CURRENT TOPIC

Hearing impairment after bacterial meningitis: a review

H M Fortnum

Postmeningitic hearing impairment is an important public health problem with implications for both paediatric and audiology services. A recent population study has shown that, by the age of 3 years, the proportion of children with a known bilateral profound hearing impairment who have an *acquired* impairment is approximately 20%. Of these acquired impairments, 90% are probably due to bacterial meningitis.¹ Furthermore, studies of cohorts of children born in the 1970s and early 1980s indicate that 6% of all childhood hearing impairment is due to bacterial meningitis.^{2 3}

Not all children surviving bacterial meningitis suffer permanent sensorineural hearing impairment. How many do, and why are certain children affected but not others? Are there any factors within the illness, within the children, or within the medical treatment that could predict the children at greatest risk? This article reviews the recent literature as a source of answers to these questions and recommends management guidelines in the light of current knowledge of the pathology. (Except where otherwise stated, 'impairment' in this article refers to *sensorineural* hearing impairment, that is permanently raised hearing thresholds and loss of other auditory functions such as frequency resolution, due to damage to the eighth nerve or to the receptor cells of the inner ear.)

Total loss of hearing disrupts the development of communication skills, particularly in young children who have not fully developed speech and language. It can also lead to regression to an earlier stage.⁴ This disruption is an important sequela of bacterial meningitis, justifying the effort of early identification to enable appropriate habilitation to begin as soon as possible. Partial hearing impairment and/or unilateral losses also occur⁵⁻¹⁰ and also need to be identified with minimal delay, because these children may also suffer auditory and linguistic disabilities that are only subtly symptomatic. Such children often display behavioural compensations and may appear to hear normally. Unaware of what he is missing, a young child will not complain. Crucial stimulation may be missed,¹¹ which is particularly important at school entry. Parents and teachers should be aware of any degree of impairment, even if it is too mild for hearing aids to be beneficial.

Bacterial meningitis may also cause more widespread damage. If a child is left with multiple handicaps, any hearing impairment is more easily overlooked and difficult to detect. In such children assisting any impairment to

hearing may be of even greater benefit than in less complex cases.

What is the incidence of postmeningitic hearing impairment?

From a review of the recent literature, the incidence of hearing impairment in children surviving bacterial meningitis may be as low as 3.5%¹² or as high as 37.2%.¹³ The 10-fold range certainly reflects the large sampling errors associated with small samples, but probably also reflects some bias due to case selection and methodology, for example, the type and severity of the hearing impairment included, the timing of assessment after the onset of the illness, the age range of the children, the profile of infecting organisms, and the sophistication of the audiological tests used. Table 1 summarises the recent literature and includes only those studies considered to provide the most trustworthy estimates. The criteria for inclusion of a study were (a) publication in 1977 or later (that is in the last 15 years), (b) sample size over 50 in a consecutive series, (c) a well defined age group including children up to at least 3 years of age, (d) the use of age appropriate audiological testing methods, and (e) audiological testing of more than 80% of the original cases. From the selected papers an overall rate and confidence intervals were computed (weighted by the number of cases in each study) for permanent sensorineural hearing impairment of any degree among survivors of bacterial meningitis. Table 2 gives the results of these calculations for all causes of the illness and for each of the three main infective agents. This synthesis gives an incidence of 9.6%.^{8 10 14-20} Interpreting the computed confidence intervals, the risk of permanent sensorineural hearing impairment lies between one in 12 and one in eight. This compares with the risk in the background childhood population (<3 years) of approximately one in 600 for any degree of permanent sensorineural hearing loss. Thus the raised relative risk is 50- to 75-fold. However, in countries other than those studied, mainly North America and north west Europe, the contribution of each of the infecting organisms is very different and caution must be used in interpreting and generalising these figures.

For bilateral profound or total impairment the range in reported incidence is between 1% and 4%.^{8-10 14 16-18 21-23} Projected on to an incidence of bacterial meningitis of about 0.3 per 1000 per year aged 0 to 14 years and a mortality rate of approximately 10% (H M

MRC Institute of
Hearing Research,
University of
Nottingham,
University Park,
Nottingham NG7 2RD

Correspondence and requests
for reprints to:
Dr Fortnum.

