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# EXPERIMENTAL STUDY ON THE PERILYMPHATIC PRESSURE

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## ABSTRACT

The hydrostatic pressure was successfully and accurately measured through the round window membrane of the cat over a wide pressure range and long duration using glass micropipets of 1-5 $\mu$m tip inner diameter and an active nulling pressure measuring system. The dynamic changes in perilymphatic pressure occurring after inhalation of different gas mixtures (5 percent $CO_2$ and 95 percent $O_2$/carbogen, 5 percent and 10 percent $CO_2$ in room air) were recorded. The maximal oxygenation of the perilymph combined with minimal increase in pressure was achieved following inhalation of carbogen. The correlation between variations of pressure of the perilymph and of the systemic blood circulation shows that a regulatory system is present in the inner ear vessels. The pressure measuring system used has proven to have all the requirements that are needed for its use in humans.

Among existing pressure measuring devices, only the so-called servo micropipet system has an adequate dynamic performance and a sufficiently small displacement capable of accurate measurements of rapid pressure changes in a small fluid volume like peri- or endolymph.

Wiederhielm and colleagues applied this principle to measure blood pressure in the capillaries of the frog with micropipets smaller than 1 $\mu$m in diameter.[1] Recently a number of investigators have used similar systems for measuring the pressure in arterioles, capillaries, venules, lymphatic capillaries, and in the interstitial space of different microvascular beds.[2-9]

The aims of the present study were (1) to test experimentally the use of a servo-controlled pressure system in view of its later clinical use, and (2) to obtain the basic experimental data required to interpret later clinical findings.

## METHODS

The block diagram of the servo micropipet system (Instrumentation for Physiology and Medicine, model 4 A, San Diego, California) used to measure the perilymphatic pressure is shown in Figure 1. It consists of an electric and a hydraulic part. The operational principle of the system is based on the fact that a change in composition of the electrolytes within the tip of the micropipet will give rise to a change in its electrical impedance.

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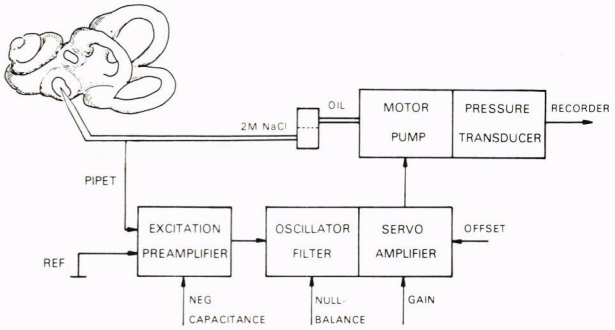


**Figure 1.** Block diagram of the servo-nulling pressure measuring system.

The micropressure system consists of a glass micropipet filled with 2 M NaCl solution. From the oil-saline interface the system is filled out to the pipet with deaerated 2 M NaCl. The conductivity of the solution within the pipet is considerably greater than that of plasma or body fluid. A change in pressure between the inside and outside of a glass micropipet will cause a change in its electric impedance.

When pressure outside the tip exceeds the internal pressure, an inward bulk flow of dilute electrolyte solution occurs. This causes a shift of the concentration profile in the electrode tip, resulting in a decreased conductivity of the fluid and thus an increase in total electrical resistance.

If a counterpressure equal to the external pressure is applied within the pipet, the entrance of the serum in the system is prevented and the pipet impedance remains constant. The required counterpressure is generated by a servo-system, which senses a change in the pipet impedance and translates it into a pressure change within the micropipet. This latter is incorporated into the arm of a Wheatstone bridge. When the impedance of the pipet is increased, the bridge becomes unbalanced, giving rise to an error voltage.

The Wheatstone bridge, with resistance and capacitance adjustments as well as a high input impedance differential cathode fellower, is mounted on the manipulator to minimize electrical noise.

The resistance of the pipet is one element in AC Wheatstone bridge, which is adjusted for zero at a resistance within the operating range of the pipet. When the pressure outside the pipet changes, the change in pipet resistance causes an imbalance in the Wheatstone bridge, producing an error signal. The voltage is amplified and applied to a motor (bellows), which generates a counterpressure inside the pipet, restoring the resistance to its original value.

Since the operating range of a larger pipet is narrow, it is safe to assume that the internal and external pressures are essentially identical. Thus, by monitoring the applied internal pressure, a measure of the outside pressure is obtained. This is achieved by means of a commercial pressure transducer (Statham p23d) connected to a Philips recorder.

