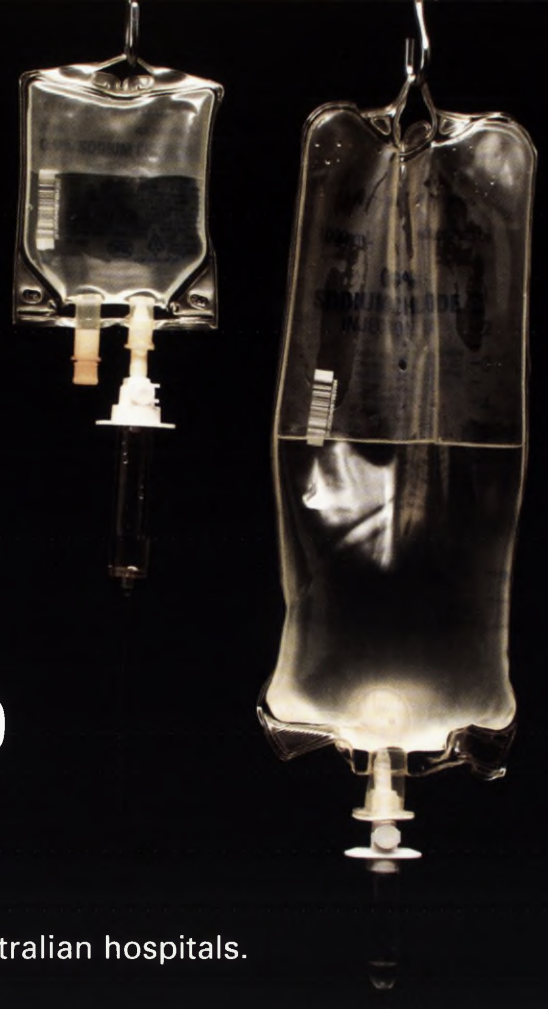
By Ngaire Watson



Gentamicin – an antibiotic to use with care

Gentamicin is an antibiotic widely used in Australian hospitals.

It is known to lawyers due to the damage it can do to the apparatus inside the ear (ototoxicity) and the kidney (nephrotoxicity).[1] This article focuses on ototoxicity and how to assist a client who presents with this life-changing problem.

Gentamicin was discovered in 1963 and belongs to a class of drugs called aminoglycosides. Other aminoglycosides (which can all be toxic) are tobramycin, amikacin, paromomycin, framycetin, neomycin and streptomycin. Streptomycin was the first, discovered in 1945. Right from the start, when streptomycin was discovered, it was known that these drugs were ototoxic and nephrotoxic, and that great caution was required to get the dose correct.[2]

Despite government and private sector interest in the topic, iatrogenic (health practitioner-caused) injury still occurs at an alarming rate in Australian hospitals.

GENTAMICIN CHECKLIST

One of the most important aspects in assisting a client through the maze of a claim against a medical practitioner is the fact that there will usually be a denial of liability. This makes it necessary to gather all the medical evidence available and examine it carefully. The following information is needed:

- What dose of the medication was administered?
- Over what period of time was the dose run into the client? A bolus dose means it was pushed in rapidly rather than left to drip.
- Was the client weighed?
- What other medications were being administered at the same time? If more than one drug was being administered that was excreted by the kidneys, this puts a strain on the kidneys to work overtime.
- Were the kidneys in good working order?
- Was the client receiving intravenous fluid? Could the client have been dehydrated? Dehydration causes the concentration of the drug to increase in the blood stream.
- Was the client given any information or warnings about the side-effects of gentamicin?
- Did the client ever have any pervious balance or hearing problems?

Gentamicin is currently used to treat a wide range of infections in Australian hospitals. It is not absorbed orally, so it is usually administered intravenously, intramuscularly or topically – such as in ear drops. The toxic effects can be encountered after any injected administration or via topical ear drops.[3]

It is a popular drug with doctors because it is effective against a number of serious infections, including Golden Staph.[4] However, an audit conducted at The Royal Melbourne Hospital found that gentamicin prescribing practices were 'suboptimal' and that '[p]rovision of a guideline and education sessions with doctors do not necessarily lead to widespread adoption of recommended practices'.[5]

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Body weight and dosage

Hilmer et al[6] conducted a study into the rate at which patients were weighed in hospital. They referred to 'The Quality Use of Medicines Framework', which identifies three key steps to prescribing:

- Decide on the best treatment.
- Select medicines wisely.
- Use medicines based on the best evidence (right dose and right duration).

