## Alveolus Micro Anatomy

Advanced, Organ-Based and Clinical Sciences

The average alveolar diameter is between 0.05 to 0.33 mm, with the largest alveoli at the pulmonary apex and the smallest at the base when in the upright position. The walls of the alveoli are asymmetrically arranged. Gas exchange occurs on the thin side of the alveolar epithelium. The thick side of the alveoli is where fluid and solute exchange occurs, and also provides structural support for the alveolus. Gas exchange occurs between the alveolar epithelium and capillary epithelium which are separated only by their respective cellular and basement membrane. On the thick side, the alveolar and capillary endothelium are separated by the pulmonary interstitial space which is made up for elastin, collagen and possibly nerve fibers.

The pulmonary epithelium contains two main cell types. Type I pneumocytes, which are flat, form tight junctions with one another that prevent the passage of large oncotically active molecules into the alveolus (i.e. albumin). Type II pneumocytes are much more numerous than Type I pneumocytes, and are round cells that contain cytoplasmic inclusions called lamellar bodies, which contain surfactant. Unique to type II pneumocytes is the ability to divide and produce type I pneumocyte if need be. Additionally, they are resistant to O2 toxicity.

### Sources

Morgan and Mikhail's Clinical Anesthesiology 5th Edition.

**48%**

Answered correctly

**2020**

Year asked

## Glycocalyx layer: Function

Advanced, Organ-Based and Clinical Sciences

The glycocalyx is a complex layer between the endothelium and flowing blood. It is composed mostly of glycoproteins and proteoglycans. Proteoglycans have a protein core which is attached to negatively charged GAG (glycosaminoglycan) side chains. There are 5 types of GAG side chains, of which heparin sulphate makes up 50-90% of

the chains.  The glycocalyx layer regulates interactions between endothelial cells and blood cells, vascular permeability, coagulation and thrombosis, and vascular tone.

● The glycocalyx modulates blood viscosity and hematocrit in the microcirculation. It repels red blood cells from the endothelium and shields it from leukocyte and platelet interactions.

● The glycocalyx also plays a large role in hydrostatic and oncotic pressure gradients between the blood vessel lumen and interstitial space. Disrupting the glycocalyx layer results in increased hydraulic conductivity, anionic protein flux, and fractional filtration of albumin.

● The glycocalyx facilitates an antithrombotic surface through the binding of AT III. The anticoagulant activity of ATIII is also enhanced by the GAG side chain heparan sulphate.

● The glycocalyx also regulates vascular tone in response to shear stress. Movement of the glycocalyx cytoskeleton transduces mechanical stimuli into intracellular signals that results in vasodilation mediated by endothelial nitric oxide release.

● The glycocalyx layer can be damaged by hypervolemia, hyperglycemia, ischemia-reperfusion, inflammation, sepsis, or bypass surgery. Damage to this layer can result in platelets aggregation, leukocytes adhesion, and a prothrombotic state. Damage will also cause increased vascular permeability leading to interstitial edema and diminished vascular responses to shear stresses.

## Sources

## Alveolar gas equation: Altitude

Advanced, Clinical Sciences: Anesthesia Procedures, Methods, and Techniques, Statistics

The alveolar gas equation estimates alveolar oxygen content given a few readily measurable variables. The pAO2 derived from performing the calculation can then be used to discern the degree of shunt present in a patient. Practical simplification of the complex formula allows for the following equation:

$pAO_2 = FiO_2 (Patm – pH20) – (paCO_2/RER)$

Where in the average person the respiratory exchange ratio (RER) (or respiratory quotient) is typically considered to be 0.8 (varies depending on the diet and primary source of fuel the patient is utilizing such as fat, protein or carbohydrates)

At sea level, the atmospheric pressure is 760 mmHg and the vapor pressure of water at body temperature is 47 mmHg. Plugging these rough numbers into the aforementioned equation leads to the following simplification at sea level:

$pAO_2 = (FiO_2 \times 713\ mmHg) - (paCO_2/0.8)$

Given that increasing altitude decreases the atmospheric pressure, for any given $FiO_2$ you would expect a lower $pAO_2$ and, consequently, a lower $paO_2$. For example, whereas breathing 100% oxygen at sea level would result in an alveolar $pO_2$ of 663 mmHg, breathing 100% oxygen on Mt. Everest at a barometric pressure of 263 mmHg would result in a $pAO_2$ of 166 mmHg (assuming the $pH_2O$, $paCO_2$ and RER to be the same). This results in hypoxia which triggers all manner of physiologic changes that can include but are not limited to: respiratory alkalosis (as seen in acute mountain sickness), mental status changes, increased heart rate and cardiac output, decreased systemic vascular resistance, pulmonary vasoconstriction/hypertension (as seen in chronic mountain sickness with potential evolution of cor pulmonale), and cerebral edema, among others.

