Useful and relevant research

Many physical after effects of bacterial meningitis and septicaemia such as hearing loss, epilepsy, neuro-motor problems and amputations are extensively described in the scientific literature and are well recognised as consequences of meningitis and septicaemia by health professionals. However, cognitive, behavioural and emotional or psychological after effects tend to be less well recognised as do some of the more subtle or late developing physical effects such as problems with bone growth following septicaemia.

The table over the next few pages lists research papers which document some of the after effects of bacterial meningitis and meningococcal septicaemia. We have specifically included research which describes some of the less well recognised or late onset effects.

Some parents find it helpful to be able to point to research which demonstrates that certain after effects can be caused by meningitis and septicaemia when trying to access care for these problems. For example, pointing your child's GP towards research that shows that these diseases can lead to behavioural problems may help you to get a referral to Child and Adolescent Mental Health Services more promptly if this is required. It may also be helpful to point other professionals involved in the care of your child towards this research so that they can have a clearer understanding of the difficulties affecting your child.

While research shows that meningitis and septicaemia increase a child's risk of developing cognitive, behavioural and emotional or psychological problems, it is important that you do not interpret this to mean that these problems will necessarily apply to your child. Most children recover well with no lasting effects. The reason we are presenting the evidence that associates meningitis and septicaemia with these after effects is to help parents get help for their child who is already showing signs of having developed problems in some of these areas.

How to use the table

Column 1 - After effects: Lists the after effects that were looked at in a particular research study which were found to be more likely to occur in children who had survived meningitis than in healthy children of a similar age.

Column 2 - Age group and pathogen: Describes how many children took part in the study, their age and the type of bacteria that caused the illness.

Column 3 – Findings: Provides more detailed information on the findings of the research study and in most cases describes the proportion of children who were found to have specific problems following meningitis and septicaemia.

Column 4 – Ref: Provides the reference number for the study. References are listed on page 9 in the following format: Lead author of the research, title of the research, scientific journal that the research was published in, the year the research was published followed by the journal issue number and page numbers.

After effects	Age group and pathogen	Findings	Ref.
Epilepsy, Neuro-motor, VP shunts for hydrocephalus (water on the brain), Blindness, Deafness, Learning problems, Behavioural and emotional (psychological) problems,	130 children who had meningitis vs 130 age matched controls Children aged 3 months to 14 years when acutely ill and re-evaluated 6.7 years after illness (mean age 8.4) Bacterial meningitis (Hib was the disease causing pathogen in 74% of cases)	Neurologic abnormalities (4.7%) • Epilepsy (3.9%) • Cerebral palsy (1.5%) • VP shunts to treat hydrocephalus (1.6%) • Blind (0.79%) Auditory • Sensorineural deafness (6.4%) • Reduced central auditory function e.g. auditory figure-ground problems (distinguishing speech from background noise) 58% of children who had meningitis displayed problems vs 32% of controls (excl children with neurologic abnormalities) Nuero-psychological *Mean scores often fell within the average range, but were significantly lower in children who had meningitis compared to controls* • Lower full scale IQ compared to controls • Poorer reading ability • Poorer visuo motor co-ordination – could impact on writing and drawing • Poorer memory and learning • Reduced executive skills (executive skills help people achieve goals and can include the ability to manage time and attention and plan and organise. Reduced executive skills can lead to behavioural problems) Behavioural and emotional problems • Teachers rated children who had survived meningitis as having more behavioural problems than controls	[1]

