LETTERS TO THE EDITOR

The discovery that *Helicobacter pylori* is the prime cause of peptic ulcer disease, is one of the most important advances in medicine in the 20th century. Subsequently, its importance in the causation of gastric cancer has been recognised. It is a rare cause of gastric lymphoma. Despite its significance as a pathogen, this organism colonises the gastric mucosa in up to 50 percent of the world's population. Not surprisingly research interest is intense. There has been much speculation (though little proof) that it might have a role in various other gastrointestinal and non-gastrointestinal disorders, including failure-to-thrive in infancy, short stature, anaemia, and even cardiovascular disease. Now a link has been proposed between *H pylori* and sudden infant death syndrome (SIDS). Recently, Kerr *et al* examined gastric, tracheal, and pulmonary tissue, looking for evidence of *H pylori* in SIDS victims and controls.[1] Based on polymerase chain reaction (PCR) techniques, they reported a highly significant association between SIDS and the presence of two *H pylori* genes (UreC, cagA) in these tissues. Not surprisingly, this reported association has evoked a lively correspondence. Important questions have been raised regarding both methodology and interpretation.

M STEPHEN MURPHY
Associate Editor

1 Kerr JR, Al-Khattaf A, Barson AJ, *et al*. An association between sudden infant death syndrome (SIDS) and Helicobacter pylori infection. *Arch Dis Child* 2000;**83**:429–34.

Association between SIDS and *H pylori* infection

EDITOR,—The article in the November issue of the *Archives* on the association between sudden infant death syndrome (SIDS) and *H pylori* infection is confusing.[1] I am very familiar with *H pylori* colonisation in gastric biopsies in children and its association with gastritis, peptic ulcer, and gastric cancer. However, the implication that the organism can cause an unexpected infant death—that is, SIDS, is shocking!

Unexplained infant deaths (SIDS) are "fertile soil" for speculators that apply new technology—polymerase chain reaction (PCR)—to uncover new associations. Unfortunately, these observations are not based on an infrastructure of knowledge of the causes of infant mortality. Caution needs to be exercised when applying PCR technology to postmortem tissue and "discovering" an answer. The possibility of contamination is real, and in addition infants can die with something, and not of it.

I would value a response from Drs Fleming, Blair, Bacon, and Berry who co-authored the CESDI study of SUDI.

RALPH A FRANCIOSI
Pediatric Pathologist,
Children's Hospital and Medical College of Wisconsin,
Wisconsin, USA
ralph@mcw.edu

1 Kerr JR, Al-Khattaf A, Barson AJ, *et al*. An association between sudden infant death syndrome (SIDS) and Helicobacter pylori infection. *Arch Dis Child* 2000;**83**:429–34.

Ammonia—not the culprit

EDITOR,—We were interested to read the article by Kerr *et al* on the SIDS problem. With regard to the interesting results we would like to point out some related findings. As pointed out by Kerr *et al*, *H pylori* is abundant in less advantageous parts of society where smoking is often frequent, and sometimes where SIDS occurs. The fact that smoking is often inversely related to the ability of *H pylori* to colonise and to be transmitted from mother to child[1] might indicate that it is sensitive to smoke itself, or products generated after smoke inhalation. It is interesting to note that endogenous products of smoke, like nitrate and nitrite, often inhibit bacterial growth.[2 3]

Furthermore, we have previously shown that total breakdown of all ingested urea takes place in all normal infants without causing problems of ammonia intoxication.[3] This is in contrast to SIDS victims, most of whom have unmetabolised urea in their faeces.[4] Due to these related circumstances it may seem a little adventurous to suggest that ammonia produced by *H pylori* could cause death in SIDS.

