LETTERS TO THE EDITOR

Allicin: a possible answer to antibiotic resistant campylobacter diarrhoeal infection?

EDITOR,—Several *Campylobacter* spp are a frequent cause of gastroenteritis in children, particularly those younger than 2 years in developing countries.[1] Recent articles have reported the emergence of campylobacter isolates resistant to quinolones, which are commonly used for the treatment of this infection.[2] We have observed the emergence of *Campylobacter* spp resistant to nalidixic acid, a commonly used quinolone. We propose that due consideration be given to the research and development of allicin, the primary antimicrobial component in garlic (*Allium sativum*) as an alternative form of enteral treatment in cases of campylobacter infection that fail to respond to conventional antibiotic regimens. Allicin, a naturally occurring antibiotic, has been shown in vitro to have a broad spectrum of activity against Gram positive and Gram negative bacteria, yeasts,[3] *Candida* spp, *Cryptococcus neoformans*, and *Helicobacter pylori*.[4]

The antibacterial effect of an aqueous garlic extract was investigated against 38 clinical isolates of campylobacter from children presenting with diarrhoeal infections, and 32 isolates of *H pylori* from adults with peptic ulcers. The campylobacter strains tested were *C jejuni* sub *jejuni* (n = 20), *C fetus* (n = 5), *C coli* (n = 4), *C upsaliensis* (n = 3), *C jejuni* sub *doylei* (n = 2), and one strain of each of the following: *C hyeintestinalis*, *C ureolyticus*, *C mucosalis*, and *C helveticus*.

An aqueous garlic extract was prepared according to a modified method of Fromtling and Bulmer.[5] Cloves of garlic were dehusked, crushed, and homogenised. Distilled water (100 ml) was added to each 50 g of garlic pulp. The aqueous mixture was mixed for one hour and allowed to stand for a further two hours at 4°C. The resulting aqueous supernatant was decanted to remove the larger tissue particle. The supernatant was centrifuged for 15 minutes to remove smaller particles and then passed through a 0.45 µm acetate membrane filter followed by storage at 4°C for up to seven days before in vitro testing.

The Nathan agar well diffusion assay[6] was used to test the susceptibility of the 70 clinical isolates of campylobacter and *H pylori* to allicin in the aqueous garlic extract at a concentration of 0.5 g/ml. Blood agar plates were inoculated with the different strains and a well (6 mm diameter) made in the centre of each plate. The well was filled with 100 µl of the aqueous extract and incubated at 37°C in an H_2 increased atmosphere for 48 hours. Plates were examined, re-incubated, and examined frequently for an additional four days.

The 70 clinical isolates were all susceptible to allicin as seen by zones of inhibition (range 16–32 mm in diameter, mean 21 mm) (table 1). Subcultures from the zones of inhibition produced no growth after 48 hours, suggesting that the mode of action of allicin against campylobacter is bactericidal.

These results suggest that allicin should be investigated as a possible enteral treatment for gastroenteritis involving antibiotic resistant campylobacter strains and as a possible cure for *H pylori* infections.

Table 1 Effect of allicin on Campylobacter and Helicobacter spp

Organism	Tested (n)	Zone size (mm) Range	Mean
H pylori	32	18–32	23
C jejuni sub *jejuni*	20	6–26	20
C fetus	5	17–24	20
C coli	4	16–18	18
G upsaliensis	3	18–20	19
C jejuni sub *doylei*	2	16–18	17
C hyointestinalis	1		18
C ureolyticus	1		22
C mucosalis	1		22
C helveticus	1		20

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ACTH treatment for gelastic seizures

EDITOR,—Gelastic seizures are recurrent attacks of inappropriate laughter not precipitated by external stimulation. Usually, they are poorly responsive to antiepileptic drugs.[1] I report a case of tuberous sclerosis with gelastic seizures that disappeared after treatment with adrenocorticotrophic hormone (ACTH).

A 6 month old girl had repetitive tonic spasms of her head and arms and was referred to hospital. There was no significant family history. Pregnancy and delivery were uncomplicated and developmental milestones were normal. Physical examination revealed retinal hamartomas and hypomelanotic macules on her chest and back. The EEG showed hypsarrhythmia. Computed tomography and magnetic resonance imaging (MRI) of her brain showed multiple subependymal calcified nodules and cortical tubers. She was diagnosed with tuberous sclerosis and treated with ACTH (synthetic ACTH, 0.015 mg/kg/day).[2] Her seizures and hypsarrhythmia on the EEG disappeared soon after ACTH treatment, which was administered every day for two weeks and tapered gradually.

Six months later, she started to have episodes of sudden inappropriate laughter followed by salivation and unconsciousness for a few minutes. These episodes occurred a few times a week. The EEG showed sporadic spikes or polyspikes in the left posterior temporal region. MRI showed no hypothalamic masses. These gelastic seizures were difficult to control and lasted for three months, despite the administration of valproate, zonisamide, and nitrazepam. Repetitive tonic spasms of her head and arms recurred. She was treated with ACTH in the same way as before and gelastic seizures disappeared. Her tonic spasms also diminished but still occurred a few times a week after eight weeks of ACTH treatment.

The sudden laughter observed in this case is consistent with the criteria of gelastic seizures.[3] ACTH might be useful to treat gelastic seizures in selected cases.

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Less diarrhoea but no change in growth: 15 years' data from three Gambian villages

EDITOR,—The paper by Poskitt and colleagues from The Gambia[1] indicates that there has been a disappointing lack of improvement in the nutritional status and mortality of young African children during the 25 years' existence of the famous field station. Previous research from Keneba suggested a relation between diarrhoeal diseases and growth faltering, but despite considerable reductions in diarrhoea incidence and duration of attacks over the past 15 years, nutritional status has not improved, implying that these children were malnourished primarily because of a lack of food rather than because of high rates of diarrhoea.