Table 1 Incidence of sensorineural hearing impairment after bacterial meningitis

Author(s)	Study date	Place	Age	No tested	Organism	Incidence of SNHI of any degree (%)	Incidence of profound bilateral SNHI (%)
Salwen <i>et al</i> ¹⁴	1956–80	Sweden	1 month–16 years	181	All	11.6	3.9
				115	<i>H influenzae</i>	9.6	—
				51	Meningococcus	10	—
				15	Pneumococcus	33	—
Koskiniemi <i>et al</i> ⁵³	1960–74	Finland	2 months–9 years	101	<i>H influenzae</i>	13.9	—
					(>moderate)	18.1	—
Rosenthal <i>et al</i> ⁹	1968–75	Sweden	0–22 years	83	<i>H influenzae</i>	18.1	3.6 (bilateral >70 dB)
Moss ⁵⁴	1971–74	UK	1 month–8 years	60	Meningococcus	5.0	—
Claesson <i>et al</i> ²¹	1971–80	Sweden	0–15 years	128	<i>H influenzae</i>	14.8	1.4
Pomeroy <i>et al</i> ¹⁵	1973–77	USA	1 month–14 years	185	All	9.7	7.2 (bilateral >80 dB)
Dodge <i>et al</i> ¹⁰	1973–77	USA	2 months–14 years	185	All	10.3	2.2
				118	<i>H influenzae</i>	5.9	1.7
				19	Meningococcus	10.5	0
				29	Pneumococcus	31	6.9
				19	Other	5.3	0
Dawson <i>et al</i> ¹⁶	1975–87	New Zealand	1 month–13 years	143	All	6.3	3.5
				99	<i>H influenzae</i>	—	2
				24	Pneumococcus	—	12.5
Richner <i>et al</i> ³⁰	to 1977	Switzerland	3 months–8 years	97	<i>H influenzae</i>	15.5	—
Edwards and Baker ³¹	1977–79	USA	0–16 years	79	Meningococcus	6.3	0
Guiscafre <i>et al</i> ¹⁷	1978–79	Mexico	1 week–15 years	100	All	8	1 (bilateral >70 dB)
				30	<i>H influenzae</i>	6.7	—
				18	Other	22.2	—
				52	Not known	3.8	—
Ozdamer <i>et al</i> ¹⁸	1978–81	USA	3 weeks–3.5 years	60	All	11.7	3.3
				46	<i>H influenzae</i>	6.5	—
				8	Pneumococcus	50	—
Vienny <i>et al</i> ⁸	1979–82	Switzerland	1 week–16 years	51	All	9.8	2
Cartwright <i>et al</i> ²²	1981–86	UK	0–24 years	63	Meningococcus	9.5	3.2
Smith <i>et al</i> ²³	1982–83	West Africa	0–14 years	126	Meningococcus	7.1	2.4
Lebel <i>et al</i> ¹⁹	1984–85	USA	2 months–16 years	176	All	9.1	—
				137	<i>H influenzae</i>	9.5	—
				14	Pneumococcus	21.4	—
				25	Other	0	—
Odio <i>et al</i> ²⁰	1990	Costa Rica	6 weeks–13 years	94	All	10.6	—

All, all bacteria; SNHI, sensorineural hearing impairment.

Table 2 Overall rate for incidence of permanent sensorineural hearing impairment after bacterial meningitis as computed from studies included in table 1

Type of meningitis	Study reference number	No in study	No hearing impaired	Estimate (%)	Range of studies (%)	Computed weighted confidence intervals (%)
Unselected	8, 10, 14, 16, 17, 18, 19, 20	1175	113	9.6	6.3–11.7	7.9 to 11.3
<i>H influenzae</i>	9, 10, 14, 17, 18, 19, 21, 30, 53	871	99	11.4	5.9–18.1	9.3 to 13.5
Meningococcal	10, 14, 22, 23, 31, 54	398	30	7.5	5.0–10.5	5.0 to 10.1
Pneumococcal	10, 14, 18, 19	66	21	31.8	21.4–50.0	20.7 to 42.8

Fortnum, A Davis, and P Ispahani, in preparation), this would amount to 60 or 70 profoundly impaired children each year in England, Scotland, and Wales.

