration occurs by virtue of elastic recoil of lungs.



Medullary Respiratory Neurons
Input to Dorsal Respiratory Group (DRG)

- The most important sensory comes from the adjacent central Chemoreceptors (chemosensitive area in medulla)
- Input from peripheral Chemoreceptors via afferent sensory of vagus (X) & glossopharyngeal (IX)
- Stimulatory input from Apneustic centre prolonging its activity
- Inhibitory input from Pneumotaxic centre terminating its activity

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Medullary Respiratory Neurons
Output from Dorsal Inspiratory Group (DIG)

- Efferent nerves to spinal motoneurons supplying diaphragm (C3-5) & external intercostals (T1-T12).
- Stimulatory to Pneumotaxic centre

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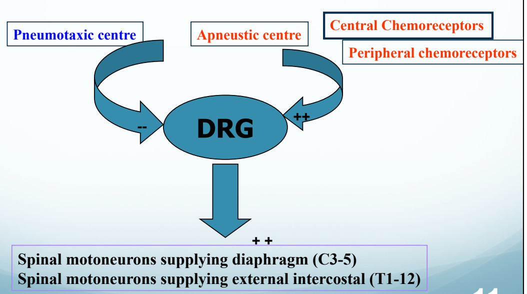
Inputs & output of DRG



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Medullary Respiratory Neurons
Ventral Respiratory Group (VRG)

- Anterolateral to DRG
- Activated during heavy breathing; e.g. exercise
- During such conditions, the increased activity of inspiratory neurons activates the VRG
- In turn, the activated VRG discharge:
  - inhibiting inspiratory group
  - stimulating the muscles of expiration; internal intercostals (T6-L3), abdominal recti (T4-L3)

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Rhythmicity Center

- I neurons located primarily in dorsal respiratory group (DRG):
  - Regulate activity of phrenic nerve.
- E neurons located in ventral respiratory group (VRG):
  - Passive process.
- Activity of E neurons inhibit I neurons.
  - Rhythmicity of I and E neurons may be due to pacemaker neurons.

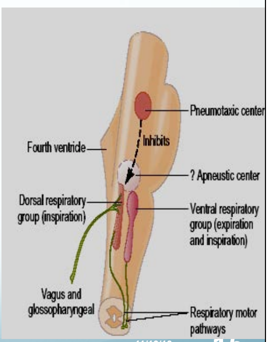
Pontine Respiratory Centre

- **2 pontine centres that modify the rate & The Pattern of respiration**

Pontine Respiratory Centres

Apneustic centre:

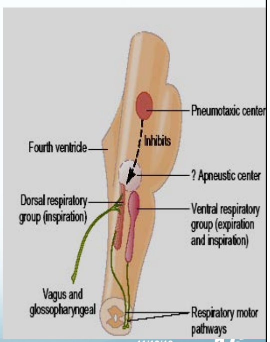
- **In the lower 1/3 of pons, close to medullary groups**
- **sends stimulatory discharge to inspiratory neurons promoting inspiration**
- **Removal of its stimulatory effect→ respiration becomes shallow & irregular**



Pontine Respiratory Centres

Pneumotaxic centre

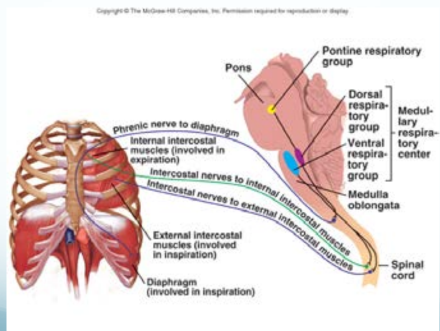
- **In upper 2/3 of pons**
- **Its major role is regulation of respiratory volume & rate**
- **Controlling cessation of inspiratory ramp signal from DRG;**
- **Switch-off DRG & apneustic centre → expiration occurs**
- **Hypoactivation of this centre →prolonged deep inspiration with limited brief expiration**
- **Hyperactivation →shallow inspiration**