LARS WIKLUND
GUNNAR RONQUIST
MARY GEORGE
Department of Anaesthesia,
Uppsala University Hospital,
Uppsala, Sweden
Lars.Wiklund@anestesi.uas.lul.se

1 Brenner H, Bode G, Adler G, *et al*. Does maternal smoking hinder mother-child transmission of Helicobacter pylori infection? *Epidemiology* 2000;**11**:71–5.
2 Goretski J, Zafiriou OC, Hollocher TC. Steady-state nitric oxide concentrations during denitrification. *J Biol Chem* 1990;**265**:11535–8.
3 George M, Nord KE, Ronquist G, *et al*. Faecal microflora and urease activity during the first six months of infancy. *Ups J Med Sci* 1996;**101**: 233–50.
4 Wiklund L, George M, Nord CE, *et al*. Sudden infant death syndrome and nitrogen metabolism: further development of a hypothesis. *Eur J Clin Invest* 1998;**28**:958–65.

Control your controls and conclusions

EDITOR,—In a retrospective study, Kerr and coworkers investigated formalin fixed, paraffin embedded tissues (stomach, trachea, and lung) of 32 infants who had died of SIDS, and eight control cases, with nested polymerase chain reaction (PCR) and ELISA of the amplicons. A child was considered as infected with *H pylori* if the optical density of the ELISA was above the mean value plus 2 SD obtained in the tissue of control infants. The authors found that 28 of the 32 SIDS cases, but only one of the eight control cases fulfilled these criteria. They conclude from their results that *H pylori* infection may play a causative role in SIDS. We have serious doubts about their results and conclusions.

The control group was extremely small in size and we would expect most, if not all, of these eight infants to have received one or more antibiotics in high doses intravenously over several days before death, as the causes of death were bacterial meningitis, septicaemia, pneumonia, necrotising enterocolitis, ileal perforation, and prematurity. In contrast, few if any of the SIDS victims would have received intravenous antibiotics. Therefore, if control children had been colonised with *H pylori*, the bacteria may have been suppressed. These eight infants are certainly not appropriate controls for this kind of study.

Nested PCR is a very sensitive method with a high risk of false positive results caused by contamination. The applied ELISA is yet another amplifying method which also increases the risks of unspecific binding. Although the authors stated that they tried to minimise contamination, no precautions have been performed at the time of autopsy and preservation of the tissue due to the retrospective character of the study. Because of the low specificity of the methods used, it is mandatory to prove the identity of the PCR amplicons as *H pylori* specific by sequencing the products. Such confirmation is not reported in the paper. To show the specificity of their method, the authors could have also performed analyses on control tissues—for example, brain, which are unlikely to be *H pylori* infected even when other tissues were assessed as "positive".

The fact that *H pylori* was not shown in the stomach, trachea, or lung by histology in any of the children must raise major concerns that the applied methods were not specific. Other methods for detection of *H pylori* infection like fluorescence in situ hybridisation (FISH) have not been applied.[1] The authors do not report whether any of the children had histological signs of acute or chronic gastritis, which is found even in young children with *H pylori* infection.[2] If the bacterial load was so small that neither the bacteria nor the associated inflammation could be detected by histology, it seems questionable that metabolic products produced by *H pylori*—for example, ammonia, may play a causative role as a cause of SIDS as suggested by the authors.

Finally, the authors mention that both *H pylori* infection and SIDS are more common in poor socioeconomic populations but fail to provide any information on the ethnic and socioeconomic background of their cases and control infants. From many epidemiologic studies and our own experience, it seems extremely unlikely that 28 of 32 infants (87%) under 28 weeks of age are infected by *H pylori* in a country such as the UK, unless these children are from immigrant groups. We are, for example, following a cohort of German children from birth with regular testing for *H pylori* infection by two non-invasive tests: the detection of *H pylori* antigen in stool (HpSA, Meridian Diagnostics, Cincinnati, USA) and the ^{13}C-urea breath test corrected for estimated individual CO2 production rate.[3] Although a quarter of the children have at least one *H pylori* infected parent (positive serology and/or a positive ^{13}C-urea breath test) only 1.5% of the children have positive tests during the first three years of age.

