

# **MECHANISM (MECHANICS) OF BREATHING**

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❑ Breathing is produced by rhythmic discharge of signals from the spinal motor neurons (= anterior horn cells) that supply the respiratory muscles, which are located in the cervical and thoracic parts of the spinal cord.

❑ This discharge is controlled by 2 mechanisms :

1. **An involuntary automatic (subconscious) mechanism** : This is the *principal mechanism that controls respiration*, and is performed by the *respiratory centres*

(2) **A voluntary (conscious) mechanism** : Breathing can voluntarily be stopped (e.g. during talking) or accelerated (when required)

❑ However, this can be performed for *only a short time*, and is produced by signals discharged from the *motor area of the cerebral cortex* via the corticospinal (= pyramidal) tract, which *directly affect the activity respiratory spinal motor neurons*.

❑  **Ondine's curse**: This is an old legend that tells about a man who had lost his automatic control of respiration.

❑ In such case, respiration can occur only by voluntary control, and to maintain life, he should stay awake to remember to breathe voluntarily, which is evidently fatal due to either exhaustion or the resulting apnea if he fell asleep

## Historical background

❑ In the early 1920s, Lumsden performed brainstem transections and concluded that respiratory control was provided by centers which he called the **pneumotaxic center** (in the upper pons), the **apneustic center** (in the lower pons) and the **inspiratory and expiratory centers** in the medulla oblongata

❑ The pontine centers were postulated because a transection between upper and lower pons effectively removing the pneumotaxic center, produces slow deep breathing

❑ If done in conjunction with a bilateral vagotomy, to remove vagal sensory input from the lungs, inspirations become prolonged, separated by only brief expirations (a pattern referred to as apneustic breathing)

❑ This led to the conclusion that the pneumotaxic center normally promoted expiration and the apneustic center normally promoted inspiration

❑ Postulation of the medullary inspiratory and expiratory centers arose because, after a transection between the pons and medulla, breathing was dominated by prolonged expiratory spasms and irregular short inspiration

❑ However, more refined techniques for pons ablation have since demonstrated that the medulla by itself will produce a relatively normal pattern of rhythmic inspiration/expiration.

❑ This pattern becomes slower and deeper when the incoming vagal sensory information is blocked.

❑ As breathing is abolished only by a transection between the medulla and spinal cord, the rhythmic drive to the respiratory muscles must be generated within the medulla

## Recent Developments

- ❑ No specific group of neurons has ever been found in the so-called apneustic center, so that it and any theories of respiratory control involving it, have been abandoned
- ❑ The pneumotaxic center is now referred to as the pontine respiratory group (PRG)
- ❑ It is now known to comprise expiratory neurons in the nucleus parabrachialis medialis and inspiratory neurons in the parabrachialis lateralis and laterally sited Kolliker-Fuse nucleus.

❑ Modern evidence indicates that rather inspiratory and expiratory centers, the medulla is composed of three bilateral aggregations known as the DRG, VRG and Botzinger complex.