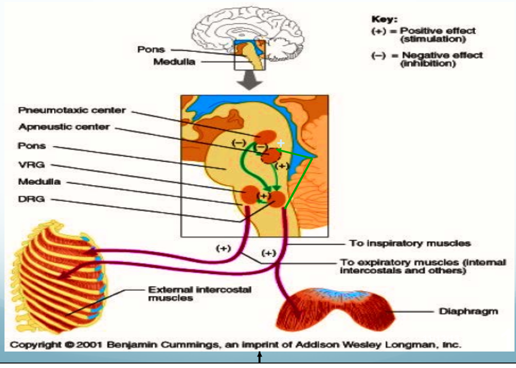
Pontine Respiratory Centres

- **Thus, the pontine centres work in co-ordination to regulate rhythmic respiratory cycle; How**
- **Active inspiratory neurones→ stimulation of ms. of inspiration& pneumotaxic centre .**
- **Active pneumotaxic centre → inhibits apneustic & DRG → initiation of expiration**
- **Spontaneous activity of inspiratory neurons in DRG then starts another cycle**

Respiratory Structures in Brainstem



The co-ordinated work of neurons of respiratory centre



Overall Control of Activity of Respiratory Centre

- **A). Involuntary (Automatic) Control:**
- I- Chemoreceptor Reflexes
- II- Neurogenic Reflexes
- **B). Voluntary Control**

A). Involuntary Automatic Control
I- Chemoreceptor Reflexes

- Chemical regulation of activity of Respiratory centre which involves 2 pathways:

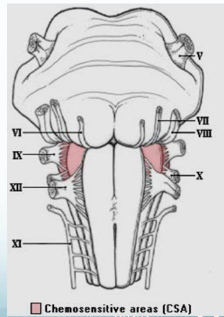
1- Central Chemoreceptor Pathway

2- Peripheral Chemoreceptor Pathway

- These chemoreceptors sense changes in PCO_2, PO_2 & pH

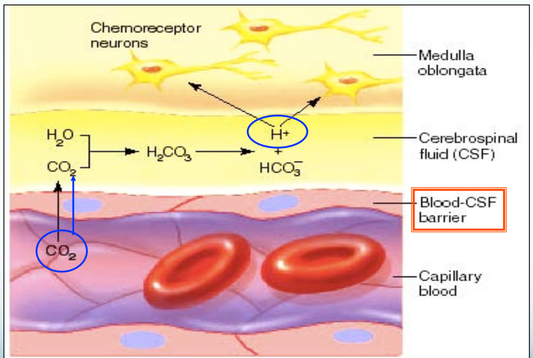
1- Central Chemoreceptors Pathway
Central chemosensitive area

- Lying just beneath ventral surface of medulla
- Relaying most important sensory input about changes in their close environment to respiratory centre in medulla & pons
- **Most sensitive to change in PCO_2, H^+ conc., but not to PO_2**



1- Central Chemoreceptors Pathway
Central chemosensitive area

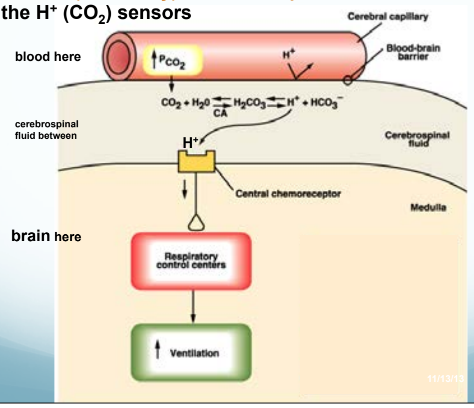
- Under normal conditions, ~75-85% of respiratory drive is due to stimulation of central chemoreceptors by CO_2
- Central chemoreceptors are **directly stimulated only by H^+**
- But H^+ can not cross blood brain barrier while CO_2 can
- So, how central chemoreceptors are stimulated by an increase in arterial PCO_2?