In our experiments pipets of 1-5 $\mu$m tip diameter have been used. Pipets with less than 1 $\mu$m were discarded because of their low intrinsic gain, high sensitivity to resistance of the measuring fluid, temperature change, and higher occurrence of plugging.[10]

Rubio and Zubieta pointed out that a significant electro-osmotic effect occurs in a smaller pipet.[11] Furthermore, the presence of a DC electric current through the pipet causes a small movement of fluid at the tip, with a resulting shift in concentration profiles and hence a change in pipet resistance.[12] For this reason it is important to have stable potentials in the electric connections to the fluid in the pipet and to the animal tissues when using small pipets. To zero this DC electric current, capacitance coupling is used between the pipet and the Wheatstone bridge.[13] Larger pipets, such as those used in our experiments, have the advantage of being relatively insensitive to temperature, resistance of the measuring fluid, DC contact potentials, surrounding electric disturbances, and plugging. We have not noticed considerable distortion in the range of pressure up to 50 mm Hg or more.

Pulling and filling micropipets requires complete cleanliness. Pipet glass (Omega DOT. OD = 1.5 mm, lD = 0.75 mm) was first cleaned; rinsed with 10 percent acetic acid, 100 percent ethanol and bidestilled water; ultrasonically cleaned; and dried by compressed air. After pulling on a two-stage David-Kopf puller, the pipets were bevelled to approximately 30° angle by a grinder that has a surface made of 3 $\mu$ aluminum oxide (3M Company, St. Paul, Minnesota). Patency check and blowing out the small particles left inside were done by applying compressed air in acetone solution through the micropipet. As the Omega dot capillaries have a fine fiber attached inside the wall,

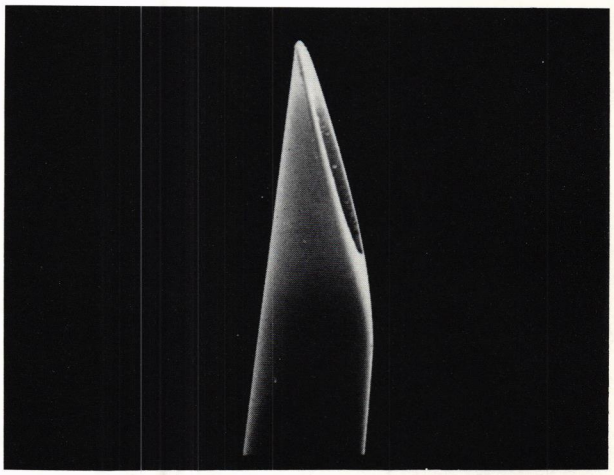

**Figure 2.** Excitation signal (back pressure signal) in response to increasing pressure outside the micropipet. The inner diameter of the pipet tip was of 3 $\mu$m. Note the good correlation ($r = 0.9996$, $p < 0.0001$).