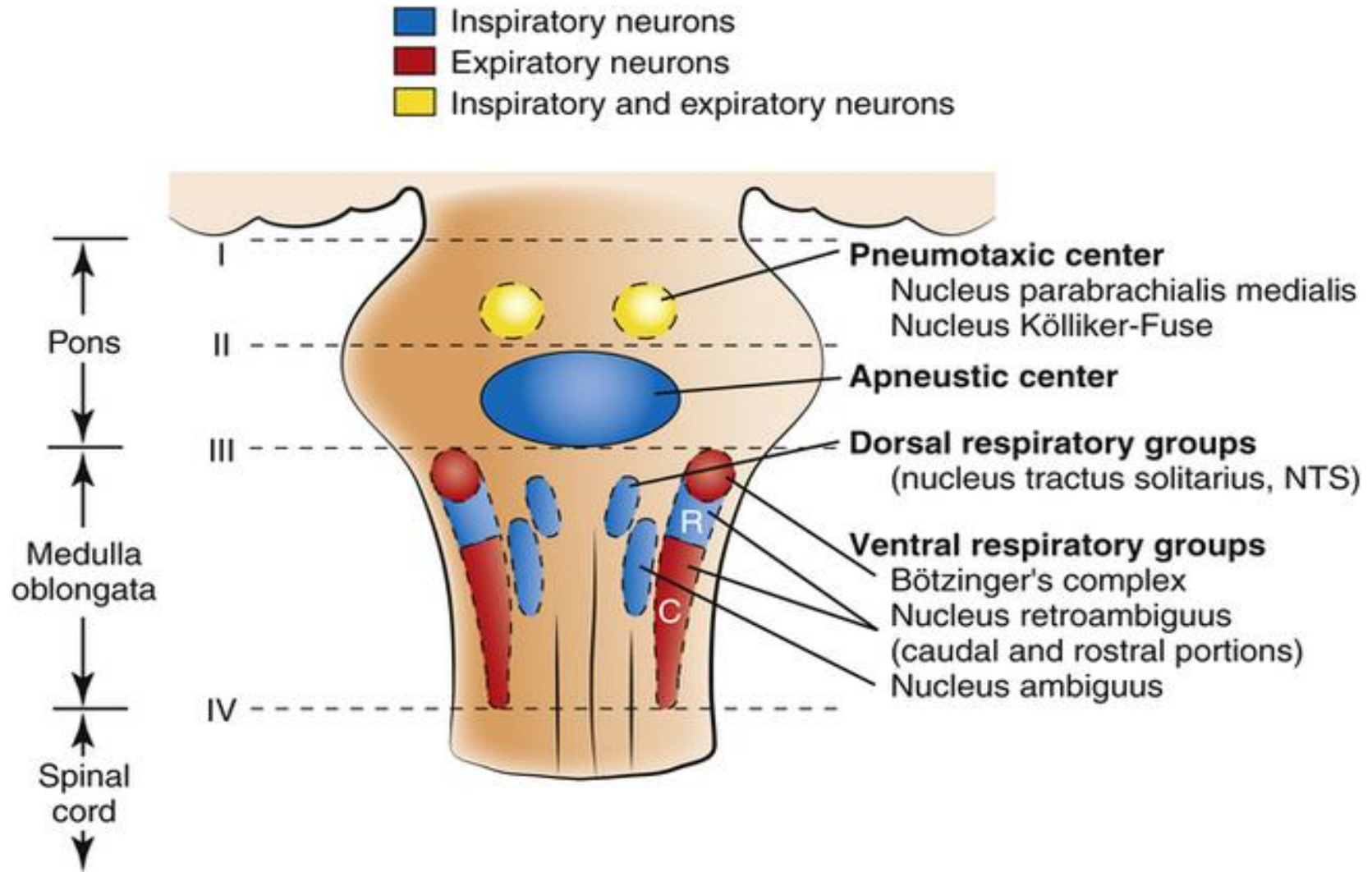
❑ They receive sensory information and after integration adjust appropriately the efferent activity to the respiratory muscles

❑ The pontine nuclei somehow modulate DRG and possibly VRG activity



# THE RESPIRATORY CENTRES

❑ These centres *control breathing automatically*, and each consists of a collection of neurons. They are located bilaterally in the reticular formation of the *brain stem*. and include the following:



## (A) MEDULLARY CENTRES

❑ There are 2 groups of neurons in the *medulla oblongata* that indirectly control the respiratory muscles (by discharging signals downwards via special respiratory tracts to the spinal motor neurons that supply these muscles)

### 1- A dorsal respiratory group (DRG)

- ❑ It is part of the nucleus tractus solitarius
- ❑ The NTS receives information from respiratory-related mechanoreceptors and chemoreceptors
- ❑ It is composed mainly of i-neurons
- ❑ These are the upper motor (premotor) neurons that project downward to the lower motor neurons of mainly the phrenic nerves which supply the diaphragm
- ❑ The DRG i-neurons exert inhibitory effect on the e-neurons in the VRG

## 2- A ventral respiratory group (VRG)

- ❑ Located rostrally in the nucleus ambiguus and caudally in the nucleus retroambiguus
- ❑ The nucleus ambiguus contains not only premotor i-neurons but also motor neurons to the laryngeal muscles and parasympathetic neurons to the bronchioles and heart
- ❑ The rostral part of the nucleus retroambiguus contains more i-premotor neurons and like those of the nucleus ambiguus supply the external intercostal and accessory muscles rather than the diaphragm
- ❑ The caudal part of the nucleus retroambiguus contains mainly e-neurons to the internal intercostals and abdominal muscles

❑ During resting breathing, in which expiration is passive, the activity in these VRG expiratory neurons is insufficient to discharge their lower motor neurons