Central chemoreceptors are stimulated by an INCREASE in H+ & PCO2

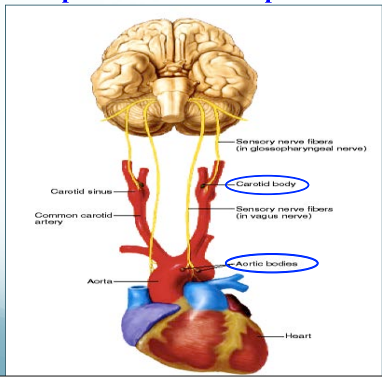
Central (medullary) Chemoreceptors (mechanisms)

the H^+ (CO_2) sensors



2- Peripheral Chemoreceptor Pathway

Peripheral Chemoreceptors

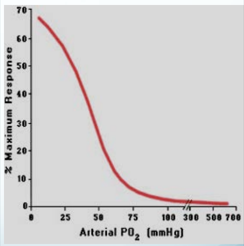


Peripheral chemoreceptors are the only sensors detecting a fall in PO2

2- Peripheral Chemoreceptor Pathway

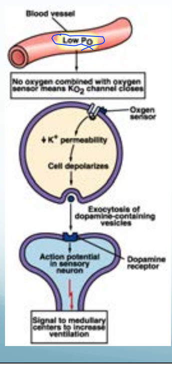
Stimulation of Peripheral chemoreceptors

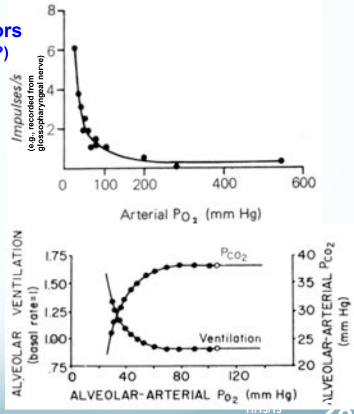
- The carotid & aortic bodies are **sensitive to fall in PO_2, an increase in PCO_2 or H^+ concentration**
- They **maximally stimulated when PO_2 decreases below 50-60mm Hg**
- They **detect changes in dissolved O_2 but not in the O_2 that is bound to Hb** (e.g. in anaemia there is normal PO_2 but reduced content of O_2 bound to Hb)



The Oxygen Sensors

(How do they work?)





What if Carotid bodies are removed?

- if there is decreased PO_2 (Hypoxia) with absence of peripheral chemoreceptors Hypoxia will inhibit respiration

Why?

- hypoxia depresses neuronal activity including that of respiratory centre
- Hypoxia →VD of cerebral vessels →↓PCO_2 in CSF →↓CO_2-mediated stimulation of central chemoreceptors → hypoventilation

A). Involuntary Automatic Control
II- Neurogenic Reflexes

- Hering-Breuer Inflation Reflex
- Hering-Breuer Deflation Reflex
- J-receptor Reflex
- Baroreceptors Reflex
- Cough & sneezing Reflexes
- Other influences (mediated via hypothalamus)

Neurogenic Reflexes

1- Hering-Breuer inflation reflex (inhibito-inspiratory reflex)

- Over-Inflation of lungs→ stimulation of slowly adapting stretch receptors in smooth muscles of large & small airways →afferent vagal signals → inhibitory to apneustic centre →termination of inspiration
- Pulmonary stretch receptor are present in the tracheobronchial tree and viseral pleura but not in lungs

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Neurogenic Reflexes

2- Hering-Breuer deflation reflex (excito-inspiratory reflex)

- Deep expiration → Deflation of the lungs → ↓activity of previous stretch receptors or stimulate other propioceptors in respiratory muscle → vagal afferent signals → inhibition of expiratory neurons

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Neurogenic Reflexes

3- J-receptor Reflex

- Pulmonary emboli or oedema →juxtapulmonary-capillaries receptors stimulated dues to increase in interstitial fluid volume which increase the polmonary cappilaries pressure→vagal afferent to respiratory centre → rapid shallow respiration
- These receptors are responsible for the sensation of air hunger (Dyspnea; shortness of breath)

