NERVOUS REGULATION OF THE CIRCULATION

- Nervous control affects more global functions, such as redistributing blood flow to different areas of the body, increasing pumping activity of the heart and especially, providing very rapid control of arterial pressure
- Nervous system control of the circulation occurs almost exclusively through the autonomic nervous system
- Parasympathetic contributes specifically to regulation of heart function, but only plays a minor role in regulation of the circulation
    - Controls heart rate via vagal stimulation of the SA node
    - Results in decreased heart rate and decreased contractility
- **Parasymp has big control of heart, but minimal control of BVs (TPR)**

AUTONOMIC NERVOUS SYSTEM:

- SYMPATHETIC NERVOUS SYSTEM ANATOMY:
    - Vasomotor nerve fibres leave the spinal cord through all the thoracic and the first one or two lumbar spinal nerves
    - Pass immediately into a sympathetic chain
    - Pass by two routes into the circulation
        - Through **specific sympathetic nerves** that innervate mainly the vasculature of the internal viscera and the heart
        - Via **spinal nerves** which are then distributed to the vasculature of the peripheral areas
    - Sympathetic outflow goes to all blood vessels **except** the **capillaries, precapillary sphincters** and most of the metarterioles
    - **I.e. no sympathetic control of capillaries and precapillary sphincters**
    - Innervation of the small arteries and arterioles allows increase resistance and thereby decrease the rate of blood flow
    - Innervation of the large vessels, particularly the veins, allows translocation of blood from these reservoirs back to the heart and resultant increase in cardiac output

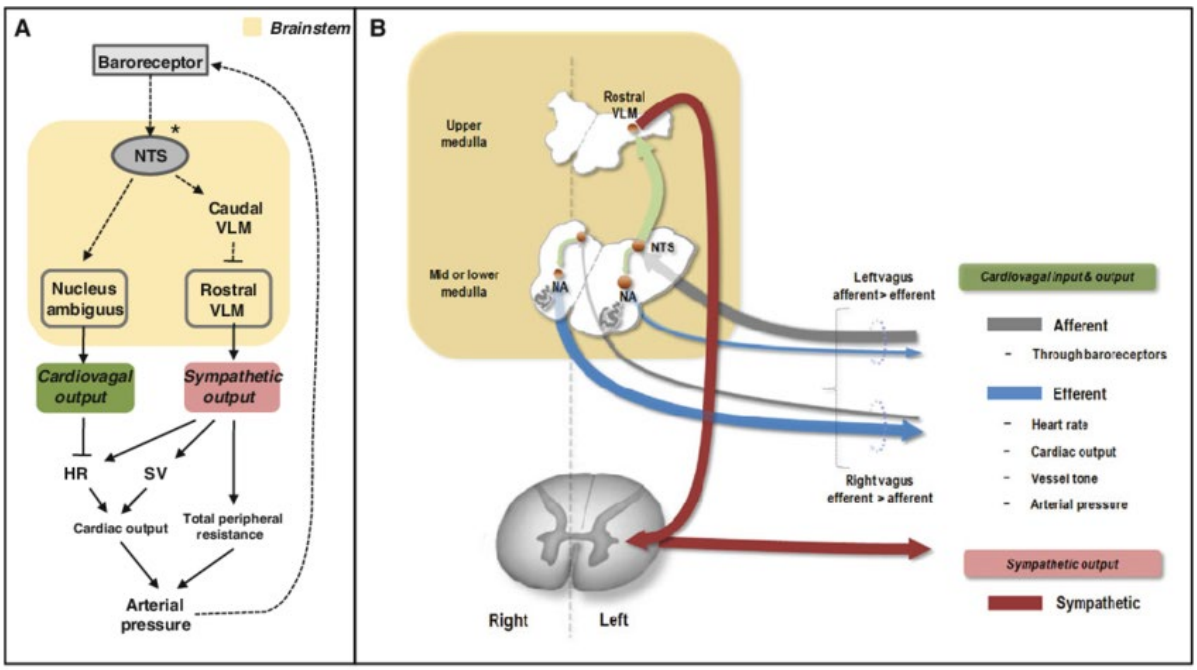
- SYMPATHETIC VASOCONSTRICTOR SYSTEM:
    - SNS carries huge numbers of vasoconstrictor fibres and only a few dilator fibres
    - Unequal distribution throughout tissues
        - Especially powerful in the gut, kidneys, skin and spleen
        - Much less potent in skeletal muscles and brain