❑ The VRG expiratory neurons appear to have inhibitory effects on inspiratory neurons late in the inspiratory phase, contributing to the termination of inspiration, the so-called inspiratory cut-off switch

# Botzinger Complex

- ❑ Rostral to the nucleus ambiguus
  - ❑ Contains entirely e-neurons
  - ❑ Receives sensory inputs relayed through the NTS
  - ❑ Exerts inhibitory effects on the i-neurons in the nucleus ambiguus and nucleus retroambigualis
  - ❑ Exerts excitatory effects on the e-neurons of the VRG
- ❑ It is not known where respiratory rhythmicity originates in the medulla.
- ❑ It maybe that the DRG inspiratory neurons have pacemaker properties and spontaneously discharge in a phasic manner, inhibiting when they do so the expiratory neurons.

❑ An alternative hypothesis, is a neural network of local re-excitation within each of the inspiratory and expiratory neuronal pools and oscillating reciprocal inhibition between the phasic firing of the two pools

# Genesis of the breathing rhythm (role of the respiratory centres)

□ During *eupnea* (= normal resting breathing), the breathing rhythm (i.e. the alternation of inspiratory and expiratory phases) occurs as follows :

□ The Ap. C. has an inherent tonic (=continuous) activity and is called the pacemaker of respiration

□ It discharges stimulatory signals to the i neurons in the medulla oblongata. Such discharge is rendered rhythmic by 2 mechanisms that potentiate each other :

- 1- The Pn C discharges rhythmic inhibitory signals to the Ap. C.
- 2- The afferent vagal nerve fibres carry inhibitory signals to the Ap. C from the inflated lungs during inspiration

❑ Accordingly, the medullary i-neurons discharge rhythmically at a rate of *12-16 bursts per minute, which* produces rhythmic inspirations.

❑ On the other hand, the e-neurons remain quiet all the time (i.e. do not discharge), and expiration follows inspiration passively

❑ The signals discharged from the i-neurons start weakly then increase in a *crescendo manner (= ramp signals)* for about 2 seconds, after which they stop for 3 seconds (during which expiration occurs), then a new cycle starts



# MECHANISM (MECHANICS) OF INSPIRATION

- ❑ Inspiration is an *active process*.
- ❑ The signals discharged from the I neurons are conducted downwards *via special respiratory tracts* to the spinal cord, where they *stimulate the spinal motor neurons that supply the inspiratory muscles*, which are located in the 3rd, 4th and 5th cervical segments as well as in all thoracic segments.
- ❑ The phrenic nerves arise from the cervical neurons and supply the diaphragm, while the intercostal nerves arise from the thoracic segments and supply the external intercostal muscles which extend obliquely downward and forward between the ribs.

❑ When the diaphragm contracts, *it moves down* leading to an increase in *the vertical diameter of the chest* (about 1.5 cm during eupnea and up to 7-10 cm during deep inspiration)

❑ On the other hand, contraction of the external intercostal muscles leads to:

*(a) Elevation and eversion of the ribs (a bucket-handle movement)*

*(a) Movement of the sternum forwards and its tilt upwards* These movements *increase the antero-posterior diameter of the chest markedly* and its *lateral (or transverse) diameter to some extent.*

❑ Accordingly, the chest cavity expands in all dimensions, leading to movement of the parietal pleura outwards. This decreases the intrapleural pressure, becoming more negative, which causes expansion of the lungs.

❑ As a result, the intrapulmonary pressure decreases from zero to about - 1 mmHg, which causes rush of about 500 ml of atmospheric air (= tidal volume) into the lungs, leading to its inflation.

# The inspiratory muscles

(1) During eupnea (normal resting breathing), the basic inspiratory muscles are the *diaphragm and external intercostal muscles*

(2) During forced inspiration : In addition to the basic muscles, the following accessory inspiratory muscles also contract to widen the chest cavity

- 1- The sternomastoid and scaleni muscles (elevate the upper ribs).
- 2- The levator costarum and serratus posterior superior muscles (help rib elevation).
- 3- The quadratus lumborum and serratus posterior inferior muscles (prevent inward movement of the lower ribs when the diaphragm contracts).