On publication, this paper was widely reported by the media, a process actively assisted by the authors. This is likely to result in considerable anxiety among young parents and pregnant women, feelings of guilt in parents of SIDS children and unjustified *H pylori*

eradication therapy in asymptomatic children. Since neither the selection of the control group nor the methodology used is fully robust, this study does not, however, permit valid conclusions on the association of *H pylori* infection with SIDS. We believe it is irresponsible to promote inconclusive results in the light of such inadequate data.

SIBYLLE KOLETZKO
NIKOLAOS KONSTANTOPOULOS
Kinderklinik und Kinderpoliklinik, Dr v. Haunersches Kinderspital, Ludwig-Maximillians-University, Pettenkoferstrasse 8a, D-80336 Munich, Germany
koletzko@pk-i.med.uni-muenchen.de

NORBERT LEHN
Institute of Med. Microbiology and Hygiene, University Regensburg, Regensburg, Germany

DAVID FORMAN
Unit of Epidemiology and Health Service Research, The Medical School, University of Leeds, Leeds, UK

1 Trebesius K, Panthel K, Strobel S, *et al*. Rapid and specific detection of Helicobacter pylori macrolide resistance in gastric tissue by fluorescent in situ hybridisation. *Gut* 2000;**46**:608–14.
2 Radhakrishnan S, Al Nakib B, Kalaoui M, *et al*. Helicobacter pylori-associated gastritis in Kuwait: Endoscopy-based study in symptomatic and asymptomatic children. *J Pediatr Gastroenterol Nutr* 1993;**16**:126.
3 Sauerwald T, Demmelmair H, Tasch C, *et al*. Improving accuracy of the ^{13}C-urea breath test in children by normalizing results for CO2-production-rates. *Gut* 2000;**47**(suppl I):A93.

Association is not the same as causation

EDITOR,—The paper by Kerr *et al* describes an association between SIDS and colonisation with *H pylori*. In the introduction, the authors state that both SIDS and colonisation with *H pylori* are known to be linked with poor socioeconomic status and overcrowding. This clearly suggests that some common factor (possibly smoking, possibly something else) may predispose to both conditions. Yet, in the discussion, the authors ignore this possibility and prefer to postulate on how *H pylori* might cause sudden unexpected death. Not only is this approach unscientific, it is also irresponsible. The proposed causation has been taken up by the media and I have already been asked to see a mother who is receiving eradication therapy for *H pylori*. She fears that her child may already be infected and will die from cot death.

MARTIN RICHARDSON
Consultant Paediatrician, Peterborough District Hospital, Peterborough, UK
martin.richardson@pbh-tr.anglox.nhs.uk

Death kisses for newborns?

EDITOR,—Kerr *et al* claim *H pylori* as a potential etiologic factor in SIDS. Fatal systemic ammonia intoxication through hydrolysis of urea by *H pylori* produced urease in the lungs and trachea, following aspiration of gastric juice, was proposed as a possible pathogenic pathway. In general we cannot agree with this hypothesis. The molecular procedure (nested PCR and ELISA based detection) used in this study could explain some inconsistent data—for example, *H pylori* DNA detection in lungs or trachea but not in the stomach. Furthermore, it is debatable whether haematoxylin and eosin (H&E) routine staining is an efficient method to visualise *Helicobacter* like organisms. A Warthin-Starry-silver stain, modified Giemsa or immunochemistry would have been more advisable.

We also regret that no histopathological data were given which could have provided essential information about a possible infectious etiology. From our experience, we observed that an acute *H pylori* infection always causes marked inflammatory changes of the gastric mucosa.

We also find that the negative control group was not a good reference, as this group did not comprise enough cases and was too heterogeneous (including two premature cases with apparently no normal environmental contact, one case with pneumonia (aspiration pneumonia?)).