Table 3 Risk factors for hearing impairment from various studies (study reference numbers given)

Clinical measure	Significantly raised risk of hearing impairment	No raised risk of hearing impairment
Factors within the illness:		
Low CSF glucose	5, 8, 10, 19, 24, 25, 26	18, 31
Increased CSF protein		5, 8, 10, 19, 25, 29, 30, 31
Increased CSF white cell count	5, 31	8, 10, 19, 25, 29, 30
Ataxia or vestibular disturbance	20, 27, 28	10
Severe neurological deficits	5, 10	18, 30
Organism:		29, 35
Meningococcus	5 (>2.5 years)	
Pneumococcus	18	
Coincident middle ear disease		5, 18
Hospital >14 days	18	
Seizures	26	10, 14, 18, 35
Hydrocephalus		18
Subdural effusions		10, 18, 53
CSF pressure		5
Factors within the child:		
Age		5, 10, 18, 29, 30
Sex		5, 10, 18
Factors within the treatment:		
More time from symptoms to treatment	5, 14, 30, 55	8, 10, 18
No steroid treatment compared with steroid treatment	19, 48 (<i>S pneumoniae</i>)	20, 48 (meningococcus and <i>H influenzae</i>)
Partial antibiotic treatment		25
Delayed CSF sterilisation	56	

CSF, cerebrospinal fluid.

Can any factors predict hearing impairment?

Table 3 lists several factors which have been studied in sufficient numbers of children to give quantitatively stable results, and lists those studies which found an association with the various factors and those which did not. All of these studies are, inevitably, descriptive with data derived from clinical judgments. In terms of the quality of evidence presented, only one of the quoted papers reports relative risk values with confidence intervals.²⁰

CLINICAL SIGNS

For those studies that measured it, an initial low concentration of glucose in the cerebrospinal fluid almost universally carried a much raised risk of hearing impairment.^{5 8 10 19 24–26} The three studies that reported values gave a statistically significant raised risk at concentrations of <0.6 mmol/l,²⁵ <1.1 mmol/l,¹⁰ and <2.15 mmol/l.⁸ The presence of ataxia or vestibular disturbance also indicates a child at a higher risk of hearing impairment.^{20 27 28} However, this is likely to be a correlated effect rather than a useful causal predictor and is, anyway, difficult to recognise in very young, very sick infants.

Most studies agree that a raised cerebrospinal fluid white cell count^{8 10 19 25 29 30} or a raised

cerebrospinal fluid protein concentration^{5 8 10 19 25 29-31} is not predictive of hearing impairment.

CAUSATIVE ORGANISM

Different risks have been reported from different organisms,^{5 18} particularly a higher risk of hearing impairment after infection with *Streptococcus pneumoniae*. Where a study has reported differences between organisms this is shown in table 1 and the overall computed incidence rates are shown in table 2. For *Haemophilus influenzae* and meningococcal infections these rates are reliable estimates. The numbers for pneumococcal infections are small and are hence the most open to any selection bias that might have a large effect on the rate, so the apparently higher contingent incidence should be viewed with caution. Permanent sensorineural hearing impairment is not truly organism specific, having been documented for almost all possible causes of bacterial meningitis. There have also been a few documented cases of hearing impairment after viral meningitis,^{13 17} but there has been no comprehensive epidemiological study of this and further research is needed.

AGE

Bacterial meningitis has been documented in children of all ages from neonates to 16 years.^{5 8 10 13} It does occur beyond infancy, although the greater vulnerability of very young children to more severe infections may result in a higher proportion of them suffering sequelae of all forms. The fact that some studies have restricted their population by age may explain some of the differences in incidence figures reported in table 1.

In summary, the evidence to date on risk factors indicates that hearing impairment cannot be exclusively predicted by a small number of risk factors. It should be assumed to be a possibility in every case until proved otherwise by thorough audiological testing.

How is the damage mediated?

Hearing impairment after meningitis may have several different causes. Most likely is the effect of suppurative labyrinthitis, due to direct spread of the infection from the subarachnoid space through the cochlear aqueduct.^{5 6 10 32 33} This leads to destruction of sensory structures and no recovery of hearing. On the other hand, a toxic or serous labyrinthitis is thought to be the mechanism responsible for partial and reversible losses.^{5 32 34} Other possible mechanisms include direct nerve fibre damage^{8 14 35} and secondary ischaemic damage.^{6 8 19 35}

Recent studies of experimental animal models have provided more details of the possible mechanism of the damage.^{36 37} These studies have shown that lysis of bacterial cells by antimicrobial agents produces endotoxin from Gram negative bacteria and lipoteichoic acid from Gram positive bacteria. These lead to the release of cytokines such as tumour necrosis factor and interleukin-1 which initiate a generalised inflammatory response. This inflammation

may be responsible for the hair cell damage in the inner ear observed in experimentally infected animals.³⁶ Roos provides a good review of recent work.³⁸

Is the impairment permanent and stable?