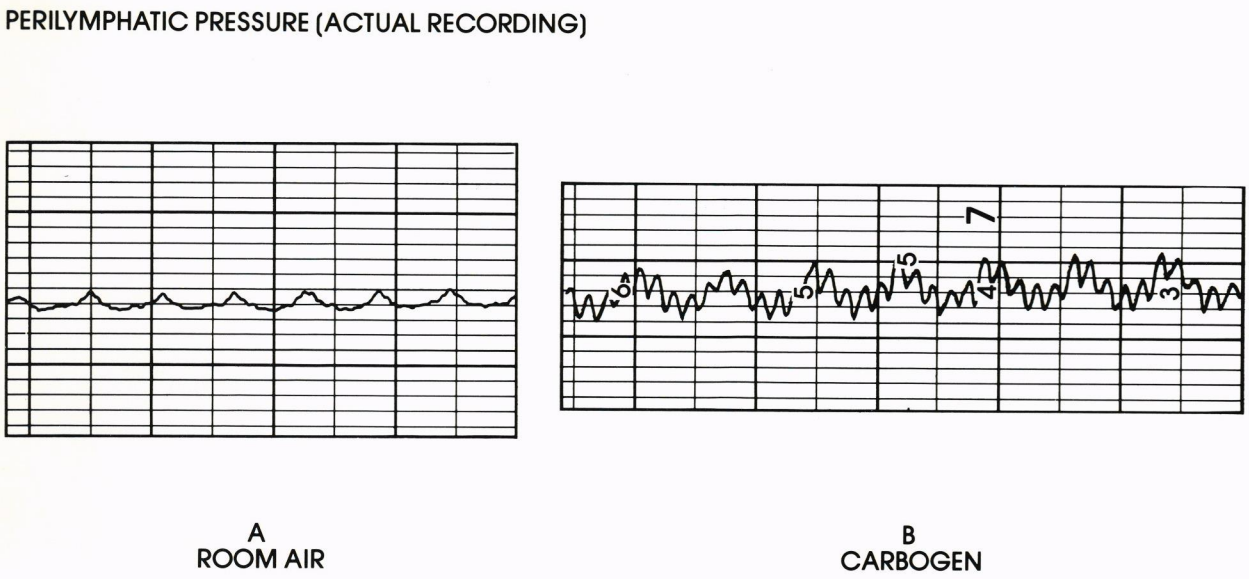


**Figure 3.** With the servo-nulling pressure measuring system the smallest vascular pulsations of the perilymph are recorded.

A, The heartbeats are clearly seen with the respiratory movements when recording the perilymphatic pressure during room air inhalation.

B, The heartbeats are enhanced when recording the perilymphatic pressure during inhalation of carbogen.

pipet filling was achieved easily as follows. The beveled tip of the micropipet was dipped in 2 M NaCl solution for about 10 minutes. During this time the solution usually climbed up to the shoulder of the pipet. The remaining portion of the pipet was then filled using 30 Gx2½ hypodermic needle. An alternative way was to fill the micropipets by boiling them tip down in a storage receptacle under partial vacuum.

The servo-nulling pressure system used in our experiments is commercially available (Instrumentation for Physiology and Medicine, Model 4A, San Diego, California). A pipet holder with an Ag/AgCl (WP Instruments Inc., New Haven, Conn.) as well as an Ag/AgCl reference electrode were used to provide a stable contact between the bridge and the pipet solution or the surrounding tissue. The frequency response of the hydraulic system was maintained higher than 40 Hz by using low compliance tubing and by eliminating microscopic air bubbles.

The evaluation of a pressure measuring device requires the determination of the frequency response, the transient response, the linearity, and the base-line stability (drift). Figure 2 shows the linearity of the system used in the range required for pressure measurements in the inner ear fluids. As mentioned above, the frequency response was 40 Hz and therefore sensitive enough to pick up the smallest vascular pulsations of the perilymph (Fig. 3). The drift was in order of 0.1 mm Hg/hr.

## MATERIAL

Fifteen pyrogen-free cats weighing between 2.8 to 3.8 kg were used. The pressures of the tympanic perilymph and of the arterial blood were recorded simultaneously via the round window membrane and the femoral artery. In 12 cases the perilymphatic pressure was measured over 5 hours without visible leakage of perilymph.

The animals were premedicated with atropine sulphate (0.1 mg/kg sc), anesthetized with sodium pentobarbital (Nembutal), 50 mg/kg im, and intubated with 3.5 to 4.0 mm endotracheal tubes. Alucronium dichloride (Alloferin), 0.5 mg/kg im was used for muscle relaxation.

Nonrebreathing intermittent positive pressure breathing was provided by a Harvard Model 660 respirator. The following gas mixtures were given for respiration: compressed air, 95 percent $O_2$ and 5 percent $CO_2$ (carbogen); 90 percent compressed air and 5 percent $CO_2$; 90 percent compressed air and 10 percent $CO_2$. The uniformity of the respiratory condition was ascertained by repeated blood gas analysis using an AVL microanalyser. The animal temperature was kept constant (35° C) throughout the experiment by a heating pad. The volume of the intravenous infusion of lactated Ringer's solution was adjusted to maintain normal hematocrit values.

The head of the animal was rigidly fixed by a specially constructed holder and placed on several rubber dumpers.