This challenge to the orthodox "diarrhoea–malnutrition vicious cycle" theory, first voiced by Briend in an analysis of morbidity and growth data from Bangladesh,[2] is also supported by our findings in rural Zimbabwe.[3 4] Children from commercial farm labour compounds were enrolled in a prospective study of diarrhoea morbidity and growth. Growth faltering in the 2nd year of life was severe but there was little difference in the average rates of growth between children with frequent and infrequent diarrhoea. The results of an interval based data analysis similar to that employed by Briend, were consistent with there being only a transient effect of diarrhoea on weight gain. Estimation of weight faltering following episodes of diarrhoea and the rate of return to the trend in the 9–14 month age group indicated that weight loss associated with each episode was small (around 2% of body weight), and return to the child's trend was 90% complete within a month.

Our observations lend weight to the hypothesis that recurrent episodes of diarrhoea are not a potent cause of growth faltering in early childhood except in a small number of largely catastrophic cases. Inadequate food intake is a more plausible explanation.

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Need to consider other causes of poor growth in Gambian children

EDITOR,—The paper by Poskitt and colleagues[1] suggests that diarrhoea does not contribute significantly to malnutrition in Gambia and proposes that poor diet is likely to be the main cause. The accompanying commentary by Weaver puts forward the idea that *Helicobacter pylori* may also be implicated. The reality is that there are many causes of malnutrition in African children including those mentioned in the paper.

The paper points out that catch up growth after acute diarrhoeal disease requires energy intakes 50% in excess of recommendations. In Gambia micronutrient and macronutrient supplementation has been tried over 14 years without obtaining significant catch up growth,[2] as quoted in the paper. Mention is made of the role of enteropathy in causing malnutrition and poor growth. The evidence for this was published in 1991,[3] and suggested that impaired mucosal integrity, secondary to chronic inflammation, is largely to blame with 40% of poor growth attributable to poor small bowel function. Thus the effect of enteropathy appears to be significantly greater than any response to dietary supplementation.

Enteropathy is widespread in the tropics and has been termed "tropical enteropathy", the cause of which is uncertain and could include infection, nutrient deficiency or postenteritis food allergy. Although acute diarrhoeal disease may not contribute significantly towards poor growth, the underlying enteropathy undoubtably does. Clearly, adequate nutrition is crucial for growth, but for many African children this may not be enough.

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BCG and tuberculosis

EDITOR,—There is no doubt that BCG increases sensitivity to tuberculin but this cannot be taken to equate with protection against tuberculosis as is implied by a number of studies including 2 cited in the article by Bannon.[1] Evidence from the large Medical Research Council (MRC) trial in the UK showed that after BCG vaccination, non-responders to a 3 tuberculin unit (TU) Mantoux test had the same degree of protection against tuberculosis as responders.[2] The delayed hypersensitivity reaction should not be regarded as evidence of immunity but as evidence of infection. Distinguishing a BCG infection from tuberculosis infection may be difficult and the tuberculin test is only one element in the assessment. In a high risk population in Leicester who had neonatal BCG vaccination, use of a 1 TU Mantoux test (0.1 ml of 1 in 10 000) can significantly and safely reduce the number of children who need chemoprophylaxis.[3]

The larger tuberculin response that follows later vaccination[4] is not evidence that neonatal BCG is less effective. The present system of universal vaccination at 13 years is illogical and derives from the original MRC trial design. This age was chosen for operational and statistical reasons that have nothing to do with the clinical effectiveness of the vaccine.[5] A more rational approach would be to dispense with school BCG in favour of universal neonatal BCG, which is logistically much easier and protects those most at risk of the disease (young children) from its most serious manifestations. Funding for tuberculosis services could then be directed more towards case finding and treatment compliance, which will break the transmission of disease to the next generation.

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Dr Bannon comments:

The tuberculin protein skin test should never be used in isolation in the diagnosis of childhood tuberculosis. A more rigorous approach is required that includes good history taking, meticulous clinical examination, and judicious use of appropriate investigations. A positive tuberculin protein skin test merely indicates that a child's immune system has been exposed to certain strains of mycobacteria. However, there is now some agreement that a reaction is more likely to be indicative of infection rather than prior BCG immunisation if:

- it is strongly positive
- BCG had been given at least five years previously
- there had been close contact with a sputum positive adult
- the child is a recent immigrant form a part of the world where there is a high prevalence of TB.[1]

All children fulfilling these criteria must be referred for specialist opinion.

It would be illogical to discontinue with the school BCG programme at this present time. Even if universal neonatal BCG immunisation were to be implemented immediately, there would still be a large cohort of children who would remain unprotected for many years. School attendance is an ideal opportunity for opportunistic health promotional activities, and tuberculin protein testing of adolescents should continue to detect those children who have subsequently become infected with the *Mycobacterium tuberculosis* bacillus or who, despite receiving neonatal BCG, have developed active tuberculosis.

For the foreseeable future, we should continue with existing TB prevention and eradication programmes. In addition, TB must achieve a higher profile in medical education programmes and in future strategic health care planning. Incidentally, how many readers were aware that 24 March 1999 was world TB awareness day?

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Varicella: to vaccinate or not vaccinate?

EDITOR,—Gershon summarised the rationale for universal varicella immunisation and strongly advocated its implementation in developed countries.[1] While the reduction of varicella associated morbidity is indeed an important public health goal, it seems warranted to draw attention to epidemiological, political, economic, and cultural characteristics of Europe that may affect the success of a universal varicella vaccination programme.

Recent epidemiological data indicate that severe complications of varicella are uncommon in Europe.[2 3] Persuading primary care physicians of the need for universal varicella vaccination will face obstacles similar to those reported from the state of Washington,[4] where fewer than 50% of physicians surveyed followed the policy of universal varicella vaccination. One of the main reasons for non-adherence was the impression that varicella is a benign illness. While ongoing monitoring of severe complications is crucial, it is clear that an appreciable burden of the illness must be obvious to those in charge of administering the vaccine.

The demise of the East–West divide, the Balkan war, and the free employment market in the European Union contribute to an accelerated migration of people across national boundaries, the directions and flow of which are poorly predictable. Unless a multinational varicella vaccination programme can be implemented, such migration will dilute immunisation rates, and the emergence of populations of susceptible adults becomes a realistic scenario.

The cost effectiveness of the varicella vaccine relies heavily on indirect savings resulting from the prevention of parental work loss. In many European countries, most children are cared for by a housekeeping family member. Overall cost effectiveness in this socioeconomic environment is unclear.