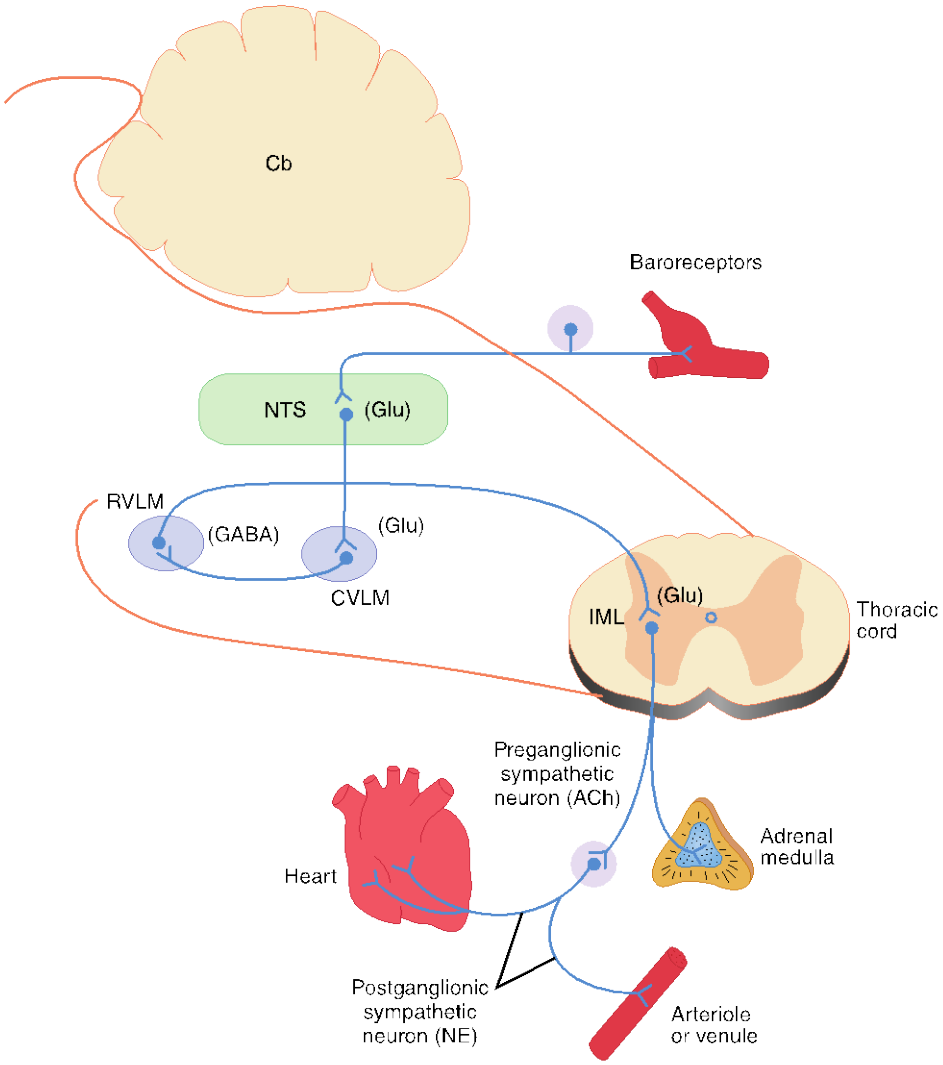
- VASOMOTOR CENTRE:
    - Located bilaterally mainly in the reticular substance of the medulla and the lower third of the pons