After fixation on the micromanipulator, the tip of the micropipet was first placed in physiologic saline solution to check the drift and noise. The bridge was adjusted to zero and the gain of the system increased just below the point of oscillation. The pipet was then placed in a small pool of saline solution covering the round window membrane. The bridge was readjusted so that the recorded

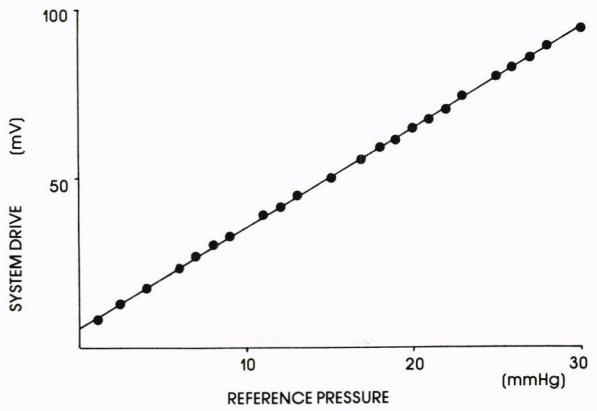


**Figure 4.** Scanning electron microscopic view of the tip of the bevelled micropipet (internal diameter 5 $\mu$m).

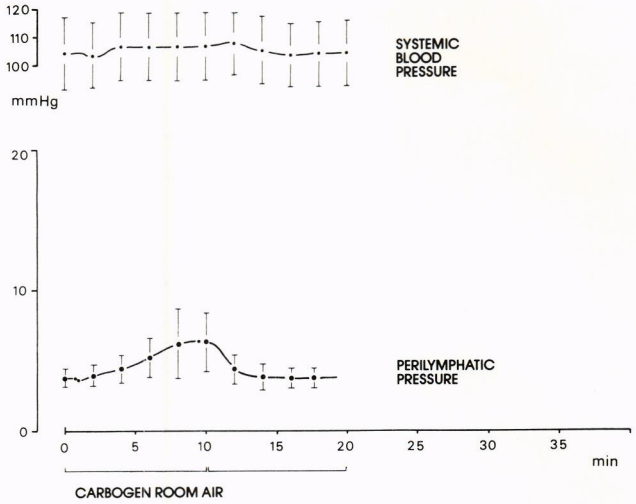


**Figure 5.** Perilymphatic and systemic blood pressure during and after carbogen inhalation for 10 minutes.

pressure was zero. The patency of the pipet was rechecked by submitting the system to a negative pressure. The resulting change of impedance was read on the oscilloscope and the bridge readjusted to the zero pressure level. At this point the system was ready for puncturing the round window membrane. Figure 4 shows the scanning electron microscope view of the bevelled electrode (average diameter 3 $\mu$m). The sharp tip of the electrode made puncturing of the tissues effortless.

After introduction, if the pipet proved to be patent and the system began to operate, plugging was unlikely, since the pressure differences at the tip were automatically maintained near zero. Electric shielding was unnecessary because environmental disturbances were negligible.

The penetration through the round window membrane was best detected by looking at the change of the curve displayed on the oscilloscope. In most instances it was impossible to determine when the puncture occurred by direct microscopic visual control. After penetration, the tip of the electrode was advanced 100 $\mu$m, and then both the tip and the round window membrane were covered with agar. No leakage of perilymph from the perforated round window membrane was observed throughout the time of measurement. No adhesive or dental cement was used for electric fixation to enable calibration and to check the condition of the electrode tip at the end of the experiment. Furthermore, we wanted to avoid the use of materials that could not be applied later on for measurements in humans.

## RESULTS

It is well established that the inhalation of carbogen as well as of 5 percent and 10 percent $CO_2$ in room air induces different degrees of oxygenation in the perilymphatic space.[14–16] The servo-micropipet system was used to record through the round window membrane the dynamic changes of the hydrostatic pressure of the perilymph during the inhalation of the above mentioned gas mixtures.

### *Perilymphatic Pressure and Inhalation of Carbogen (5 Percent $CO_2$ and 95 Percent $O_2$) (Fig. 5, Table 1)*

Figure 5 and Table 1 show the average values of the perilymphatic and systemic blood pressure obtained during 10 minutes' inhalation of carbogen in 14 cats. Following an initial decrease in pressure (occurring after a delay of 46 seconds), the perilymphatic pressure increases to a maximal value of 6.3 mm Hg (+68 percent of the initial value) after 9.5 minutes. After changing the inhaled gas from carbogen to room air, the perilymphatic pressure drops to the maximal recovery value of 3.7 mm Hg in 7.8 minutes. No signifcant overshoot or rebound phenomenon is noted. During the entire observation period the systemic