The discussion is totally speculative—for example, the role of interleukin 1 in *H pylori* infection: the main cytokines involved are (decreased production of) transforming growth factor, (local production of) tumour necrosis factor (TNF), interleukin 2 and interleukin 8. From the data presented, only the presence of *H pylori* DNA in the respiratory system (some cases without infection of the gastric mucosa) can be claimed. All other conclusions are not substantiated and should be considered as speculative until further evidence is provided—for example, culturing of *H pylori* from tracheal or lung fluid.

Even if the presence of viable *H pylori* cells in the respiratory system can be established, some kind of experimental model should be used to establish *H pylori* as a causative agent in SIDS.

Recent findings established by the Children's Hospital of Bamberg, Germany, suggest a hypoplasia of the basilar artery as a more plausible explanation for SIDS. It has been shown that this anatomical defect can cause blockage of the cerebral blood circulation especially in the prone sleeping position when the head is turned aside. This hypoplasia can be detected by ultrasound. Data of this study[1] performed by the same hospital, seem to confirm this hypothesis. Among 3506 births over the last two years, 31 newborns (0.88%) could be identified with marked hypoplasia of the basilar artery, six of these newborns were considered as high risk cases (1.7‰). The babies were given a monitor and the parents were instructed in resuscitation. None of the children born and screened in the Children's Hospital of Bamberg died from SIDS in the last years, whereas two babies not participating in the screening programme died out of 1130 house born babies in the region of Bamberg (1.8‰). For statistical significance 5000 births are necessary; a number that will be reached end of the year 2001. Further reports are pending.

M VIETH
M STOLTE
Institute of Pathology, Klinikum Bayreuth, Preuschwitzerstr. 101, 95445 Bayreuth, Germany
vieth.lkpathol@uni-bayreuth.de

D DE GROOTE
Department of Pathology, Bacteriology and Avian Diseases, Ghent University, Merelbeke, Belgium

K H DEEG
Childrens Clinic, Klinikum Bamberg, Germany

G SEITZ
Institute of Pathology, Klinikum Bamberg, Germany

1 Deeg KH, Alderath W, Bettendorf U. Insufficiency of the basilar artery—a possible cause of sudden infant death syndrome? *Ultraschall in Med* 1998;**19**:250–8.

Dwelling crowding as a pertinent factor

EDITOR,—Kerr *et al* report a highly significant association between *H pylori* infection and SIDS. This finding raises the possibility of (and a plausible mechanism for) a link between dwelling crowding and SIDS, as there are a number of studies that have documented a strong relation between dwelling crowding and *H pylori* infection.[1 2] Close person to person contact and increased exposure to the infective agent is a likely cause of this relationship. Dwelling crowding has also been associated with increased passive exposure to tobacco smoke, and this, coupled with parental smoking being strongly associated with SIDS,[3] provides yet another clear link between dwelling crowding and SIDS.

There are likely to be many causes of dwelling crowding. It has often been associated with low socioeconomic status, but the study by Elitsur *et al*[4] suggests that there may be a direct link between crowding and *H pylori* infection, which is independent of socioeconomic status. SIDS has also been associated with lower environmental temperature and it is possible that the increase in SIDS rate during winter is in part relate to the increased dwelling crowding during such times.

Very few studies have examined the links between dwelling crowding and SIDS. One recently published study found only a non-significant increase in relative risk for SIDS associated with dwelling crowding.[5] Given the importance of SIDS and the growing body of evidence suggesting *H pylori* as a cause of SIDS, it would be pertinent for future studies to consider dwelling crowding in more detail.

PAUL J BEGGS
Senior Lecturer, Department of Physical Geography, Division of Environmental and Life Sciences, Macquarie University, Australia
paul.beggs@mq.edu.au