After effects	Age group and pathogen	Findings	Ref.
Intellectual impairment, Behavioural and emotional (psychological) problems, Reduced academic achievement	109 of the meningitis survivors from the previous study[1] re-evaluated 11.5 years after illness. 96 of the controls re-evaluated Bacterial meningitis (Hib was the pathogen in 74% of cases)	Children who became acutely ill under 12 months of age had increased risk of neuro-psychological deficits 12 years on. 12 months post illness • Delayed expressive language development 7 years post meningitis • Expressive language has developed *but* • Deficits in reading • Mildly decreased IQ • Decreased verbal skills • Decreased organisational capacity 12 years post meningitis • Children post meningitis were more than twice as likely to require special educational assistance (27% vs 12.5%) • They were more than twice as likely to have a minor impairment (IQ70-80 – borderline learning difficulty, educational deficits, deaf (25-69DB), behaviour problems (29% vs 11%) • Neuro-behavioural effects were still evident in post meningitis survivors 12 years on. *Mean scores often fall within average range, but are significantly lower than controls* ○ Took longer to complete tasks ○ Made more errors ○ Less organised ○ Struggle with problem solving • Reduced literacy skills (verbal fluency) amongst meningitis survivors compared to controls It is suggested that children who survive meningitis may experience an ongoing lag in development because some basic skills such as attention, processing speed, immediate memory capacity improve from below age expected levels to normal at the 7 and 12 year assessments respectively. High level cognitive skills continue to be impaired at the 12 year assessment compared with controls. The risk of neurological impairment in children who survive meningitis is greater in those who experienced acute complications, but not limited to this group. Authors recommend that families and school teachers be made aware of possible language deficits and problems comprehending language based material. Hearing problems that prevent children from distinguishing speech from background noise compound these difficulties and in a noisy classroom, children may not always understand what they hear. Early learning programmes that include quieter classrooms, sitting close to the teacher, small group teaching, repetition of information, rephrasing verbal material and practice may help compensate for these learning deficits, resulting in improved academic achievement, behaviour and self esteem.	2-3

After effects	Age group and pathogen	Findings	Ref.
Neuro-motor problems, Epilepsy, Hearing loss, Visual impairment, Intellectual impairment, Hydrocephalus, Behavioural and emotional (psychological) problems,	1717 Infants (under one) who had meningitis during the first year of life in E&W between 1985 and 1987 Followed up 5 years after meningitis (1584 subjects) with 1391age and sex matched controls Mainly Hib (26%), meningococcal (25%), pneumococcal (9%), E.coli (4.4%) and GBS (6.2%). Unknown organism (20%)	Severe disability (5.8% vs 0.07% for controls) • Unable to attend a mainstream school • Includes children with multiple problems such as ○ Severe neuromotor impairment ○ Significant intellectual impairment ○ Severe seizure disorders ○ Severe visual or hearing impairment Moderate disability (9.8% vs 1.4% for controls) • Impaired functioning, but no severe intellectual or developmental impairment • Attend mainstream schools with or without additional support • Mild neuromotor disabilities • Intellectual impairment • Moderate sensorineural hearing loss • Mild or moderate visual impairment • Epilepsy controlled with treatment • Hydrocephalus without complications Mild disorders (29.1% vs 19.8% for controls) • Have a condition which is prevalent amongst children of the same age, but not typically associated with meningitis • Children with middle ear disease • Squint • Febrile convulsions • Behavioural problems Neonates(under one month of age) had higher rates of severe and moderate disability compared to children under one year of age.	4
Neuro-motor problems, Global delay Epilepsy, Hearing loss, Intellectual impairment, Hydrocephalus	Neonates (under 28 days) who had meningitis between 1985-1987 in E&W This study followed up 111 children at 9-10 years of age compared to 113 matched controls GBS E.coli Listeria Gram -ve	Severe outcomes were noted in 10.8% survivors vs 0% controls • Cerebral palsy • Significant learning problems (IQ <55) • Global delay • Special education Moderate outcome in 10% survivors vs 1.8% hospital controls • Mild cerebral palsy • Mild learning problems (IQ 55-69) • Sensorineural hearing loss Mild outcome in 17.1% survivors vs 11.5% hospital controls An impairment without disability: • Neuromotor signs without overt functional loss • Isolated hydrocephalus • Isolated epilepsy • Borderline learning problems (IQ 70-80) • Isolated occurrence of all mABC movement assessment battery for children component scores being below the 5th centile ○ ball skills (Visual Motor Integration), manual dexterity (fine motor), static and dynamic agility (gross motor). Low birth weight was indicative of poorer outcome. The authors conclude that around 10% of neonatal meningitis cases will need significant follow up for severe outcome and a further 10-20% will require ongoing support for mild to moderate problems They recommend that comprehensive developmental assessment is needed before school entry, to identify less evident but important after effects.	5