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Neurogenic Reflexes

4-Baroreceptor Reflex

- ↑in ABP → stimulation of baroreceptors →afferent signals via X & IX → inhibitory to respiratory centre → decrease rate & depth of respiration → ↓venous return → ↓COP → ↓ABP

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Neurogenic Reflexes

5- Cough, Sneezing reflexes

- Dust, smoking, irritant substances → stimulation of irritant receptors in upper airways →afferent signals via vagus (Upper airways, {larynx, cough}) or trigeminal or olfactory (nose, sneezing) → respiratory centre → deep inspiration followed by forced expiration against closed glottis →opening of glottis →forceful outflow of air

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Reflexes involved in Respiratory Control

Stimulus	Reflex	Receptor	Afferent Pathway
Lung inflation	Hering-Breuer inflation	Airway Stretch Receptors	Vagus
Lung deflation	Hering-Breuer deflation	Airway Stretch Receptors	Vagus
Pulmonary emboli or congestion in lung		J-receptors in lung capillaries	Vagus
Mechanical irritation of airway	cough	irritant receptors of upper airway	Vagus
Systemic arterial blood pressure	arterial baroreceptors reflex	Aortic and carotid bodies	Glossopharyngeal & Vagus
Stretch of muscle and tendons		Muscle spindles, tendon organs and proprioceptors.	Various spinal pathways

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Neurogenic Reflexes

Other Influences from higher centres hypothalamus & limbic system

- Temperature: Increases respiratory rate
- Pain: Sudden pain decreases, prolonged pain increases rate
- Alcohol: Decreases rate

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B). Voluntary Control of Breathing

Cortical Influence

- Through descending tracts from the cerebral cortex to motor neurons of the respiratory muscles (dorsolateral corticospinal tracts)
- This provides CNS the ability to override the automatic regulation of respiration for short time e.g. holding breath but the involuntary control will take over (↑ PCO_2, H^+), or deliberate hyperventilation (↓PCO_2)

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Summary in Figures

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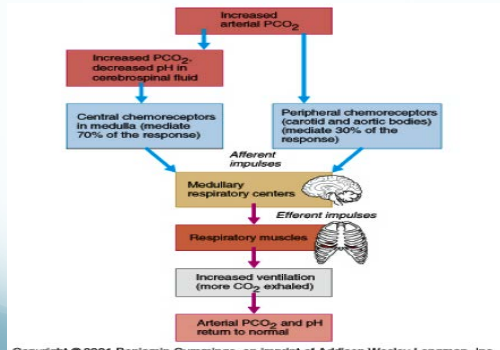
Summary of the Effect of ↑arterial PCO_2 on ventilation



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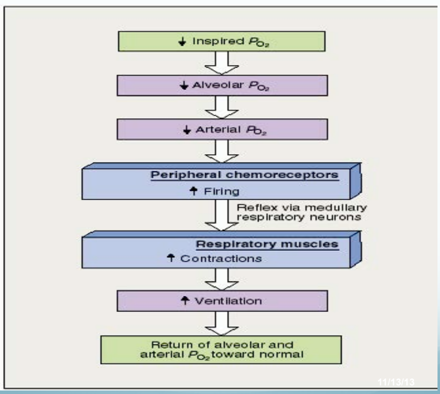
Effect of a decreased arterial PO_2



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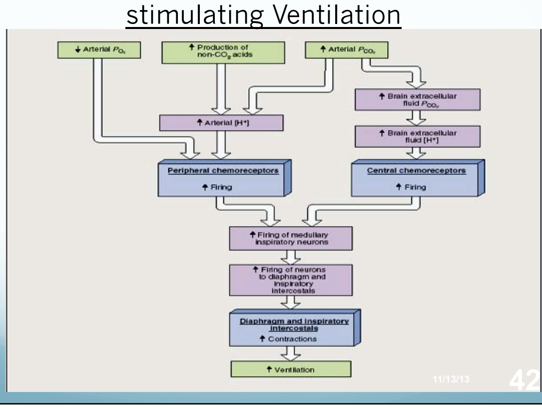
Summary of Chemical Pathways stimulating Ventilation



