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EDITORIAL

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Infections are a potentially preventable cause of hearing impairment in children and adults, and particularly cause permanent hearing loss in developing countries. In sensorineural hearing loss the damage is mainly in the cochlea but the vestibulocochlear nerve or auditory pathways may also be involved. Whereas conductive hearing impairment as a result of otitis media is an important cause of hearing loss in developing countries and may be long-lasting, a sensorineural hearing impairment, particularly if severe or profound, is even more disabling for the individual and is, therefore, the focus of this Issue of the Journal.

Infections which cause a bilateral or unilateral sensorineural hearing impairment can be congenital or acquired. The main congenital infections are rubella, cytomegalovirus and syphilis, whereas acquired infections include meningitis, measles and mumps. HIV/AIDS and malaria are also implicated in studies of the causes of a hearing impairment, but the evidence for a causative role is confused by the occurrence of opportunistic infections (in people with HIV/AIDS) and the use of ototoxic drugs in treatment.

Diagnosis

In diagnosing an infection, a history of contact, clinical features and medical examination are helpful but a definitive diagnosis depends upon the results of laboratory investigations, e.g., on blood and sometimes urine samples. Diagnosis of an infection known to be a risk factor for hearing loss should alert clinicians to ensure that the affected individual has their hearing tested subsequently. Simply asking the parent of a young child if they have noticed a problem is useful only if testing facilities are not available. This is because observers may miss mild or moderate hearing loss or a hearing loss in only one ear, yet these could adversely affect a child's speech and language development and lead to behavioural problems.

A pupil at the SERVE Hearing Impairment Project (SHIP), Jalalabad, Afghanistan

Photo: SHIP

Where there has been normal hearing previously, then finding a hearing loss would indicate the infection to be the cause. More problematic is diagnosing a hearing loss and then looking back into the patient's past history to identify the cause. Having had an infection which is known to be associated with hearing loss does not necessarily mean that this was the cause of any hearing loss found years later in a teenager or adult. There may be a different cause. For instance, there may also be genetic factors such as a family history of hearing impairment or consanguinity or problems from around the time of birth. Many hearing impaired and deaf persons have more than one potential cause of hearing loss in their previous history and it is not always clear which actually caused the hearing defect.[1]

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Importance of Early Identification of a Hearing Loss

Detection and rehabilitation of a hearing impairment as early as possible is essential. A child is more likely to develop speech and language skills within the normal range if a congenital or early onset hearing impairment is effectively rehabilitated in the first six months of life.[2] Research has shown that there is a 'critical' period for language development in early childhood. Although not everyone agrees as to how long this period lasts, it is probably time-limited and mainly during the first 3 years of life.[3,4] In many centres, new tests are now available for detection of a hearing impairment soon after birth. Even when there is no equipment available for these, longer-established tests such as the distraction test can be used to detect hearing impairment in infants. [5]

Animal research too has shown that the development of the central auditory system is affected if there is early sound deprivation. For example, auditory neurones in the central auditory cortex take on a different function if there is no sound stimulation.[6]

Adults and older children benefit from early detection of an acquired hearing impairment. An infection such as meningitis, causing a very severe/profound bilateral hearing loss, can result in speech deterioration within only a month or two, unless the experience of sound is restored. They can also suffer from balance problems which could result in injury. Importantly, the cochlea can also become filled with bone within months of meningitis. In countries where cochlea implants are available, clinicians try to implant these early after meningitis - before bone formation has taken place.

Summary

Detection and rehabilitation of a sensorineural hearing loss of any causation, as early as possible, has benefits for both children and adults. Where an infection, known to be associated with hearing loss takes place, then all health care workers involved in treating the patient should ensure that hearing is checked subsequently. Prevention is preferable to treatment and remediation and so efforts should be made to ensure that all those eligible to receive vaccinations against infections are encouraged to have them. A reduction in the prevalence of sensorineural hearing impairment will be one of the many benefits of such action.

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CONGENITAL INFECTIONS AND HEARING IMPAIRMENT

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Congenital Infection

Congenital infection is a common cause of hearing impairment. The most frequent associations are with cytomegalovirus, rubella virus, and *Treponema pallidum* (syphilis). Until recently *Toxoplasma gondii* (toxoplasmosis) would be included in this list as it was thought to be a significant cause of congenital ear and eye defects. However, recent evidence emerging across Europe suggests that although it is a significant cause of blindness, the association with hearing impairment is poor.[1] The relative risks of congenital transmission with each of these agents and the associated risk to hearing is shown in Table 1. Congenital hearing impairment is sometimes seen as part of a severe syndrome as in the congenital rubella syndrome (CRS) – but more commonly hearing impairment or loss is the first and/or only manifestation of intrauterine infection and may not even be recognised as due to a congenital infection. In many cases, impairment is not detected until the child reaches 2 to 4 years of age and at this age definition of the causative agent is difficult.

Cytomegalovirus

Human cytomegalovirus (HCMV) is a human herpesvirus. In the developing world, acquisition of HCMV is nearly universal in early childhood. Transmission is assumed to be through the close physical contacts that result from crowded living conditions as the virus is spread in bodily fluids such as saliva. Infection is usually asymptomatic but, like all herpesviruses, after first infection HCMV remains in the body for life in a latent state. However, the virus undergoes regular periods of reactivation when new virus is produced that is shed in bodily fluids to infect a new host. Although in a healthy person this is usually of no consequence, problems arise when the virus causes a congenital infection. This may occur if the mother becomes infected for the first time during pregnancy causing a primary infection which affects her baby, or less often because the virus reactivates during pregnancy. A baby born with a severe symptomatic, congenital HCMV infection will be very poorly; most have a pinpoint purplish-red rash, jaundice and an enlarged liver and spleen. Many will also have an abnormally small head associated with mental retardation and other neurological problems such as lethargy and floppiness, poor sucking and/or seizures and will often be small for gestational age. However, most have no apparent symptoms at birth but may develop symptoms later. For both symptomatic and asymptomatic congenital HCMV

infection, sensorineural hearing loss is the most frequent symptom. The loss is usually bilateral, but may affect only one ear and typically becomes progressively worse over time. The majority affected in this way eventually have severe to profound loss (≥71 dB). In both groups of children, the hearing loss may have delayed onset occurring over a wide age range, from 6 months to 16 years, but the median age of onset of loss is 3 to 4 years.[2]

Previously, primary infection with HCMV during pregnancy was considered to be the only risk for congenital infection and, as most new mothers in the developing world are likely to be seropositive, it might be assumed that congenital CMV infection would not be a problem there. However, it is now known that primary infection, re-infection and reactivation of infection in the mother can all lead to congenital infection. Also HCMV infection and reactivation is very common in AIDS patients, thus, it is likely that a considerable burden of congenital CMV exists in developing nations.

The only treatment currently available for congenital CMV infection, that has been evaluated for its effect on preventing hearing loss is ganciclovir therapy. Ganciclovir is an antiviral agent that prevents replication of the virus. It is not ideal as a treatment option for infants as it has high bone marrow toxicity, so careful monitoring of dosage is required. There have been a number of reports describing the benefits of ganciclovir treatment for preventing hearing loss in a congenitally infected infant. However, in most cases control populations were unavailable and no firm conclusion can be reached about this until further studies are carried out. As yet, the prospects for an effective vaccine are slight. Although several different vaccines have been developed, limited studies carried out so far suggest they do not protect against re-infection or reactivation of the virus. Thus, their usefulness remains to be determined.

