# MODERN VIEWS ON VESTIBULAR PHYSIOLOGY*

By Professor GÖSTA DOHLMAN (London)

MR. PRESIDENT, twenty-three years ago I stood in this same place, in this same room and talked about the same subject which I am to talk about to-day. A great deal has however been added to labyrinthine physiology in these years and views have changed. To cover the whole field of this subject here and now, would, however, be impossible. Therefore I wish to confine the subject of my paper to a more limited field: the mechanism of transformation of mechanical movements of the cupula into nerve-signals, and this for two reasons. Firstly because it is a very central problem in the physiology of the labyrinth and secondly because this is the problem which has occupied me, since my retirement from my appointment in Lund, while I have been a guest at the Institute of Laryngology and Otology in London. For this I feel very much obliged to this country, its institutions and my colleagues.

I start as I did 23 years ago—by mentioning the work of the Edinburgh physiologist Crum-Brown, who incidentally simultaneously with Mach and Breuer, published his work on *The Physiology of Equilibrium* in 1874. All three of these investigators independently came to the same conclusion that the semicircular canals were, in their shape and in their orientation, most suited for the detection of head movements, and that such movements must produce a streaming of the fluid in the canals.

This explanation solved the problem of how and where the reactions for normal maintenance of equilibrium originated and also where the origin of disturbance in equilibrium might be found.

It explained to his contemporaries how head movements could give rise to fluid movements in the semicircular canals which in some way must stimulate sensitive areas in these canals. Extensive physiological experiments by Breuer, Ewald and others made it clear that only the movement of the endolymph was of importance for the reactions and that the sensory area was restricted to the cristae of the ampullae.

*Paper read to the Section of Otology, Royal Society of Medicine, London on November 7th, 1958, incorporating experimental work at the Institute of Laryngology and Otology carried out with the generous assistance of the Trustees of the Leverhulme Research Fund.



https://doi.org/10.1017/S0022215100055109 Published online by Cambridge University Press

These investigations and physiological experiments could, however, not give an adequate explanation of how these endolymph movements could possibly stimulate the neuro-epithelium. It was supposed that the endolymph, when streaming through the ampulla, bent the hairs of the haircells in the direction of the endolymph flow and that this gave the reactions in the neuro-epithelium.

Histological investigations, however, showed that the crista and the hairs were evidently covered by a gelatinous mass, which was not an artefact, as it was previously believed.

The cupula as seen in microscopic sections appeared only as a small cap over the sensory epithelium of the crista and it was therefore difficult to explain the mechanism of stimulation, recognizing the extremely high sensitivity of these organs on one hand, and on the other hand the evidence from physical facts that the movements of the endolymph must be much smaller than previously believed. Therefore, about 1930, when Steinhausen by injecting Indian ink into the endolymph, was able to show that the cupula extended from the crista up to the vertex of the ampulla; this demonstrated that the cupula filled the whole cross-section of the ampulla and therefore was bent or deflected by *even the slightest* displacement of the endolymphatic fluid.

At that time the investigations then had shown that movements of the endolymph, due to inertia of the fluid, could transmit the movements to the cupula in a physically predictable way as a deflection over the sensitive neuro-epithelium of the crista and, that the effect of the reaction is in conformity with the stimulus.

It could be argued that this is enough from a practical point of view to explain the normal physiological reactions and the effects of clinical investigational methods.

However, there are many questions to be answered regarding the mechanism in which the cupula can transform the mechanical movements into neural signals, before we can say that we know enough to explain the function of the vestibular apparatus even from a practical point of view.

Ménière's disease has to-day been dealt with in the presidential address. Much has been done from a diagnostic and therapeutic point of view and through the work of Hallpike and Cairns most important contributions have been made to the pathology of the disease, but still there are great empty regions in our knowledge of the pathogenesis of these changes and also of the action of the destructive process which deteriorates the hearing and initiates the attacks of vertigo.

Therefore I would like to show the results of some investigations, which have been carried out at the Institute of Laryngology and Otology during the last two years with Professor Ormerod and the staff of the Institute. There is no pretension of having solved the problems of any



https://doi.org/10.1017/S0022215100055109 Published online by Cambridge University Press

clinical questions but only trying to add some basic knowledge for a further understanding of the mechanism of vestibular reactions, as a support for what perhaps later could be interpreted in terms of practical importance.