Conversely, increasing the barometric pressure can have significant effects by increasing the amount of dissolved oxygen. It is for this reason that hyperbaric oxygen therapy has been implemented for the treatment of nonhealing wounds, decompression sickness, and carbon monoxide poisoning, among others.

Though not specific to altitude necessarily, the alveolar gas equation illustrates that, by definition, hypoventilation (and increases in $PaCO_2$) will result in a relative hypoxemia given all other variables in the equation are held steady. For any given patient, this fact may or may not have any clinical relevance.

Most variable bypass canisters can compensate for adjustment in atmospheric pressure automatically. So you will not have to adjust the percent concentration for isoflurane or sevoflurane at different altitudes. The partial pressure of the anesthetic gases will remain the same.

However, you will have to make adjustments for desflurane. The percent of desflurane delivered will not change with altitude, but the partial pressure will. A desflurane vaporizer is kept at a constant temperature (39 degrees Celsius) which maintains a constant vapor pressure of 2atm. At higher altitudes, the total pressure decreases. Dalton’s law states that the total pressure equals the sum of the partial pressures, so if the percent concentration is constant, the partial pressure will decrease proportionally at a lower atmospheric pressure. Because potency of an anesthetic agent is related to its partial pressure rather than its percent

concentration, you would need to increase the dial of percent concentration of a volatile anesthetic to achieve the same MAC at a higher altitude.

Required dial setting = desired % x (760mmHg/current atmospheric pressure)

### Sources


Barash, Clinical Anesthesia, 6th edition, pp. 414-416, 667-668.

Dorsch, Understanding Anesthesia Equipment, 5th edition, pp. 122-169.

Miller, Miller's Anesthesia, 6th edition, p. 291.


## *Critical temperature: Nitrous oxide*

Nitrous Oxide is an anesthetic gas with a low potency with a MAC value of 104%. It is commonly used during mask inductions in pediatric patients, as an adjunct for labor analgesia, and in dentistry offices for conscious sedation. Among anesthetic gases, it has a unique physical chemical profile.

**Triple Point:** -90.82° C

The triple point of a substance is that at which it can exist in a solid, liquid and gaseous phase depending on the pressure or lack thereof applied (i.e. this is the freezing, boiling and sublimation point)

**Critical Temperature:** 36.37° C

The critical temperature of a substance is that at which it can no longer be converted from a gas to a liquid no matter the pressure applied to it.

In between these two temperatures, nitrous oxide can exist as a liquid or a gas depending on the pressure applied. Immediately below to the critical point, nitrous will boil at 1050.1 PSI (71.45 ATM) – above this pressure, nitrous oxide exists as a liquid; however, above this temperature, no matter the pressure applied, nitrous oxide is a gas. With such a low critical temperature, nitrous oxide cylinders have the potential for explosion if heated or handled improperly.

# Nitrous oxide: Closed spaces

*Basic pharmacokinetic principles*

- NO has a blood:gas partition ratio of 0.47 and is thus 30 times more soluble in blood than nitrogen, which has a blood:gas partition ratio of 0.015
- Thus, NO accumulates in closed gas spaces that contain N2 faster than the N2 can diffuse out. In other words, the highly blood soluble NO is brought to the space faster than the poorly soluble N2 can be carried away from the space.
- Volume of distensible space will increase until the NO concentration in the space is equal to the concentration in the alveoli and blood concentration in volume percent
- As a consequence, an alveolar concentration of 50% might double the gas space volume and 75% might quadruple the volume
- This phenomenon is time-dependent based on the location of the air space

*Closed gas spaces*

- Compliant spaces
    - Pneumothorax – increased volume from NO diffusion into the air space can impair cardiorespiratory function, use of NO is thus contraindicated in presence of pneumothorax
    - Air embolism – expansion in blood occurs rapidly (seconds vs. minutes), increased risk in procedures at risk for embolism (posterior fossa craniotomies, laparoscopy), if suspect air embolism must discontinue NO immediately
    - Equipment cuffs – increased ETT cuff volume can lead to increased pressure on tracheal mucosa, increased volume in catheters (Swan-Ganz) can cause issues if in the pulmonary artery etc., increased volume in LMA will increase volume and exert pressure on surrounding tissue

    - Other compliant spaces include bowel gas (especially in setting of obstruction), pneumoperitoneum
- Noncompliant spaces
    - Middle ear – can cause adverse effects on hearing after tympanoplasty
    - Pneumocephalus – following dural closure or pneumoencephalography, leads to increased ICP

# Nitrous oxide: bowel distention

**Definition**

Nitrous oxide will move into air-filled cavities in the body that normally contain nitrogen; so as nitrous oxide transfers from the blood into the space, nitrogen transfers out. However, nitrous oxide is 34 times more soluble than nitrogen in blood. Thus, substantial quantities of nitrous oxide leave the blood and enter the bowel, but not much nitrogen can leave the bowel to enter the blood. The result is that during exposure to nitrous oxide, like in other compliant spaces, the volume of gas in the bowel increases. The amount of the increase depends on the alveolar partial pressure of nitrous oxide, the intestinal blood flow, and the duration of nitrous oxide administration.

