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GUEST EDITORIAL

Editor's Note—At the 1990 Midwinter Meeting of the Association for Research in Otolaryngology, the Award of Merit of the Association was presented to Dr. Robert S. Kimura in recognition of his contributions to the field. During the introduction to his more formal comments, Dr. Kimura stressed the importance of team research, particularly the collaboration of clinicians and basic scientists. Dr. Kimura's association with Dr. Schuknecht over the past two decades at Harvard Medical School serves as an exemplary model for such collaboration.

Dr. Kimura's comments come out of a mind which developed the best animal model in existence for endolymphatic hydrops (in guinea pigs). Thus, one must carefully consider his words. Young investigators would do well to read carefully everything Dr. Kimura has written, and to spend as much time as possible with him.

Dr. Kimura's address to the Association follows.

Mr. President, Dr. Nadol, Dr. Lim, Dr. Kiang, and members of the ARO. It is a great honor for me to receive this award, and I will cherish this moment for the rest of my life. Not only does it provide recognition for my past work, but it instills in me a stronger commitment for future research. I was fortunate to be associated with great mentors, Dr. Lindsay, Dr. Perlman, Dr. Schuknecht, and Dr. Wersall. Above all, I owe my deepest gratitude to Dr. Schuknecht, who gave me the opportunity to get involved in inner ear research. I have worked in many different areas of the inner ear, as Dr. Lim has mentioned, but I would like to briefly comment on one particular subject, endolymphatic hydrops in relation to Meniere's disease, and possibly make some suggestions which may be worthwhile for further investigations.

This is a controversial subject, and opinions on the etiology and treatment of Meniere's disease are diverse. Almost every investigator interested in this subject has his or her own pet theories. Our research is primarily based on pathological findings observed in Meniere's specimens. These findings are endolymphatic hydrops, and fine morphological changes in the cochlear and vestibular sensory cells, their nerve endings, and the stria vascularis. We are able to produce animal models for endolymphatic hydrops whose morphological characteristics are similar in some areas bu differ in others from those shown in Meniere' cases. More detailed study is needed on th nerve endings and secretory cells, possibl combined with immunological techniques. I experimental hydrops, NA^+ and K^+ concen trations are often reported to be norma whereas the concentration of Ca^{++} ions i the endolymph is increased. Similar observa tions have been reported in some cases o Meniere's disease. However, the exact mech anisms leading to the hydropic condition hav not been clarified. Perfusion of various chem icals and drugs may provide a clue to th cause of hydrops. Most of us are aware tha endolymphatic hydrops occurs also in non Meniere's cases. The experimental model ma belong to this category since the animals d not show episodic vestibular symptoms; how ever, these animals are reported to demon strate flat hearing loss or even fluctuations i hearing, and spontaneous nystagmus in dark ness. I have only once observed spontaneou nystagmus in daylight in one animal. Exper imental studies on hydropic animals to ini tiate these symptoms may be valuable t follow-up.

The site responsible for producing hydrop is often held to be the endolymphatic sac Certainly this is proved to be true in guine pig ears; by blocking the endolymphatic duct

hydrops is consistently produced. When sac function is impaired, fluid dynamics or chemical composition of the inner ear fluid may be altered and hydrops may ensue. Morphological features of the endolymphatic sac are extremely variable within normal animals of the same species, however, and firm conclusions on the sac's functioning remain elusive. The question is raised as to whether there is a site other than the endolymphatic sac which is capable of producing endolymphatic hydrops. Perhaps there is or are. These sites could be Reissner's membrane and the vestibular endolymphatic walls. In acoustic trauma, Reissner's membrane is damaged and hydrops is sometimes observed. These pathological Reissner's membranes are also demonstrated in Meniere's cases and in experimental hydrops resulting from blockage of the endolymphatic duct. It is difficult to interpret whether these changes precede hydrop formation or result from the hydropic condition. A change in permeability of the membranous walls could be the cause of hydrops. The factors affecting permeability could be vascular spasm, ischemia, hormonal imbalance or immunological reactions. Evidence for or against this generalized physiological change in the inner ear may be supplied by clinical statistical studies showing the location of the initial symptoms of Meniere's disease, whether it is distributed randomly between the cochlear or vestibular system or occurs consistently in one or the other. Also, what are the causes of the sudden attacks of the symptoms? A rapid change in ionic concentration in the fluid is suspected, but the precise mechanisms are at present unknown. More detailed understanding of the biochemistry of the inner ear fluids and the cytochemistry of the Meniere's cases is essential.

As to treatments, I often ask clinicians, "How do you treat Meniere's disease?" A strong cooperative effort is needed between basic scientists and clinicians, since our research directions are and should be considerably influenced by clinical observations. Some treatments do not "make sense" scientifically, but seem to improve the patient's condition nevertheless. In animal models we have tried surgical fistulization techniques and used various types of drugs to attempt to control endolymphatic hydrops. The fistulae were healed in the majority of cases. There was no visible effect on hydrops from administration of massive doses of steroids, prednisone and hydrocortisone. Another approach for possible reduction of inner ear pressure is administration of β-adrenergic blocking agents which are known to be effective in controlling intraocular pressure. The β-adrenergic receptor has been identified in the eye, but it is not identified histologically in the inner ear. Another form of drug treatment is the use of aminoglycosides. Although a systemic or transtympanic injection shows improvement of the clinical symptoms, there is risk of damaging the sensory cells. A more recent development is the application of these drugs through the lateral semicircular canal. Our studies and others have shown that sensory cell lesions are essentially confined to the vestibular system. Improvements of this method may be valuable to investigate. Another method could be a noninvasive technique utilizing a pressure chamber. This treatment is based on the assumption that inner ear pressure can be reduced by decreased external pressure. In experimental animal models, its effect, if any, on endolymphatic hydrops could be assessed or initiation of vestibular symptoms investigated.

These are some of my thoughts. Challenges are there. I am sure that you can meet these challenges. My comments can be interpreted as an appeal to the ARO members who excel in each specialized area. Together with strong input from clinical groups, we can resolve this puzzling and perplexing Meniere's disease. Before I close, I would like to express my thanks to Dr. and Mrs. Takahashi and Dr. Hashimoto who came especially to attend this award ceremony from Japan. I thank you all.

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