THE DRUGS

LIDOCAINE (lignocaine, xylocaine)

The only consistently tinnitus reducing or alleviating drug has been Lidocaine. This was first observed by Barany (1935). This is a drug with local anaesthetic, anti-arrhythmic and anticonvulsive properties. The effect of this on tinnitus has been studied by many especially Shea et al. (1981), Emmett and Shea (1984). Unfortunately this can only be administered intravenously for tinnitus suppression. Its effect lasts between some minutes and some hours and can have unacceptable side effects.

Although the intravenous injection of lidocaine is seldom used in treatment at present, it provides fertile grounds for research into its mechanism of action. Research using lidocaine so far indicates that it has effects upon central auditory pathways as well as on the cochlea.

Iontophoresis of lidocaine through the skin of the external auditory canal was used in the past with no apparent benefit.

Although intratympanic lidocaine injection was advocated by Sakata and Umeda (1976), Coles et al (1992) in their study did not find support for this and the complication of vertigo was very common. It is still used in some centres.

Lidocaine is one of the group of cardiac arrythmic or membrane stabiliser drugs. In the same class there are drugs that can be taken orally:

Tocainide hydrochloride (Tonacard) 400mg tablets.
Flecainide Acetate (Tambocor) 100mg tablets.
Mexiletine (Mexilin) 100mg tablets.

Although these drugs were found to be quite effective in tinnitus alleviation they cannot be used in patients with a variety of health problems including heart disease. When used, co-operation with the cardiologist is required. Emmett and Shea concluded that due to lack of tolerance of the drug's adverse effects, which include cardiovascular problems and blood dyscrasias, there usefulness is not supported. Clinical use of these drugs has been virtually abandoned.

ANTIEPILEPTIC (anticonvulsant) DRUGS WITH MEMBRANE STABILISING PROPERTIES

It is likely these drugs were trialled because the anticonvulsant property of lidocaine inspired investigation into the effect of anticonvulsant drugs on tinnitus. The following were tried:

Amylobarbitone sodium
Phenitoine sodium
Sodium valporate
Primidone

Although some patients benefited from these drugs, they had undesirable side effects and therefore are seldom used.

BENZODIAZEPINES WITH ANTICONVULSANT PROPERTIES

Carbamazepine (Tegretol) 100-200mg tablets.

The studies of Goodhill (1981) gave promising results, however later studies (Goodey 1981, Lechtenberg and Schulman 1984) did not support these levels of effectiveness and the unpleasant side effects of gastrointestinal distress, drowsiness and unsteadiness limit its usefulness.

Clonazepam (Rivotril) 500micrograms tablets.

Lechtenberg and Schulman found clonazepam to have promising effect in comparison with other benzodiazepines such as diazepam, flurazepam and oxazepam. Recently Bumby and Stephens (1997) in a double-blind placebo controlled crossover pilot study found significant reduction in the annoyance caused by tinnitus in comparison with cinnarizine and placebo. It was concluded that it would be helpful to use it in brief and intermittent courses when patients' tinnitus is very troublesome and unresponsive to other management. The effect was explained in terms of the GABAergic effect of the drug on the excitability of auditory neural activity of the cochlea.

Alprazolam (Xanax) 250mg tablets.

Some patients experienced relief of their tinnitus while on alprazolam. This led to a controlled study by Johnson et al (1993). Of the 17 patients who completed the trial, 13 had a reduction of their tinnitus (76%). The authors also explained the action through its GABAergic effect. Although this result sounds promising, alprazolam is known to lead to dependence/addiction, therefore, as with diazepam, utmost care is needed in the consideration of the use of this drug.

Other antiepileptic drugs suggested for tinnitus treatment:

Vigabatrin (Sabril) 500mg tablets.

This drug is a GABA agonist. A trial by Perucca et al (1991) suggested benefit but Coles failed to replicate this (personal communication).

Lamotrigine (Lamictal) 25mg tablets.
This candidate, like vigabatrin, is under research.