A considerable proportion of parents object to immunisations against common childhood illnesses. A recent survey[5] of vaccine coverage at the age of 36 months among Swiss children found immunisation rates for diphtheria–tetanus, pertussis, and poliomyelitis of 98%, 90%, and 98%, respectively, while the rate for measles–mumps–

rubella (MMR) was as low as 76%. The last rate does not reflect the lack of opportunity, but the lower acceptance of the MMR vaccine. The varicella vaccine is likely to fall into the same category.

Both the safety and efficacy of the varicella vaccine are undisputed, and the prospect of preventing herpes zoster may become a powerful argument supporting its use. However, strategies for overcoming the issues described must be available before universal vaccination should be recommended. Equally important, new vaccines of high priority, such as the pneumococcal conjugate vaccine, will soon be available. It seems prudent not to waste the cooperation of both paediatricians and parents with a vaccine of lower priority.

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Nurse-led asthma education and childhood asthma readmission rates

EDITOR,—Wesseldine and colleagues showed a significant decrease in asthma readmission rates in children whose parents received 20 minutes of structured asthma education before their child was discharged from hospital.[1]

In October 1992, a community based, nurse-led, children's asthma service was established in Central Manchester, UK with the aim of informing and empowering asthmatic children and their parents to undertake day to day management of asthma through a structured education programme.[2] Over a third of the educational encounters take place in the patient's home. Parents and teenagers have direct access to asthma nurse specialists by telephone during working hours and to the weekly asthma education drop-in clinic.[3]

All children admitted to our inner city general paediatric unit with acute asthma are routinely referred to asthma nurse specialists. We undertook a retrospective case note audit to test the hypothesis that this structured nurse-led education programme would lead to a reduction in the hospital readmission rates for acute asthma. Hospital admission and readmission rates of all patients with acute asthma between the ages of 2 and 15 years were compared during 24 month periods before (January 1990 to December 1991) and after (January 1994 to December 1995) establishment of the nurse-led asthma education service (table 1). Over 90% of patients and their parents were seen within a week of discharge from hospital and each educational session lasted around 20 minutes.

We accept the limitations of using a retrospective case note audit; nevertheless, given the intensity of the educational input provided in the community and in the patient's home, we were disappointed to observe a small increase in the rate of readmission of children with asthma in the "posteducation" period. The relatively deprived population that we serve (the average Jarman score of families studied was 44), cultural beliefs of some of our patients about asthma, and the content and timing of the education programme might have contributed to the failure of our service in reducing hospital readmissions. Results of the study by Wesseldine and colleagues[1] and our audit suggest that the delivery of an asthma education programme to the captive population in hospital rather than after discharge may be more effective in preventing readmissions. If these findings are confirmed by further studies, it poses an important challenge in the delivery of a predischarge asthma education programme in the setting of short stay or ambulatory paediatric units, which are increasingly being proposed as models of care for all but very ill children.

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Table 1 Hospital admission and readmission rates of patients aged between 2 and 15 years with acute asthma before (January 1990 to December 1991) and after (January 1994 to December 1995) establishment of a nurse-led asthma education service

	Before	*After*
Total paediatric medical admissions	3134	4652
Total acute asthma admissions	252 (8.2%)*	300 (6.5%)*
Total patients with asthma	162	180
Patients readmitted with acute asthma	43	55
Asthma readmission rate	26.5%	30.6%
Patients referred to asthma nurse specialists	NA	92%
Nurse-led educational sessions/patient (median (range))		
Overall	NA	4 (1-25)
Re-admission group	NA	7 (1-25)

*Percentage of total acute general paediatric hospital admissions.

Kearns Sayre syndrome initially presenting as hypomelanosis of Ito

EDITOR,—Hypomelanosis of Ito (HI) is a neurocutaneous syndrome characterised by hypopigmented skin lesions along Blaschko's lines, frequently associated with neurological, musculoskeletal, ocular, and other extracutaneous manifestations. Chromosomal mosaicism in skin fibroblasts is responsible for approximately 30% of the cases.[1] Kearns Sayre syndrome (KSS) is a mitochondrial multisystem disorder, usually associated with a single large scale muscle mtDNA deletion. Its main clinical characteristics are progressive external ophthalmoplegia and pigmentary retinopathy but virtually all organ systems can be involved.[2]

We report a 13 year old boy who, at the age of 5 years, was diagnosed with HI and who later, at the age of 12 years proved to have KSS. At the age of 5 years the patient had short stature, mild mental retardation, corneal opacities and myopia, irregularly spaced teeth with hypoplastic dental enamel, hypopigmented patchy lesions on the left side of the trunk, and linear streaks on the left limbs. The laboratory investigations were negative for malabsorption disease, endocrine abnormality or metabolic disorder. Skin histology showed decreased melanin in the hypopigmented skin. Karyotype analysis, using G banding technique, in peripheral blood lymphocytes and skin fibroblasts was normal, 46 XY

At the age of 10, he presented with hypocalcaemic tetany. He had also bilateral ptosis of the eyelids, slurred speech, and limb muscle weakness. Parathyroid ultrasound, serum 25(OH)D vitamin, muscle enzymes, tensilon test, and brain magnetic resonance imaging (MRI) were normal. At the age of 12, ophthalmologic examination revealed bilateral limitation of horizontal eye movements. Fundoscopic examination was normal but the electroretinogram was compatible with pigmentary retinopathy. Hearing acquity and cardiac function were normal. The laboratory investigations, relevant to mitochondrial cytopathy showed serum lactate, 2.80 mmol/l (normal 0.33–1.33), serum pyruvate, 0.235 mmol/l (normal 0.33–1.85), cerebrospinal fluid lactate, 7.25 mmol/l (normal 0.33–1.85), cerebrospinal fluid pyruvate, 0.209 mmol/l (normal 0.03–0.08), cerebrospinal fluid protein, 300 mg/dl (normal < 20 mg/dl). Brain MRI showed abnormal signals in the lenticular nuclei. Gomori trichrome stain of quadriceps muscle biopsy demonstrated ragged red fibres; biochemical analysis of mitochondrial enzymes in muscle revealed low cytochrome c oxidase activity. Analysis of muscle mtDNA showed a large scale deletion (5 kb).