- **Vasoconstrictor area:**
  - Located bilaterally in the anterolateral portions of the upper medulla **(RostoVLM)**
  - Excite vasoconstrictor neurons at all levels of the spinal cord
- **Vasodilator area:**
  - Located bilaterally in the anterolateral portions of the lower half of the medulla **(caudal VLM)**
  - **Caudal VLM (vasodilator area) inhibits the RVLM (vasoconstrictor area).**
- **Sensory area:**
  - Located bilaterally in the **nucleus tractus solitaries** (NTS) in the posterolateral portions of the medulla and lower pons
  - Receive sensory **nerve signals mainly through the vagus and glossopharyngeal nerves**
  - Output signals control activities of both areas above
  - Involved in reflex control of the circulation (e.g. baroreceptor reflex)

NTS = sensory area (CNIX, X afferents)
CVLM = vasodilator (inhibits RVLM)
RVLM = vasoconstrictor (⇑sympathetic output via IML column of T-L spine)
NA = parasymp efferents (X)

In this system excitatory = glutamate, inhibitory = GABA

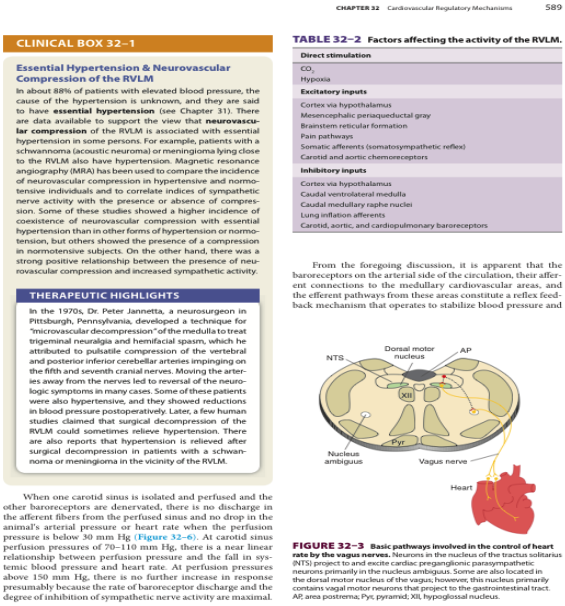




- VASOCONSTRICTOR TONE:
  - Continuous partial constriction normally caused by sympathetic vasoconstrictor tone
  - Aka VASOMOTOR TONE
- VASOMOTOR CENTRE CONTROL OF HEART:
  - Lateral portions of the vasomotor centre transmit excitatory impulses through sympathetic nerve fibres to increase heart rate and contraction
  - Medial portions, which lie in immediate apposition to the dorsal motor nucleus of the vagus nerve, transmit signals to decrease heart rate and contraction
- HIGHER CENTRE CONTROL OF VASOMOTOR CENTRE:
  - **Reticular substance of the pons**

- Hypothalamus
- Motor cortex ->excitation
- Anterior temporal lobe, orbital area of frontal cortex, anterior cingulate gyrus, amygdala, septum, hippocampus

- NORADRENALINE:
  - The substance that is released at sympathetic nerve endings
  - Acts directly on the alpha receptors of the vascular smooth muscle to cause vasoconstriction
  - Adrenal medulla stimulation results in release of both adrenaline and noradrenaline



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CLINICAL BOX 32–1

Essential Hypertension & Neurovascular Compression of the RVLM

In about 88% of patients with elevated blood pressure, the cause of the hypertension is unknown, and they are said to have **essential hypertension** (see Chapter 31). There are data available to support the view that **neurovascular compression** of the RVLM is associated with essential hypertension in some persons. For example, patients with a schwannoma (acoustic neuroma) or meningioma lying close to the RVLM also have hypertension. Magnetic resonance angiography (MRA) has been used to compare the incidence of neurovascular compression in hypertensive and normotensive individuals and to correlate indices of sympathetic nerve activity with the presence or absence of compression. Some of these studies showed a higher incidence of coexistence of neurovascular compression with essential hypertension than in other forms of hypertension or normotension, but others showed the presence of a compression in normotensive subjects. On the other hand, there was a strong positive relationship between the presence of neurovascular compression and increased sympathetic activity.