The authors looked into the rate at which patients were weighed on admission to two wards at Royal North Shore Hospital, and found that less than one-third of patients had been weighed. Additionally, unweighed patients had more complications than patients who were weighed.[7]

Gentamicin belongs to a category of drugs that are excreted via the renal system, which means that a person's kidneys need to be in good working order to eliminate the drug from their system. People with poor renal function should either not receive gentamicin or should have a reduced dose calculated for them. The dose is based on body weight, expressed as mg per kg. Typically, an adult should not get more than 5-7mg/kg/day.

Online information and resources

The federal government is interested in the prevention of adverse effects of medication, and has compiled a list of links to websites containing relevant information and resources.[8] Of these, a website operated by healthlinks.net[9] is particularly useful for legal practitioners wanting to gather quality information about medications, including their side-effects. The information contained on this website is organised so as to be accessible to consumers as well as health practitioners. A search of 'gentamicin' revealed all the pertinent side-effect information that would be required by an individual who is concerned about their medication.

SAFETY FIRST WHEN PRESCRIBING GENTAMICIN

The *Therapeutic Guidelines* is a very well-known and accepted pocket-sized guide. It is inexpensive and widely available throughout Australia – in short, there is no excuse for a medical practitioner not to have a current edition. It is regularly updated as new drugs come on to the market and as new research is published. The current 2009 edition on antibiotics states:

> 'Patients should be informed where possible that there is a chance of balance or hearing problems related to aminoglycoside use, especially if treatment is prolonged. Patients should be regularly asked about any hearing or balance problems and told to report it immediately if they occur. For prolonged aminoglycoside courses (>5 days), formal vestibular function testing and high-frequency audiometric testing should be considered, if available.'[10]

Prescribing doctors are aware of the propensity of gentamicin to be toxic. This toxicity has been thought to be dose dependent, but a group of Sydney doctors has found that 'even in accepted therapeutic doses, [gentamicin] can occasionally cause bilateral vestibular loss (BVL) due to hair cell toxicity'.[11] Some people have an inherited predisposition which makes them highly sensitive to the ototoxic effects of gentamicin and a single dose in such a person can cause permanent hearing loss. It is thought that the sensitivity is passed down the maternal line.[12] Studies have shown that gentamicin damages the vestibular apparatus at a rate of 1.4 to 3.7 per cent. This can be higher if other ototoxic drugs are also administered, such as ethacrynic acid.[13]

The problem arises because our sense of balance is achieved when tiny bones (otoliths) move across tiny hairs inside the middle ear. As we move our heads the otoliths move across the hairs and cause signals to be sent by the hairs about the otoliths' position. In turn, this provides information about the position of our head in space. In some individuals, gentamicin destroys these hairs, and they do not grow back.

A person who develops ototoxicity can develop the following signs and symptoms, which are largely irreversible:[14]

1. Vestibular toxicity: initially nausea, vomiting, sweating and vertigo, then –
   a. oscillopsia – a visual sensation that objects are moving or bouncing; and/or
   b. ataxia – loss of balance when walking, which may be perceived as dizziness.
2. Cochlear toxicity: tinnitus, later loss of hearing at high frequency.

QUESTIONS ON CAUSATION

To assess liability, the following questions need to be considered:

1. Was gentamicin an appropriate choice of antibiotic? There are other antibiotics (such as the widely available but potentially more expensive class called the beta lactams) which can be used to treat the same organisms; these antibiotics are generally safer.
2. Was an appropriate dose of gentamicin used? Doses should be calculated according to the age and weight of the patient. If the person has impaired renal function, the dose should be reduced.
3. Was appropriate monitoring of the person performed? Tests of gentamicin blood levels should be ongoing to avoid toxicity.
4. How long was the length of treatment with gentamicin? The longer the treatment, the greater the risk of toxicity.

Surgical antibiotic prophylaxis occurs when a person is operated on and the doctor decides there is a risk of infection. Antibiotics can be administered prophylactically, as a protective measure. However, some surgery is identified as 'clean surgery', such as when healthy skin is cut. Examples of this are when cosmetic surgery is performed or when urinary, respiratory or gastric tracts are entered but not punctured. Such 'clean' surgical sites do not require antibiotic prophylaxis.[15]

It is not immediately obvious if a person has oscillopsia or ataxia if they are bed-bound or very ill. If they are not mobile, they may not become aware of the problem until they have left hospital.

In *Strempel v Wood* [2005] WASCA 163, the plaintiff had

undergone a knee replacement and developed 'permanent giddiness, vertigo, imbalance, nausea, hearing loss and tinnitus as a result of gentamicin-induced toxicity'.