**TABLE 1. MEAN VALUES OF THE PERILYMPHATIC AND SYSTEMIC BLOOD PRESSURE DURING AND AFTER INHALATION OF 5% $CO_2$ AND 95% $O_2$ (CARBOGEN) FOR 10 MINUTES**

| *Carbogen (n = 14)* | *Initial Value (mm Hg)* | *Delay to Initial Response (sec)* | *Initial Decrease (mm Hg) (sec)* | *Maximal Response (mm Hg) (sec)* | *Maximal Rebound (mm Hg) (min)* | *Maximal Recovery (mm Hg) (min)* |
|---|---|---|---|---|---|---|
| Perilymph | 3.8 ± 0.7 | | 3.6 ± 0.8 | 6.3 ± 1.9 | 3.5 ± 1.1 | 3.7 ± 0.8 |
| | | 46 ± 25 | 114 ± 47 | 9.5 ± 1.3 | 2.8 ± 0.9 | 7.8 ± 3.3 |
| Systemic blood pressure | 105 ± 13 | | 102 ± 13 | 109 ± 13 | 109 ± 10 | 104 ± 12 |
| | | 61 ± 38 | 123 ± 36 | 6.1 ± 2 | 3.3 ± 1.4 | 8.1 ± 2.9 |

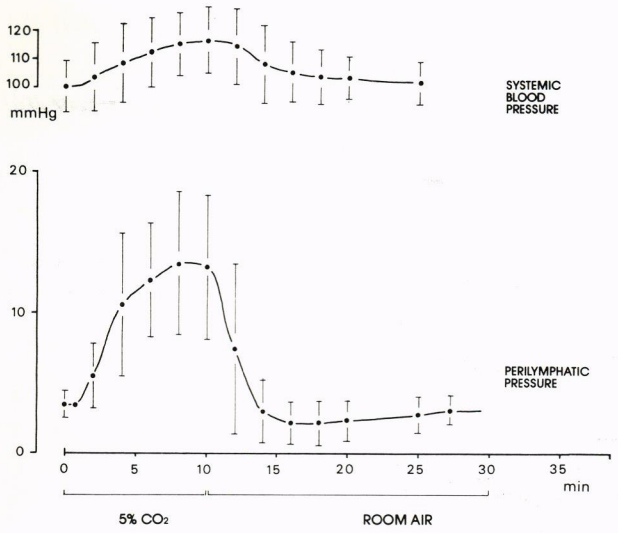


**Figure 6.** Perilymphatic and systemic blood pressure during and after inhalation of 5 percent and room air for 10 minutes.

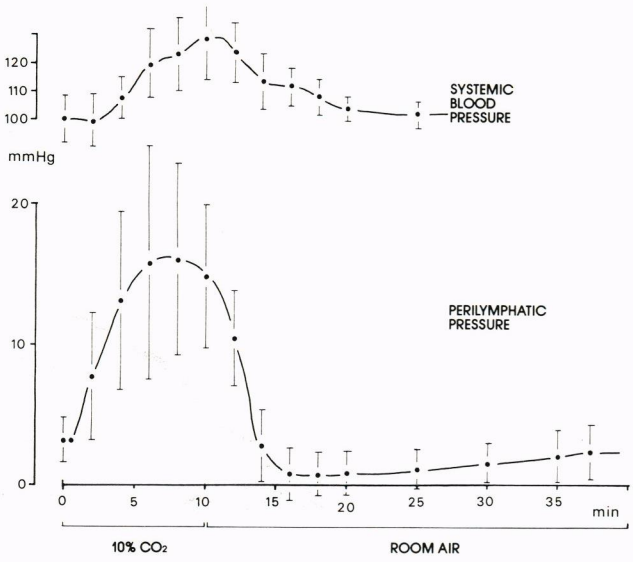


**Figure 7.** Perilymphatic and systemic blood pressure during and after inhalation of 10 percent $CO_2$ and room air for 10 minutes.

blood pressure shows a maximal increase of 3.8 percent, which is reached 2.8 minutes after beginning the carbogen inhalation. There is no significant correlation between the perilymphatic and systemic blood pressures ($r = -0.2738$, $n = 70$, $p < 0.025$).