Rubella (German Measles)

Rubella causes a mild childhood illness characterised by a slight fever, swollen lymph nodes and a red rash. Until 1941, it was considered to be relatively unimportant and with no serious sequelae. However, following a large epidemic of rubella in 1940, N M Gregg, an Australian ophthalmologist noted a large proportion of babies born with cataracts, heart defects and deafness.[3] Severe congenital rubella infection is known as congenital rubella syndrome (CRS). Of all the problems associated with CRS, deafness is the most common and the only one that appears alone, probably because development of the inner ear occurs over a longer period (during the second to fourth month of gestation) than most other organs. As with CMV, rubella-induced hearing loss usually affects both ears and may develop as a late symptom of the infection. It is useful to remember that in a child with hearing loss due to a suspected congenital rubella infection, a characteristic, patchy 'salt and pepper' pigmentation can sometimes be noted at the back of the eye even when the eye is apparently unaffected.

Rubella is a highly contagious infection and circulates freely in unvaccinated populations spreading by the respiratory route. To date, no effective antiviral drugs have been developed to treat it. Therefore, prevention of infection is needed: it is essential that women of childbearing age are immune to the virus before they become pregnant and a number of different strategies have been tried to achieve this in developed countries. However, worldwide, congenital rubella infection is still a significant problem. No African countries currently include rubella in their immunisation schedule. Indeed, it has not been recommended for inclusion in the WHO Expanded Programme of Immunization (EPI) in developing countries because, unless sustained high coverage among the infant population can be guaranteed, rubella vaccination could actually have a negative effect on the incidence of congenital rubella syndrome as it could make women of child bearing age more

Bilateral congenital cataracts in a child with the congenital rubella syndrome. The child's mother had rubella in the first three months of her pregnancy.
Photo: John D C Anderson

Table 1: Congenital Infectious Causes of Auditory Impairment
(Adapted from Vallely et al, 2002)[4]

Congenital Infection				
	Percentage transmission risk and (percentage risk of damage[1])			
	1st trimester	2nd trimester	3rd trimester	Term
Infectious Agent				
Rubellavirus	90% (80-90%)	25-70% (5%-15%)	35% (0%)	100% (0%)
Human cytomegalovirus	40-50% (10-15%[2])	40-50% (10-15%[2])	40-50% (10-15%[2])	100% (probably 0%)
Toxoplasma gondii	4-25% (2-10%)	25-54% (2-4%)	65% (0%)	80% (0%)
Treponema pallidum	70-100% in primary syphilis (50% risk of neonatal death)			

[1]'Damage' represents risk of significant foetal damage when mother experiences infection in pregnancy (e.g., if materno-foetal transmission occurs in 60% of pregnancies and 40% of the foetuses who are congenitally infected are damaged, overall percentage risk of damage is 60/100 x 40 i.e., 24%)

[2]Known risk of damage following symptomatic infection – probably an underestimate as risk of damage, particularly hearing loss, following asymptomatic infection is unknown

susceptible by slowing but not eradicating rubella circulation. Thus, to ensure that childhood vaccination is an effective strategy in the long term, sustained high vaccine uptake levels, and periodic assessment of rubella susceptibility rates among teenage and adult women, are essential.

Syphilis

Syphilis is caused by the bacterium *Treponema pallidum*. It is a common infection in most of the developing world and has recently re-emerged in parts of the developed world. There are four stages in the course of untreated syphilis; primary, secondary, latent and tertiary syphilis. The typical syphilis lesion or chancre occurs at the primary stage. The main route of transmission is sexual contact, but syphilis can also be transmitted from an infected mother to her baby. Congenital infection can occur at any stage during pregnancy (Table 1) but the highest likelihood of damage to the foetus is when infection occurs and is untreated during the first or second trimesters. Third trimester infection is more likely to result in asymptomatic disease. During primary syphilis the rate of vertical transmission in untreated women is 70% to 100%; this drops to 10-40% in the latent stage of the disease. Thus the poorest prognosis is for an infant infected during the first or second trimester by a mother in the primary or secondary stages of disease. The symptoms of congenital syphilis at birth are varied: often the neonate is asymptomatic, or there may be clear multi-organ involvement. The manifestations of congenital syphilis can be divided into early (those occurring in the first two years of life) and late (symptoms of disease occurring after the first two years). Early manifestations typically develop within the first few months of life. These include persistent and profuse nasal discharge which may be blood-tinged and is highly infectious, as well as liver enlargement, a raised red rash, and swollen lymph nodes, indeed the appearance of a newborn with congenital syphilis has been described as 'a little wrinkled potbellied old man with a cold in his head'. Hearing loss is a late symptom of congenital syphilis and often appears as one of a group of signs known as 'Hutchinson's Triad'. These signs include inflammation of the cornea giving it an opaque appearance which leads to loss of vision, peg shaped upper incisors (Hutchinson's teeth), and eighth cranial nerve deafness. Hearing loss is the least common component of Hutchinson's triad and occurs in around 3% of children with late congenital syphilis. It typically appears when the child is 8-10 years of age, although occasionally it may be delayed until adulthood. Onset is sudden and damage to the cranial nerve is thought to result from a persistent and ongoing inflammatory response to the infection. Loss of hearing may be unilateral or bilateral and initially involves higher frequencies, with normal conversational tones affected later.

Because of the serious morbidity and risk of foetal mortality associated with the infection, all pregnant women identified with syphilis require treatment. The WHO recommendation is that asymptomatic neonates born to infected mothers should receive 50,000 units/kg of benzathine penicillin G in a single intramuscular dose. Symptomatic infants should receive intramuscular or intravenous aqueous crystalline penicillin G administered at a dose of 50,000 units/kg every 12 hours for the first 7 days of life and then every 8 hours for 3 days or intramuscular procaine penicillin G at a dose of 50,000iu/kg as a single dose daily for 10 days.[5] In the presence of HIV infection caution is warranted; the alteration of B-cell function in HIV patients can result in both false positive and false negative testing for syphilis and women identified with HIV infection, therefore, require special attention.

Prenatal screening for syphilis is commonplace in developed countries and is the main priority for prevention of the disease In developing countries. In order to reduce childhood mortality and sequelae such as hearing loss due to congenital syphilis, there is a need to improve these screening programmes. Ideally, women attending primary health centres should be tested and treated at the same clinic visit. The introduction of newly available rapid, easy to use tests to identify infection in such settings has been shown to reduce the incidence of congenital syphilis by 75% in 2 years.[6] Widespread use of such programmes could help to considerably reduce the mortality and morbidity due to congenital syphilis.

Summary

Congenital infections are an important cause of childhood hearing impairment and may be present at birth or become evident later in life.

The main organisms contributing to congenitally acquired hearing loss are cytomegalovirus, rubella virus and the bacterium *Treponema pallidum* (syphilis).

Toxoplasmosis, though an important congenital infection, is probably not a major cause of congenital hearing loss.

Few anti-viral drug treatments are available and the most effective control method for viral infection is prevention via vaccination programmes. An effective vaccine is available for rubella infection but successful implementation requires high uptake and careful monitoring of seroprevalence.

Congenital syphilis can be treated with high dose penicillin, but is best prevented by identification and eradication of the infection in the mother. This requires universal antenatal screening programmes. Such programmes are feasible with the newly available rapid tests, and implementation must be strongly encouraged.

Most hearing loss due to congenital infection can be prevented.

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HEARING LOSS IN MALAWIAN CHILDREN AFTER BACTERIAL MENINGITIS

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Introduction

Hearing impairment that results from bacterial meningitis is the most common cause of acquired sensorineural hearing loss in childhood. *Streptococcus pneumoniae* meningitis carries a particularly high risk of resulting in hearing loss, but *Haemophilus influenzae* type B and non-typhoidal salmonellae (NTS) infections also carry a great risk. All bacterial meningitis has the potential for hearing and neurological sequelae. Sequelae also follow many tuberculous infections, but are less frequent after viral meningitis. The reported incidences of hearing loss following bacterial meningitis in developing countries vary greatly. The incidence of childhood meningitis in the developing world is about 10 times higher than in developed countries, and the frequency of sequelae is higher and probably under reported.[1] The facilities for the reliable assessment of hearing are not consistently available.