If radioactive sulphur, S.35, is injected subcutaneously the labelled sulphur will be found for certain periods of time practically everywhere where sulphur in any compounds takes part in the metabolism of the tissues or fluids of the body. Having injected S.35 into pigeons which were killed after from 1 hour to 24 hours, it was possible to demonstrate the radioactivity of the labelled sulphur in the labyrinth. After the preparation of microscopic sections, these were covered with a layer of photographic film-emulsion which was then exposed for some 2-6 weeks to the radioactivity in the sections. The results of such an experiment can be seen in the next few slides.

Fig. 1 shows a cross-section of the ampulla of a pigeon killed one hour after injection. In the middle of the section the crista with the sensory epithelium and a part of the cupula is visible. On both sides, part of the lateral walls of the ampulla, known as the planum semilunatum, is apparently much darker than the surrounding tissues. This is due to the silver grains in the photographic film which have been reduced by the local underlying radioactivity in the cells and tissues. It is apparent



Fig. 1



https://doi.org/10.1017/S0022215100055109 Published online by Cambridge University Press

from Fig. 2, showing the epithelium of the planum semilunatum in higher magnification, that the concentration of these grains is low in the sub-epithelial tissue, that it is much higher in the region of the epithelial layer

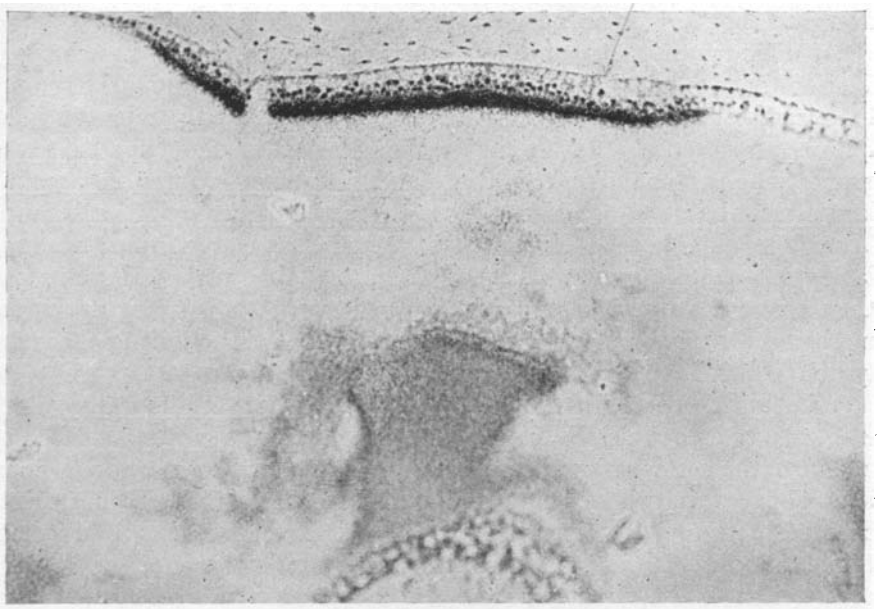


FIG. 2

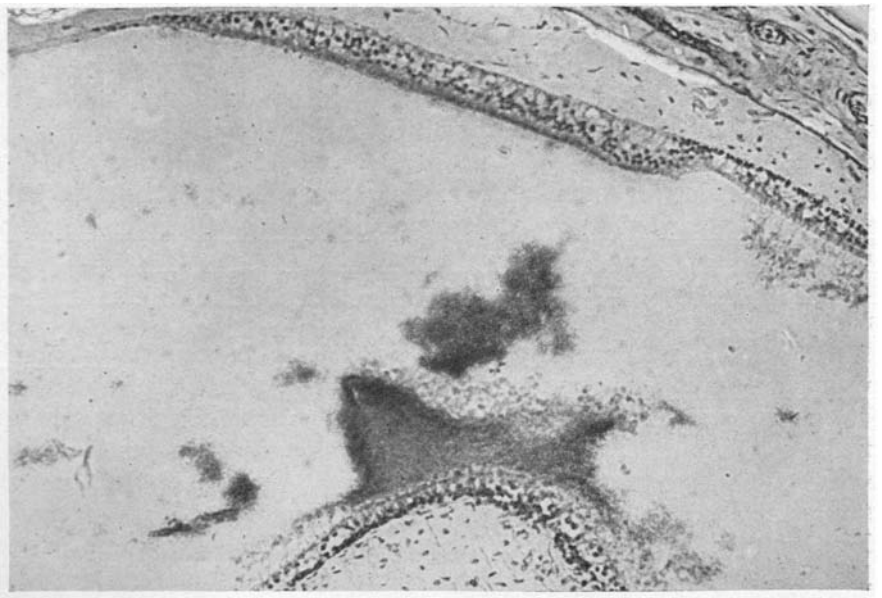


FIG. 3



https://doi.org/10.1017/S0022215100055109 Published online by Cambridge University Press

and then again lower in the endolymphatic space. In this slide which is from a pigeon killed after 4 hours the epithelium of the planum semilunatum is black from the density of the silver grains. In the cupula and in the clouds of coagulated endolymph there is only little radioactivity and thus they appear only hazily gray.

In Fig. 3 from a pigeon killed after 24 hours the picture has changed. The epithelium which was black in the 4-hour pigeon, now shows very little radioactivity, but the cupula and the coagulated patches of endolymph are intensely darkened by the density of the exposed silver-grains. The compounds which contain the labelled isotopes are accumulated on to the *cupula* and have also penetrated all through its substance. What does this show? It shows a wave of labelled material, first accumulating in a certain region of the epithelium of the walls of the ampulla, then passing into the endolymphatic space where it is taken up by the meshwork of the cupula and also appears in the compounds of the endolymph, which have been coagulated by the fixing fluids.