THERAPEUTIC HIGHLIGHTS

In the 1970s, Dr. Peter Jannetta, a neurosurgeon in Pittsburgh, Pennsylvania, developed a technique for "microvascular decompression" of the medulla to treat trigeminal neuralgia and hemifacial spasm, which he attributed to pulsatile compression of the vertebral and posterior inferior cerebellar arteries impinging on the fifth and seventh cranial nerves. Moving the arteries away from the nerves led to reversal of the neurologic symptoms in many cases. Some of these patients were also hypertensive, and they showed reductions in blood pressure postoperatively. Later, a few human studies claimed that surgical decompression of the RVLM could sometimes relieve hypertension. There are also reports that hypertension is relieved after surgical decompression in patients with a schwannoma or meningioma in the vicinity of the RVLM.

When one carotid sinus is isolated and perfused and the other baroreceptors are denervated, there is no discharge in the afferent fibers from the perfused sinus and no drop in the animal's arterial pressure or heart rate when the perfusion pressure is below 30 mm Hg (Figure 32–6). At carotid sinus perfusion pressures of 70–110 mm Hg, there is a near linear relationship between perfusion pressure and the fall in systemic blood pressure and heart rate. At perfusion pressures above 150 mm Hg, there is no further increase in response presumably because the rate of baroreceptor discharge and the degree of inhibition of sympathetic nerve activity are maximal.

TABLE 32–2 Factors affecting the activity of the RVLM.

Direct stimulation
CO_2
Hypoxia
Excitatory inputs
Cortex via hypothalamus
Mesencephalic periaqueductal gray
Brainstem reticular formation
Pain pathways
Somatic afferents (somatosympathetic reflex)
Carotid and aortic chemoreceptors
Inhibitory inputs
Cortex via hypothalamus
Caudal ventrolateral medulla
Caudal medullary raphe nuclei
Lung inflation afferents
Carotid, aortic, and cardiopulmonary baroreceptors

From the foregoing discussion, it is apparent that the baroreceptors on the arterial side of the circulation, their afferent connections to the medullary cardiovascular areas, and the efferent pathways from these areas constitute a reflex feedback mechanism that operates to stabilize blood pressure and

FIGURE 32–3 Basic pathways involved in the control of heart rate by the vagus nerves. Neurons in the nucleus of the tractus solitarius (NTS) project to and excite cardiac preganglionic parasympathetic neurons primarily in the nucleus ambiguus. Some are also located in the dorsal motor nucleus of the vagus; however, this nucleus primarily contains vagal motor neurons that project to the gastrointestinal tract. AP, area postrema; Pyr, pyramid; XII, hypoglossal nucleus.

RVLM

- Direct stimulation:
  - ⇑CO2
  - ⇓O2
- Excitatory inputs:
  - Peripheral **chemoreceptors**
  - Higher centres
- Inhibitory inputs:
  - Baroreceptors
  - CVLM
  - Lung inflation afferents (??)

RAPID CONTROL OF BLOOD PRESSURE:

- Most important function of nervous control of the circulation is its capability to cause **RAPID** increases in arterial pressure
- For this to occur, three major changes occur simultaneously:
    - Almost all arterioles of the body are constricted, increasing TPR
    - Veins and other large vessels are constricted, enhancing venous return and thus increasing cardiac output
    - The heart itself is directly stimulated by the autonomic nervous system, further enhancing cardiac contractility and output