Research studies show that benzodiazepines work through their effect on gamma aminobituric acid A (GABA A) receptors. GABA A has an inhibitory effect on ascending auditory pathways as well as at cochlea level. It has been shown that benzodiazepines enhance the GABA A effect and through this the effects are (i) sedative (ii) anxiolytic (iii) anticonvulsant (iv) attenuation of autonomic and endocrine responses. Hence in theory one expects benefit not only directly on tinnitus but also on emotional and autonomic consequences. However in the use of benzodiazepines there are problems of dependency/addiction, tolerance and rebound.

TRICYCLIC ANTIDEPRESSANTS

Earlier amitriptyline and trimipramine were thought to have a direct effect on tinnitus along with the antidepressant effect. However the direct effect is doubtful. Later another drug in this group (nortriptyline) was suggested to have tinnitolytic effect.

Nortriptyline (Allegron, Motipress, Motival) 25mg tablets.

Of studies comparing tinnitus patients and tinnitus patients with depressive disorder, (Dobie et al. 1993) this drug was found to have beneficial effect upon depression but no significant effect upon tinnitus.

ANTIHYSTAMINIC DRUGS

Cinnarizine (stugeron) 15mg tablets
Flunarizine (not available in the UK)

These are used in the management of vertigo. They have also some cerebral vasodilator effect. They have been prescribed in the hope that they may help other inner ears related symptoms along with vertigo.

VASODILATOR DRUGS

Nictoinic acid (Hexopal; 500mg tablets, Ronicol; 500mg tablets)
Naftidrofuril oxalate (Praxilene) 100mg capsules
Betahistine Hydrocholoride (Serc) 8 and 16mg tablets.

These drugs are used to improve cerebral circulation as vasodilators. Betahistine has been promoted as a specific treatment for Meniere's disease claiming to improve the labyrinthine circulation. In some patients the severity and frequency of vertiginous attacks are reduced, however its effect on tinnitus is not certain.

CALCIUM CHANNEL BLOCKERS

Based on the knowledge that i) extra and intracellular calcium concentration is of critical importance for sound transduction, ii) drug induced tinnitus can be attenuated by providing the subject with an extragenous calcium supplement and iii) L-type calcium channel blockers are effective in alleviating drug induced tinnitus (Jastreboff, 1995) an L-type calcium channel blocker, Nipodipine has been a good candidate for drug trial.

NIMODIPINE (Nimotop) 30mg tablets.

Davies et al. (1994) found in an 8 week trial that 5 of 31 patients reported great improvement, 2 found worsening of tinnitus. Four of those with improvement in their tinnitus continued a further 4 weeks of the drug, minimum masking level measures showed reduction in their tinnitus. Further research is required before conclusions may be drawn concerning these data.

THE LOOP DIURETICS

Frusemide (Frusemide, Lasix)

Based on the knowledge that frusemide reduces the endocochlear potential, it was thought that it may be suitable for the suppression of tinnitus. Although earlier trials gave promising results, the study by Jayarajan and Coles (1993) showed that, when it is administered intravenously, tinnitus was reduced in half of the subjects. However it did not appear to reduce tinnitus to a helpful degree when taken orally.

GINKGO BILOBA EXTRACTS

Ginkgo biloba is an extract from the leaves of the maidenhair tree, and is a herbal medicine with a very long history. It has been promoted for the treatment of chronic cerebral vascular insufficiency and peripheral vascular disease. It is thought to improve blood flow. It has also been used in the treatment of retinal disease and vertigo. Earlier reports on its effect on tinnitus were optimistic, however the study by Holgers et al. in 1994 did not find grounds for this optimism. The interest in its possible value for tinnitus treatment remains and a study is currently being conducted by Ewart Davies.

RECENTLY TRIED DRUGS WHICH TAKE THE PATHOPHYSIOLOGICAL MECHANISMS OF TINNITUS INTO CONSIDERATION

GAMMA AMINOBUTYRIC ACID (GABA) AGONISTS

Baclofen (Baclofen, Lioresal) 10mg tablets.