After effects	Age group and pathogen	Findings	Ref.
Behavioural and emotional (psychological) problems,	Infants (under one) who had meningitis between 1985-1987 in E&W This study followed up 739 children at a mean 13.3 years of age compared to 606 matched controls Mainly Hib (26%), meningococcal (25%), pneumococcal (9%), E.coli (4.4%) and GBS (6.2%). Unknown organism (20%)	Undertook a strengths and difficulties questionnaire (SDQ) for both parents and teachers of children. It has 25 questions divided into five categories: • Emotional symptoms • Conduct problems • Hyperactivity • Peer problems • Prosocial behaviour There were additional questions on impact of the child's behaviour on the family or classroom to try and measure the burden of behavioural problems. The meningitis group received extra help at school compared to controls. 8 children from the meningitis group had been excluded from school compared to 0 from the control group. SDQ scores • Parents of meningitis cases were more than twice as likely to have scored their children outside of the normal range compared to parents of controls (46% of parents whose children had complicated meningitis, 38% of parents whose children had uncomplicated meningitis vs 21% for controls) • For teachers the difference was less marked, but still statistically significant. Impact score • Parents whose children had "complicated" meningitis were three times more likely to report a negative impact on home and social life than parents of control children. • There was also a significant difference between "uncomplicated" cases and controls. This study shows that 13 year old children who had bacterial meningitis during the first year of life have significantly more behavioural problems than matched controls when assessed by both parents and teachers	6
Behavioural and emotional (psychological) problems,	Children aged 3 to 16 years Median age at recruitment 6.8 Under 3's excluded as no standardised way to assess psychiatric status 60 subjects followed up at 3 months Meningococcal disease	The research looked at psychiatric symptoms of children and parents 3 months after illness. Both families admitted to PICUs and general paediatric wards were included. 11% of children indicated high risk for PTSD. All of these children had been admitted to PICU. Children who were more severely ill on admission were more likely to have hyperactivity and conduct problems. Psychiatric symptoms in children may be as a result of: • biological effects of the acute illness on the brain • a consequence of the stress of the illness • a combination of the two Psychiatric symptoms in children and parents were positively correlated, which emphasises how parents play an important role in helping their children cope with the emotional impact of serious illness.	7

After effects	Age group and pathogen	Findings	Ref.
Behavioural and emotional (psychological) problems,	Children aged 3 to 16 years Median age at recruitment 8. 66 children followed up 9-12 months later Meningococcal disease	Looked at psychiatric outcome in children and parents in the year after illness. More than half of the children over 6 had a psychiatric disorder during the course of the year after discharge from hospital. It was still present at the 12 month assessment in almost one third of children. Most common was impairing depressive and oppositional defiant disorders (ODDs). Anxiety disorders were also common including specific phobias regarding medical procedures. Depressive disorders tended to be relatively short lived, but ODD and anxiety disorders tended to persist at 12 month follow up. Persistent problems are associated with septic shock and higher illness severity, suggesting that it has an organic cause. However, length of hospital PICU admission is also associated and this may reflect the psychological stress derived from the admission itself. The authors suggest that screening for psychological problems seems highly appropriate for the more severely affected children and for those with pre-morbid psychological vulnerability.	8
Behavioural and emotional (psychological) problems,	Children aged 3-16 years The study followed up 56 families Meningococcal disease	An extension of previous research [7-8], aiming to see if the increase in psychological problems observed at 3 months is sustained at 12 months. In children, hyperactivity problems identified at 3 months after illness tended to have decreased again at 12 months, but conduct and emotional problems increased over time. The percentage of children at high risk of developing post traumatic stress disorder (PTSD) stayed at around 11% at both 3 and 12 months after illness. Admission to the hospital with meningococcal disease is followed by an increase in psychological symptoms in children at home, some of which are persistent and impairing, and by continuing PTSD symptoms in a proportion of children and parents.	9
Hearing impairment, Headache, Balance problems, Behavioural and emotional (psychological) problems,	Children aged 0-4 years who had meningitis between 1987-1989 in Sweden Followed up 457 children between the ages of 6-14. Haemophilus influenzae, pneumococcal, meningococcal	Sent questionnaires to the parents of children who survived meningitis with no obvious after effects at the time of discharge from hospital using nearest age siblings as a comparison group. The majority of children were healthy and attended normal school after surviving meningitis but they had more hearing impairment, headaches and problems with balance than their siblings. When the distributions of answers regarding behaviour were compared, the children who had survived meningitis had significantly more symptoms in the fields of inattention, hyperactivity and impulsiveness than their siblings.	10