The wide spectrum and severity of manifestations of HI as well as its genetic heterogeneity led several authors to believe that HI is not a single clinical entity.[3] As far as we know, hypopigmented skin lesions have not been described in KSS but they might have been overlooked. It must be noted that except for external ophthalmoplegia and hypoparathyroidism, all other extracutaneous abnormalities of our patient could be found in KSS as well as in HI.[4] Although one case could be a chance association, we suggest that KSS or other mitochondrial disorders should be suspected in patients fulfilling the criteria of HI.

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Controlled trials from history

EDITOR,—Craft[1] is right to point out that steps to control selection bias by alternation or randomisation to treatment groups did not begin with the Dutch trials of paludrine in malaria and the Medical Research Council's (MRC) first trial of streptomycin in pulmonary tuberculosis. However, neither were these important design features introduced with the trial of patulin conducted in the early 1940s, as he suggests. Readers interested in earlier examples of efforts to control biases in treatment comparisons should enjoy visiting the "Controlled trials from history" web site, which has been established by the Royal College of Physicians of Edinburgh and the UK Cochrane Centre. The web site currently contains over a dozen examples of reports of controlled trials published before 1940 in which investigators used randomisation or alternation to create comparison groups (www.rcpe.ac.uk/cochrane).

The design feature of the MRC's streptomycin trial that makes it a methodological milestone was the care taken by the investigators to prevent knowledge of the allocation schedule among those responsible for recruiting patients to the trial. Empirical evidence has shown just how important this precaution against biased allocation is, and how difficult it is to achieve if the allocation schedule is based on alternation.[2]

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The vitamin K debacle and infants with cholestatic liver disease

EDITOR,—We write in support of Tripp and McNinch's paper[1] recommending daily oral administration of 25 μg phytomenadione to all breast fed infants up to the age of six months. However, we remain concerned that high risk infants with cholestatic jaundice (up to 1 in 500 births[2]) are still liable to develop bleeding secondary to vitamin K deficiency.

An audit of all infants younger than 3 months admitted between 1 January 1998 and 30 June 1998 was carried out by retrospective review of case notes. The aim of the review was to evaluate vitamin K prophylaxis and the prevention of coagulopathy in jaundiced neonates. The setting was a supraregional centre for paediatric liver disease in Birmingham, UK.

Twenty seven jaundiced infants were admitted during the study period with the following diagnoses: extrahepatic biliary atresia (7), acute liver failure (4), α_1 antitrypsin deficiency (3), neonatal hepatitis (4), Alagille syndrome (3), Niemann pick disease (2), other (4). The mean age at presentation was 6 weeks (range 4–10). Three children with extrahepatic biliary atresia presented with gastrointestinal bleeding. All three children had rectal bleeding and one of them had haematemesis while another had extensive bruising, which his parents were initially accused of inflicting. All three had prothrombin times in excess of 100 seconds, which was corrected after a single 1 mg dose of intravenous vitamin K. All three babies had been exclusively breast fed before presentation and had received two to three doses of oral vitamin K. Despite this, these high risk infants developed a life threatening coagulopathy and it is fortunate that none had an intracranial haemorrhage.

It is now recommended that all babies with jaundice persisting beyond 14 days of age be evaluated medically.[3] We would like to add to Tripp and McNinch's recommendation about oral vitamin K prophylaxis, that breast fed infants who are referred for evaluation of conjugated hyperbilirubinaemia have coagulation measured. Intramuscular vitamin K (1 mg) should be given without delay if coagulation studies cannot be easily obtained. In this group of children with liver disease, the risk of vitamin K deficiency bleeding was 11%, which exceeds the putative risk of childhood leukaemia.[4]

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The role of the Glasgow meningococcal septicaemia prognostic score in the emergency management of meningococcal disease

EDITOR,—Pollard *et al* give an excellent review of the emergency management of meningococcal disease.[1] We strongly support the involvement of the paediatric intensive care unit (PICU) at an early stage; however, only a third of all admissions with meningococcal disease are admitted to a PICU. Deciding which children need PICU admission can be a major clinical challenge. It would be inappropriate to transfer all children—they would occupy beds better used for other patients. Although the algorithm in fig 1 of Pollard *et al*'s article is useful in assessing children who may need PICU admission, it does not cover most children seen in district hospitals who have milder disease. We were disappointed that no mention was made of the role of severity scores, especially the Glasgow meningococcal septicaemia prognostic score (GMSPS)[2]; which has been validated retrospectively[3] and prospectively.[4]

In a multicentre study of 152 patients in four district general hospitals and one secondary–tertiary centre, Marzouk[4] compared the performance characteristics for mortality of eight meningococcal scoring systems and laboratory markers of disease severity. The GMSPS performed best, a score ⩾ 8 identifying children at risk of dying from meningococcal disease (odds ratio of 87.0). Prospective validation in 278 children showed a GMSPS of ⩾ 8 to have 100% sensitivity, 75% specificity, a positive predictive value of 29%, and a negative predictive value of 100%.[5]

The GMSPS is particularly valuable because it can be repeated. This identifies deteriorating disease in patients who initially scored < 8 but then moved into the ⩾ 8 category despite early treatment, as well as patients who were ⩾ 8 but deteriorated further. Characteristics of the score do not seem to change when used by frontline medical staff.[5] The GMSPS is useful in identifying severity of disease and predicting mortality. We recommend it to paediatricians to identify children needing PICU admission as an adjunct to Pollard *et al*'s algorithm.

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Dr Pollard et al comment:

We are grateful that Carrol *et al* have raised the important issue of scoring systems in the evaluation of children with meningococcal disease. Such scores were designed and validated to predict death in cohorts of patients. In contrast, the emphasis of our algorithm is on the emergency management of meningococcal disease and prevention of death in the individual child. However, we recognise that the GMSPS may be useful in alerting the clinician to the important signs of critical illness in children with meningococcal disease and, when used for repeated review of such children, could aid the monitoring of stability or deterioration of the patient. GMSPS is also an important research tool allowing cohorts of patients to be categorised and compared between groups in audit, drug trials, and health planning.