This is a selective GABA receptor drug. It is used for the treatment of trigeminal neuralgia and increased muscle tone and spasticity. L-Baclofen has been shown in animals to have suppressing effects within the cochlear nucleus (Caspary et al. 1984, Szczepaniak and Moller, 1995). Baclofen appeared to hold promise for the treatment of tinnitus. Recently Westerberg et al. (1996) made a double blind placebo controlled study on the effect of baclofen on tinnitus and found that of the 32 patients in the placebo group, 1 (3.4%) reported improvement and of the 31 subjects on baclofen 3 (9.7%) reported improvement, no significance was found. Side effects such as confusion, drowsiness, dizziness and gastrointestinal upset were related to

the drug. Despite this disappointing finding, the drug may have effects on the mechanisms involved in tinnitus and further research is indicated.

PROSTAGLANDINS

Based on the knowledge that aspirin, some non-steroid anti-inflammatory drugs and aminoglycoside antibiotics have toxic effects on the cochlea with resultant hearing loss and tinnitus could partly be related to an alteration in the prostaglandin mechanism in the cochlea, Briner et al. (1993) thought it would be worth trying a synthetic prostaglandin E1 (Misoprostol) in the treatment of tinnitus. 8 of their 24 patients reported improvement during the active drug phase, together with improvement in sleep and concentration. The researchers felt that this promising result was worthy of further investigation.

DRUGS ACTING ON GLUTAMATE RECEPTORS

Caroverine

This is a drug used as a spasmolytic in some countries. It has also agonist effect on glutamate receptors in the cochlea. There is growing evidence that glutamate and glutamate receptor dysfunction is implicated in a wide range of inner ear diseases including presbycusis, noise induced hearing loss, Meniere's disease and sudden hearing loss. Denk et al. (1997) based on their earlier clinical experience, carried out a single blind study on its effect on tinnitus. Caroverine is administered only by intravenous infusion. The authors investigated the immediate effects. They found reduction in the tinnitus in 50% of the subjects. They concluded that the positive respondents had tinnitus of cochlea origin and that caroverine is probably beneficial in these cases. It is impractical to use this drug for tinnitus treatment at the moment. However it implies that in the future some drugs which can be taken orally and act on the glutamate function would be efficacious. This knowledge stimulates further research.

CONCLUSION

Although one would not discount the possibility that a drug or drugs may be found to relieve tinnitus, as yet no safe, reliable drug to cure or consistently alleviate tinnitus has been found.

DRUG TREATMENT OF INNER EAR DISEASE ASSOCIATED WITH TINNITUS

Meniere's disease

The pathology of Meniere's disease is endolymphatic hydrops. It is characterised by a)episodic attacks of vertigo, lasting from several minutes to hours, b)autonomic imbalance manifested by nausea/vomiting, c)fluctuating hearing loss, d)usually low-pitched tinnitus, e)sense of pressure/fullness in the ear. In many patients tinnitus is present between the attacks but it increases and may change in quality in association with the attacks.

There is no known specific drug treatment for Meniere's disease. Individual attacks are treated by drugs to alleviate vertigo, nausea and vomiting.

Diuretics, betahistine hydrochloride and a variety of other drugs have been used for the purpose of reducing the frequency and severity of the attacks. The effectiveness of drug treatment is uncertain. Patient-management with counselling and elimination of precipitating factors such as stress, possible dietary factors and high salt intake appear the best way of helping the patient at present.

If there is constant tinnitus, the ideal approach is habituation with cognitive therapy or retraining therapy (consult audiologist).

Sudden deafness

This may or may not be associated with tinnitus or vertigo. Depending on the cause, vasodilators, corticosteroids, dextran perfusion or hyperbaric oxygen therapy, or a combination of any of these are used.

Autoimmune inner ear disease.

In the case of an inner ear malfunction associated or not associated with tinnitus through to be due to an autoimmune abnormality revealed by immunological studies, corticosteroid or immunosuppressant drug therapy is worth trying.

Syphilitic inner ear disease.

If diagnosis is certain it requires specific drug treatment.