After effects	Age group and pathogen	Findings	Ref.
Hearing loss, Amputations, Intellectual impairment, Behavioural and emotional (psychological) problems,	Children aged from 1 month to 13 years who had meningitis between July 2004 and December 2006 The study followed up 245 children3 years after disease (mean age 6.5) Group B meningococcal (MenB) disease	Looked at physical and psychological health of children 3 years after illness compared with age matched controls. Children with MenB disease were more likely than controls to have: • Bilateral sensorineural hearing loss 40dB or more (5% vs <1% for controls) • Lower full scale IQ (mean of 99.5 vs 107.2 for matched controls) • Psychological disorders (26% vs 10% for controls) • Disabling amputations (1% vs 0% for controls) • Deficits in executive function and multiple aspects of memory (36% vs 15% of controls) No significant differences were noted for post traumatic stress disorder or attentional function between children with MenB disease and controls. • About one tenth of survivors had major disabling after effects: intellectual disability (full-scale IQ <70) • Seizures • bilateral sensorineural hearing loss of 40 dB or more • disabling motor impairment (eg, amputation of part of a limb or more than one digit) • significant visual loss • major communication disability (unintelligible speech or unable to understand speech). More than one third had one or more deficits in physical, cognitive and psychological functioning.	11
Behavioural and emotional (psychological) problems,	5-16 yr olds treated from Jan 91-Jan 07 Followed up 100 children with confirmed meningitis Meningococcal (34%), pneumococcal (26%), haemophilus influenza (5%), GBS (4 %) and Entervirus (3%), other (7%) Unknown organism (21%)	Followed up children at a mean of 8 years post illness. Psychosocial outcomes were measured via parent and teacher report using the strengths and difficulties questionnaire (SDQ) and the paediatric quality of life (PedsQL) inventory. • 32% of parents and 19% of teachers reported clinically significant behavioural difficulties on the SDQ. • Parents reported significantly lowered health related quality of life (HRQoL) on PedsQL measures. • Children with learning disability, epilepsy and visual impairment were associated with increased risk of behavioural problems and reduced HRQoL outcomes.	12