The permanence and stability of hearing impairment after bacterial meningitis are important for at least two reasons. Firstly, for the profoundly impaired child one option for rehabilitation now available is a cochlear implant. Postmeningitic children, who have been deafened perilingually or postlingually, are a highly successful group of implantees.³⁹ Implantation involves insertion of a single or multichannel electrode through the round window into the cochlea with the aim of stimulating the sensory nerve endings. In implantation there is potential risk of destruction of the receptor cells directly or via rupture of membranes separating fluids of different ionic content, leading both to poisoning of the cells and disruption of the primary hydromechanical and chemical properties of the cochlea. If aidable hearing is present, or is likely to return, this procedure is obviously not in the best interests of the child. Thus, any evidence that profound hearing losses may not be permanent has important implications. Rosenhall and Kankkunen report three cases of improvement from bilateral profound losses over periods of 18 months, 4.5 years, and 6 years.³⁴ However, improvements in hearing after meningitis have more often been reported among cases with less severe hearing losses.^{5 6 8 17} Reports of complete or partial recovery may be due to improvements in the accuracy of testing as the child gets older or to resolution of simultaneously present conductive hearing losses due to fluid in the middle ear,^{7 10 13 40} particularly if the first measurement is soon after the infection.

Secondly, any instability in hearing impairment is important as a potential obstacle to a child's development of communication skills. It also has implications for the resources needed in continued follow up of such children. Fluctuations have been documented, again notably by Rosenhall and Kankkunen.⁴¹ Their explanation was a form of endolymphatic hydrops caused by suppurative labyrinthitis. Alternatively, these children may have had coincident middle ear conductive problems.⁴⁰ Underlying sensorineural impairments probably do not fluctuate. A few cases of a deterioration in threshold levels between 5 and 12 years after the episode of meningitis have been noted,^{6 42} but attributing these losses solely to the meningitis is questionable.

Can we reduce the risk?

There have been recent advances in both the prevention and treatment of bacterial meningitis. The potential value of immunisation has been acknowledged and researched for many years^{43 44} and in October 1992 immunisation for *H influenzae* infections will become a reality in the UK. The new *H influenzae* b vaccine, given to children at the time of the standard triple

vaccine (diphtheria, pertussis, and tetanus) is intended to prevent the majority of cases. An estimate of the potential health gain may be made by projecting the optimistic assumptions of 100% uptake and 100% effectiveness onto figures from a recent 10 year retrospective study (H M Fortnum, A Davis and P Ispahani, in preparation) in Nottingham District Health Authority (1989: total child population 0 to 14 years=113603, 18% of all age total). Such a vaccine given at 3 months of age might have prevented 78 cases of meningitis over 10 years including one death and three cases of permanent sensorineural hearing impairment (one profound bilateral and two severe to profound unilateral). It would not have prevented six cases in children aged less than 4 months, two of whom died. Projecting these figures on to the population of England, Scotland, and Wales, a vaccine might prevent up to 700 cases of meningitis due to *H influenzae* per year. Applying the overall incidence rate from table 2 would predict a consequent reduction of 65 to 95 children per year with permanent hearing loss but these figures may not truly represent the UK population in the 1990s and should be used with caution.

The role of factors within treatment is uncertain. In the past the discussion has mainly concentrated on the question of appropriate antibiotics^{45 46} and delay to treatment. Well conducted studies have found both for and against an increased risk if treatment is delayed more than 48 hours (table 3). It is likely that this conflicting evidence is the result of the involvement of other factors, as it is generally accepted that any damage to hearing occurs early in the infection.^{6 10 17 24 47} More recently, in the search for effective treatment, steroids have received much attention. If given at the same time as antibiotics, dexamethasone lessens the inflammatory response³⁷ and may block much of the cochlear damage.³⁶ Three studies reported a lesser risk of neurological sequelae in steroid-treated children,^{19 20 48} but only two of the three found a lesser risk of hearing impairment.^{19 48} Other studies have reported benefit from the use of non-steroidal anti-inflammatory agents,^{49 50} but more and larger studies are needed to determine the true benefits and costs of introducing anti-inflammatory drugs as routine treatment.