- EFFECT OF EXERCISE:
    - At the same time as motor areas of nervous system are activated in exercise**, RAS of the brain stem is also activated**, greatly increasing stimulation of the vasoconstrictor and cardioaccelatory areas of the vasomotor centre **(RVLM)**
    - Local blood flow also increased by local vasodilation caused by increased metabolism of the muscle cells

REFLEX MECHANISMS FOR MAINTAINING NORMAL ARTERIAL PRESSURE:

- BARORECEPTOR REFLEXES:
    - Initiated by stretch receptors (BARORECEPTORS) located in the walls of several large systemic arteries
    - Rise in pressure -> stretch of baroreceptor -> CNS -> feedback signals to reduce arterial pressure downward
    - Baroreceptors located extremely abundantly in:
        - CAROTID SINUS (carotid sinus nerve → IX):
            - Wall of **ICA** slightly above bifurcation
            - **Hering's nerve (aka carotid sinus neve)→ CN IX → NTS**
        - WALL OF AORTIC ARCH (X):
            - Signals carried through the **vagus** into same area of medulla
    - BARORECEPTORS RESPOND TO CHANGES IN PRESSURE:
        - Carotid sinuses are NOT stimulated until pressures greater than 50mmHg
        - Reach a maximal response at about 180
        - Aortic arch respond similarly, but 30mmHg higher
        - Carotid sinuses more sensitive
        - Optimal operating range around 100mmHg, meaning even a slight change in pressure causes a strong change in the baroreceptor response
        - RESPOND to **CHANGES** in pressure rather than stationary pressure

- THE REFLEX:
  - Baroreceptor signal carried to **NTS** (via IX, X)
  - **Signals to vasodilator centre (CVLM) → inhibition of vasoconstrictor centre (RVLM).**
  - **NTS also activates vagal parasympathetic centre (NA)**
  - NET EFFECT: ⇑parasymp, ⇓symp
    - VASODILATION
    - DECREASED HEART RATE AND CONTRACTILITY
    - DECREASED ARTERIAL PRESSURE
  - CONVERSELY, LOW PRESSURE HAS THE OPPOSITE EFFECT
    - Reduced carotid sinus pressure -> decreased baroreceptor activity -> decreased inhibitory effect on the vasomotor centre->increased HR, vasoconstriction -> increased BP
- Very important during changes in body posture:
  - On standing, falling pressure at the baroreceptors elicits an immediate reflex, resulting in strong sympathetic discharge throughout the body
- ALSO CALLED BUFFER NERVES:
  - Maintain blood pressure at near constant levels throughout the day
  - NOTE:
    - Big fluctuations in denervated individuals
- RESETTING OF BARORECEPTORS:
  - Baroreceptor control is of little or no importance in long-term control
  - Baroreceptors reset themselves in 1-2 days regardless of whatever pressure they are exposed to.
  - If BP increased acutely -> initially receptors fire off numerous impulses
  - Rate of firing diminishes considerably and eventually ceases, despite continued elevation of BP

- **CHEMORECEPTOR REFLEXES:**
  - Reflex similar to baroreceptors, except initiated by chemoreceptors
  - **CHEMORECEPTORS** PRESENT IN:
    - **Carotid bodies** (each bifurcation)
    - **Aortic bodies**
    - Peripheral chemoreceptors excited by:
      - **⇓O2**
      - **⇑CO2**
      - **⇑hydrogen ions (acidosis)**
    - Pass through Hering/Vagus nerve into vasomotor centre

- If arterial pressure drops below critical level, above stimuli result in chemoreceptor activation, excite vasomotor centre and elevates arterial pressure back to normal
  - Not stimulated until the arterial pressure drops below 80mmHg
- **I.e. chemoreceptors feed into vasomotor areas and contribute to BP control (sympathetic stimulation)**
- **Are activated at pressures lower than baroreceptors (i.e. only come into play at lower BP)**

Baroreceptor activation → ⇓Symp
Chemoreceptor activation → ⇑Symp

ATRIAL AND PULMONARY ARTERY REFLEXES:

- **Low pressure receptors**
- Especially important in minimising arterial pressure changes in response to changes in **blood volume**
- Respond to **stretch**

- ATRIAL REFLEXES THAT ACTIVATE THE KIDNEYS:
  - Also causes very significant reflex dilation of the afferent arterioles in the kidneys
    - Causes glomerular capillary pressure to rise, with resultant increase in filtration of fluid into the kidney tubules
  - Transmitted simultaneously from the atria to the hypothalamus to decrease the secretion of ADH
    - Reduces an increased blood volume back toward normal
    - Also atrial stretch elicits a hormonal effect on the kidneys via ANP, further fluid loss
  - **ATRIAL STRETH →**
    - **⇑HR** (Bainbridge reflex via vagal afferents to medullary vasomotor)
    - **⇑ANP (humoral)**
    - **⇓ADH (neural)**
    - **⇑GFR (neural)**

  - **ANP effects:**
    - Natriuresis + diuresis:
      - ⇑GFR
      - ⇓Renin release
      - ⇓circulating angiotensin II
      - ⇓ circulating aldosterone
    - Systemic vasodilation

        - ⇓TPR (⇓afterload)
        - ⇓Venous return (⇓preload)

    - **BAINBRIDGE REFLEX:**
        - Increase atrial pressure also causes an increase in heart rate
            - Stretches SA node with increased HR
            - Additional 40-60% increase in HR caused by nerve reflex caused by Bainbridge Reflex
                - Atrial stretch receptors transmit afferent signals through vagus nerves to the medulla of the brain, then efferent signals to increase HR and prevents damming of blood in the veins
        - **⇑RA pressure → Bainbridge reflex → ⇑HR**

- **CNS ISCHAEMIC RESPONSE:**
    - When blood flow to the vasomotor centre in the lower brain stem becomes decreased severely enough to cause nutritional deficiency, that is, to cause cerebral ischaemia, the neurons in the vasomotor centre itself respond to the ischaemia and become strongly excited
    - Vasomotor ischaemia → ⇑⇑RVLM output
    - Believed to be related to slowly flowing blood to carry CO2 away from the vasomotor centre
    - Very great response
        - Can elevate the MAP for as long as ten minutes to as high as 250mmHg
        - Can sometimes be so intense that it decreases perfusion to peripheral organs
    - Does not become significant until the arterial pressure falls far below normal, down to 60mmHg and below, reaching its greatest at 15-20mmHg
    - EMERGENCY PRESSURE CONTROL SYSTEM
    - **CNS ischaemia due to very low BP → profound excitation of vasomotor area → ⇑⇑BP**

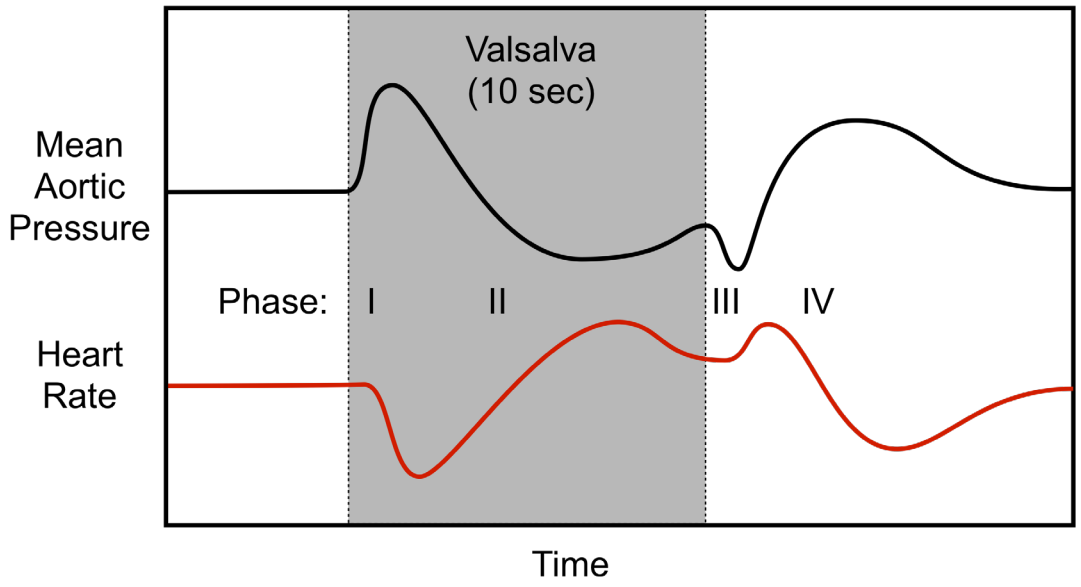
- CUSHING RESPONSE:
    - Special type of CNS ischaemic response that results from increased pressure of the CSF around the brain in the cranial vault
    - If CSF pressure equals systemic pressure ->occlusion of cerebral vessels ->initiates response that causes arterial pressure to rise, allowing cerebral blood flow to recommence
    - **Cushings reflex: ⇑ICP → ⇑BP, ⇓HR**