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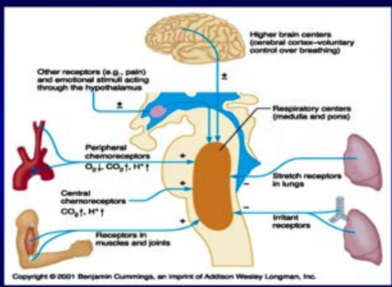
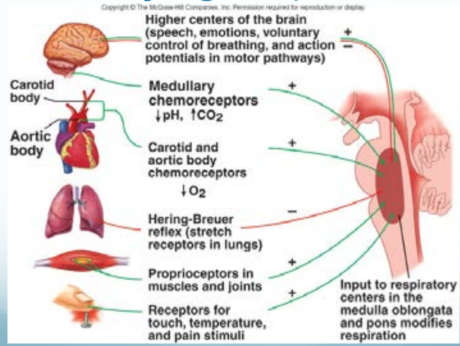
Summary Of the Overall Control of Activity of Respiratory Centre



Modifying Respiration



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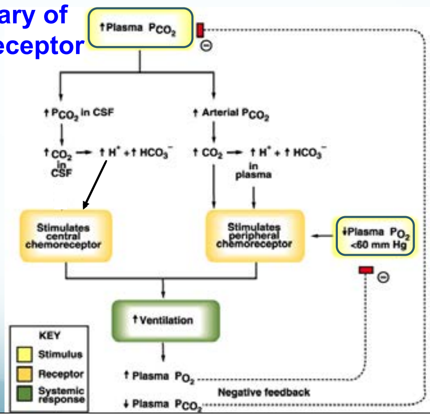
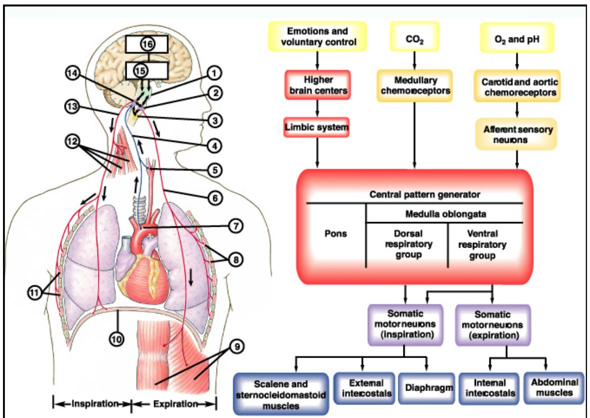
A Summary of Chemoreceptor Reflexes





Mark the following T or F

Respiratory chemoreceptors:

a). in the carotid and aortic bodies are most important in the ventilatory response to an elevated PCO2

b. in the carotid and aortic bodies are strongly stimulated by the low arterial O2 content in anaemic patients

c). in the medulla are responsive to changes in arterial PCO2

d. transducer a chemical changes into electric signals

e. may be sensitive to H+

Choose the best answer

- **Which of the following is the correct chain of events in the response to low Oxygen level?**

a) peripheral chemoreceptors activated·impulses sent to respiratory centre· respiratory muscles stimulated

b) central chemoreceptors activated· impulses sent to respiratory centre· respiratory muscles stimulated

c) increased ventilation· impulses sent to respiratory centre· respiratory muscles stimulated

d) peripheral and central chemoreceptors activated· impulses sent to respiratory centre· respiratory muscles stimulated

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- **What is the function of the Apneustic centre in the brain?**

a) monitor changes in CO2, O2 & H+ ions

b) sends inhibitory signals to Inspiratory area in medulla

c) sends stimulatory signals to Inspiratory area in medulla

d) monitors changes in blood pressure

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- **Peripheral chemoreceptors are sensitive to which of the following?**

a). increased PO2

b). elevated arterial blood pressure

c). elevated pH

d). decreased PO2

e). decreased PCO2

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