In the post-operative period, one of the arteries which flows into the lower leg became occluded. This ultimately led to the lower leg swelling and the plaintiff developing a condition known as 'compartment syndrome'. The only way to relieve the pressure in the leg and save it from becoming necrotic (dead) was to do further surgery – to open up the layer of tissue which surrounded the leg – a fasciotomy. In the meantime, as a result of the surgical intervention and lack of blood flow, the plaintiff was at risk of serious infection in his leg. The plaintiff was prescribed intravenous gentamicin which was continued for approximately two months. On appeal, their Honours Malcolm CJ, McLure JA and Le Miere AJA found that:

> 'Gentamicin should not be given for any longer than 10 days, because it involves a risk of permanent side-effects. The known risks include permanent loss of hearing and permanent vestibular dysfunction symptoms including nausea and dizziness. Approximately four to five weeks after his initial prescription, the appellant [plaintiff] started developing side-effects. Principally, these were loss of hearing and loss of balance.'[16]

A WORD ON DRUGS AND BUGS

Medicos are faced with an ongoing challenge around the overuse of particular antibiotic drugs and the propensity of infections to become resistant to the drugs – such as MRSA (Methicillin Resistant Staphylococcus Aureus – better known as Golden Staph). MRSA is resistant to many antibiotics, but gentamicin can have a place in treating this difficult-to-treat infection. This is why gentamicin is likely to remain with us for some time into the future and to continue to come to the awareness of legal practitioners.

CONCLUSION

It could be argued that gentamicin has no place in today's armoury of antibiotic treatment. The drug's positive features are mainly that it is cheap and that it is effective against a range of infective organisms (medically referred to as 'gram negative organisms'). However, despite these positive attributes there are other drugs which, while potentially more expensive, are safer to use.

The central problem appears to be that doctors do not follow the guidelines. If they did, they may find more patients opting for the more expensive but safer antibiotics. Additionally, if more routine monitoring was done, more people might be saved from this debilitating problem. ■

Notes: **1** Therapeutic Guidelines Ltd, *Therapeutic Guidelines: Antibiotic*, Version 13 (2006) p13. **2** Evan J Begg and Murray L Barclay, 'Aminoglycosides – 50 Years On' (1995) 39(6) *British Journal of Clinical Pharmacology* 597-603, p597. **3** Robert J Black et al, 'Ototoxic Ear Drops with Grommet and Tympanic Membrane Perforations: A Position Statement' (2007) 186(11) *Medical Journal of Australia* 605-6. **4** MIMS, revision date 2009. **5** CL Leong et al, 'Providing Guidelines and Education is Not Enough: An Audit of Gentamicin Use at The Royal Melbourne Hospital' (2006) 36 *Internal Medicine Journal* 37-42. **6** SN Hilmer et al, 'Failure to Weigh Patients in Hospital: A Medication Safety Risk' (2007) 37 *Internal Medicine Journal* 647-50, p647. **7** *Ibid*, p647. **8** Australian Government, 'Preventing Adverse Effects of Medication' (2010) available at http://www.healthinsite.gov.au/topics/Preventing_Adverse_Effects_of_Medication, accessed 8 March 2010. **9** Available at http://www.medicines.org.au, accessed 8 March 2010. **10** Therapeutic Guidelines Ltd, *Therapeutic Guidelines: Antibiotic*, Version 13 (2006) p342. **11** KP Weber et al, 'Horizontal Head Impulse Test Detects Gentamicin Vestibulotoxicity' (2009) 72(16) *Neurology* 1417-24. **12** M Bitner-Glindzicz & S Rahman, 'Ototoxicity Caused by Aminoglycosides is Severe and Permanent in Genetically Susceptible People' (2007) 335 *BMJ* 784-5. **13** Richard A Santucci & John N Kriger, 'Gentamicin for the Practicing Urologist: Review of Efficacy, Single Daily Dosing and "Switch" Therapy' (2000) 163 *Journal of Urology* 1076-84. **14** GM Halmagi, 'Diagnosis and Management of Vertigo' (2005) 5(2) *Clinical Medicine* 159-165; R Janknegt, 'Aminoglycoside Therapy Current Use and Future Prospects' (1990) 12(3) *Pharmaceutisch Weekblad Scientific edition* 81-90. **15** W Munckhof, 'Antibiotics for surgical prophylaxis' (2005) 28 *Australian Prescriber* 38-40. **16** *Strempel v Wood* [2005] WASCA 163 at [149].

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