Bacterial meningitis is common in Malawi and accounts for 2.7% of admissions in the Queen Elizabeth Central Hospital, a large governmental tertiary and referral hospital.[2] Human immunodeficiency virus (HIV) prevalence has increased and both meningitis and the chronic otitis media associated with AIDS cause hearing impairment.

Presenting Signs and Symptoms in Meningitis

The signs and symptoms of acute bacterial meningitis are different in children and infants. Older children present with fever, headache, often vomiting, and neck stiffness. Infants with meningitis have the signs of any very sick baby - they feed poorly, are irritable, may develop a grey colour and may not have a fever. A bulging fontanelle is a rather late sign of meningitis. All ages may have seizures and these can be quite subtle and need to be carefully looked for. Meningococcal meningitis may be accompanied by a purpuric rash when there is also a septicaemia.

Causes of Bacterial Meningitis

The common bacterial causes of meningitis in children are *Streptococcus pneumoniae*, *Haemophilus influenzae* type b (in places where the Hib vaccine is not given), and *Neisseria meningitidis*. In children under 2 years of age, non-typhoidal salmonella (NTS) occurs, especially in post-malarial anaemic and malnourished children. In infants, Group B streptococcus is the single most common cause of meningitis, though the Gram negative bacteria, collectively, cause most infections. In Malawi, in children, S. *pneumoniae* is the most common and NTS (*Salmonella typhimurium, Salmonella enteritides*) the second most frequent cause of meningitis. This is against a background of a high prevalence of HIV infection and malaria.

Diagnosing Meningitis

Lumbar puncture (LP) is the 'gold standard' for diagnosing meningitis. It is important to be ready to carry out an LP, as it is disastrous to mismanage meningitis. Sometimes a child is too sick for an LP, in which case antibiotics should be started and an LP done when it is safe to do so. Some children present with difficulty in breathing and to curl them into a suitable position for a lumbar puncture would compromise their breathing even more. Some children have evidence of raised intracranial pressure – posturing, abnormal eye reflexes, irregular breathing pattern, and in the older child, papilloedema on examination of the fundus. If the LP has to be delayed, the cerebrospinal fluid (CSF) will still be cloudy in appearance, at this stage, though on Gram stain no bacteria are likely to be seen.

Treating Bacterial Meningitis

Children with bacterial meningitis are treated with parenteral antibiotic therapy (benzyl penicillin 100,000 iu/kg/ 6 hourly and chloramphenical 25mg/kg 6 hourly) according to the national guidelines - amended appropriately when the sensitivity of the organism was known. Most national guidelines follow the recommendations of the World Health Organization given in the Integrated Management of Childhood Illnesses (IMCI).[3] Infants require parenteral penicillin (100,000 iu/kg/8hourly and gentamicin 2.5mg/kg/8 hourly). Antibiotics are continued for 10 days in children, and 14-21 in infants, in all cases other than meningococcal meningitis (7 days) and *Salmonella* spp. meningitis (30 days). It must be remembered that gentamicin is itself ototoxic and should be used with great caution in children with poor renal function. In premature babies, both the penicillin and the gentamicin doses are given less frequently, the frequency depending on prematurity and body weight. In Malawi, since 2002, pentavalent vaccines that include *Haemophilus influenzae* type b have been part of the childhood vaccination programme. Also, increasing resistance of common bacteria to first line antibiotics has led to reconsideration of antibiotic therapy for meningitis. Some hospitals are advocating the use of parenteral intramuscular or intravenous broad spectrum cephalosporins (called third generation cephalosporins).

Other supportive therapy is provided - maintenance IV fluid, treatment of malaria, anaemia, seizures and reducing a high fever. It is important to ensure adequate nutritional intake and prevent, or treat if it develops, hypoglycaemia.

Table 1: Hearing Outcome by Causative Agent

Hearing test results (% with loss)				
	Normal	**Bilateral loss**	**Unilateral loss**	**Total**
Cause				
S. pneumoniae	41	42 (81)	10 (19)	93
H. influenzae	61	14 (82)	3 (18)	78
N. meningitidis	29	3 (30)	7 (70)	39
Salmonella spp	1	5 (83)	1 (17)	7
Other	3	2 (67)	1 (33)	6
No Growth	32	12 (92)	1 (8)	45
Total	**167**	**78 (30)**	**23 (0.85)**	**268**

Hearing Assessments and Results

Hearing is assessed by a combination of asking the carer's opinion of a child's response to loud and quiet sounds, the level of vocalisation or speech attained; age appropriate behavioural testing; tympanometry; and otoacoustic evoked emissions.

In one study that we undertook in Malawi - of children surviving meningitis - we showed that *Streptococcus pneumoniae* caused 33.6% of the infections, *Haemophilus influenzae* type b caused 30%, *Neisseria meningitidis* a further 15% and in 16% no growth was found on culture of the CSF.[4]

Hearing was impaired in 38%. Hearing loss was bilateral and profound in most (77.2%), and 22.8% had unilateral hearing impairments.

The mortality from bacterial meningitis of 31%, is similar to that reported from other developing countries, but much higher than in developed countries. Similarly, a hearing loss of 38% in survivors is much higher than the 7 – 10% reported from well resourced countries.[5]

Hearing loss is most common following pneumococcal meningitis. Neither age nor sex affected hearing outcome (Table 1). We did not assess infants less than 2 months of age, and do not know the hearing loss in this age group. If children with histories >7 days are excluded, as the symptoms are often non specific and may be unrelated to the onset of meningitis, we found a non-significant increase of hearing loss in those with a longer history of fever (half were affected compared with a third). Antibiotics given in the week prior to admission did not affect outcome. This may be because the antibiotics commonly given were in small amounts (1/2 or one tablet) and often inappropriate (such as cotrimoxazole or oral penicillin).

The presence of a low coma score, but not of seizures on admission, predicated a poorer outcome in our study.

We did find that a high CSF protein, a positive CSF Gram stain and a low total white cell count / cmm each, individually, predicted an increased likelihood of hearing impairment. Adjuvant steroid therapy did not benefit the children in our study. Children left with neurological sequelae were much more likely to have hearing loss than other survivors. This is not surprising as neurological sequelae are the outcome of severe infection.

- Meningitis is a medical emergency – treatment should be started as soon as possible
- The only sure way of diagnosing meningitis is by lumbar puncture
- Infants often present with very non-specific signs and symptoms
- Supportive care – turning the comatosed child, reducing fevers, treating seizures, ensuring feeds (by mouth if able, or by nasogastric tube if unconscious) are important
- Give the full course of antibiotics – no short cuts!
- If fevers persist, even though the child is improving, look for injection abscesses, any other focus of infection and consider complications of meningitis such as a brain abscess or subdural empyema
- If the fever has not settled after 10 days, consider TB meningitis
- Hearing loss, other neurological damage, and hydrocephalus are all sequelae of meningitis. Early diagnosis and treatment will reduce these.

Vaccinations to Prevent Bacterial Meningitis

The *Haemophilus influenzae* type b (Hib) vaccine is highly effective and in developed countries has reduced the number of invasive Hib infections by 98%. It is part of the pentavalent vaccine given to children in the Expanded Programme of Immunization (EPI), in combination with tetanus, diphtheria, and hepatitis B vaccine. Oral polio is given separately but at the same clinic visits. Only about 5 countries in Africa have this as part of their national vaccination programmes. *Haemophilus influenzae* infections are common in under five-year-old children and, if it were widely available in EPI programmes, many cases of meningitis would be prevented. A conjugate pneumococcal vaccine is also available. It is a 7 valent vaccine which is effective against the 7 most common serotypes of the pneumococcus to affect developed countries. These 7 serotypes also cause problems in the resource constrained parts of the world but there are 2 other serotypes which are particularly problematic and are not covered by the 7 valent vaccine (The 2 serotypes are called type 1 and type 5). The 9 valent vaccine has been tried in studies in The Gambia and in South Africa and found to be very effective and even beneficial in the immunosuppressed HIV infected children. The meningococcal vaccines are available for type A which causes the epidemics across the meningitis belt of Africa, and type C. There is, as yet, no vaccine to prevent type B.