Recommendations

All children recovering from bacterial meningitis should be referred for audiological assessment before discharge from hospital.⁵¹ For administrative and motivational reasons immediate cross referrals are more likely than later ones to result in an appointment actually being made. The appointment should take place about four to six weeks later. If a child is seen too early an associated conductive loss may be identified, requiring further follow up before the possibility of an underlying sensorineural impairment can be discounted. However, if the appointment is made later the impact of the acute life threatening disease on the parents may have lessened and they may not think it important enough to bring the child for the appointment. In this way

a significant degree of hearing impairment could go undetected until the child meets a circumstance where unimpaired auditory input becomes a higher priority (for example at school entry). Also a non-attended appointment at a specialist centre is a waste of scarce resources.

Another reason for minimising the delay to referral, and therefore to assessment and identification of any hearing impairment, is the process of ossification of the cochlea that can occur within a few months of meningitis. This process is important in profound hearing losses because if ossification has progressed too far an intracochlear implant becomes surgically very difficult to insert⁵² and extracochlear implants confer less benefit.³⁹ Thus the window of four to six weeks reconciles the increased resource implications of referral too early with the dangers of referral too late.

The professional responsibility for initiating referral of the child for hearing assessment has to lie with the paediatrician responsible for the child in hospital. It is an obligation of the paediatric service to ensure that a fail-safe administrative system exists to make certain that referral actually occurs. Any subsequent non-attendance should be followed up with close cooperation between the general paediatric and audiology services.

Assessment of the hearing of young children is not easy. It requires great skill and patience particularly to detect mild or unilateral impairments and particularly in younger children. Conventional pure tone audiometry can be reliably used in children over the age of 3 or 4 years with minimal modification, but 80% of bacterial meningitis occurs before age 3. Accurate testing of younger children is possible if the relevant skills are available. Usually this will require referral to a subregional or regional centre specialising in paediatric audiology. Stressing the importance of the potential problem to the parents will help to ensure attendance. On no account should the child's hearing be tested by informal and imprecise methods in an outpatient clinic or at the bedside, as this could give an incorrect result and a false sense of security. Neonates and very young infants should have their hearing assessed with brainstem auditory evoked potentials.

This article has concentrated on bacterial meningitis but the question often arises of the possibility of hearing impairment after viral meningitis. This is a more difficult link to study but until further research proves otherwise, any child with encephalitis, or ill enough with viral meningitis to merit hospital admission, should also have a formal assessment of hearing after discharge. This should also apply to any child with viral meningitis treated outside hospital, even some time before, where there is concern over hearing, speech or balance. There will also be children known to have had meningitis before the introduction of fail-safe mechanisms of referral. If concern is expressed over the hearing or speech of such children, the possibility of meningitic damage should be considered and referral made for audiological assessment to exclude this cause before other aetiologies are sought.

Summary

The recent literature reports the incidence of permanent sensorineural hearing impairment in children surviving bacterial meningitis to be approximately 10%. The question of why some children surviving bacterial meningitis suffer a hearing impairment while others recover completely remains unanswered. Very few of the factors so far studied have any predictive power. Knowledge of those that do, for example low concentrations of cerebrospinal fluid glucose, may improve our understanding of the pathological mechanisms involved and ultimately possibly lead to methods of prevention, but at present do not allow useful prediction of those who will be affected.

The role of steroids and non-steroidal anti-inflammatory agents needs further investigation. These may yet prove to be useful interventions to prevent mortality and morbidity caused by bacterial meningitis. The best hope of preventing serious sequelae of bacterial meningitis is primary prevention and currently vaccination offers the most promising solution. Further research will no doubt expand the range of causative organisms covered. Up to date epidemiological studies of the UK population are needed to enable an accurate assessment of the extent of the problem and the potential health gain from advances in prevention or treatment.

Children will continue to suffer bacterial meningitis. Most will survive but some of them will be left with impaired hearing. Such children must be identified as quickly as possible to enable timely secondary prevention of disability or handicap.

My thanks go to Professor Mark Haggard, Professor David Hull, Dr Adrian Davis, and Dr Michael Tarlow for constructive comments on an earlier draft of this paper.

