High-resolution gas volume change measurements bring new insights in pressure regulation of the middle ear

IN THIS ISSUE, the paper by Kania et al. (7) presents measurements and modeling results on the role of nitrogen in the gas exchange processes in the middle ear. The middle ear is a semirigid biological gas pocket that is closed most of the time. External influences, such as changing weather conditions, taking an elevator, diving in a pool, or even blowing the nose constantly, cause pressure differences between the closed space and the ambient air. Some changes are slow, others very fast, and the amplitude can vary from some pascals to several kilopascals. For acoustic pressures, the pain threshold is ~120-dB sound pressure level, corresponding to pressure amplitudes of ~10 Pa. At the same time, the ear deals with these quasi-static pressures of several kilopascals in everyday situations. There is a connection between systematic deregulation of middle ear pressure and important middle ear pathologies, but the underlying basic mechanisms still elude us.

Contrary to past beliefs, the eustachian tube is closed most of the time and, therefore, certainly not a ventilation hole that keeps pressure inside the middle ear equal to the outside. Only at large pressure differences, over 2 kPa, will the eustachian tube open spontaneously (4). During swallowing, a peristaltic action takes place, injecting a small bolus of air into the middle ear cavity.

Deformation of the eardrum causes a volume change of the semirigid middle ear cavity and can, therefore, compensate partly for fast pressure changes. In the past, the pars flaccida was regarded as a pressure-regulating buffer. Recent results in animal models show, however, that the pars flaccida volume displacement is <0.2% of middle ear volume, limiting its pressure buffering role to ~200 Pa (1). Based on their measurements of pars flaccida motions, Helström and Stenfors (6) already argued that the pars flaccida may act as a pressure receptor, a view that was supported by the discovery of nerve endings in the tympanic membrane (9, 11). Middle ear pressure is continuously regulated during the day (2, 10), possibly through neural feedback loops (5).

The third regulatory mechanism is gas exchange through the mucosal lining, which covers the interior walls of the middle ear. Although this process has long been overlooked, it may be the most important regulatory process in terms of volume change under normal conditions, and its deregulation may be directly connected to development of eardrum and middle ear pathology. Attempts have been made to measure the magnitude of the exchange process by measuring middle ear pressure change with an inactive eustachian tube (3, 4). As baroreceptors most probably are present, however, pressure itself will change the mechanism. Moreover, pressure-based measurements are prone to technical pitfalls, such as gas exchange through the walls of plastic connection tubes and unknown dead space, which make it difficult to calculate gas amounts from measured pressure changes. Gas exchange under normal conditions can only be accurately studied by measuring volume change at constant pressure. For such studies, custom-made detectors are necessary that can measure volume change with zero pressure difference so that the middle ear remains at ambient pressure throughout the entire measurement. To perform studies in animal models such as rat, where middle ear volumes are <50 μl, the detector needs to have extraordinary accuracy.

A system was developed in which the displacement of a droplet of fluid in a horizontal air-filled capillary is followed as a result of changing gas volume, and Kania et al. (8) applied this detection system to measure gas volume changes with sub-microliter accuracy at (nearly) zero pressure difference. Improved versions of the technique allow continuous automated monitoring of gas volume changes.

The several gases present in the middle ear can all be involved in the gas exchange process, and up until now it was unclear which gases were the main governing factor. Oxygen and carbon dioxide have far higher solubility than nitrogen, and they are also consumed and produced by the mucosa itself. The inert nitrogen is only exchanged with the blood, and it diffuses much slower. It is, therefore, unclear which of these gases is the more important in the exchange processes. In their experiments, Kania et al. (7) replaced the normal middle ear gas with ambient air and with pure nitrogen and discovered that, after initial changes, which depend on initial gas composition, a steady-state decrease of volume is obtained that is independent of the initial disturbance. They developed a model describing the different phases, and the model agrees well with observations. From this result, it can be concluded that nitrogen is the limiting factor in the gas exchange process. The relative fraction of nitrogen in the middle ear is higher than in the mixed venous blood, causing a constant decrease of middle ear gas volume. A next step will be to see if reducing pressure triggers regulatory mechanisms or perhaps regulates the “pumping speed” by changing the blood flow. The model will prove useful in the study of gas economy in pathological conditions.

To obtain a correct mathematical model of the regulation process, several parameters need to be estimated. In middle ears with a simple bulla structure such as in rat, the “active” area for gas exchange can be estimated relatively easily. A second important parameter is the diffusion barrier: Kania et al. (7) estimated this from thickness measurements of the mucosa. Their modeling results agree well with experiments so at least the combination of the estimated parameters is correct.

From measurements such as these, estimations of blood flow through the middle ear mucosa could be made. Values for the several modeling parameters could be “solved” on the basis of gas exchange rate measurements for different kinds of foreign gases with different solubility and diffusion parameters. The gas itself should be physiologically inert and not trigger edema in the mucosa. Hydrogen or helium may be valid choices in view of their high solubility and diffusion. Further research will also be necessary to determine the actual thickness of the diffusion pathway: up until now, mucosa thickness was measured, but the average distance to the capillaries can only be estimated. Also, the actual distribution of blood flow in different zones of the mucosa is unknown. Only a full three-dimensional model of general blood vessel distribution in the
middle ear, completed with high-resolution details of capillary density and position in the mucosa, will bring this information.

Middle ear pressure deregulation is connected to the development of important eardrum and middle ear pathologies, such as recurrent retraction pockets. The basic underlying mechanisms may be connected to impaired eustachian tube function and most probably to deregulation of gas exchange. Accurate knowledge of the gases involved, of the blood flow, and of the gas exchange rates are the key to understanding how the normal ear manages its pressure balance. Together with pinpointing the baroreceptors involved in this complex regulation mechanism, accurate knowledge of the gas exchange mechanisms forms the key to understanding the basic physiological reasons why some ears tend to develop systematic underpressure and its clinical consequences. The techniques and models presented by Kania et al. (7) are important to further progress in this developing field.

REFERENCES


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