Conclusion

Meningitis in settings such as ours has a high mortality and many survivors are left with profound hearing loss. Children with hearing impairment face enormous challenges in trying to maintain speech, if it is acquired already, to learn at school, avoid injuries in busy, undisciplined traffic and be given the opportunity to learn a skill or trade. *Haemophilus influenzae* type b and pneumococcal immunisations would prevent many cases of meningitis. Treatment with third generation cephalosporins would probably improve the outcome in those with meningitis. Community assistance for the deaf would help children with hearing impairment and their families to overcome some of their difficulties. Deaf children in poorer parts of the world need advocates to help them help themselves.

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MEASLES, MUMPS AND HEARING LOSS IN DEVELOPING COUNTRIES

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Studies among deaf children in developing countries have implicated infectious and communicable diseases such as measles and mumps as notable aetiological factors.[1,2,3] This article describes the clinical features of these two conditions and the associated risks to hearing in early childhood. It also highlights necessary steps to address the disease burden in this region.

Measles

Measles is a highly infectious viral sickness which presents as an acute illness with high fever, running nose, characteristic Koplik's spots on the buccal mucosa and a distinctive generalised maculo-papular rash – large flat, red to brown spots that flow into one another and completely cover the skin (Figures 1A &1B).

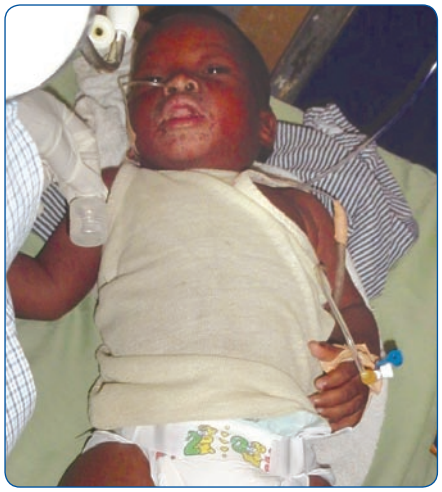

Fig. 1 A: Severely ill 6 1/2 month-old infant, not yet due for measles vaccination, on the 2nd day of the eruptive stage with conjunctivitis, oral inflammation, aspiration pneumonitis, and generalised maculo-papular rash.

Photo: Bolajoko Olusanya

It occurs worldwide but its incidence has reduced significantly in developed countries since the introduction of an effective vaccine in 1968.

Measles is transmitted by droplet infection from the respiratory tract. It is predominantly a disease of infants and young children and occurs mostly after the age of 6 months. It also affects pre-school children but is rare in infants less than 6 months old because of protective maternal antibodies. In some developing countries, measles is endemic and occurs all year-round, but may show periodicity in late winter/early spring and during cold hammattan/rainy seasons in communities where poor housing conditions or overcrowding is widespread.

Where malnutrition is common, mortality from measles may be as high as 25%. Measles accounts for about 745,000 deaths annually, representing 50-60% of an estimated 1.6 million deaths attributable to vaccine-preventable diseases in childhood worldwide.[4] Globally, measles is the leading cause of vaccine-preventable child deaths. About 98% of the death toll from measles occurs in developing countries. In fact, Africa alone accounts for about 500,000 measles deaths per year.

Clinical features

Measles infection is characterised by four distinctive stages of illness:

1. The first stage is the incubation period (IP) of 8-14 days, during which there are no visible clinical signs of the disease.
2. The IP is followed by a prodromal period (PP) of 3-5 days, characterised by a severe constitutional upset, high fever, running nose, conjunctivitis, a harsh dry cough and irritability. Small greyish white lesions, which appear on the buccal mucosa during this stage, known as Koplik's spots, are the most characteristic sign of the disease.
3. The eruptive stage (ES) is the third stage of the disease characterised by the eruption of maculo-papular rash, which starts from the back of the ears, becoming a generalised rash within 2 days (Figures 1A & 1B).

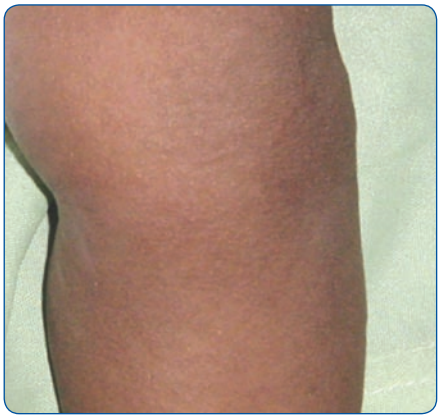

Fig. 1B: Close-up view of the confluent maculo-papular rash on the lower limb of the child in Figure 1A.

Photo: Bolajoko Olusanya

4. The fourth stage is the recovery phase (RP) characterised by the fading of the rash. This phase occurs by the third day of the eruption when the maculo-papular rash is replaced with brownish staining (Figure 2), and sometimes in severe cases, especially in malnourished children, a fine desquamation with extensive ulceration may occur (Figure 3).

Complications

Measles has been reported as a major aetiological factor for severe to profound bilateral hearing loss in deaf children. As it was known that mucous membranes all over the body were affected, the observed hearing loss was previously thought to be conductive and attributable to suppurative otitis media, chronic perforation and mastoiditis. For instance, none of the three children (Figures 1, 2 & 3) highlighted in this report, recorded normal otoacoustic emissions during the recovery phase when tested for hearing impairment. The involvement of the middle ear with extensive mucosal lesions, as demonstrated by these cases, was previously perceived as the main course of measles - related hearing loss, until the documented report of measles virus within the cochlea[5] besides the measles virus-associated otosclerosis,[6] thus providing the needed evidence in favour of the sensorineural component. This finding, therefore, explains the often-reported severe and sometimes progressive/delayed sensorineural hearing loss among deaf children.

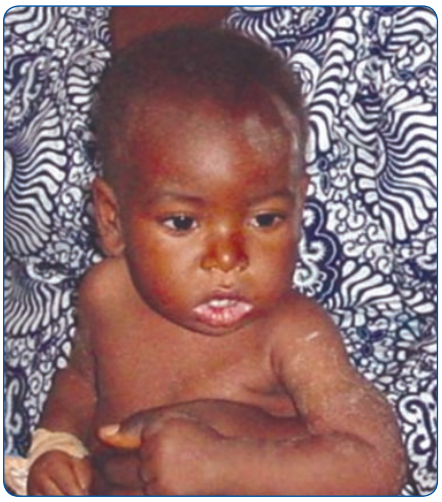

Fig. 2: A 13 months old well-nourished boy who had measles vaccination at the age of 9 months. He is now recovering from measles infection. The generalised maculo-papular rash has been largely replaced by a yellowish stain in the upper limb.

Photo: Bolajoko Olusanya

Apart from the ear and hearing organ, measles infection affects respiratory, ophthalmic, gastrointestinal and the central nervous systems. Complications may occur anytime from the prodromal phase to the recovery stage of the disease. As a result, high fever or febrile convulsion, which may occur towards the end of the second stage or early in the eruptive stage, remains one of the most common complications (Table1). Similarly, severe gastro-enteritis may result from the extensive viral damage of the inner linings, at anytime from the eruptive stage. Severe oral inflammation, due to secondary infection, is more commonly seen in malnourished children towards the end of the eruptive stage.

