Cold and the Airways

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J. Regnard
Laboratoire de Physiologie, Faculté de Médecine, Besançon, France

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Abstract

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Physiological and pathological respiratory responses are triggered by various conditions of exposure to cold climates. Beside airway smooth muscle, both the pulmonary and the tracheobronchial vasculatures are major effectors of respiratory responses to cold. General exposure to cold causes pulmonary vasoconstriction known as "Raynaud's phenomenon of the lung" in subjects with primary Raynaud syndrome and favors acute pulmonary oedema in subjects with congestive heart failure. In healthy subjects acute hyperventilation of very cold air has led to acute respiratory failure closely similar to hypoxic pulmonary oedema. In outdoor exercising people years long repetition of hyperventilation of subfreezing air causes "eskimo lung" made of obstructive lung disease and increased wall thickness of pulmonary arteries. At a lesser degree hyperventilation of dry air cools the central airways and triggers subclinical bronchial obstruction in healthy subjects. In asthmatic subjects hyperventilation of dry air causes asthma attacks. Results of recent animal and human experiments point to a key role of mucosal vessels in thermal balance of the airways. Simultaneously, there is increasing evidence that hyperventilation-induced asthma is triggered by a thermal stimulus.

Key words

Cold, pulmonary circulation, Raynaud syndrome, bronchial reactivity

Conditioning Inspired Air: a Main Function of the Airways

The airway mucosa is directly exposed to the physical and chemical features of the atmosphere. In fact the airways are not only a passage for gas critical to respiratory function, but also a first line agent of protection of the body's integrity. Breathing in the cold requires both warming up and humidification of inspired air. In normal subjects, temperature of alveolar gas is 37 °C, even in very cold climates, and alveolar gas is fully saturated with water vapour for this temperature, i.e. there are 45 mg of water vapour per liter of alveolar gas, whatever the total barometric pressure e.g. at the summit of Mount Everest (ambient pressure = 1/3 of sea level barometric pressure) as well as in deep dives at a depth of 600 m of seawater (ambient pressure = 601 atmospheres). However, the water content of cold air is very low (less than 2 mg/l in subfreezing air). Thus inspired air has to be warmed and loaded with water vapour before reaching the alveoli. Heat and water vapour are provided by the walls of air passages. Mucosa of the nose is powerful for this purpose, and at rest, inspired air is almost completely conditioned before reaching the larynx. However during physical exercise and high levels of minute ventilation, narrow passages in the nose have a too large resistance to air flow and mouth breathing occurs. Although the mouth mucosa is very efficient in conditioning inspired air, complete conditioning is not performed at the glottis level so that incompletely conditioned air flows through trachea and the main bronchi. Therefore tracheobronchial walls have to cope with lowered temperatures and low water content, up to subsegmental bronchial divisions (14, 23). Depth and degree of cooling depend on both the level and duration of ventilation of dry air (22, 23). In normobaric and hypobaric conditions, most of the energy expenditure of the airway wall results from latent heat loss i.e. evaporation of water from the airway lining fluid (34). Convective heat loss becomes larger than evaporative only in hyperbaric atmospheres, or when helium or hydrogen replace nitrogen as dilutant in breathing mixtures. Both heat transferred to inspired gas and water of the airway lining fluid are provided through the airway epithelium by blood flow.

Tracheobronchial circulation: a Main Effector of Physiology and Physiopathology of the Airway

In the peripheral small bronchi branches of pulmonary arteries are closely parallel to bronchi in the same bundles, but in the central airways and even in segmental bronchi, most of mucosal blood flow is derived from the tracheobronchial circulation which spreads a dense capillary and venular subepithelial networks (9). At rest tracheobronchial blood flow is about 1 percent of cardiac output. In dogs and sheep thermal panting and hyperventilation of dry air increase tracheal blood flow (4, 28, 36). Circumstantial evidence that ventilation of dry air increases tracheobronchial blood flow has also been obtained in humans during cardiopulmonary by-pass (1). Vasomotor control in the airway mucosa is mediated by the parasympathetic and sympathetic nerves in the airways, and neuropeptides such as Substance P and Calcitonine Gene Related Peptide (CGRP) seem to be potent vasodilators (21). Also inhaled substances (e.g. histamine, methacholine, noradrenaline, methoxamine) or substances locally released (e.g. prostaglandins and mediators of inflammatory cells) act on bronchial blood flow.

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Vasodilatation of bronchial vessels has been shown to cause thickening of the airway mucosa, whereas vasoconstriction reduces thickness of the airway wall (16, 20). Therefore, vasodilatation of the tracheobronchial bed is an essential factor of airway obstruction in allergenic bronchial provocation (24, 29), when inflammatory state is underlying bronchial responses to various stimuli, e.g. exercise-induced asthma. Because intra-parenchymatous bronchial blood flow drains into the left heart through pulmonary veins, haemodynamic conditions such as left ventricular failure also result in congestion of tracheobronchial vasculature and cause bronchial hyperresponsiveness (6). Blood flow of the trachea and main bronchi drain into the right atrium through the azygos vein, which might result in congestion of the airway wall when right heart filling is increased and right atrial and arterial pulmonary pressures are increased. There is indirect evidence that vasodilatation in the airway mucosa contributes to exercise-induced airway obstruction, which can be more or less prevented by inhalation of a vasoconstrictor agent prior to bronchial challenge (10). However, the interplay of blood flow in the airways and the airway patency is more complicated than a simple geometrical effect on the thickness of the airway wall (19, 31).