That means that the epithelium of the planum semilunatum which embraces and encircles the cupular structures, is a secretory epithelium and that the compounds which are secreted are sulpho-mucopolysaccharides. The fact that these compounds are substances with highly negatively charged molecules and that they are secreted directly to the cupula seems to me to indicate that they are of the greatest importance for the function of the cupula. The transformation of mechanical movements to electrical charges is what we have reason to believe to be the fundamental potential change, influencing the generation of excitatory reactions in the nerve endings at the crista.

The historical conception of the function of the sense organ in the ampullae, pictured the hairs of the hair cells waving like seaweed in streams of endolymph, or bending of the hairs following displacement of the cupula.

From all that is known about such structures it must be considered extremely unlikely that a bending of the hairs in one direction should be able to effect nystagmus to one side and that bending of the same hair in the opposite direction should produce a nystagmus to the contra-lateral side.

It has in other experiments been possible to show that the cupula responds to much smaller movements than it has earlier been assumed, (to only fractions of a degree of arc). Even much smaller fluid movements in the endolymph, movements produced by sound waves from clicks or tones can still give reactions from the crista. Under these circumstances it is impossible to assume a bending of the whole cupula or its hairs caused by these small and rapid waves. It is more likely that fluid movements *in* the cupula substance itself are the consequence of such distortions of the cupula.



https://doi.org/10.1017/S0022215100055109 Published online by Cambridge University Press

If these facts are linked together it seems necessary to abandon the traditional conception of the action of the cupula effectuating a bending of the hairs of the haircells as the relevant effect of an endolymph movement. On the other hand the presence of mucopolysaccharides absorbed into the cupula, as it has been shown in these experiments, might suggest reversible electrical changes due to flow potentials, known to exist under similar conditions in the meshwork of the cupula, which might be collected by the hairs, acting as antennae for the hair cells, thereby raising or lowering their cell potential.

Such a variation in the cell potential of the sensory cells are known to influence the nerve endings surrounding these cells.

From the investigations of Lowenstein and Sand it is further known that the reaction in the nerve fibre due to a stimulation of the semicircular canal is an increase or decrease respectively of the frequency of action-potentials depending upon the direction of the endolymph movements.

Accordingly the signal from the peripheral vestibular organ is a *pattern of frequency*. This opinion is nowadays generally accepted. If so, it must be of great importance that the normal resting frequency of the nerve fibres is controlled and kept within normal limits, while otherwise it must be assumed that a varying frequency might as a result give a feeling of imbalance or even vertigo.