Fig. 4: Measles immunisation

Preventive measures

WHO and UNICEF have emphasised primary prevention of measles in its global campaign against the prevailing childhood illnesses in the developing world, for several decades. Immunisation for measles is currently administered at the age of 9 months at the earliest, in developing countries. However, the cases presented in this present article highlight two major concerns. Firstly, children between the ages of 6 to 9 months are vulnerable to severe measles attack before vaccination (Figures 1A & 1B). Secondly, severe infections after vaccination cannot be ruled out completely (Figure 2).

Currently, there is only a single-dose vaccine for measles in many developing countries (Figure 4), unlike some other vaccine-preventable diseases such as diphtheria, polio, pertussis and tetanus. The need for a second dose of measles immunisation has been suggested and is currently advocated by WHO and UNICEF - to catch those who have not responded to, or have missed the first dose. In addition, national programmes on immunisation currently exclude mumps vaccination in several developing countries. The triple MMR vaccine against major causes of hearing loss in the region (i.e., measles, mumps and rubella) would easily provide a much better alternative to the current single vaccine for measles.

Good nutrition and breast-feeding should safeguard from middle ear complications, while early diagnosis and intervention remains the mainstay of management. The early recognition of clinical features would provide lead-time for instituting appropriate and effective support treatment. It will also often prevent avoidable complications such as febrile convulsions and corneal ulceration, early in the disease process.

Photos: Christian Blind Mission

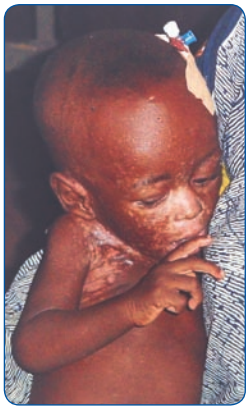

Fig. 3: A 10 months old malnourished infant who missed measles vaccination at 9 months now in the protracted post-measles phase of the illness. The maculo-papular rash is now replaced with widespread desquamation of the skin and buccal ulceration. In addition, the child received treatment for bronchopneumonia, zinc deficiency and electrolyte imbalance.

Photo: Bolajoko Olusanya

Mumps

Mumps, also known as endemic parotitis is a milder disease, relative to measles. It is caused by infection with the mumps virus. A decline in the incidence of mumps has been reported since the introduction of Measles, Mumps, and Rubella (MMR) vaccine which is now administered routinely, mainly in developed countries.

Mumps tends to affect older children and is transmitted by droplet infection from the respiratory tract. The incubation period is about 18-22 days.

Clinical features

Mumps infection is a non-suppurative enlargement of the salivary glands, particularly the parotids. Symptoms are most pronounced during the first two days after the incubation period but subside slowly over the next five days. The clinical features are quite varied and range from inapparent infection in one-third of the cases. In several others, the first presentation may be the appearance of complications.

Complications

Mumps is frequently associated with sudden unilateral sensorineural hearing loss, which is often total, but bilateral involvement has also been reported. Although the incidence of mumps-related sensorineural hearing loss has been documented as 5/100,000,[7] its patho-

physiology has not been fully described. Other complications include aseptic meningitis, post-infectious encephalitis, as well as transient facial paralysis, without prior infection of the salivary glands.

Preventive measures

No preventive measure for mumps is currently available under the Expanded Programme of Immunization in developing countries, in contrast to the practice in most of the developed world where MMR vaccines are routinely administered. This illness and its complications will therefore persist in this region until an appropriate vaccine is introduced.

Conclusion

Measles and mumps are significant aetiological factors for permanent hearing loss in the developing world. Because of the limitations in the current primary prevention strategy for these conditions, early detection through a high index of suspicion and appropriate/timely intervention should be actively promoted - to reduce devastating and long-term complications particularly in 'endemic' communities.

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CONGENITAL RUBELLA SYNDROME: A VACCINE PREVENTABLE CAUSE OF DEAFNESS

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Congenital Rubella Syndrome and Vaccines

The World Health Organization (WHO) estimates that globally there are 100,000 new cases of congenital rubella syndrome (CRS) in infants each year.[1] Most of these CRS cases occur in countries where widespread introduction of rubella vaccine has not been implemented. Rubella vaccine is highly effective; a single dose of the most commonly used RA27/3 rubella vaccine strain leads to seroconversion in at least 95% of vaccinees and is thought to afford lifelong protection. All studies that have examined cost-effectiveness of rubella vaccination, including studies in developing countries have found a positive cost-benefit ratio.[2]

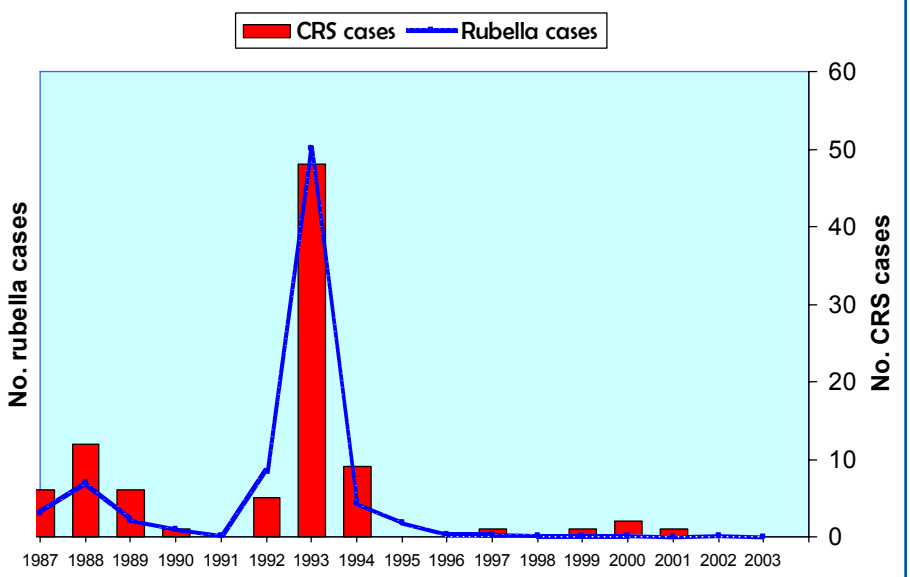
Rubella Vaccination

The WHO position paper on rubella vaccines recommends that all countries should assess their rubella situation and, if appropriate (see Box), make plans for the introduction of rubella vaccine.[1]

The primary purpose of rubella vaccination is to prevent CRS. There are two approaches:

1. Prevention of CRS by providing rubella vaccine to women of childbearing age; or
2. Prevention of both rubella and CRS through rubella immunisation of young children, as well as women of childbearing age.

Fig. 1: Annual incidence of congenital rubella syndrome (CRS) and rubella, Oman, 1987-2003



Source: Ministry of Health, Oman

Criteria for Introduction of Rubella Vaccine

The decision to include rubella vaccine in the national immunization programme should be based on:

- The level of rubella susceptibility in women of childbearing age
- The burden of disease due to CRS
- The strength of the basic immunization programme as indicated by routine measles vaccine coverage (which should be >80% for several years before implementing childhood rubella vaccination)
- Infrastructure and resources for child and adult immunization programmes
- Assurance of injection safety
- Other disease priorities.

A policy of rubella vaccination of women of childbearing age is essentially free of risks of altering rubella transmission dynamics. In contrast, inadequately implemented childhood vaccination has a long-term risk of increasing the number of 'susceptibles' among women of childbearing age, and thereby increasing the risk of CRS.[3,4] Therefore, unless rubella vaccine coverage levels can be sustained above 80% on a long-term basis, childhood vaccination programmes against rubella are not recommended.[1]

Vaccination of Women

Vaccination of women of childbearing age may be carried out postpartum, at school leaving, or during mass campaigns. Rubella vaccine should not be administered to pregnant women because of the theoretical, but never demonstrated risk of causing developmental malformations in the foetus.[1] No cases of CRS have been reported in infants of more than 1000 susceptible pregnant women who inadvertently received rubella vaccine in early pregnancy; thus, inadvertent rubella vaccination during pregnancy is not an indication for abortion. If pregnancy is being planned, then an interval of one month should be observed after rubella vaccination.