TREATMENT OF CONDITIONS WHICH MAY BE CONTRIBUTING OR AGGRAVATING FACTORS FOR TINNITUS

In some patients there may be extra-auditory factors contributing to the degree or emergence of tinnitus, e.g. hypothyroidism, anaemia, vitamin B12 and zinc deficiency, diabetes, hypoglycaemia, hypertension, hyperlipidaemia, food and drink allergies, migraine etc. Their treatment may result in diminution of the tinnitus or at least preventing it from becoming worse.

If the patient is on any known ototoxic medicine it should be discontinued unless the medicine is vitally important. Some patients may have individual susceptibility to certain drugs, foods or drinks which aggravate their tinnitus and sensible counselling which does not result in the patient becoming obsessive about food and drinks helps.

Reinstatement of sedative drugs or tranquilisers.

When suddenly discontinued, many patients may have a wide range of symptoms including emergence or aggravation of tinnitus. In Coles' experience, the reinstatement of the drug followed by very gradual withdrawal results in much reduction or abolition of tinnitus (Coles, 1997).

MEDICAL TREATMENT OF SOMATOSOUNDS OR OBJECTIVE TINNITUS

Spontaneous otoacoustic emissions (SOAEs)

Tinnitus caused by SOAEs can be treated by aspirin or quinine. (Details in Appendix 6).

Clicking tinnitus caused by palatal or middle ear myoclonus

This is a rare neurological condition in which the small muscles contract involuntarily in a quiet rhythmic fashion causing clicking noises. It has been shown that injection of botulinum toxin to the palatal muscle is effective (Saaed and Brooke, 1993). Additionally, training in deep relaxation techniques and counselling re stress related issues is highly beneficial and strongly recommended.

Pulsing (throbbing) tinnitus

If this is caused by anaemia or hypertension drug treatment of these may be effective. If it is caused by intracranial vascular malformation or occlusive cranial vascular disease the treatment approach would be surgical.

It is reported that tinnitus caused by somatosounds are amenable to habituation and this may be assisted by retraining therapy (Jastreboff and Hazell, 1993).

MEDICAL MANAGEMENT OF ASSOCIATED OR CONSEQUENTIAL PROBLEMS WITH TINNITUS

In a considerable proportion of patients the actual perception of the tinnitus sound is probably less troublesome than the accompanying emotional and autonomic consequences and the functional effects on day to day life such as sleeplessness, fatigue, difficulties with concentration and memory lapses. These can be more deleterious to the individual than the noxious experience of tinnitus. These effects may occur whether or not the individual makes negative attributes to tinnitus, but negative attributions impede habituation to tinnitus. Drug treatments for tinnitus need, in order to be effective, to take into consideration these problems which people experience with tinnitus.

Before being seen in the tinnitus clinic many patients are put on sedative/hypnotic drugs for their insomnia. It is important to be circumspect in prescribing these drugs, and they should only be given for reasonably short periods. It is advisable to provide reasonable counselling for methods of combating insomnia without drugs.

Association of anxiety and/or depression with tinnitus may be a two-way relationship, the causal direction is usually difficult to discern. If the condition is so severe as to be unable to benefit from counselling or professional psychological support, tranquilisers or antidepressants may be given careful consideration. It is best to cooperate/consult with psychologist and psychiatrist.

STIMULATORY OR PHYSICAL METHODS IN THE TREATMENT OF TINNITUS

These are treatment methods which aim to influence or affect the auditory system in ways which can rectify or modify its dysfunctional state in order to abolish or alleviate tinnitus. The following is a list of these methods of treatment:

Magnetic stimulation
Ultrasonic stimulation
Low intensity laser application
Transcutaneous electrical nerve stimulation (TENS)
Acupuncture
Hyperbaric oxygen therapy
Treatment of temporo-mandibular joint and myo-facial disorders

The above methods are beneficial in some patients but they are all open to further research and development.

Thank you to the Institute of Hearing Research, Nottingham England for permission to use the above on the properties and uses of various medications.