Unfortunately, GMSPS is of only limited value when making decisions about the management of individual patients and could be misleading.[1 2] False reassurance may be provided when the score is low. For example,

a child who has severe raised intracranial pressure or compensated shock could score just 5 on the GMSPS but still be critically ill. Carrol *et al* point out that children with scores > 8 have a 29% chance of dying and suggest that the score may be helpful in deciding which patients require intensive care. However, this is not a reliable use of the GMSPS[1] and some of the children with initial scores < 8 will also require intensive care and some of these children will deteriorate.

We do not advocate PICU admission for all children with meningococcal disease, as it is clear that most children with the disease do not develop critical illness. Our algorithm encourages clinicians to consider those signs suggestive of severe disease requiring intervention and we only advocate intensive care for those who do not improve after initial management. The algorithm also deals with recognition and initial treatment for children without shock or raised intracranial pressure, those who do not need to go to a PICU, and who should be managed on the general paediatric ward.

GMSPS may help in the evaluation of children with meningococcal disease, particularly where those in the frontline are unfamiliar with the disease, but the prognostic score must not be allowed to distract from urgent resuscitation of those who need it.

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Prolonged QTc interval as an important factor in sudden infant death syndrome

EDITOR,—Dr Davies's comments on the relation between QT prolongation and sudden infant death[1] are based on accepting the report by Schwartz *et al* at face value.[2] In that paper 9725 of 34 442 ECGs recorded over 19 years were analysed. Twenty four infants had unexplained sudden death and their ECGs were analysed retrospectively to show a mean difference in QT interval of 35 ms (< 1 mm). The paper gives no indication that the observers were blinded to the occurrence of sudden death. QT measurement depends on identification of the end of the T wave and retrospective measurement in the knowledge of sudden infant death raises doubts about the findings.

The report by Schwartz *et al* also goes against what is known about familial long QT syndrome. In long QT syndrome there is a strong association between the degree of prolongation of the QT interval and risk,[3] yet Schwartz *et al* reported the QTc only slightly prolonged in all but two of their cases. International studies have failed to demonstrate any excess of sudden infant death in families with known long QT syndrome.[4] Studies of first degree relatives of victims of sudden infant death[5] and survivors of "near miss" sudden infant death have also shown no evidence of QT prolongation.

The changes that occur in QT interval with age during infancy are normal and should not be taken as evidence of "tendency towards reduced cardiac stability". There is also no evidence of any differential risk related to different QT intervals within the normal range. Unless evidence can be provided from a blinded measurement of QT intervals in infancy it will be difficult to accept that there is any association between QT interval and sudden infant death syndrome.

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Umbilical cord blood transplantation

EDITOR,—Although Will[1] gave an informative overview of umbilical cord blood transplantation he expressed the commonly held misconception that umbilical cord blood lymphocytes are immunologically naïve. To call these cells immunologically naïve implies that the B and T lymphocytes have not encountered antigen. This is clearly not the case. Numerous groups have demonstrated antigen specific responsiveness at birth indicative of priming of the fetal immune system during intrauterine life. The range of antigens for which this has been shown include allergens (such as those of house dust mite and hens' eggs),[2] autoantigens (myelin basic protein and acetylcholine receptor), and parasite antigens (schistosomal and malarial).[3] Not only do umbilical cord blood cells show proliferative responses to these antigens, antigen specific cytokine production is also seen. Furthermore, antigen specific IgM and IgE are demonstrable in umbilical cord blood serum. As neither of these immunoglobulin types cross the placenta the fetus must be producing them.

The reduced incidence of graft versus host disease, despite the fact that umbilical cord blood cells are not immunologically naïve, probably reflects the reduced cytokine production that these cells exhibit on stimulation with either mitogen or antigen. In fact, the immunological responsiveness of fetal cells may be transiently downregulated in the last few weeks of pregnancy, perhaps in preparation for the massive antigen load to be encountered at birth. This downregulation is supported by the fact that T lymphocytes from term cord blood show minimal upregulation of CD40 ligand on stimulation, while those obtained at 21 weeks' gestation have poststimulation levels of this co-stimulatory molecule comparable to adults. This responsiveness was found to decrease with increasing gestational age.[4] Therefore, rather than calling the immune system of newborns naïve we should consider it to be in a downregulated state compared to that of adults.

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No strings attached: preventing deaths from children's clothing

EDITOR,—Drawstrings on children's clothing are a hidden hazard that can lead to death and injury when they catch on cribs, playground equipment, vehicles, and escalators.[1–3] Although rare, 17 deaths and 42 non-fatal accidents involving the entanglement of drawstrings on children's outerwear were reported from 1985–95 in the United States. At least 12 of these incidents involved the entanglement of drawstrings in the doors of school buses.[4] The recent unrelated deaths of two young boys in Ireland, following entanglement of part of their outercoats in the door of a school bus[5] and rotating powershaft of a tractor,[6] prompted us to evaluate the safety of children's outerwear.

We evaluated the safety of different designs of children's winter outerwear carrying drawstrings in nine department stores and boutiques in Cork City, Ireland. In addition, we examined the outerwear worn by children (younger than 12 years) in two local primary schools. Outerwear was defined as "safe" according to the following guidelines for children's outerwear established by the United States consumer product safety commission[4]:

- outerwear should not carry hood or neck drawstrings
- it should not have waist strings that extended beyond 7.4 cm
- the waist strings should be sewn down at the midpoint
- there should not be toggles or knots on the ends of strings.

Of the 77 different designs of outerwear examined from nine department stores and boutiques, only 23.4% (9 of 40 girls' garments and 9 of 37 boys' garments) fulfilled the safety recommendations. Almost half of the garments (28 of 59) had hood or neck strings, while 44 of 59 had excessively long waist drawstrings. Two thirds of the garments (38 of 59) were not sewn down at their midpoint and most had toggles or knots on the end (42 of 59).

Of the 183 school children's outerwear examined, only 38.8% (33 of 84 girls' garments, 38 of 99 boys' garments) met the safety recommendations. Almost half had hood strings, while the remainder had excessively long waist drawstrings, which were not sewn down at their midpoint and/or had toggles or knots at the end. There was no obvious difference in the safety profile of outerwear garments between the sexes or across different age groups.