Cuba and Oman

While the successful elimination of CRS in countries such as Finland and the USA is well known, a number of developing countries such as Cuba and Oman have also achieved CRS elimination through careful implementation of rubella vaccination. The last reported case of CRS in Cuba occurred in 1989, with the last reported case of rubella in 1995.

In the year 2000, Oman set a target for elimination of rubella and CRS by 2005.[5] In 1994, measles-rubella (MR) vaccine was introduced nationwide with a mass campaign targeted at individuals, 15 months - 18 years of age; the campaign achieved 94% coverage. In the same year, MR vaccine was introduced into the routine immunization schedule for children at age 15 months, with coverage sustained at 97% or higher since then. In 2001, rubella vaccine was introduced for women postpartum, with coverage of more than 99%. The last reported case of CRS in Oman occurred in 2001 and the incidence of rubella has dropped dramatically (Figure 1).

WHO Member States and Regions

Provisional data for 2004 indicate that 117 (61%) of 192 WHO Member States were routinely using rubella vaccine, and this represents a striking increase from 32% in 1996. The proportion of countries using rubella vaccine varies by WHO region (Figure 2). Two WHO regions - the Americas and Europe - have established targets for elimination of rubella and CRS by the year 2010.[6]

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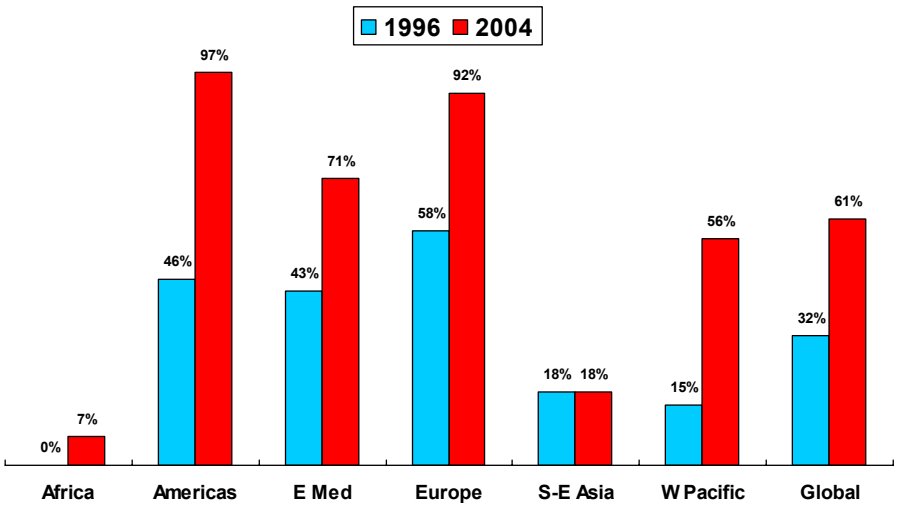
Fig. 2: Percentage of Member States, by WHO region, with routine rubella vaccination, 1996 versus 2004



Source: provisional data, WHO/UNICEF, July 2005

THE CAUSES OF HEARING LOSS IN HIV INFECTION

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HIV Infection

Infection with human immunodeficiency virus (HIV), which causes acquired immune deficiency syndrome (AIDS), is a major health problem worldwide, with approximately 38 million adults and 2.3 million children (under 15 years of age) currently living with HIV infection. In 2005, there were approximately 4.9 million new HIV infections and 3.1 million AIDS related deaths. Sub-Saharan Africa has the largest burden of infection worldwide (UNAIDS 2005; http://www.unaids.org/Epi2005/doc/EPIupdate2005_pdf_en/epi-update2005_en.pdf).

HIV can be isolated from several body fluids including semen, cervical secretions, blood and breast milk. The commonest route of transmission of HIV infection is by sexual intercourse. Other routes include receiving contaminated blood products or the use of contaminated needles. Mother to child infection, termed vertical transmission, is the commonest route of HIV infection in children, with the majority of infections occurring perinatally. Vertical transmission can be reduced by the use of antiretroviral drugs (used in the treatment of HIV infection), the avoidance of breast feeding and delivery by Caesarian section.

The HIV virus infects cells of the immune system and in particular CD4+ T cells which play an important role in the immune response to both HIV infection and many other infectious organisms. Defects in CD4+ T cell function are observed in HIV infection and their numbers in peripheral blood decline with advancing disease. When the CD4+ T cell number falls below 200 x 10^6/l an individual with HIV infection is particularly prone to certain types of infections, termed opportunistic infections.

The World Health Organization (WHO) describes four stages of HIV infection in adults and adolescents and three stages in children.[1] (http://www.who.int/hiv/pub/prev_care/en/arvrevision2003en.pdf). Antiretroviral therapy is recommended in resource-limited settings for adults and adolescents with advanced HIV infection (WHO Stage IV disease and individuals with WHO Stage III disease with a CD4+ T cell count < 350 x10^6/l) - and those with WHO Stage I and II disease with a CD4+ T cell counts ≥ 200 x10^6/l. Treatment is recommended in children with advanced disease (WHO Stage III) and those with WHO Stage I or II disease with a low CD4+ T cell percentage (the CD4+ T cell percentage threshold varies depending upon the age of the child). Currently, less than 5% of individuals in resource-limited settings who need antiretroviral therapy have access to it. The WHO '3 by 5' initiative aims to treat 3 million individuals in resource limited settings by the end of 2005 (http://www.who.int/3by5/about/initiative/en/index.html).

Four classes of antiretroviral drugs are currently available. These include:

1. Nucleoside reverse transcriptase inhibitors (NRTIs).
2. Non-nucleoside reverse transcriptase inhibitors (NNRTIs).
3. Protease inhibitors (PIs).
4. Fusion inhibitors (used to salvage therapy when treatment options are limited).

Standard treatment regimens, termed highly active antiretroviral therapy (HAART), use triple combinations of drugs usually from two different drug classes. Adherence to HAART is important to reduce the risk of developing drug resistance that would limit future treatment options. Treatment response is determined both clinically and by the measurement of surrogate markers (CD4+ T cell count and the HIV viral load in plasma). HAART is associated with a reduction in both morbidity and mortality. Information regarding the costs of antiretroviral agents in resource limited settings are provided at the following websites:

http://www.who.int/3by5/amds/untanglingtheweb07.pdf

http://www.who.int/3by5/amds/en/AFROarvindicator.pdf

http://www.who.int/3by5/amds/sourcesAug05.pdf

Table 1: Causes of Hearing Loss in HIV Infection

Aetiology	Type of hearing loss described	Ref.
Otitis externa	CHL	2
Polyps in the external ear canal	CHL	2
Acute /recurrent otitis media	SNHL/CHL	2, 3
Otosyphilis	SNHL	3, 4
Ramsay Hunt Syndrome	SNHL	5
Medications *(see Table 2)*	SNHL	6
Direct effects of HIV on 8th cranial nerve	SNHL	7, 8, 9
Opportunistic infections		
a. Cytomegalovirus	SNHL	10
b. Extrapulmonary *Pneumocystis jiroveci*	CHL	2
c. Cryptococcal meningitis	Not stated	11
d. Invasive aspergillosis (temporal bone)	SNHL	3
HIV related malignancy	CHL	
a. Kaposi's sarcoma	Not stated	2
b. Lymphoma (tympanic membrane)		12

Footnote:
SNHL = sensorineural hearing loss
CHL = conductive hearing loss

Causes of Hearing Loss: HIV

Hearing Loss in HIV Infection

Several causes of hearing loss are described in HIV infection and these are listed in Table 1, along with the type of hearing loss described, if known. Some causes of hearing loss are common to both HIV negative and HIV positive individuals, although in HIV infection the individual may present with more severe disease. Other causes are a consequence of HIV infection itself or as a result of an opportunistic infection. The main causes of hearing loss in HIV infection are described in the following sections.