## Abdominal and costal (or thoracic) breathing

- ❑ Breathing produced by contraction of the *diaphragm* is called *abdominal breathing (or respiration)* because it is accompanied by movement of the anterior abdominal wall forwards (due to rise of the intra-abdominal pressure)
- ❑ On the other hand breathing by contraction of the *external inlet costal muscles* is called the *costal or thoracic breathing*.
- ❑ During eupnea, the abdominal breathing accounts for about 75 % of the pulmonary ventilation.

❑ However, *the diaphragm is not essential* (although it is the most important inspiratory muscle) because if its movement is compromised, *costal breathing can maintain life*.

❑ The latter also becomes equally important in deep breathing *and* during measurement of the vital capacity.

## Effects of various lesions on respiration

1. A complete spinal cord transection above *the* origin of the *phrenic nerves* (the 3<sup>rd</sup> cervical segment) is fatal (e.g. hanging) due to isolation of the respiratory centres.

❑ On the other hand, if this lesion is below the origin of the phrenic nerves (the 5th cervical segment), -respiration is not markedly affected because the diaphragm is still functioning.

2. Bilateral phrenic nerve palsy does not affect pulmonary ventilation at rest (which can be maintained by costal breathing); but breathing becomes labored and the pulmonary ventilation is reduced during exercise

# MECHANISM (MECHANICS) OF EXPIRATION

- ❑ During eupnea, expiration is a passive process (i.e. no muscle activity is involved).
- ❑ It occurs after relaxation of the inspiratory muscles by the elastic property of the lungs and the surface tension of the fluid that lines the alveoli, and is aided by elevation of the diaphragm and the weight of the thoracic cage.
- ❑ These effects decrease the chest volume, so the intrapleural pressure increases, becoming less -ve, which helps the lungs to recoil.



- ❑ As a result, the intrapulmonary pressure increases to about + 1 mmHg leading to rush of about 500 ml of air (tidal volume) outwards and the lungs are deflated.
- ❑ Such deflation occurs slowly because the inspiratory muscles are partially contracted in the early expiration (which exerts a braking action on the lung recoil forces).
- ❑ On the other hand, **the muscles of expiration contract only during forced expiration** (e.g. during muscular exercise) and in cases of increased airway resistance (e.g. asthma) and diminished elasticity of the lungs (e.g. emphysema).

❑ The expiratory muscles include mainly the following :

**1. The anterior abdominal wall muscles :** The contraction of these muscles increases the intra-abdominal pressure, which causes bulging of the diaphragm upwards into the chest cavity, thus helping outward expulsion of the air.

**2. The internal intercostal muscles :** These muscles extend obliquely downward and backward in between the ribs, so their contraction causes depression of the ribs, which reduces the chest volume and helps expiration.

## Intrapulmonary (or alveolar) pressure changes during eupnea

- ❑ The intrapulmonary pressure is normally zero (i.e. atmospheric) during the expiratory pause (in the mid thoracic position).
- ❑ At the start of inspiration, It decreases to about -1 mmHg due to lung expansion.
- ❑ This allows rush of about 500 ml of atmospheric air into the lungs and as a result, it increases gradually till *becoming atmospheric again by the end of inspiration.*
- ❑ At the start of expiration, it *rises to about +1 mmHg* due to lung recoil. This allows rush of about 500 ml of air outwards from the lungs and as a result, it decreases gradually till *becoming atmospheric again by the end of expiration.*

# HERING BREUER REFLEXES

## 1. Hering Breuer inflation reflex (= inhibito-inspiratory reflex)

- ❑ Lung inflation leads to stoppage of inspiration and initiation of expiration.
- ❑ The receptors are *slowly-adapting stretch receptors* (= inflation receptors) located among the airway smooth muscle cells.
- ❑ Signals from such receptors are conducted via *afferent fibres in the vagi nerves* to the brain stem, where they inhibit the activity of the apneustic centre (thus the inspiratory process stops and expiration starts).

## 2. Hering Breuer deflation reflex (= excito-inspiratory reflex)

- ❑ *Lung deflation* leads to stoppage of *expiration* and *initiation* of *inspiration*.
- ❑ The receptors are certain *deflation receptors* which are probably a *type of irritant receptors*
- ❑ Signals from such receptors are conducted via *afferent fibres in the vagi nerves* to the brain stem, where they stimulate the apneustic centre (thus the expiratory process stops and inspiration starts).