Beside its nutrient role to bronchial walls and large pulmonary arteries, and beside its contribution to water balance in the airway lumen and to secretion of mucus, bronchial circulation likely fulfills other functions. For example, subepithelial bronchial blood flow is likely to wash out inhaled or locally released substances and, hence, play a crucial role in duration or intensity of their effects (8, 35).

Tracheobronchial Blood Flow and Cold-Related Airway Diseases

Cold is related to various acute or long term diseases of the airways (18). General exposure to cold exacerbates chronic bronchitis, triggers Raynaud's phenomenon of the lung, i.e. constriction of the pulmonary arteries and reduction of pulmonary blood volume in subjects with primary Raynaud phenomenon (11). Breathing very cold air at very high ventilation levels has led to acute pulmonary oedema or to "frozen lungs". As already mentioned tracheobronchial blood flow increases on breathing dry air or cooling the airways (1, 3, 28, 32). It has not been established if vasodilatation still occurs when very cold air is inhaled at very high ventilation rates, or if some vasoconstrictive response takes place at lower temperatures as it happens in the skin. However, vasodilatation if it occurs in the airway wall when breathing dry or cold gases is likely to protect the airways by somehow reducing or delaying the cooling effect of hyperventilation (Fig. **1**). Conversely, experiments in dogs have shown that intraparenchymal bronchial blood flow decreases when lung temperature is low (2). It is therefore tempting to speculate that in subjects who repeatedly hyperventilate very cold air, repeated episodes of decreased bronchial blood flow can lead to alterations in walls of bronchi and of pulmonary arteries, leading to the faster than average decrease of lung function and increased thickness of walls of pulmonary arteries ("Eskimo lung" [33]).

Much more commonly, exercise-induced asthma is triggered by hyperventilation of dry air. Although very high levels of ventilation of dry air can cause a slight decrease of FEV_1 in healthy subjects (27), airway obstruction is much larger in asthmatic subjects, partly because of the many inflammatory cells which are likely to release large quantities of various mediators in the airway mucosa of these subjects, and partly because nerve endings are largely exposed due to damage of the epithelial covering of airways. We reasoned that increasing the blood content in the airways during hyperventilation of dry air might delay cooling of the airway wall and hence decrease the thermal stimulus acting on nerve endings and causing release of inflammatory mediators. Indeed, performing external compression of the lower limbs to venous occlusion pressure in the mid-course of hyperventilation challenge largely blunted post-hyperventilation airway obstruction in 8 of 10 asthmatic subjects (30), an effect related to the rise in intra-airway temperatures immediately following leg compression i.e. increase in thoracic blood volume (13). Exercise-induced asthma is less frequent or less severe during swimming than during terrestrial exercising (5, 12). During immersion and swimming the thoracic blood volume is increased, and pressures are increased in right and left atria as well as in pulmonary arteries (7, 17, 26). Since bronchial vessels and pulmonary vessels communicate (9) immersion is likely to increase blood content not only in the pulmonary vessels but also in the tracheobronchial wall. Thus, a decrease in thermal stimulation related to some degree of pulmonary congestion might explain, at least partly, the lesser incidence of asthma during swimming. Finally, if vasomotor control of tracheobronchial vessels is similar to vascular control in skin vessels, i.e. in other systemic vessels also exposed to environmental conditions, it might happen that vasoconstriction is decreased as an habituation response to cold exposure. This kind of vascular adaptation is well documented in the hands of fishermen and of people living in the cold (25). If such an habituation occurs in the airways mucosa, it may contribute to the decreased obstructive effect of hyperventilation of cold air in asthmatic subjects who underwent repeated challenges (15).

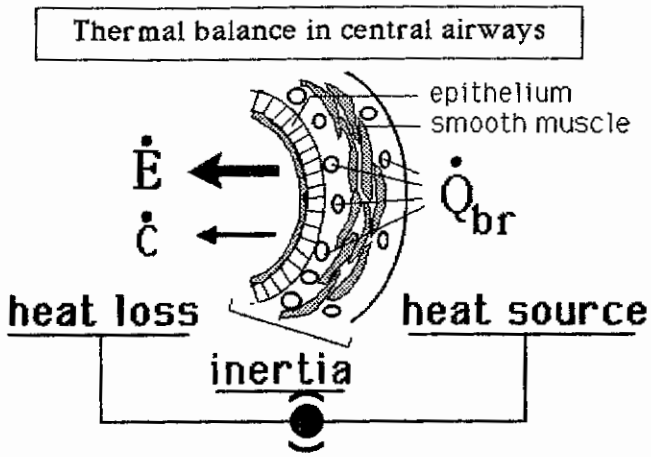

Fig. 1 Cooling of the airway wall results from evaporation of water from lining fluid of the airways (E) and also slightly from convection (C). Heat content of the wall opposes inertia to cooling, whereas blood flow in tracheobronchial vessels (Qbr) brings new heat.

In conclusion, the anatomical situation of tracheobronchial circulation promotes its key role in airway responses to cold exposure.

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J. Regnard

Laboratoire de Physiologie
Faculté de Médecine
F-25030 Besançon
France