- 1 Davis A, Wood S. The epidemiology of childhood hearing impairment: factors relevant to planning of services. *Br J Audiol* 1992;26:77-90.
- 2 Das VK. Aetiology of bilateral sensori-neural deafness in children. *Scand Audiol* 1988; suppl 30:43-52.
- 3 Martin JAM, Bentzen O, Colley JRT, et al. Childhood deafness in the European Community. *Scand Audiol* 1981;10:165-74.
- 4 Osberger MJ. Speech production in profoundly hearing-impaired children with reference to cochlear implants. In: Owens E, Kessler DK, eds. *Cochlear implants in young children*. Boston: Little, Brown and Co, 1989:257-81.
- 5 Nadol JB. Hearing loss as a sequela of meningitis. *Laryngoscope* 1978;88:739-55.
- 6 Brookhouser PE, Auslander MC, Meskan ME. The pattern and stability of postmeningitis hearing loss in children. *Laryngoscope* 1988;98:940-8.
- 7 Kronthaler M, Rauegger H, Guggenbichler JP. Sensorineural hearing loss as a sequela of bacterial meningitis (in German). *Sprache Stimme Gehor* 1991;15:9-11.
- 8 Vienny H, Despland PA, Lutschg J, Deonna T, Dutoit-Marco ML, Gander C. Early diagnosis and evolution of deafness in childhood bacterial meningitis: a study using brainstem auditory evoked potentials. *Pediatrics* 1984;73:579-86.
- 9 Rosenhall U, Nylen O, Lindberg J, Kankkunen A. Auditory function after Haemophilus influenzae meningitis. *Acta Otolaryngol (Stockh)* 1978;85:243-7.
- 10 Dodge PR, Davis H, Feigin RD, et al. Prospective evaluation of hearing impairment as a sequela of acute bacterial meningitis. *N Engl J Med* 1984;311:869-74.
- 11 Bess FH, Tharpe AM, Gibler AM. Auditory performance of children with unilateral sensorineural hearing loss. *Ear Hear* 1986;7:20-6.
- 12 Spanjaard L, Bol P, De Jong MCJW, Zanen HC. Bacterial meningitis in 366 children in the Netherlands, 1982-1983. Epidemiology and antibiotic therapy. *Tijdschr Kinder-geneesk* 1986;54:1-8.
- 13 Finitzo-Hieber Y, Simhadri R, Hieber JP. Abnormalities of the auditory brainstem response in post-meningitis infants and children. *Int J Pediatr Otorhinolaryngol* 1981;3:275-86.
- 14 Salwen KM, Viskerfors T, Olcen P. Increased incidence of childhood bacterial meningitis. A 25-year study in a defined population in Sweden. *Scand J Infect Dis* 1987;19:1-11.
- 15 Pomeroy SL, Holmes SJ, Dodge PR, Feigin RD. Seizures and other neurological sequelae of bacterial meningitis in children. *N Engl J Med* 1990;323:1651-7.
- 16 Dawson KP, Abbott GD, Mogridge N. Bacterial meningitis in childhood: a 13 year review. *N Z Med J* 1988;101:758-60.
- 17 Guisacfre H, Martinez MC, Benitez-Diaz L, Munoz O. Reversible hearing loss after meningitis. Prospective assessment using auditory evoked responses. *Ann Otol Rhinol Laryngol* 1984;93:229-32.
- 18 Ozdamar O, Kraus N, Stein L. Auditory brainstem responses in infants recovering from bacterial meningitis: audiological evaluation. *Archives of Otolaryngology* 1983;109:13-8.
- 19 Lebel MH, Freij BJ, Syrogiannopoulos GA, et al. Dexamethasone therapy for bacterial meningitis: results of 2 double blind placebo controlled studies. *N Engl J Med* 1988;319:964-71.
- 20 Odio CM, Faingezicht I, Paris M, et al. The beneficial effects of early dexamethasone administration in infants and children with bacterial meningitis. *N Engl J Med* 1991;324:1525-31.
- 21 Claesson B, Trollfors B, Jodal U, Rosenhall U. Incidence and prognosis of Haemophilus influenzae meningitis in children in a Swedish region. *Pediatr Infect Dis* 1984;3:35-9.
- 22 Cartwright KAV, Stuart JM, Noah ND. An outbreak of meningococcal disease in Gloucestershire. *Lancet* 1986;ii:558-61.
- 23 Smith AW, Bradley AK, Wall RA, et al. Sequelae of epidemic meningococcal meningitis in Africa. *Trans R Soc Trop Med Hyg* 1988;82:312-20.
- 24 Berlow SJ, Caldarelli DD, Matz GJ, Meyer DH, Harsch GG. Bacterial meningitis and sensorineural hearing loss: a prospective investigation. *Laryngoscope* 1980;90:1445-52.
- 25 Feldman WE, Ginsburg CM, McCracken GH, et al. Relation of concentrations of Haemophilus influenzae type b in cerebrospinal fluid to late sequelae of patients with meningitis. *J Pediatr* 1982;100:209-12.
- 26 Borkowski WJ, Goldgar DE, Gorga MP, Brookhouser PE, Worthington DW. Cerebrospinal fluid parameters and auditory brainstem responses following meningitis. *Pediatr Neurol* 1985;3:134-9.
- 27 Hodgson J. Meningitis and childhood deafness. Manchester: University of Manchester, 1984 (MSc dissertation.)
- 28 Kaplan SL, Goddard J, Van Kleeck M, Catlin FI, Feigin RD. Ataxia and deafness in children due to bacterial meningitis. *Pediatrics* 1981;68:8-13.
- 29 Kotagel S, Rosenberg C, Rudd D, Dunkle LM, Horenstein S. Auditory evoked potentials in bacterial meningitis. *Arch Neurol* 1981;38:693-5.
- 30 Richner B, Hof E, Prader A. Hearing impairment following therapy of Haemophilus influenzae meningitis. *Helvetica Paediatrica Acta* 1979;34:443-7.
- 31 Edwards MS, Baker CJ. Complications and sequelae of meningococcal infections in children. *J Pediatr* 1981;99:540-5.
- 32 Harada T, Semba T, Suzuki M, Kikuchi S, Murofushi T. Audiological characteristics of hearing loss following meningitis. *Acta Otolaryngol (Stockh)* 1988; suppl 456:61-7.
- 33 Igarashi M, Saito R, Alford BR, Filippone MV, Smith JA. Temporal bone findings in pneumococcal meningitis. *Archives of Otolaryngology* 1974;99:79-83.
- 34 Rosenhall U, Kankkunen A. Hearing alterations following meningitis 1. Hearing improvement. *Ear Hear* 1980;1:185-90.
- 35 Jiang ZD, Liu XY, Wu YY, Zheng MS, Liu HC. Long-term impairments of brain and auditory functions in relation to treatment from purulent meningitis. *Dev Med Child Neurol* 1990;32:473-80.
- 36 Tarlow MJ, Comis SD, Osborne MP. Endotoxin induced damage to the cochlea in guinea pigs. *Arch Dis Child* 1991;66:181-4.
- 37 Mustafa MM, Ramilo O, Mertsola J, et al. Modulation of inflammation and cachectin activity in relation to treatment of experimental Haemophilus influenzae type b meningitis. *J Infect Dis* 1989;160:818-25.
- 38 Roos KL. Dexamethasone and non-steroidal anti-inflammatory agents in the treatment of bacterial meningitis. *Clin Ther* 1990;12:290-6.
- 39 Kessler DK, Owens E. Conclusions: current considerations and future directions. In: Owens E, Kessler DK, eds. *Cochlear implants in young children*. Boston: Little, Brown and Co, 1989:315-30.
- 40 Smyth V, O'Connell B, Pitt R, O'Callaghan M, Scott J. Audiological management in the recovery phase of bacterial meningitis. *Int J Pediatr Otorhinolaryngol* 1988;15:79-86.
- 41 Rosenhall U, Kankkunen A. Hearing alterations following meningitis 2. Variable hearing. *Ear Hear* 1981;2:170-6.
- 42 Silkes E, Chabot J. Progressive hearing loss following Haemophilus influenzae meningitis. *Int J Pediatr Otorhinolaryngol* 1985;9:249-56.
- 43 Eskola J, Peltola H, Takala K, et al. Efficacy of haemophilus influenzae type b polysaccharide-diphtheria toxoid conjugate vaccine in infancy. *N Engl J Med* 1987;317:717-22.
- 44 Booy R, Moxon ER. Immunisation of infants against Haemophilus influenzae type b in the UK. *Arch Dis Child* 1991;66:1251-4.
- 45 Peltola H, Anttila M, Renkonen OV, The Finnish Study Group. Randomised comparison of chloramphenicol, ampicillin, cefotaxime, and ceftriaxone for childhood bacterial meningitis. *Lancet* 1989;i:1281-7.
- 46 Raivio M, Koskiniemi M. Hearing disorders after Haemophilus influenzae meningitis. *Archives of Otolaryngology* 1978;104:340-4.