\*\*\* The inflation receptors are not adequately excited till the tidal volume exceeds 1 litre. Therefore, *the Hering Breuer reflexes normally play a little role during eupnea in adults.*

❑ However, they become important during *deep & anaesthesia* (in which they provide *a protective mechanism against excessive inflation and deflation of the lungs*).

❑ Also, the inhibitory vagal discharge during inspiration *shares in producing rhythmic breathing*

\*\*\* It was reported that in newly-born infants, lung inflation excites the apneustic centre leading to a prolonged inspiration and more lung inflation. Such response is called the paradoxical reflex. However, its presence is doubtful.

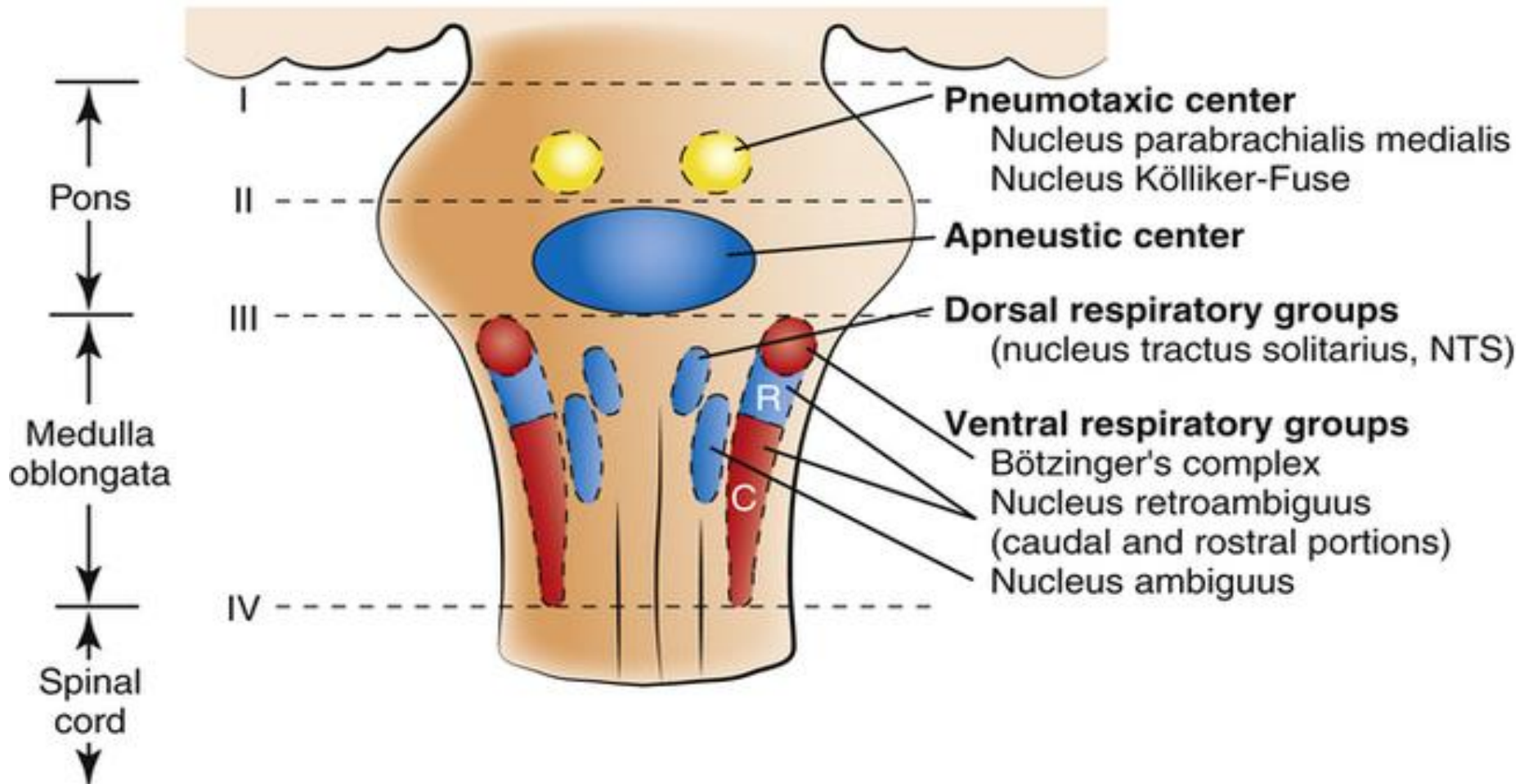
## Effects of bilateral vagotomy on breathing

❑ The inhibitory input to the apneustic centre (Ap.C) carried by the vagi nerves *potentiates the inhibitory input from the pneumotaxic centre* (Pn.C) and both produce rhythmic breathing.