The Irish Industrial Research and Standards Order 1976 states that "it is unlawful to manufacture, assemble or sell a child's outergarment if the hood is designed to be secured by means of a cord drawn through the material". This study confirms that this law is not

being enforced and that consumers are making unsafe choices in selecting outergarments. As the clothing stores we studied are common to most areas in the UK, we have no reason to believe that the design of children's clothing in the UK is safer than in Ireland, despite the recommendations of the British Standards Institution.[7]

The effectiveness of properly enforced legislative and regulatory interventions in the children's clothing industry has been well illustrated by the reduction in childhood burns from loose and flammable nightclothes.[8] However, the fact that less than a quarter of children's outerwear styles in shops were considered safe in terms of drawstrings indicates a lack of enforcement of recognised safety standards. Although some clothing hazards are difficult to correct without altering the function or aesthetic appeal, this is not the case for outerwear. Metal snaps, buttons, velcro or elastic can replace drawstrings, the main source of danger in outerwear.

Deaths due to children's clothing are uncommon but preventable. It is essential that child care professionals, the government, and clothing industry work together to ensure that established safety standards for the design, sale, and importation of children's outerwear are properly enforced.

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Where should paediatric surgery be performed?

EDITOR,—The figures quoted for surgical activity in East Anglia by Arul and Spicer in their response to the letter by Wilkinson and Crowle[1] are many years out of date. Over the four year period between 1995 and 1998 two accredited general paediatric surgeons working in Cambridge dealt with 504 neonates. Surgery requiring anaesthesia was carried out in 76% of these (table 1). However, we do support Arul and Spicer's view that specialist paediatric surgical services should be centralised to concentrate experience and so maintain high standards.

Table 1 Surgical neonatal caseload at Addenbrooke's Hospital 1995–98

	Referrals	*Surgery (%)*
1995	112	92 (83)
1996	137	96 (70)
1997	146	107 (73)
1998	109	88 (81)
Total	504	383 (76)

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1 Wilkinson KA, Crowle P. Where should paediatric surgery be performed? [letter]. *Arch Dis Child* 1999;**80**:300.

Thyroid dysfunction in Down's syndrome: relation to age and thyroid autoimmunity

EDITOR,—The paper by Karlsson *et al* describes a longitudinal study of monitoring for thyroid disease in children and young people with Down's syndrome.[1] Although the authors conclude that "annual screening is important", they do not provide any data to justify the interval being a year. We need to know the interval from changes in thyroid stimulating hormone concentrations and autoantibody titres to a subnormal thyroxine level. If the authors have such data, it would be most helpful if they could supply it.

This matter is important in the UK where many districts are introducing an enhanced surveillance programme for children with Down's syndrome, which includes thyroid function tests. The optimal screening interval for thyroid status is not known and needs to be studied unless Karlsson *et al* can provide such data.

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1 Karlsson B, Gustafsson J, Hedov G, Ivarsson S-A, Anneren G. Thyroid dysfunction in Down's syndrome: relation to age and thyroid autoimmunity. *Arch Dis Child* 1998;**79**:242–5.

Drs Annerén and Gustafsson comment:

In the group of Down's syndrome patients described in our article, 28 of 85 subjects developed hypothyroidism. Half of the subjects acquired the condition before 8 years of age and had no thyroid autoantibodies at the time of diagnosis. Most of those diagnosed after this age displayed such antibodies. However, since these were not analysed until the time of diagnosis there is no information on how long such titres preceded thyroid dysfunction. It is certainly important to measure thyroid autoantibodies annually in patients with Down's syndrome, especially those older than 8 years of age.

The rationale for annual screening of thyroid stimulating hormone (TSH) is the finding that among our patients with hypothyroidism, four girls (8–17 years) and one boy (10 years) developed significant increases of TSH between two annual controls. However, our experience is that if a child with Down's syndrome has a normal growth velocity during the preceding year and a TSH concentration well within the normal range at the previous control, hypothyroidism is rarely found.

BOOK REVIEWS

Truth and the Child 10 Years on: Information Exchange in Donor Assisted Conception. Edited by E Blyth, M Crawshaw, J Speirs. (Pp 83; £5.95.) BASW Publication, Birmingham. ISBN 1 86178 028 1.

How much information should children conceived from donor sperm be given about their origin? This is not a small problem now that 2500 children are born in the UK every year using donated gametes or embryos. I must admit that this was a problem that had never crossed my mind despite having an adopted son and being pretty much in favour of openness between parents and children on "secrets of the past". Yet, if asked, I think I would have said it is different for children born as a result of donor insemination. Why? I suppose because I feel that the relationship a child might have with "a gamete" is different from that with a real father; and the same goes for the genetic father (or mother).

However, this book convinced me that openness in this field is desirable. It is clearly a situation that will become more common, and the present regulations—genetic parents who are donors have the right not to be identified to children—will need to change. I was particularly impressed by the point of view of "donor children" in this small multiauthor volume, which brings together anthropology, genetics, psychiatry, and the law in a robust attack on the culture of secrecy.

Christine Whipp did not learn until she was 41 that she had conceived by donor insemination, but she had always had anxieties about her origins. This was partly because of a lack of resemblance to her father, and it is interesting that Lauren, the other donor insemination child who writes in the book says that "when secrets are kept the children often grow up sensing that something is different in their family". There is another interesting quote from Lauren. "When I was younger I had a particularly nasty fight with my brother and afterwards I went up to mum and said, 'His donor must have been a terrible man'. Mum asked, 'why, what makes you say that?' I replied, 'Because his nature is nothing like yours!' "

I suspect that these views may not be typical, and that it is unusual for children to observe physical differences from their parents, unless someone draws attention to it. However, I can believe that children sense something unusual about their family, in the same way as they sense disagreement between parents, or a hidden secret about cancer. Another personal chapter in this book, which is elsewhere rather dry and repetitive, is by the mother of surrogate twins, born to another woman (a friend) but genetically her own. She describes her complete openness with the children—in what for them would be a very strange and unnerving experience "we never contemplated telling our children anything but the truth". One daughter's comment was "it was a good job we had Kim as your friend mummy, otherwise you wouldn't have us." The children grew up not only knowing Kim but also her family. This mother went on to donate an egg which was used for in vitro fertilisation.