### *Inhalation of 5 Percent $CO_2$ and Room Air (Fig. 6, Table 2)*

Figure 6 and Table 2 show the average results obtained in 11 cats during inhalation of 5 percent $CO_2$ and room air. The perilymphatic pressure increases on average to a maximal value of 14.9 mm Hg (+232 percent of the initial value) in 8.1 minutes. Six minutes after changing the inhaled gas to ambient air, a drop of the perilymphatic pressure to 2 mm Hg (−43 percent of the initial value) is observed. This negative rebound phenomenon is followed by a recovery reaching the maximal value of 3.2 mm Hg 28 minutes after onset of room air inhalation. The systemic blood pressure shows a maximal increase of +21 percent of the initial value 8.8 minutes after onset of the inhalation with 5 percent $CO_2$ and room air. There is a significant correlation ($r = 0.3725$, $n = 55$, $p < 0.01$) between the increase in systemic blood pressure and perilymphatic pressure.

### *Inhalation of 10 Percent $CO_2$ and Room Air (Fig. 7, Table 3)*

Figure 7 and Table 3 show the average results obtained in 6 cats during and after inhalation of 10 percent $CO_2$ in room air. After a short delay of 31 seconds and without initial decrease, the perilymphatic pressure climbs up to a maximum of 18.1 mm Hg (+366 percent of the initial value) in 6.3 minutes. Seven point eight minutes after reassuming room air inhalation, a drop of perilymphatic pressure to 0.5 mm Hg (−84.4 percent of the initial value) is observed. The maximal recovery to 2.4 mm Hg occurs 37.3 minutes after onset of room air inhalation. The systemic blood pressure increases to a maximum of +33 percent of the initial value 10.3 minutes after onset of inhalation with 10 percent $CO_2$ and room air. There is a highly significant correlation between the observed changes of the perilymphatic and systemic blood pressure ($r = 0.5132$, $n = 55$, $p < 0.01$).

### *Statistical Analysis of the Results (Tables 1–3)*

The statistical analysis of these results (Tables 1–3) shows that there is no significant difference between the *initial values* of perilymphatic pressure

**TABLE 2. MEAN VALUES OF THE PERILYMPHATIC AND SYSTEMIC BLOOD PRESSURE DURING AND AFTER INHALATION OF 5% $CO_2$ IN ROOM AIR FOR 10 MINUTES**

| *5% $CO_2$ + Room Air (n = 11)* | *Initial Value (mm Hg)* | *Delay to Initial Response (sec)* | *Initial Decrease (mm Hg) (sec)* | *Maximal Response (mm Hg) (sec)* | *Maximal Rebound (mm Hg) (min)* | *Maximal Recovery (mm Hg) (min)* |
|---|---|---|---|---|---|---|
| Perilymph | 3.5 ± 1 | | 3.4 ± 1.2 | 14.0 ± 5.5 | 2 ± 1.4 | 3.2 ± 1 |
| | | 43 ± 22 | 56 ± 9 | 8.1 ± 2.5 | 6.1 ± 2.4 | 28.2 ± 7.8 |
| Systemic blood pressure | 100 ± 9 | | 99 ± 6 | 121 ± 15 | 100 ± 13 | 103 ± 10 |
| | | 58 ± 48 | 140± 69 | 8.8 ± 3.7 | 3.8 ± 1.7 | 12.8 ± 5.8 |

**TABLE 3. MEAN VALUES OF THE PERILYMPHATIC AND SYSTEMIC BLOOD PRESSURE DURING AND AFTER INHALATION OF 10% $CO_2$ IN ROOM AIR FOR 10 MINUTES**

| *10% $CO_2$ + Room Air (n = 6)* | *Initial Value (mm Hg)* | *Delay to Initial Response (sec)* | *Initial Decrease (mm Hg) (sec)* | *Maximal Response (mm Hg) (sec)* | *Maximal Rebound (mm Hg) (min)* | *Maximal Recovery (mm Hg) (min)* |
|---|---|---|---|---|---|---|
| Perilymph | 3.2 ± 1.6 | | — | 18.1 ± 6.9 | 0.5 ± 1.6 | 2.4 ± 2 |
| | | 31 ± 19 | — | 6.3 ± 2.6 | 7.8 ± 1.3 | 37.3 ± 9.5 |
| Systemic blood pressure | 102 ± 9 | | 95 ± 10 | 133 ± 17 | 104 ± 6 | 102 ± 4 |
| | | 46 ± 27 | — | 10.3 ± 2.2 | 10.1 ± 1.7 | 25.3 ± 3.3 |

in the three experimental situations used. The student's unpaired t-test has also been used to analyze the following further parameters:

TIME DELAY TO RESPONSE. No significant difference was noted in the time delay to the first detectable response of the perilymphatic pressure after onset of inhalation (carbogen vs. 5 percent $CO_2$: $p > 0.70$, $n_1 + n_2 = 25$; carbogen vs. 5 percent $CO_2$: $p > 0.20$, $n_1 + n_2 = 20$; and 5 percent $CO_2$ vs. 10 percent $CO_2$: $p > 0.20$, $n_1 + n_2 = 17$). The same observation was made for the systemic blood pressure.