❑ Therefore, the effects of bilateral vagotomy on breathing *depend on whether the brain stem is intact or transected, and also the level of transection* as follows:

(1) If the brain stem is intact or transected above the pons, bilateral vagotomy renders breathing to be *deep and slow*, because the *Pn. C becomes the only source of inhibition to the Ap.C.*

- Inspiratory neurons
- Expiratory neurons
- Inspiratory and expiratory neurons





(2) If the Pn.C is isolated from the Ap.C by a mid-pontine transection, bilateral vagotomy *deprives the Ap. C from all inhibitory* signals, so it discharges continuously resulting in *apneustic breathing*

(3) If the medulla is isolated from the pons breathing remains *rhythmic but becomes irregular whether the vagi are intact or cut* due to *spontaneous discharge from the i neurons* (which are stimulated by a special pacemaker in the medulla caned the *pre-Bottzinger complex*).

(4) If the medulla is isolated from the spinal cord e.g. in hanging, *breathing stops (= apnea) and death occurs whether the vagi nerves are intact or cut* because the respiratory centres are separated from the spinal motor neurons that supply the respiratory muscles.

# APNEUSTIC BREATHING (=APNEUSIS)

- ❑ This is a type of breathing that occurs as a result of *bilateral vagotomy together with a midpontine transection*.
- ❑ It can be produced in experimental animals but is rarely seen clinically. It is characterized by prolonged spasmodic inspirations interrupted by short weak expirations (due to exhaustion of the inspiratory muscles).
- ❑ This occurs as a result of continuous discharge of excitatory signals from the Ap. C to the inspiratory muscles due to its release from the inhibitory inputs of both the Pn. C and the vagi nerves. Such pattern of breathing cannot maintain life and leads to death due to asphyxia.

# THE INTRAPLEURAL AND INTRATHORACIC PRESSURES

❑ The intrapleural pressure (IPP) is the pressure inside the pleural cavity. It is normally negative (i.e. *subatmospheric*) during eupnea and it becomes *more negative during inspiration*.

❑ Such negativity is due to the *elastic properties of both the lungs and chest wall* as follows :

**1. The elastic property of the lungs :** This is due to the elastic elements in the lungs, the elastin & collagen fibres (1/3) and the surface tension of the fluid layer that lines the alveoli (.2/ 3 ).

❑ It tends to decrease the lung's volume, thus pulling the visceral pleura inwards.

2. The elastic property of the chest wall This tends to expand the thoracic cage, thus *pulling the parietal pleura outwards*

□ These opposing forces result in continuous pulling of the 2 pleural layers apart from each other which creates an equal negative pressure in both the pleural & chest cavities

## SIGNIFICANCE (IMPORTANCE) OF THE IPP NEGATIVITY

1. It prevents collapse of the lungs and keeps them inflated.
2. It helps lung expansion during inspiration (which decreases the work of breathing)
3. It helps the venous return by the *thoracic pump*.
4. It helps lymph drainage through the thoracic lymph ducts.
5. It increases the blood flow in the pulmonary vessels.

## NORMAL VALUES OF THE IPP

❑ The IPP varies with the body position as well as in the different parts of the pleural cavity due to the *effect of gravity*

❑ The following are the average normal values *in the standing position* .

1. In the **midthoracic position** (after a normal expiration), the IPP averages -4 or- 5 cm H<sub>2</sub>O (about -3 mmHg), varying from - 2.5 cm H<sub>2</sub>O in the lung bases to - 10 cm H<sub>2</sub>O in the lung apices

2. **During normal inspiration**, the IPP decreases to - 7.5 or- 8 cm H<sub>2</sub>O (about -6 mmHg) due to the increase in the lung recoil forces.

3. During forced inspiration , the IPP decreases to about - 40 cm H<sub>2</sub>O, i.e. about- 30 mmHg, and is further decreased on performing the *Muller's maneuver* (= forced inspiration against a closed glottis)

4. During forced expiration, the IPP increases and becomes positive at the lung bases, and is further increased on performing the *Valsalva's maneuver*(= forced expiration against a closed glottis).