VIRAL THEORY FOR MENIERE’S DISEASE

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Meniere’s disease was first described by Prosper Ménière in 1861. His idea that vertigo was caused by an inner ear disorder was not accepted by the scientific community who supported the concept that vertigo was a brain disorder.

Ménière accurately described the condition but his original paper was not published because of the adverse scientific opinions. Fortunately several of his subsequent papers were published. Prosper Ménière died in 1862 after contracting pneumonia. It was ten years later that Ménière’s ideas became accepted so he never received any acknowledgement during his lifetime.

Meniere’s disease causes four major symptoms; attacks of vertigo which tend to occur in clusters, a fluctuating and usually progressive hearing loss in the affected ear, tinnitus and a sensation of aural fullness. Other symptoms such as tiredness, ‘brain fog’, and poor memory are less commonly mentioned.

It is estimated that approximately 50,000 people in Australia suffer from Meniere’s disease. Meniere’s disease tends to occur initially in mid adult life with a median age of 50 years. The attacks of vertigo tend to occur in clusters lasting a few months followed by variable periods of remission. Eventually the attacks of vertigo peter out when the hearing becomes poor, which is known as ‘burn out’ or stage 3 of the condition.

The attacks of vertigo cause great distress. The sensation of spinning can last for several hours associated with nausea and vomiting. The attacks are unpredictable and often the bread winner cannot continue work or a parent is unable to cope with the family. Often the sufferer hopes for ‘burn out’ even though they become very deaf in the affected ear and may continue to be plagued by tinnitus. Discovering the cause of the attacks of vertigo must be the first step towards finding the cure for this terribly disabling condition.

Discovering the cause of the attacks of vertigo

The initial concept was that the vertigo was due to vascular spasms within the inner ear. In the period after WW2, this belief led to the use of medications which dilate the blood vessels such as nicotinic acid and an operation called cervical sympathectomy [1]. To avoid the skin of the face reddening, Betahistine (Serc®) was developed and this still remains a popular treatment. The concept that constriction of the blood vessels in the inner ear caused the attacks was the reason why doctors told their patients to avoid coffee, caffeine drinks and nicotine. As Meniere’s disease occurs in a younger age group than vascular disease and there is no increased prevalence of Meniere’s disease amongst people with vascular problems, the concept that Meniere’s is due to vascular spasm has been mostly abandoned.
In the 1930’s, Swedish doctors noticed that many people noticed that salty foods could precipitate attacks of vertigo [2]. In the 1950’s two English researchers (Harrison and Naftalin) gave Meniere’s disease sufferers salt loads and demonstrated that vertigo attacks occurred when increased salt was excreted in the urine [3]. It is not possible to do a proper ‘double blinded trial’ of salt but the anecdotal evidence does suggest that salt loading is a significant factor.

In 1960, Schucknect at Boston showed small ruptures had occurred in the membranes in the inner ear which had healed up but left some tell-tale scarring. He proposed a rupture theory [4]. This theory suggested that an increase in the inner ear fluid called endolymph bulged the membrane causing ruptures which allowed potassium from the endolymph to poison the balance nerve endings leaving the ear. This caused a temporary loss of function resulting in vertigo until the rupture was closed off and the ionic balance restored. This theory has been favoured for the past 50 years.

The cause of the increased endolymph volume was attributed to a failure of the flow of endolymph to the endolymphatic sac. It was thought that there was a constant ‘longitudinal’ flow of endolymph toward the sac, and if a blockage occurred there was a build up of endolymph in the inner ear until the membranes ruptured. This led to the concept of endolymphatic shunt surgery, where a tube or sialastic sheeting was placed in the endolymphatic sac to facilitate its ability to absorb the fluid. This concept has now been largely discounted. Swedish workers have shown that the endolymphatic sac is a sponge like structure and not a sac which passively accepts endolymph [5]. Endolymph is only attracted into the sac when it secretes and reabsorbs glycoproteins. Salt and his co-workers have demonstrated that there is no constant flow of endolymph to the endolymphatic sac but longitudinal flow only occurs when there is a sudden increase in endolymph volume [6]. Furthermore, audiological studies and electrophysiological studies undertaken by the author and others have shown no loss of cochlear function during the attacks of vertigo [7]. In a controversial study the author has shown that removal of the endolymphatic sac rather than shunt surgery provides a better outcome as it hastens the ‘burn out’ stage of MD [8].

The search is now on to find the real cause of the attacks of vertigo. The Meniere’s Research Laboratory has been established in Sydney under the care of Dr Daniel Brown. Here work has been undertaken to increase the volume of endolymph in the inner ear while observing the changes in the firing of the vestibular and cochlear nerves. Studies suggest that sudden changes in endolymph volume cause a stretching or collapse of the vestibular hair cells within the cristae of the semicircular canals. The author proposed a ‘drainage theory’ which postulates that the increased volume of endolymph inside the utricle (vestibular portion) is due to reflux of endolymph from the cochlear part of the inner ear during periods of longitudinal drainage [9]. Further studies are presently occurring.

Gibson’s drainage theory proposes that there is an initial increase in endolymph volume due to an inflammatory reaction inside the inner ear. Once this extra volume of fluid is present minor fluctuations in the level of excess endolymph could be the trigger for each attack: for example, after ingestion of salt or when stress causes a hormone (vasopressin) to be released. After a series of attacks the excess volume decreases and a period of remission from attacks occurs until another inflammatory event occurs causing another cluster of attacks.