Essentially, *Truth and the child* is a one sided argument for telling children about their background. I support this, but I went away thinking I should know more about the other side of the argument, which does not appear in this book.

TONY WATERSON
Consultant Paediatrician (Community Child Health)

Clinical Guidelines and the Law. Negligence, Discretion and Judgment. Hurwitz B. (Pp 152, paperback; £19.95.) Oxford: Radcliffe Medical Press, 1998. ISBN 1 857 75044 6.

Brian Hurwitz is a general practitioner and in this small book he has linked literature on clinical guidelines with views on how these might be applied in a legal context. He contrasts the views of the British Medical Association in 1946, which were that individual doctors retain full responsibility for the care of the patient, practising medicine according to its traditions, standards, and knowledge but with freedom of judgment and without interference in professional work, with patterns of practice that pertain today.

In discussing the nature and context of clinical guidance, Hurwitz briefly reviews the large variety of terms in use ranging from protocols to codes of practice, and concludes that there is no single definition or guideline and, moreover, that guidelines vary in their quality and in the standards of health care they seek to establish.

He offers helpful criteria on how the authority of guidelines can be assessed and then goes on to discuss their developing legal status. He quotes examples of interaction between statute law and clinical guidelines in the UK, Europe, and the USA, emphasising the higher degree of development and sophistication of this interaction in the USA compared to Europe.

He then applies this interaction to negligence case law, focusing particularly on UK practice. He concludes that guidelines are regarded by the courts as hearsay evidence only and are not a substitute for expert testimony. He nevertheless very reasonably raises the issue that doctors acting outside guidelines are exposed to the possibility of being found to be negligent in their practice.

There is a particularly interesting discussion on the potential liability of authors or sponsors, such as Royal Colleges, which recommends that the legal status of recommendations from bodies such as these should be made clearer to doctors. In contrast, he goes on to make the reasonable points that autonomous clinical thought is undermined by unthinking conformity and that despite pressure from purchasers, rigid adherence to guidelines cannot and should not be a formal managerial or legal expectation in the National Health Service.

While the issues presented and discussed by Hurwitz are of particular relevance to doctors with an interest in medicolegal practice, no paediatrician can be immune from an involvement with the issues he details.

This is a relevant and lucid exposition of the current status of clinical guidelines and how they can be, and are, applied in the legal situation. Its content is wholly applicable to paediatric practice and the book deserves to be widely read.

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Educational video: Primary Ciliary Dyskinesia—How to Treat it and Live with it. Primary Ciliary Dyskinesia Family Support Group.

The last time my Godsons came to stay, their father brought a video player along. He believed (wrongly) that I would not cope with the boys for the weekend without video diversion. Videos have become the mainstay of family life and are potentially a great educational resource. The Primary Ciliary Dyskinesia (PCD) Family Support Group have recently produced a video aimed primarily at families with PCD sufferers.

The video aims to promote better understanding of the disease, its management, and most importantly, how to live with it. In this final objective it succeeds best. The individuals with PCD on the video give a clear cut, positive, and robust description of how they deal with their disorder, and this should be enormously helpful to newly diagnosed families. Another highlight is the beautiful video pictures of ciliary motion (produced I suspect by Chris O'Callaghan's group).

I was slightly disappointed that the narrator did not use more simple language. This was a missed educational opportunity, although, in practical terms, it could be overcome by a member of the team going through the video with some families.

I have two other minor quibbles. A throwaway line suggested that children aged 2–3 years could learn the active cycle of breathing technique. This is incorrect although they can certainly be taught how to huff and to blow. It is unfortunate that alternative remedies such as reflexology are given some credence towards the end of the video. Patients with PCD have enough to put up with without being exposed to cranks and charlatans. However, grind your teeth and put up with it, for on the whole your patients and your staff will be better off for having seen this video.

ANNE THOMSON
Consultant Paediatrician

Exploring Infant Health. Conroy S, Smith M. (Pp 184, A4; £7.50.) London: Foundation for the Study of Infant Deaths.

The relation between social disadvantage and infant health is at the core of this topical and comprehensive book comprising three extensive literature reviews. It is timely in view of the recent publication of the Acheson report into health inequalities (*Inequalities in health: report of an independent inquiry*. London: HMSO 1998).

Parental smoking is a known risk factor for a range of adverse infancy and childhood outcomes. Socioeconomic status is a risk factor for the same adverse outcomes. The review presents unequivocal evidence for the link between increasing social disadvantage and parental smoking. The problems of disentangling the influence of these related factors on sudden unexpected death of infants (SUDI) and other adverse outcomes are considered, and the authors conclude that the extent to which smoking acts as a marker for socially disadvantaging factors and the extent to which it is a contributory or causal factor in the aetiology of SUDI is uncertain.

Parenting has been correlated with infant health outcomes. There is less clarity, however, in the association between specific aspects of parenting and specific health outcomes, with the possible exception of child abuse and neglect, and in the association between parenting and social disadvantage. The review concludes that, while there are significant differences in behaviour towards children and attitudes to child care associated with social variables, there is rather less evidence about differences in parenting knowledge and health beliefs. Further, the authors conclude that, with the exception of response to risk reduction recommendations, the mechanism by which any of the differences highlighted in the review may be related to SUDI is not clear.

The parenting review is helpful in that it focuses on the association of social disadvantage with specific aspects of parenting, and makes useful recommendations for future research; however, there are some glaring omissions. The major research programme into cycles of disadvantage in the 1970s by Brown and Madge is missing as is the work in the USA by Elder *et al* and others, which document the direct effects of economic hardship on parenting. Brown and Madge concluded that multiple deprivation and its effects on children were based on structural and material factors and not on family psychopathology.

Within the narrow context which the authors set themselves, their methodological review will be of great value to future researchers. They address the problems associated with studying parenting among families living in socially disadvantaged environments with a particular focus on the multiply disadvantaged. They consider in detail the complex, innovative, and challenging research strategies required to overcome the difficulties of engaging such families in research, and ensure their representation in population based studies.