After effects	Age group and pathogen	Findings	Ref.
Bone growth problems	24 children aged between 15 months to 11 years presenting with bone growth problems following meningococcal septicaemia between 1990-2001	The median time that children presented to hospital with bone growth problems was 32 months since being acutely ill with meningococcal septicaemia. Reasons for referral: • Angular bone growth deformity • Uneven limb length • Joint contracture • Problems with prosthetic limb fitting for amputees Most common reason for referral: Angular bone growth deformity caused by partial growth arrest 14 of the children had bone growth problems in multiple locations	13
Skin scarring, Bone growth problems Amputation	Children treated in intensive care from 1988- 2001 120 followed up 4 – 16 yrs later Meningococcal septicaemia	48% of patients had skin scarring varying from barely visible to disfiguring scars • Most scars were on the legs (86% and arms (55%) 6% had uneven limb length mostly together with angular bone growth deformity. The most common presenting symptoms in these patients were: • Limping • Pain in the limbs • Difficulty in walking • Angular deformity of the limb 8% had amputations ranging from one toe to both legs and one arm Patients with scars or bone growth problems tended to have more severe illness than those without these after effects.	14
Skin scarring, Bone growth problems Amputation	Children admitted to Royal Children's hospital Melbourne with meningococcal septicaemia from 1985-2002 143 children's records reviewed	122 patients survived the disease and had a mean age of 4 yrs 4 months at the time of illness. Of these patients: • 28 had surgical skin debridement. Of these, 12 developed bone growth problems later on. • 17 had amputations ranging from digits to limbs • 16 were identified with bone growth problems in a total of 41 locations. Of the 41 locations identified 23 of these occurred under areas of skin scarring. Bone growth problems were diagnosed between 2 and 9 years after the acute illness.	15

References

1. Grimwood, K., et al., *Adverse outcomes of bacterial meningitis in school-age survivors.* Pediatrics, 1995. **95**(5): p. 646-56.
2. Anderson, V., et al., *Cognitive and executive function 12 years after childhood bacterial meningitis: effect of acute neurologic complications and age of onset.* J Pediatr Psychol, 2004. **29**(2): p. 67-81.
3. Grimwood, K., et al., *Twelve year outcomes following bacterial meningitis: further evidence for persisting effects.* Arch Dis Child, 2000. **83**(2): p. 111-6.
4. Bedford, H., et al., *Meningitis in infancy in England and Wales: follow up at age 5 years.* BMJ, 2001. **323**(7312): p. 533-6.
5. Stevens, J.P., et al., *Long term outcome of neonatal meningitis.* Arch Dis Child Fetal Neonatal Ed, 2003. **88**(3): p. F179-84.
6. Halket, S., et al., *Long term follow up after meningitis in infancy: behaviour of teenagers.* Arch Dis Child, 2003. **88**(5): p. 395-8.
7. Shears, D., et al., *Short-term psychiatric adjustment of children and their parents following meningococcal disease.* Pediatr Crit Care Med, 2005. **6**(1): p. 39-43.
8. Shears, D., et al., *Psychiatric adjustment in the year after meningococcal disease in childhood.* J Am Acad Child Adolesc Psychiatry, 2007. **46**(1): p. 76-82.
9. Garralda, M.E., et al., *Longer-term psychiatric adjustment of children and parents after meningococcal disease.* Pediatr Crit Care Med, 2009. **10**(6): p. 675-80.
10. Berg, S., et al., *Long-term follow-up of children with bacterial meningitis with emphasis on behavioural characteristics.* Eur J Pediatr, 2002. **161**(6): p. 330-6.
11. Viner, R.M., et al., *Outcomes of invasive meningococcal serogroup B disease in children and adolescents (MOSAIC): a case-control study.* Lancet Neurol, 2012. **11**(9): p. 774-83.
12. Sumpter, R., et al., *Health-related quality-of-life and behavioural outcome in survivors of childhood meningitis.* Brain Inj, 2011. **25**(13-14): p. 1288-95.
13. Belthur, M.V., C.F. Bradish, and P.J. Gibbons, *Late orthopaedic sequelae following meningococcal septicaemia. A multicentre study.* J Bone Joint Surg Br, 2005. **87**(2): p. 236-40.
14. Buysse, C.M., et al., *Long-term skin scarring and orthopaedic sequelae in survivors of meningococcal septic shock.* Arch Dis Child, 2009. **94**(5): p. 381-6.
15. Bache, C.E. and I.P. Torode, *Orthopaedic sequelae of meningococcal septicemia.* J Pediatr Orthop, 2005. **26**(1): p. 135-9.