- 47 Kaplan SL, Catlin FI, Weaver T, Feigin RD. Onset of hearing loss in children with bacterial meningitis. *Pediatrics* 1984; 73:575-8.
- 48 Girgis NI, Farid Z, Mikhail IA, Farrag I, Sultan Y, Kilpatrick ME. Dexamethasone treatment for bacterial meningitis in children and adults. *Pediatr Infect Dis J* 1989;8:848-51.
- 49 Tuomanen E, Hengstler B, Rich R, Bray MA, Zak O, Tomasz A. Non-steroidal anti-inflammatory agents in the therapy for experimental pneumococcus meningitis. *J Infect Dis* 1987;155:985-90.
- 50 Kadurugamuwa JL, Hengstler B, Zak O. Cerebrospinal fluid protein profile in experimental pneumococcal meningitis and its alteration by ampicillin and anti-inflammatory agents. *J Infect Dis* 1989;159:26-34.
- 51 Hall DMB, ed. *Health for all children. A programme for child health surveillance*. 2nd Ed. Oxford: Oxford University Press, 1992.
- 52 Jackler RK, Bates GJ. Medical and surgical considerations of cochlear implantation in children. In: Owens E, Kessler DK, eds. *Cochlear implants in young children*. Boston: Little, Brown and Co, 1989:153-81.
- 53 Koskiniemi M, Pettay O, Raivio M, Sarna S. Haemophilus influenzae meningitis. A comparison between chloramphenicol and ampicillin therapy with special reference to impaired hearing. *Acta Paediatr Scand* 1978;67:17-24.
- 54 Moss P. Outcome of meningococcal group B meningitis. *Arch Dis Child* 1982;57:616-21.
- 55 Bohr V, Hansen B, Jessen O, et al. Eight hundred and seventy-five cases of bacterial meningitis. Part 1 of a three-part series: clinical data, prognosis and the role of specialised hospital departments. *J Infect* 1983;7:21-30.
- 56 Lebel MH, McCracken GH. Delayed cerebrospinal fluid sterilization and adverse outcome of bacterial meningitis in infants and children. *Pediatrics* 1989;83:161-7.