Recurrent Otitis Media

Recurrent episodes of acute otitis media (AOM) are common in children, both in HIV negative and positive individuals, and can result in hearing loss. However, AOM may be the first presentation of HIV infection in children and should always be considered in children presenting with severe disease, particularly if they fail to respond to conventional therapies, have frequent relapses or have otitis media secondary to an unusual organism(s).

The number of episodes of AOM per year in children born to HIV infected mothers, who either acquired HIV infection vertically or were subsequently found to be HIV negative (by 18 months of age), were studied by Barnett et al.[13] In the HIV negative group, the mean number of episodes of AOM per year decreased during the first three years of life whilst it increased in the HIV positive group. By three years of age, all HIV positive children had experienced at least one episode of AOM, compared to 75% in the HIV negative group - and 80% of the HIV positive children had experienced 6 or more episodes of AOM compared to 0% in the HIV negative group. The frequency of AOM episodes in the HIV positive children was associated with their CD4+ T cell counts; children with lower CD4+ T cell numbers had more episodes of AOM compared to those with normal CD4+ T cell counts.

Otosyphilis

Syphilis, is caused by the spirochaete, *Treponema pallidum*, and should always be considered in any HIV positive individual presenting with a unilateral or bilateral sensorineural hearing loss that often rapidly progresses. The hearing loss may fluctuate in severity and be relatively sudden in onset. The majority of HIV positive individuals described presenting with hearing loss secondary to syphilis infection had latent syphilis at the time of diagnosis.[4] It has been hypothesised that co-infection with HIV may accelerate the development of otosyphilis. Little information is available regarding the treatment of otosyphilis in HIV infection and, in particular, whether steroids should be used in addition to penicillin therapy.

Ramsay Hunt Syndrome

Herpes zoster virus infections occur more frequently in HIV positive individuals and are often associated with more severe disease, such as the involvement of multiple dermatomes in shingles or the presence of disseminated disease. Ramsay Hunt syndrome is well described in HIV negative individuals and it remains unclear whether HIV positive individuals have a more severe form of the condition. It usually presents with unilateral ear pain, a vesicular rash and a facial palsy on the side of the ear lesions.[5] Unilateral hearing loss and impairment of balance mechanisms are described. The facial weakness often fails to completely recover.

Medications

Several medications are used in the treatment HIV infection. Complications are potentially ototoxic and may result in a sensorineural hearing loss; see Table 2. Damage to the auditory pathways may be a consequence of direct effects on the hair cells within the inner ear or as a result of toxic metabolic effects on the stria vascularis in the inner ear.[6] The reversibility of the hearing loss observed is usually drug dependent and dose related.

A few individuals receiving antiretroviral therapy containing at least one or two of the NRTIs listed in Table 2 have subsequently developed a hearing loss.[17,18] It is unclear whether certain NRTIs or combinations of NRTIs are more likely to cause otoxicity and whether the damage is potentially reversible, if detected early. The proposed mechanism of the ototoxicity is direct damage to mitochondrial DNA. Mitochondrial toxicity has been associated with other side effects related to NRTIs including peripheral neuropathy, pancreatitis and the development of lactic acidosis. It is possible that mitochrondrial DNA damage could be responsible for the development of hearing loss, as several hereditary conditions with known mutations in mitochondrial DNA have hearing loss as a clinical feature.

There is only one report of hearing loss in a HIV positive individual receiving

Table 2: Drugs used in the Treatment of HIV Infection and its Complications that may be Associated with Hearing Loss

Drug Class	Examples	Organism	Reference
Antibiotics			
Aminoglycosides	e.g., amikacin	*Mycobacterium tuberculosis*	6, 14
	streptomycin	*Mycobacterium tuberculosis*	6, 14
Macrolides	e.g., azithromycin	MAI	6
	clarithromycin	MAI	6
		Toxoplasmosis gondii	
Co-trimoxazole (Trimethoprim - (sulphamethoxazole)		*Pneumocystis jiroveci*	15
Antifungal agents	e.g., amphotericin	*Cryptococcus*	16
Antiretroviral agents			
NRTIs	e.g., zidovudine	HIV	17, 18
	didanosine	HIV	17, 19
	stavudine	HIV	18
	lamivudine	HIV	18
Antiviral agents Nucelotide analogue	cidofovir	Cytomegalovirus infection	20

Footnote:
MAI = *Mycobacterium avium-intracellulare*
For information on the treatment of these infections in HIV infection see reference 21.

antiretroviral therapy with a protease inhibitor based regimen, namely lopinavir-ritonavir.[22] The patient was also taking azithromycin, a known ototoxic drug.[6] A potential drug interaction between ritonavir and azithromycin may have been responsible for the hearing loss observed, as ritonavir is a potent inhibitor of cytochrome P450, a liver enzyme that is involved in the metabolism of many drugs. Inhibition of this enzyme may have resulted in increased blood levels of azithromycin.

HIV

HIV can infect the central nervous system and may potentially affect the eighth cranial nerve directly causing a sensorineural hearing loss. In one case series, 4 out of 18 HIV positive patients described a hearing loss that could not be attributed to another cause.[7] Seven of these individuals had abnormal pure tone audiometry (PTA) findings, of which four had bilateral changes.

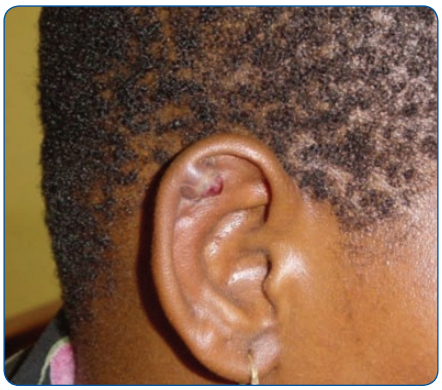
Sudden bilateral sensorineural hearing loss has been described in one patient who presented with symptoms compatible with primary HIV infection but at the time of testing had a fully positive HIV antibody response (no IgM detected).[8] Examination of the cerebrospinal fluid revealed oligoclonal bands directed against HIV-1 p24 antigen, consistent with HIV infection within the central nervous system.

Opportunistic Infections

Hearing loss has been described in several opportunistic infections associated with HIV infection (see Table 1).

Cytomegalovirus (CMV) infection usually occurs in individuals with advanced HIV infection, with a persistent CD4+ T cell count less than 50 x10^6/l. Common presentations include a retinitis (may result in blindness), colitis, pneumonitis or an encephalitis. Hearing loss associated with CMV infection has been described in a few cases and improvements in hearing have been described following antiviral therapy.[10]

Pneumocystis jiroveci (formerly *Pneumocystis carinii*) often presents subacutely with a potentially life-threatening pulmonary infection. It usually occurs in HIV positive individuals with a CD4+ T cell count less than 200 x 106/l. Manifestations outside the respiratory system are rare and include otitis media and mastoiditis.[3]



Kaposi's sarcoma of the pinna
Photo: Piet van Hasselt

Cryptococcal meningitis, caused by the fungus *Cryptococcus neoformans*, usually presents with a headache and a fever in HIV positive individuals with a CD4+ T cell count of less than 100 x10^6/l. It can present with confusion and seizures and may be insidious in onset. Involvement of cranial nerves has been described and hearing loss documented in a few instances.[11] It is unclear whether the hearing loss observed is a direct result of infection of the eighth cranial nerve or a consequence of the raised intracranial pressure frequently seen in this condition.

Chronic osteomyelitis of the temporal bone, due to *Aspergillus* infection, has been described in at least one HIV positive individual presenting with a unilateral hearing loss.[3] The diagnosis was confirmed histologically and by culture.

HIV Related Malignancies

There are only a handful of case reports of HIV positive patients developing a hearing loss as a consequence of a HIV related malignancy such as Kaposi's sarcoma (KS) or a lymphoma. Both these malignancies are AIDS defining illnesses.