INITIAL DECREASE. The initial decrease of perilymphatic pressure is significantly stronger—when expressed in percentage of the initial value—after inhalation of carbogen than after respiration with 5 or 10 percent $CO_2$ ($p < 0.10$, $n_1 + n_2 = 25$, $p < 0.025$, $n_1 + n_2 = 20$). On the other hand, the corresponding changes of the systemic blood pressure were not statistically different from each other (carbogen vs. 5 percent $CO_2$: $p < 0.40$, $n_1 + n_2 = 27$; carbogen vs. 10 percent $CO_2$: $p > 0.10$, $n_1 + n_2 = 21$); 5 percent $CO_2$ vs. 10 percent $CO_2$: $p > 0.50$, $n_1 + n_2 = 18$).

MAXIMAL VALUE. The maximal increase in perilymphatic pressure calculated as a percentage of the initial value was less following carbogen than following $CO_2$ inhalation (carbogen vs. 5 percent $CO_2$: $p < 0.001$, $n_1 + n_2 = 25$; carbogen vs. 10 percent $CO_2$: $p < 0.001$, $n_1 + n_2 = 20$). The difference between the maximal value after 5 and 10 percent $CO_2$ inhalation was, however, not significant ($p >= 0.30$, $n_1 + n_2 = 17$). The maximal change in systemic blood pressure showed a statistical difference for each inhaled gas mixture (carbogen vs. 5 percent $CO_2$: $p < 0.001$; carbogen vs. 10 percent $CO_2$: $p < 0.0001$; and 5 percent $CO_2$ vs. 10 percent $CO_2$: $p < 0.10$).

DELAY TO MAXIMAL VALUE. The delay to maximal value was statistically different when the response to carbogen and to the $CO_2$ inhalation was considered (carbogen vs. 5 percent $CO_2$: $p < 0.10$; carbogen vs. 10 percent $CO_2$: $p < 0.0005$). There was no difference, however, between the delay to maximal response observed after 5 or 10 percent $CO_2$ inhalation ($p > 0.10$, $n_1 + n_2 = 17$). The systemic blood pressure did not show a similar effect.

MAXIMAL NEGATIVE REBOUND. If the maximal decrease in pressure following onset of room air inhalation (maximal negative rebound) is calculated in percentage of the recovery value, the strongest maximal negative rebound phenomenon is noticed following inhalation of 10 percent $CO_2$. Significant pressure differences are measured among the three experimental situations (carbogen vs. 5 percent $CO_2$: $p < 0.05$; carbogen vs. 10 percent $CO_2$: $p < 0.005$; and 5 percent $CO_2$ vs. 10 percent $CO_2$: $p < 0.05$). The inhalation of carbogen was followed by no rebound phenomenon. No significant differences were noticed in the systemic blood pressure ($p > 0.20$) after inhalation with the different gas mixtures.

DELAY TO MAXIMAL REBOUND VALUE. The analysis of the time that had elapsed between the reassumption of room air inhalation to the maximal rebound value showed a similar situation as that described for the maximal negative rebound.

TIME DELAY TO MAXIMAL RECOVERY. In regard to this parameter significant differences were observed in the three experimental groups. The inhalation of carbogen required the shortest and that of 10 percent $CO_2$ the longest recovery time (carbogen vs. 5 percent $CO_2$: $p < 0.001$; carbogen vs. 10 percent $CO_2$: $p < 0.001$; and 5 percent $CO_2$ vs. 10 percent $CO_2$: $p < 0.005$). The systemic blood pressure showed the same tendency ($p < 0.002$, $p < 0.001$, and $p < 0.001$, respectively).

MAXIMAL RECOVERY. No significant differences were found between the values of the maximal recovery obtained after inhalation of the different gas mixtures, with the exception of carbogen vs. 10 percent $CO_2$ inhalation ($p < 0.025$). There were no differences in the values recorded for the systemic blood pressure in all experimental groups.