It has been calculated that the volume of and enclosed air pocket can be doubled be inhalation of by 50% N2O and quadrupled by inhalation of 75% N2O after several hours.

# Aspiration mgmt: LMA

The patient should be placed in the head-down position, oxygen 100% administered, anesthesia deepened, suctioning performed and the severity of the regurgitation/aspiration event assessed fibreoptically. The decision about whether to intubate the trachea or continue with the LMA will depend on how well the LMA is functioning, the severity of the regurgitation/aspiration event and the anticipated risk of further regurgitation/aspiration. Removal of the LMA may result in further regurgitation and consideration should be given to intubating the patient fibreoptically via the LMA. Consideration should also be given to passing a gastric tube, but this may also provoke further regurgitation.

**Updated definition 2020:**

• GI Risks: known or suspected full stomach, hiatal hernia, GERD, bowel obstruction, known or risk factors for delayed gastric emptying.

• Airway Risks: poor lung compliance, high airway resistance, glottic or subglottic obstruction, small mouth opening (<1.5cm).

• Signs of Aspiration? What Now!?

o Increase FiO2

o Deepen anesthetic

o Place the patient in head-down position

o Suction/NGT

o +/- Intubation

o Assess severity and potentially remove particulate matter with fiberoptic bronchoscopy

o PEEP

o +/- Bronchodilators if bronchospasm has been induced or is suspected.

• Should you intubate!? The decision to intubate may be appealing in order to secure the airway and allow for more advanced ventilation. While it may prevent aspiration of additional gastric contents, any contents that have already been aspirated may be introduced further into the airway. Ultimately, this decision should be made based on careful clinical assessment of patient and situation. If the decision to intubate is made, consider adding PEEP ton improve oxygenation by opening distal airways.

Delivering PEEP through an unprotected airway could increase the risk for further aspiration.

• Outcomes: Most patients that aspirate will be asymptomatic. Of those who develop symptoms, non-invasive or invasive ventilation may be temporarily required, and mortality is ~10%. Longer duration of ventilation is associated w/ higher mortality.

• What NOT to do...

o Bronchial lavage. May flush aspirate further into the lungs.

o Empiric antibiotics.  Has been shown to increase the risk of developing ventilator acquired pneumonia.

o Empiric corticosteroids. Has been shown to increase mortality in critically ill patients.

## Sources


Keys to the Cart: January 16, 2017; A 5-minute video review of ABA Keywords

Artime CA, Hagberg CA. (2020). Basic Principles of Pharmacology. In Groper MA (Eds). Miller's Anesthesia (9th edition). Elsevier Inc. 44, 1373-1412.e7.


# *Corneal reflex.*

Overview

The corneal reflex plays an important role in the evaluation of a comatose patient particularly in the neurocritical care setting. This brainstem reflex is used for determination of neurological prognosis in cardiac arrest survivors and for the determination of brain death in those with irreversible, catastrophic brain death. The test is ideally performed between the limbus and central cornea while avoiding the central field of vision (See Figure). The test can be performed with a puff of air or water but is most specific with a cotton-tipped swab. The test assesses the integrity of trigeminal nerve (afferent pathway) and the facial nerve (efferent pathway).

Anatomy

Afferent Limb

The afferent pathway of the reflex is via the nasociliary branch of the ophthalmic division (V1) of the trigeminal nerve (CN V). Multiple receptor types are present on the cornea and contribute to the afferent innervation. (1) The afferent pathway is conducted through both the pons and medulla. (1)

Efferent Limb

The efferent pathway of the reflex is via the cranial nerve VII (facial nerve) to the orbicularis oculi muscle. The efferent signal takes two pathways, a rapid conduction through an oligosynaptic arc reflex and a less direct route via descending spinal tract of the trigeminal nerve. While both the V and VII nuclei are within the pons, there is some degree of signal conduction through the medulla. (1,2) A normal response is blinking of both eyes in response to stimuli, blinking of one eye indicates an impaired reflex, and blinking of neither eye indicates an absent reflex. (2)