A fundamental difficulty with methodological review is the narrow focus on multiply disadvantaged families as the main "problem". This arises from the findings of the Confidential Enquiry into Sudden Infant Death (CESDI) study that, following the "Back to sleep" campaign, SUDI deaths are concentrated in the most disadvantaged families. Although an important observation, SUDI, in common with other adverse infant, child, and adult health outcomes, shows a finely graded social patterning, also shown in the CESDI study. Focusing on the extreme group fails to address the true nature of the social gradient in infant and child health. Why, for example, are infants born to parents with incomes above £200 per week at less risk than those with incomes between £100 and £199 per week? These fundamental questions cannot be addressed by studying the most disadvantaged.

These reviews are refreshing and rewarding in that they treat social disadvantage as a serious risk factor rather than focusing exclusively on the attributes and behaviour of individual parents outside the social context of that behaviour; they should be of particular value to those with a serious commitment to promoting infant and child health.

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Growth, Stature and Psychosocial Well-Being, edited by Eiholzer U, *et al*. (Pp 214, hardback; £24.75.) Gottingen: Hogrefe & Huber Publishers, 1998. ISBN 0 889 37197 0.

Copious information about the efficacy of growth promoting treatment for short stature of varying aetiology has been accumulating in recent years. Substantial insights are also developing into whether being taller (if achievable) is necessarily desirable or beneficial.

In the context of paediatric practice, children are commonly referred for short stature or pubertal delay and often demonstrate (apparently) short stature related psychosocial stress and distress. Is short stature psychologically stressful in itself? Do children with short stature, whether those with underlying pathology or those at an extreme of the normal height distribution, have clinically significant behavioural, emotional, or educational problems? Do children and adolescents with short stature or pubertal delay who are not referred have the same psychological problems as some of those who are? Do the psychological stresses of being short contribute to the development of psychological problems? How do we measure the emotional cost of coping? Does increased growth, in the short or long term, reduce or eliminate the "at risk" psychological status of such children? What are the effects of emotional disorders on growth?

Some of these questions were addressed and discussed at a symposium in Zürich, Switzerland entitled "Growth and psyche" and this book contains the substance of the papers presented. There are 17 contributions from psychologists, psychiatrists, clinicians, and auxologists from Europe, Scandinavia, and the United States with contributions from a number of well known names in the field. The intention of the symposium was to examine the quality of life of small children, to discuss why results in this area have been contradictory, to develop insights into the problems of psychometric methods, and to examine the effects that psychological factors may have on growth.

This book reflects the strengths and deficiencies that would be expected given its origin in a symposium, with chapters that are very variable in quality. Two of the best have already been published in virtually identical form in peer review journals. However, there is an outstanding review by Sandberg on the experiences of being short. In contrast, the two chapters in the section "Variation of normal growth patterns and their consequences" are respectively too superficial and out of date (at one point referring to "an excellent review on recent research" dated 1989) and totally unreferenced apart from the author's own previous review from 1991.

Helpful insights can be gained from a number of chapters—for example, Lindemann's comment from an evolutionary perspective that "the power of height stereotypes should not be overemphasized—we are not at the mercy of our evolution and stereotypes are often short lived and narrow." Some chapters are of particular interest and can be read with profit by anyone involved in this area (including all paediatricians). Nevertheless, the book fails to deliver the "clear overview of the current state of knowledge" promised in the foreword.

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Epidemiology of Childhood Cancer. By Little J. (Pp 386, paperback; £36.00.) Oxford University Press, 1999. ISBN 9 283 22149 4.

Paediatric oncology textbooks often open with a chapter on epidemiology, usually rather brief and tending to reflect the particular interests of the authors or editors. Numerous review articles have dealt with a few putative risk factors, but until now there has been no comprehensive review of the evidence on childhood cancer aetiology.

Epidemiology of Childhood Cancer represents a Herculean feat of almost single handed compilation and synthesis (only one chapter has any co-authors). Therein lies its main strengths and weaknesses. The introductory chapter contains a lucid discussion of study design, including methods of control selection and the principal sources of bias. This underpins the review of analytic studies that occupies most of the book and could be read with profit by anyone contemplating setting up an epidemiological study. Chapter 2, on descriptive epidemiology, sets a pattern by considering all relevant studies published by early 1997 relating to each major type of cancer in turn. The next eight chapters form the core of the book, each covering a group of possible risk factors. The best of these provide detailed reviews of the evidence on environmental factors such as ionising radiation, electromagnetic fields (one chapter each), and exposure to chemicals and dusts. Where a factor has been the subject of several studies, their characteristics and results are tabulated. The tables do not usually give confidence intervals for relative risks, and some are very long and hard to follow; the one relating to birth weight occupies five pages and has 41 footnotes.

The book could on occasion be more critical. For example, the author remarks that smoking in pregnancy is the most important single determinant of low birth weight but does not comment on how few analyses of birth weight and childhood cancer have allowed for maternal smoking or social class. The estimates of risks for siblings of children with cancer appear not to take into account the need to allow for method of ascertainment, and are of limited value for genetic counselling. A useful concluding chapter summarises factors investigated in relation to each diagnostic group, in each case ranging from those generally accepted to be associated with the specific cancer to those not generally associated. The bibliography of over 1000 references includes virtually every epidemiological study since 1990, but is less complete for earlier publications and relevant clinical and laboratory work. The index is not very helpful. Many entries for types of cancer are unnecessary, given the structure of each chapter, while factors such as paternal age (in chapter 3, six chapters away from maternal age) are unlisted.

Inevitably, the book is already out of date. The past two years have seen the publication of series of papers from case control studies in North America, Germany, and New Zealand, major studies of childhood cancer in relation to vitamin K, and parental occupational exposure to ionising radiation, volume 2 of *International Incidence of Childhood Cancer*, and yet more studies of parental smoking. What is now needed is a continuously updated, truly systematic review of childhood cancer epidemiology, with studies evaluated according to explicit, uniform criteria. Notwithstanding the criticisms above, *Epidemiology of Childhood Cancer* is unrivalled in scope and level of detail.

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