## DISCUSSION AND CONCLUSIONS

The obtained experimental data permit us to conclude that the servo-micropipet system can be used successfully for the prolonged record of perilymphatic pressure changes in the cat. The inhalation of carbogen and of 5 or 10 percent $CO_2$ in room air (Figs. 5–7; Tables 1–3) induces an increase in perilymphatic pressure.

This effect is much stronger for 5 to 10 percent $CO_2$ in room air than for 5 percent $CO_2$ and 95 percent $O_2$ (carbogen). The observed difference must be ascribed to the vasoconstricting effect of oxygen. The clinical conclusion to be drawn from

the presented results is, therefore, that carbogen should be preferred to 5 percent $CO_2$ in room air as a vasodilating gas mixture for the inner ear, because it associates a better perilymphatic oxygenation to a limited increase of the inner ear fluids pressure. This is important in view of the fact that in a prospective study performed in our department, carbogen has proven statistically superior to the conventional vasodilating regimen in the treatment of sudden sensorineural hearing losses.[17]

Measurements of the perilymphatic pressure can also be used to analyze the regulatory function of the inner ear vessels. For this purpose the correlation coefficients between the perilymphatic pressure and the systemic blood pressure were calculated for each inhaled gas mixtures at 2-minute intervals. The negative correlation coefficient obtained for carbogen inhalation ($r = -0.2738$, $n = 70$, $p < 0.001$) indicates that when the systemic blood pressure rises, the perilymphatic pressure is reduced according to a well-preserved regulatory function of the vessels. On the contrary, the correlation coefficients obtained during 5 and 10 percent $CO_2$ inhalation ($r = 0.3725$, $n = 55$, $p < 0.01$; and $r = 0.5132$, $n = 30$, $p < 0.005$) show that in this situation the perilymphatic pressure also depends, to some degree, on the change in systemic blood pressure. This positive correlation is the expression of a failure of the regulatory system and is probably caused by the excessive $CO_2$ accumulation. This is why the observed positive correlation between perilymphatic pressure and systemic blood pressure is particularly pronounced following inhalation of 10 percent $CO_2$ in room air. The analysis of the regulatory function of the inner ear vessels according to the perilymphatic pressure measurements speaks again in favor of the use of carbogen rather than of 5 or 10 percent $CO_2$ in the treatment of sudden hearing loss.

Further applications of the very sensitive and stable servo-micropipet pressure measuring system will be directed not only to the analysis of the pressure changes of the inner ear fluids under pathologic conditions (as, for example, the endolymphatic hydrops) but also to the better understanding of the regulatory system of the inner ear vessels. The data accumulated from our previous experiments with measurements of the perilymphatic oxygen tension have yielded enough evidence to state that the vascular system of the inner ear has a regulatory system similar to the brain vessels but more dependent than the latter on changes of the systemic blood pressure.[14-16,18] This particular hemodynamic situation must be considered when analyzing vascular pathology in the human inner ear.

One of the aims of this study was to develop a pressure measuring system for the inner ear fluids for possible application in humans. Our experience with the servo-micropipet system in cats was sufficient to warrant its use in the operating theater. Successful perilymphatic pressure measurements have already been obtained in a patient in whom the normal inner ear had to be destroyed in the course of the extirpation of a carcinoma invading the temporal bone. Further experiments of this type will be undertaken in the near future.

The difficulties we have encountered with the servo-micropipet system in recording the perilymphatic pressure are as follows: the calibration of the pipet in vivo can be very tedious and time consuming when plugging or mechanical injury of the electrode tip occurs. In this regard the results obtained by Klinger may be helpful in eliminating the need for repeated calibration.[19] According to Klinger, one can eliminate the gain dependence of the servo system at frequencies below 25 Hz; this means in a range sufficient for the hydrostatic pressure measurements in the inner ear fluids. Movements of the head of the experimental animal (or patient) are disturbing the stability of the tip of the microelectrode. Larger head movements may result, in spite of the small tip diameter of the electrode, in leakage of perilymph through the punctured round window membrane and induce exaggerated respiratory pressure changes. This is why agar was used not only to prevent perilymphatic leakage but also to decrease possible shifts in the position of the round window membrane. For prolonged recordings the head of the cat was fixed with a specially constructed head holder. In our human recording the Mayfield's head holder in combination with muscle relaxation permitted a good stability during more than 30 minutes of measurements.

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