KS is a tumour arising from vascular and lymphatic endothelium (cell layer lining the vascular and lymphatic vessels). It is characterised by palpable, firm, purple/brownish plaques or nodules on the skin (Figure 1) and may be a result of infection with Kaposi's sarcoma herpes virus type 8 (KSHV8). Three clinical presentations of KS are recognised: a) a sporadic/classic form, originally described in Jews b) an endemic form, described predominantly in males from central Africa, and c) the immunosuppressed form seen in HIV infection.

HIV related KS is commonly seen in homosexual men and often presents with widespread skin and mucous membrane involvement (especially in the mouth on the hard palate). Lesions affecting the skin of the outer ear may potentially obstruct the external auditory canal resulting in a conductive hearing loss. KS may also affect other organs including the gastrointestinal tract, the lungs and the lymph nodes. Specific treatment is often not required as the lesions usually regress once the patient commences HAART. For localised disease radiotherapy, or intralesional chemotherapy (injection directly into the lesion) is sometimes indicated.

Lymphoma of the tympanic membrane has been described in one HIV positive patient presenting with left sided ear pain, hearing loss and facial weakness.[12] Examination of the ear revealed a mass behind the tympanic membrane which histologically was confirmed as a high grade, B-cell lymphoma.

Discussion

Hearing loss is an important and often overlooked clinical manifestation of HIV infection and may represent the first sign of an individual's HIV disease. A high level of suspicion is, therefore, required to consider HIV infection in the differential diagnosis of an individual presenting with a hearing loss. The severity of the clinical presentation, the frequency of relapses (if relevant) and the identification of unusual causative organisms (e.g., opportunistic infections) should alert the health worker to the possibility that the patient is immunosuppressed.

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MALARIA AND DEAFNESS

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An estimated 2.7 million people die from malaria annually, the majority of whom are children and, in fact, account for 11% of childhood deaths in developing countries. Like all serious infections, for example, meningitis and encephalitis, malaria has been implicated as a cause of deafness and, according to Sowumni (1997)[1] is a recognised complication of cerebral malaria. Several studies in West Africa have confirmed the link between malaria and deafness.[2] Many factors, among them age, type of fever, low immunity, and type of malarial parasite may be responsible for auditory changes. Problems of balance after malaria are not often reported.

The mechanism is not clear but the hearing loss is usually sensori-neural suggesting damage to the cochlea itself or somewhere along the eighth nerve pathway.

Anti-malarials and Otoxicity

It has been known for many years that most anti-malarials are ototoxic and, in fact, the most commonly used anti-malarial, quinine, has developed very many side effects, known as cinchonism which include deafness and tinnitus. The mechanism of action of quinine has not been determined but it appears to interfere with the function of plasmodial DNA. It can also be used for night cramps and is found as a 'filler' for narcotic drugs. Much of the information available about toxicity is in relation to oculotoxicity and cardiotoxicity.[3] There have been no longitudinal studies on children with cerebral malaria and, mainly because of its high mortality, the hidden disability is not recognised.

Ototoxicity and neurotoxicity have been implicated with other anti-malarials, mefloquine and chloroquine.[4] It has been suggested that the ototoxicity of the anti-malarials may have a common pathway, involving the exposure of the auditory neurones to harm. Studies of the hearing loss attributed to quinine drug treatment show that it is usually reversible, pointing to drug rather than disease as a cause of deafness.

More recent clinical experience with artemisinins has shown them to be the most rapidly acting anti-malarial available.[5] They tend to be used in those areas where there is widespread resistance by *Plasmodium falciparum*. The artemisinins have been viewed favourably as a critical intervention. They have a short half life and should be used in combination with lumefantrine. This combination is known as a co-artemether and its ototoxic effect has been shown in a study by Toovey and Jamieson in South Africa.[6] The disease and treatment of malaria can give rise to loss of hearing and/or tinnitus. Fortunately, many of the effects are reversible but when managing malaria in the ideal situation, pre-treatment auditory assessment should be made - and the possibility of residual tinnitus or deafness should be kept in mind when treating a patient for malaria.

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Abstract

Study of the hearing loss in children and adolescents, comparing the periods of 1990-1994 and 1994-2000

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Introduction: In 1994, a study was performed with 200 children and adolescents suffering from hearing loss. It concluded that the diagnostic confirmation of hearing loss within 2 years of age occurred in just 13% of the cases, although 56% were suspected in that phase. The loss of time of over 2 years between suspicion and confirmation of hearing loss occurred in 42% of the cases.

Objectives: The comparison of the main hearing loss etiologies–genetic cause, consanguinity, congenital rubella, meningitis, perinatal events and unknown causes – in children and adolescents in the periods of 1990-1994 and 1994-2000; comparison of incidence, in males and females, for each etiology and among the others; comparison of age at the first consultation, for each and among them; and the investigation as to whether the time between suspicion and diagnosis of hearing loss was different for each etiology and among the others.

Methods: During the period of 1990-2000, of the 519 children and adolescents with hearing loss, 442 individuals were selected, in the two moments of the study: 1990-1994 and 1994-2000. The variables used were: sex, age at first consultation, suspected etiology and time between suspicion and confirmation of hearing loss.

Results: Congenital rubella, genetic and perinatal causes, meningitis, consanguinity and unknown causes were responsible for over 80% of all etiologies, in both periods. There were no differences between the sexes in the periods studied. There was no relation among age, sex and etiology. Among the etiologies studied, there were no differences in the lengths of times between suspicion and confirmation of hearing loss, in each period separately. The comparative study showed that congenital rubella, genetic and unknown causes took longer times between suspicion and confirmation of hearing loss, for the period of 1990-1994, as compared with 1994-2000.

Conclusions: Congenital rubella remains as an important etiology, as well post-meningitis deafness. Age at first consultation did not show relationship to the hearing loss etiology nor to sex. Independently of whether the etiology being pre-natal, perinatal or post-natal, congenital or acquired, the length of time between suspicion and confirmation of hearing loss did not differ between the periods studied, separately.

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Congenital rubella syndrome in Iran

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Background: Congenital rubella syndrome (CRS) can be prevented with appropriate vaccination programs. The prevalence rates of rubella and CRS in Iran are unknown; therefore, the risk of exposure in pregnant women is not clear. The prevalence of CRS in the pre-vaccine period can be estimated by evaluating the proportion of children in the population with sensorineural hearing loss attributable to rubella.

Methods: This was a case-control study to estimate prevalence of CRS in Tehran (Iran) by evaluating the proportion of children with sensorineural hearing loss attributable to rubella. The study used rubella antibody titer as an indicator, and compared the prevalence of rubella antibody between children with and without sensorineural hearing loss. Using these findings, the proportion of cases of sensorineural hearing loss attributable to rubella was estimated.

Results: A total of 225 children aged 1 to 4 years were entered into the study (113 cases and 112 controls). There was a significant difference between cases and controls with regard to rubella antibody seropositivity (19.5% vs. 8.9%, respectively, odds ratio = 2.47, 95% CI = 1.04-5.97). The proportion of sensorineural hearing loss cases attributable to rubella was found to be 12%, corresponding to a CRS prevalence of 0.2/1000.

Conclusion: The prevalence of CRS was approximately 0.2/1000 before rubella vaccination in Iran. Moreover; the results suggest that implementation of appropriate rubella vaccination programs could potentially prevent about 12% of cases of sensorineural hearing loss in Iranian children. This data could potentially be used as baseline data, which in conjunction with an appropriate method, to establish a surveillance system for rubella vaccination in Iran. An appropriate surveillance system is needed, because the introduction of a rubella vaccine without epidemiological data and an adequate monitoring program could result in the shifting of rubella cases to higher ages, and increasing the incidence of CRS.

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