- ROLE OF SKELETAL NERVES AND MUSCLES:
    - Abdominal compression reflex
        - Whenever **sympathetic outflow is stimulated, nerve signals are transmitted simultaneously through skeletal somatic nerves to skeletal muscles, especially abdominal muscles**
        - Increased basal tone of these muscles, compresses all the venous reservoirs of the abdomen, helps to translocate blood out of the abdominal reservoirs into the heart
        - Results in increased CO and arterial pressure
        - **⇑Sympathetic outflow → concurrent ⇑ in somatic outflow to abdominal skeletal muscle → contraction of abdominal musculature → ⇑venous return**
    - Skeletal muscle contraction during exercise also compresses blood vessels increasing venous return and cardiac output

- RESPIRATORY WAVES IN ARTERIAL PRESSURE:
    - Inspiration → ⇓arterial BP
    - During each respiratory cycle, arterial pressure changes by 4-6mmHg in wavelike manner due to:
        - Impulses arising in the respiratory centre spill over into the vasomotor centre
        - On inspiration, thoracic cavity pressure becomes negative, causing expansion in thoracic cavity vessels, decreasing return to the left heart, decreasing cardiac output.
    - **Inspiration → small ⇓BP**
        - **Linking between central resp and vasomotor centres**
        - **Negative intrathoracic pressure (→ ⇑pooling of blood in pulmonary vessels and ⇓return of blood to LV)**

- **Pulsus paradoxus** is an abnormally large decrease in stroke volume, systolic blood pressure and pulse wave during inspiration.
- The normal fall in pressure is < 10 mmHg.

Testing baroreceptor reflex – VALSALVA



Start valsalva:

1. ⇑Thoracic pressure transiently ⇑ thoracic aortic pressure → ⇑ BP. Reflex ⇓HR
2. ⇓Venous return → ⇓BP. Reflex ⇑HR + ⇑TPR

Stop valsalva:

3. Transient ⇓BP when the person starts to breathe normally again, as the external compression on the aorta is removed. Reflex ⇑HR
4. ⇑BP due to
    a) restoration of venous return
    b) ⇑TPR which was a reflex during the valsalva

TABLE 32–3 Factors affecting heart rate.

Heart rate accelerated by:
Decreased activity of arterial baroreceptors
Increased activity of atrial stretch receptors
Inspiration
Excitement
Anger
Most painful stimuli
Hypoxia
Exercise
Thyroid hormones
Fever
Heart rate slowed by:
Increased activity of arterial baroreceptors
Expiration
Fear
Grief
Stimulation of pain fibers in trigeminal nerve
Increased intracranial pressure

Inspiration → ⇑HR but ⇓BP
Expiration → ⇓HR

Most pain → ⇑HR
But pain from trigeminal nerve fibres → ⇓HR

Grief → ⇓HR