Control of the airways is a complex process involving multiple pathways. Airway diameter is controlled by smooth muscle which has a variety of receptors responsive to neuronal stimuli, chemicals (e.g. adrenaline) and inflammatory mediators (e.g. prostaglandins). This tutorial explains briefly how neuronal control affects lung function.

How is lung function controlled?

Like other involuntary mechanisms in the body including those regulating the heart and gastrointestinal tract, breathing is controlled by the autonomic nervous system.1 This comprises two branches:

• The sympathetic branch is responsible for generating the ‘fight or flight’ response, which includes bronchodilation
• The parasympathetic branch maintains resting vagal tone and basal mucus production in the airways.1

On route to their effector organ, in this case the lungs, preganglionic autonomic nerve fibres from the central nervous system synapse with postganglionic efferent fibres in autonomic ganglia. Postganglionic fibres leaving these ganglia then carry impulses to the bronchial smooth muscle cells and/ or mucus glands in the lungs.

Stimulation of the sympathetic nervous system produces bronchodilation, while parasympathetic stimulation produces bronchoconstriction.1

Which neurotransmitters are involved?
The postganglionic neurotransmitter for the sympathetic nervous system is noradrenaline. Another name given to this branch of the autonomic nervous system is, therefore, the ‘adrenergic’ system. Because the main neurotransmitter for the parasympathetic system is acetylcholine, it is also known as the ‘cholinergic’ system and resting airway tone is termed ‘cholinergic’ tone.

How is the cholinergic system activated?
Cholinergic pathways may be activated by inflammatory mediators and by inhaled irritants such as tobacco smoke.1 This activation increases airway tone, producing reflex bronchoconstriction, and also stimulates mucus secretion – thereby decreasing air entry into the lungs.

Boehringer Ingelheim hold the copyright for these images which were developed with Professor P J Barnes for Boehringer Ingelheim

In the adrenergic, or sympathetic branch of the autonomic nervous system, postganglionic neurons release the neurotransmitter noradrenaline. This binds to and activates β2 adrenergic receptors on bronchial smooth muscle cells, thus acting as an ‘agonist’. The resulting effect is one of bronchodilation. In the cholinergic system, acetylcholine is released firstly at preganglionic synapses, where it activates postganglionic nerve fibres via M3 type cholinergic receptors (also known as ‘muscarinic’) and augments signal transmission.2 Subsequently, in response to this activation, acetylcholine is released also at postganglionic synapses with bronchial tissues. This latter release activates M2 cholinergic receptors in bronchial smooth muscle and mucus glands, producing bronchoconstriction and mucus secretion. In addition, acetylcholine agonism and activation of M2 autoreceptors located on the ends of postganglionic nerve fibres inhibits further acetylcholine release – a mechanism of autoregulation.2

www.COPDexchange.co.uk
How quick are the effects of autonomic stimulation?
The sympathetic nervous system is primarily reactive, so its effects happen quickly (‘fight or flight’). The parasympathetic nervous system is primarily regulatory, so its effects happen more slowly (‘rest and digest’).

What happens in COPD?
Normal airways have a small amount of resting vagal tone, but because in healthy people the airways are open and unblocked, this has no noticeable effect on airflow. In patients with chronic obstructive pulmonary disease (COPD), the effect of cholinergic tone is magnified because these individuals already have irreversibly narrowed airways. This resting vagal tone is the main reversible component determining airflow in COPD. This means that in patients with COPD, the effects of blocking acetylcholine-mediated parasympathetic nerve transmission are proportionally greater than they would be in healthy people.

What you need to know
Breathing and lung function are controlled by the autonomic nervous system which comprises two branches:

- The sympathetic branch, responsible for generating the ‘fight or flight’ response, which includes bronchodilation.
- The parasympathetic branch which maintains resting vagal tone and basal mucus production.

There are two principal neurotransmitters regulating autonomic function:

- The postganglionic neurotransmitter for the sympathetic branch of the autonomic nervous system is noradrenaline, hence another name for this system is the ‘adrenergic’ system.
- The main neurotransmitter for both the pre- and postganglionic portions of the parasympathetic system is acetylcholine; this branch is also known as the ‘cholinergic’ system.

Cholinergic control of the lungs regulates resting tone and response to irritants:

- Resting airway tone is also termed ‘cholinergic’ tone.
- The parasympathetic, or cholinergic, system is activated by inflammatory mediators and inhaled irritants like cigarette smoke; this process produces reflex bronchoconstriction and stimulates mucus secretion, decreasing airflow into the lungs.

In patients with COPD, baseline cholinergic airway tone has a proportionally greater effect than it does in healthy people:

- In healthy people the airways have a small amount of resting cholinergic tone, but because healthy airways are open and unblocked, this has no marked effect on airflow.
- In patients with COPD, the effect of cholinergic tone is magnified because the airways are already irreversibly narrowed.
- Because of this, blocking acetylcholine-mediated parasympathetic nerve transmission has a comparatively greater effect in COPD patients than in their healthy counterparts.

Think about...

- What is the impact of the cholinergic component of autonomic control of the lungs in your patients with COPD?
- How does it relate to their symptoms and what are the stimuli that might trigger these?
- Which types of treatment might be more effective in these patients?

References

GLOSSARY
Autonomic: describes the involuntary portion of the nervous system which controls the functioning of internal organs; bronchoconstriction: narrowing of the airway diameter due to tightening of surrounding smooth muscle; bronchodilation: opening of airway passages due to relaxation of surrounding smooth muscle; efferent: indicates nerve fibres originating in the brain and/or spinal cord and going towards the end organ; ganglia: plural of ganglion, being a collection of nerve cell bodies; neurons: nerve cells; neurotransmitter: a substance that transmits nerve signals across a synapse; synapse: the junction between the end of a neuron and either another neuron or a muscle or gland cell; vagal: relating to the vagus nerve, being a nerve involved in the parasympathetic control of the airways.