Turning off the bilirubin tap

If there's too much water in your bucket you can syphon it off, enlarge the hole in the bucket, make new holes, or turn off the tap. Treatment of hyperbilirubinaemia has been aimed at syphoning (exchange transfusion), enlarging the hole (enzyme induction), or creating new holes (phototherapy) but little attention has been paid to the possibility of turning off the tap, although some children have been given a new bucket.

In the production of bilirubin from haem the rate-limiting enzyme is haem oxygenase and this enzyme is inhibited by tin-containing porphyrin molecules which act as competitive, non-metabolised inhibitors. Tin protoporphyrin is one such molecule but tin mesoporphyrin is apparently more potent.

A report from the Rockefeller University Hospital in New York (Richard A Galbraith and colleagues, *Pediatrics* 1992;89:175-82) describes the effect of giving tin mesoporphyrin to two 17 year olds with Crigler-Najjar disease type I. The study was complex and difficult to interpret because phototherapy and repeated plasmapheresis were continued at the same time and patients were estimated to have a very large tissue load of bilirubin. Nevertheless there seemed to be some effect from the tin mesoporphyrin in so far as mean serum bilirubin concentrations were lower during this treatment and the rebound increase in serum bilirubin after plasmapheresis was slower. Both of the patients had shown recent neurological deterioration, which appeared not to progress during the treatment.

These studies seem to be of more theoretical than practical interest. Long term treatment with phototherapy has been practised in Crigler-Najjar disease for at least 20 years. It is very difficult to maintain, home phototherapy being fraught with severe practical and psychological problems, and neurological deterioration during the teenage years has been described by several authors. Liver transplantation in childhood has been performed in various centres on patients with this disease and currently seems to be the most attractive option. A major drawback of the haem oxygenase inhibitors is severe photosensitization, although otherwise they seem to be non-toxic.

The idea of turning off the bilirubin tap seems an attractive one but at present its application seems likely to be very limited in practice.

ARCHIVIST