Triggering Stimuli

The test can be performed with a puff of air or a squirt of water but is most specific with a cotton-tipped swab. In the setting of life-or-death decision-making, escalating stimuli may be necessary, but has not been proven superior in head-to-head studies. The ideal location for application of a stimulus is between the limbus and central cornea. (1)

Anesthetic Considerations

General anesthesia and varying levels of sedation can ablate the corneal reflex in a dose-dependent manner. Some recommend waiting five half-lives from the last administration of anesthetics to determine brain death. (1) The common anesthetic use of the “eyelash reflex” is an approximation of the more precise corneal reflex.(2)

Key Points:

Corneal reflex: afferent = V1 branch of trigeminal nerve, efferent = facial nerve

Steps:

Pain receptors in cornea detect an irritating stimulus

C fibers are activated

Signal travels to cell bodies of C fibers in trigeminal ganglion, then via trigeminal sensory root ----> spinal trigeminal tract----> spinal trigeminal nucleus of the pars caudalis

Pars caudalis neurons cross midline and branches into two routes

1. Branches to bilateral facial motor nuclei ----> facial nerve ----> through the stylomastoid foramen ----> zygomatic branch of facial nerve ----> orbicularis oculi muscle ----> close bilateral eyelids

2. Ascending anterior trigeminothalamic fibers ----> ventral posteromedial thalamic nucleus ----> recognition of painful stimulus

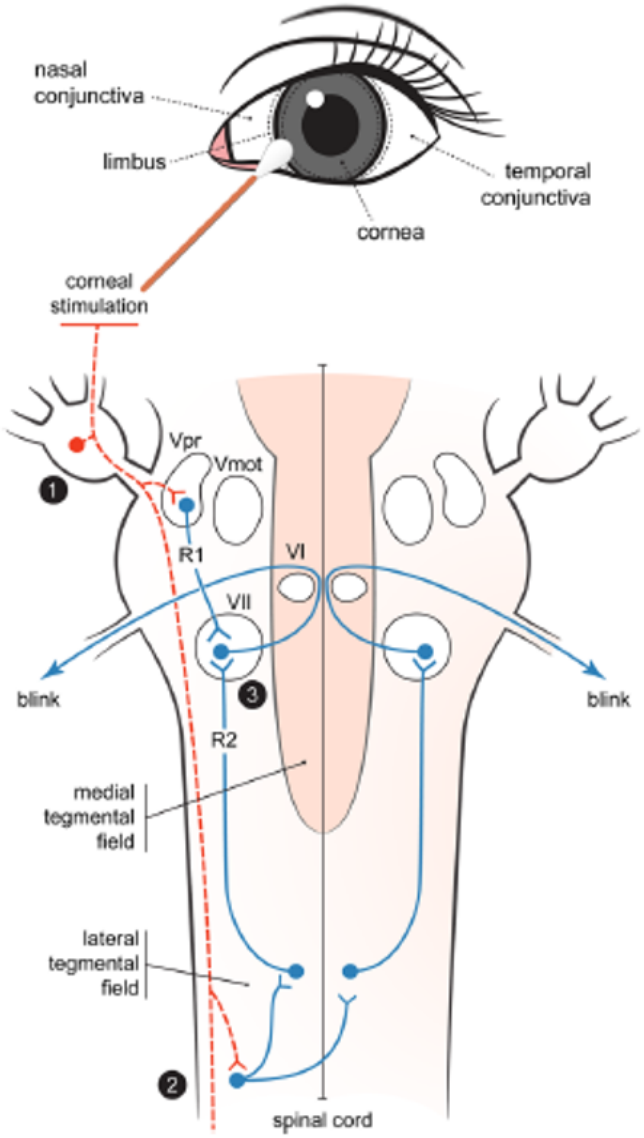


**Fig. 1** Schematic representation of the corneal reflex pathway in relation to the blink reflex pathways (R1, R2). The stimulus on the left cornea is perceived by the supraorbital nerve (1) and conducted to the trigeminal motor nucleus where the ipsilateral R1 response is obtained via an oligosynaptic arc to the CN VII nucleus. This response is not visible clinically. The supraorbital nerve also conducts the afferent impulse through the descending spinal tract of the trigeminal nerve in the lower brainstem (pons and medulla) to the caudal spinal trigeminal nucleus (2) (dotted orange line demarcates the afferent pathway). The efferent impulse (full blue line) is conducted via the medullary pathway that ascends bilaterally to connect to the facial nuclei (pons) (3) and yields the R2 responses which are clinically apparent through the blinking response. Adapted from Aramideh et al. [8]. VII = facial nucleus. VI = abducens nucleus. $V_{pr}$ = principal trigeminal nucleus. $V_{mot}$ = trigeminal motor nucleus