What causes the initial increase in endolymph volume and the recurrent attacks of vertigo?
Many researchers consider that Meniere’s Disease is multifactorial and there are many different causes which lead to the situation which results in Meniere’s disease.

It is known that the bony vestibular duct which contains the membranous duct leading to the endolymphatic sac is narrow in Meniere’s disease sufferers although it is also narrow in some people who do not suffer with Meniere’s disease. Furthermore, there is a genetic abnormality associated with Meniere’s disease.

Possible causes include congenital disorders such as viral illness during the pregnancy including rubella (German measles) and toxoplasmosis. Diseases of the bone surrounding the ear such as otosclerosis or Padgets disease, tumours of the endolymphatic sac or vestibular nerve, allergies especially to food substances, various infections caused by syphilis, yaws or viruses, autoimmune problems and failure of the immunodefence mechanism.

If the cause of the increased endolymph is due to an inflammatory reaction inside the inner ear, then steroids should limit this inflammation. There has been a vogue towards using oral or intratympanic steroids to stop clusters of attacks of vertigo. The validity of this approach has yet to be clearly shown although clinical evidence does seem to suggest it is an effective treatment.

Is a virus the most common cause of Meniere’s disease?

Over fifty years ago Lempert and his co-workers suggested that Meniere’s disease was caused in the majority of ears by a herpes virus [10]. The herpes family of viruses consist of at least 8 members including HSV1 (causes cold sores), HSV2 (causes genital herpes), VCV (causes chicken pox and shingles), EBV (causes glandular fever) and CMV (causes birth defects).

The herpes virus has been found in autopsy specimens obtained from Meniere’s disease sufferers in both the endolymphatic sac and in the ganglion of the vestibular and cochlear nerves. However ears from non Meniere’s disease sufferers often also contain the virus.

The idea of a herpes virus causing the initial inflammatory response in the inner ear is compelling. For example, herpes simplex virus causes cold sores which erupt on the lip and then the virus lies latent or hides in the nerve for a while and then can erupt again causing more cold sores. It is postulated that a similar virus causes an initial inflammatory response in the ear and results in inflammation which causes excess endolymphatic fluid (endolymphatic hydrops). As the virus lies latent within the ear, it can erupt again causing another cluster of attacks.

Unfortunately there is no medical treatment which can kill the virus when it goes into its latent state. Anti-virals may be effective in stopping eruptions of the virus but would have to be taken continually.

The need for research into a viral cause

The first step in the research will be to find out which Meniere’s disease sufferers have a viral cause for their condition. A prolonged, double blind trial needs to be undertaken to determine if antiviral drugs can prevent clusters of attacks occurring. A double blind trial means that a placebo which looks exactly like the antiviral agent is used in some subjects and the actual antiviral medication is used in others. Neither the doctor nor the patient will know which is being used. If a subject has
another cluster of attacks, the secret is revealed and if that person is on the placebo, they will be offered the active medication.

**Why do some ears have the virus present but do not develop Meniere’s disease?**

While the virus lies latent (hidden) within the inner ear structures, the function of the ear is unaffected. When the virus erupts it causes the inflammatory response resulting in the production of excess endolymph. If the ear can mount an adequate defence mechanism, the virus can be destroyed before it causes an excessive inflammatory reaction. Some ears can mount this defence mechanism, whereas ears affected by Meniere’s disease cannot.

The immune system clears viruses and other pathogens from the body using special cells called lymphocytes. Lymphocytes are developed in the bone marrow (B lymphocytes) and in the thymus (T lymphocytes or T cells). Viruses are cleared by a specific lymphocyte known as Th1 and the ear needs lots of these Th1 lymphocytes to prevent the virus from causing the inflammatory reaction.

T cells are made specifically for certain tasks. T cells develop from immature T cells in the thymus and these can differentiate into specific types with highly specialised tasks. Some may develop into T1 cells and these can be measured with a blood test using a special marker called CD8+. Other immature T cells develop into Th2 cells which communicate with B lymphocytes (which produce anti-bodies to combat bacterial infections and parasites). Th2 cells have a CD4+ marker.

Furthermore, other T cells are produced that limit the immune system so the body does not attack its own tissues, a process known as autoimmunity.

Perhaps if a person with Meniere’s disease has insufficient or inefficient specialised immune cells, they may be unable to prevent the virus erupting and causing inflammation in the inner ear. This may be the reason why some ears which contain the virus do not suffer from Meniere’s disease.

Stephen Spring, himself a Meniere’s disease sufferer, has discovered a possible means of altering the T1/T2 balance which may provide long term relief and we hope to be able to properly evaluate his ideas at the University, but such is the fickle nature of Meniere’s disease that isolated cures cannot be taken as definite proof of efficacy.

**Our hopes for the future**

It is our aim at the University of Sydney to be able to explain the mechanism which causes Meniere’s and to find an eventual cure. We feel that some definite strides towards this goal have already been made. We are desperately keen to be able to complete the tasks and hope that there will be sufficient funding to make this possible. The Meniere’s Research Fund under the superb leadership of Bruce Kirkpatrick has been the lifeline and we urge all Meniere’s disease sufferers and their families to continue to support this cause.

We need to recruit Meniere’s disease sufferers who are willing to become part of our research programme. Specifically we need sufferers who are experiencing clusters of attacks of vertigo so that we can discover if antiviral medication can be effective.

If a reader wishes to help us, please contact me (Professor Gibson at 02 9844 6801).
References