Comments on Dr. Kobayashi's Paper
—Effects of Endolymphatic Application of Furosemide on Cochlear Potentials—

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Furosemide is one ototoxic diuretic and its systemic application induces a reversible depression of the endocochlear dc potential (EP). It has been suggested that this EP depression is caused by an interference with the energy utilization of ATP at the stria vascularis (Kusakari, et al., 1978). Syka and Melichar (1981) reported that the perilymphatic application of furosemide decreased EP and cochlear microphonics (CM), and increased summating potentials (SP). It is, therefore, assumed that furosemide acts on both the stria vascularis and the hair cells. In the present study the effects of furosemide applied into the scala media on cochlear potentials were investigated to ascertain more precisely the locations of energy utilization in the cochlea.

Material and method
Guinea pigs weighing 250 g to 450 g were anesthetized by an intraperitoneal injection of 30 mg/kg pentobarbital sodium and tracheotomy and muscle relaxation were executed for artificial respiration. The tympanic bulla was opened through a ventro-lateral approach. The position of the animal's head was adjusted so that the round window was directly under the microscope. Glass capillary electrodes were filled with the solutions of 160 mM KCl or 160 mM KCl-30 mM furosemide. The tip of the electrodes was cut at 2 μm to 5 μm in diameter for recording and endolymphatic application by diffusion and iontophoresis. Their electrode resistance was between 10 M ohm and 20 M ohm.

DC potentials were fed into a preamplifier and were recorded with a poly-recorder. The cochlear responses that were fed in the preamplifier were displayed on a cathod-ray oscilloscope and were led to an X-Y recorder through an averaging data processor. Sound stimulations between 2 kHz and 10 kHz in bursts of 100 ms were delivered from a tweeter through a closed system to the external ear canal. The reference electrode with a silver plate was placed on the neck muscles. The iontophoretic current was applied in square pulses of 500 ms duration once a second for 2 min.

The electrode was inserted through the round window membrane and the basilar membrane into the scala media. The position of the electrode tip in the scala media was verified by recording of about 80 mV dc potential, EP.

In the penetrations of 160 mM KCl electrodes into the scala media EP, CM and -SP maintained their original values quite steadily for 30 min to 60 min as described in the penetration of the artificial endolymph (Tanaka and Brown, 1970). In 7 animals with the penetrations of 160 mM KCl-30 mM furosemide electrodes, EP was unchanged but CM and -SP were altered; CM decreased to the values from 20% to 77% of the initial size in 6 of the 7 animals and -SP increased to the values from 112% to 180% in all 7 animals. The maximum values of these reversible -SP increase
Figure-Time course of changes in cochlear potentials caused by endolymphatic diffusion of furosemide. CM and -SP responded to sound, 2.8 kHz, 105 dB and 9.4 kHz, 90 dB respectively. Ordinate: 100% represents the pre-diffusion value of EP, CM and -SP. Abscissa: time in minutes after initiation of diffusion.

Two animals of iontophoretic furosemide applications revealed CM decrease and -SP increase similar to the application by diffusion. The figure shows the time course of cochlear potential change in a furosemide application by diffusion. EP remained almost unchanged and its value at 30 min was 94%. CM decreased to 75% at 10 min and recovered to 97% at 30 min. Negative SP increased to 150% at 10 min and returned to near its initial value at 30 min.

It has been reported that SP is altered by the perilymphatic application of furosemide but not by the systemic application (Syka and Melichar, 1981; Evans and Klinke, 1982). The endolymphatic application of furosemide in the present experiment produced a simultaneous increase of -SP with a decrease of CM despite no change of EP. This result implies that the change of CM and SP induced by the perilymphatic application of furosemide is not only a secondary effect of EP depression but also is a direct action on hair cells. This seems to agree with the morphological study showing Na⁺K-ATPase activity on the cells in the organ of Corti (Nakai and Hilding, 1967) and with the histochemical data demonstrating a reversible disturbance of energy metabolism caused by ototoxic diuretics on outer hair cells (Akiyoshi, 1981).

Furthermore the furosemide action of the stria vascularis seems to exist not on the scala media side of the strial cells but on the basal side surrounding the vessels. This result is in accord with the morphological results indicating that a high ATPase activity is present at the endoplasmic reticulum of strial cells (Nakai, 1965) and that the dark cells, even the finger-like extensions of the cells, contain many mitochondria (Ades and Engström, 1974).
References