The anatomical works of Rasmussen and of Portmann, jr. have shown the pathways and distribution of a system of efferent nerve fibres *from* cells close to the olivary nucleus *to* the cochlea. Using a method devised by Friedenwald-Koelle it has been shown by Schuknecht that these fibres are cholinergic. This means that acetylcholine is the chemical mediator at the nerve endings of these fibres and that the enzyme for hydrolyzation of acetylcholine, the acetylcholinesterase must be present. Using the method of Friedenwald-Koelle it is possible to demonstrate the site of acetylcholinesterase activity by means of a sedimentation of copper sulphide. As it is generally accepted that the first neurons of afferent, sensory nerves do not contain acetylcholine, the presence of cholinesterase-activity therefore demonstrates a different system of nerve fibres which in the cochlea is in conformity with the known efferent fibres of Rasmussen.

Using the same method, it has been possible to demonstrate the presence of a cholinesterase-activity also in the sense organs of the vestibular apparatus. Fig. 4 shows the brown sedimentation of copper sulphide in some specimens treated according to the method of Koelle, thus demonstrating a cholinesterase activity in nerves and nerve-endings in the region of the hair cells of the vestibular sensory epithelium.

Using a modification of this method by Holmstedt the reaction is stopped at the stage when copper thiocholin is formed. This modification has certain advantages, giving more distinct localization, fewer artefacts



https://doi.org/10.1017/S0022215100055109 Published online by Cambridge University Press

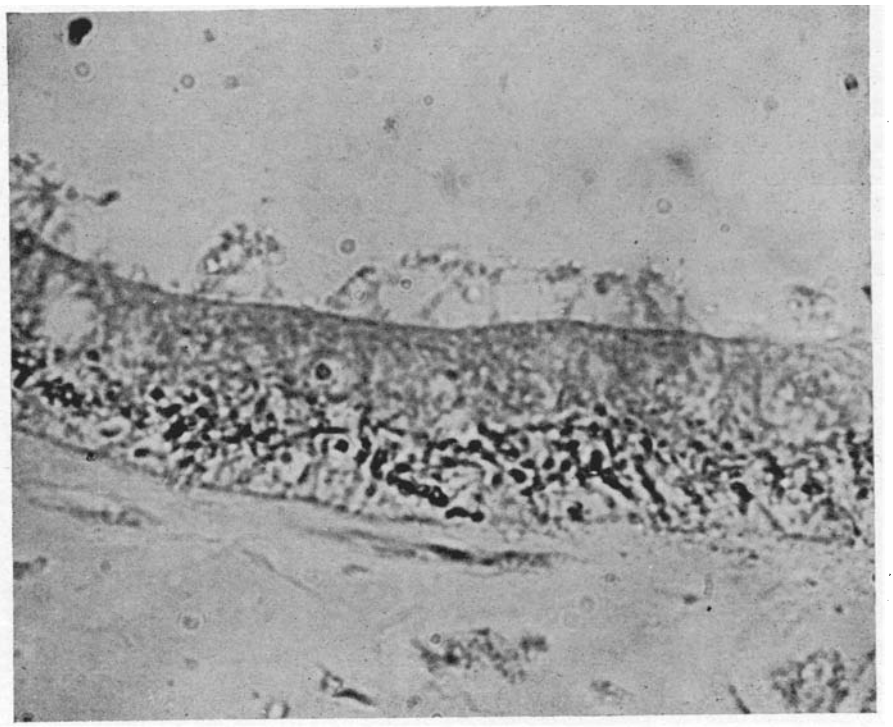


FIG. 4

and more exact results of the action of inhibitors, which must be used to sort out the non-specific enzymes which might give rise to mis-interpretation of the results.

As a result of these experiments it is possible to state that a system of efferent nerve fibres, of a cholinergic type, are passing to and ending in the sense organs of the vestibular apparatus. The origin and pathways of these efferent fibres are unknown as also their physiological function. From what has already been said, however, one might assume that this efferent system in some way might be connected with a mechanism for the regulation of the activity of the sensory nerve fibres in the vestibular system.

In conclusion I hope that the results of the investigations which have been described here and the theory of electrical transmission which has been mentioned may help to keep alive an interest for future investigations in this enchanting field of our specialty.

Institute of Laryngology and Otology,
330 Gray's Inn Road, London, W.C.1



https://doi.org/10.1017/S0022215100055109 Published online by Cambridge University Press