1 Fall CHD, Goggin PM, Hawtin P, *et al*. Growth in infancy, infant feeding, childhood living conditions, and Helicobacter pylori infection at age 70. *Arch Dis Child* 1997;**77**:310–14.
2 Webb PM, Knight T, Greaves S, *et al*. Relation between infection with Helicobacter pylori and living conditions in childhood: evidence for person to person transmission in early life. *BMJ* 1994;**308**:750–4.
3 Henderson-Smart DJ, Ponsonby AL, Murphy E. Reducing the risk of sudden infant death syndrome: a review of the scientific literature. *J Paediatr Child Health* 1998;**34**:213–19.
4 Elitsur Y, Short JP, Neace C. Prevalence of Helicobacter pylori infection in children from urban and rural West Virginia. *Dig Dis Sci* 1998;**43**:773–8.
5 Schluter PJ, Ford RP, Mitchell EA, *et al*. Housing and sudden infant death syndrome. The New Zealand Cot Death Study Group. *NZ Med J* 1997;**110**:243–6.

H pylori DNA may not imply infection

EDITOR,—Kerr *et al* report an association between SIDS and *H pylori* infection. In 32 SIDS cases aged up to 28 weeks old, the H pylori ureC gene was amplified from the stomachs of 15, from the trachea of 19, and from the lungs of 16. The *H pylori* cagA gene was amplified from the stomachs of 13 (of which seven were positive for the ureC gene), from the trachea of 20, and the lungs of 20 (of

which 14 were positive for the ureC gene). Amplified DNA was detected semiquantatively using an ELISA, with a cut off value calculated from the mean of eight controls. The authors offered little explanation for the discordant detection of *H pylori* DNA between the two PCR assays used. It may be appropriate to compare the prevalence of *H pylori* in SIDS and controls, but inappropriate to make these two groups the basis for defining cutoffs for an *H pylori* assay.

The presence of *H pylori* DNA does not itself imply infection and no visible bacteria were observed in any tissue sections. *H pylori* can be acquired early in life[1] probably from other members of the family. Infection has only previously been detected in the microenvironment of the gastric mucosa and its presence is closely related to socioeconomic status,[2] as is SIDS. No details of the socioeconomic status of the infants from whom tissues were obtained, nor details of familial contact were given. Four of the controls died under eight weeks of age from what could possibly be neonatal complications and no details of whether they had been discharged home were provided.

The authors propose that primary gastric infection and subsequent aspiration into the lungs led to lethal production of ammonia in infants as young as two weeks of age. It is difficult to imagine that an organism specifically adapted to the microaerophilic and acidic conditions of the gastric mucosa thriving well enough in the lungs to produce toxic amounts of ammonia in infants that presumably had normal livers, particularly when no organisms were visible on histology.

This interesting report could well describe a proxy for the already widely known association between *H pylori* and poor socioeconomic status. Arguing that the discordant presence of *H pylori* DNA in various organs of SIDS cases represents causation is premature, but warrants further investigation.

C P DOHERTY
W G MACKAY
L T WEAVER
Department of Child Health, University of Glasgow, UK
cd1c@clinmed.gla.ac.uk

A J SHEPHERD
Department of Nursing and Midwifery, Stirling University, UK

C L WILLIAMS
Department of Microbiology, Royal Alexandra Hospital, Paisley, UK

1 Thomas JE, Dale A, Harding M, *et al*. Helicobacter pylori colonisation in early life. *Pediatr Res* 1999;**45**:218–23.
2 Drumm B, Perez-Perez GI, Blaser MJ, *et al*. Intrafamilial clustering of Helicobacter pylori infection. *N Engl J Med* 1990;**322**:359–63.

Drs Kerr, Barson, and Burnie respond

EDITOR,—Following the publication of our paper,[1] we would like to thank the above authors for their comments and respond in order to clarify our study methodology, interpretation of the data, the impact of the media, and comment on the directions of future work in this area.

The possibility of PCR contamination has been suggested by Franciosi and Koletzko and we agree that this is a potential problem in studies of this type. We guarded against this by utilisation of separate laboratory areas and pipettes for pre-PCR, PCR and post-PCR stages of the procedure, use of sterile bunged pipette tips, and inoculation of the positive control as a last step in the pre-PCR preparation. In each run, we used sterile distilled water and DNA extract from human ureter as negative controls, and we examined samples in duplicate. Throughout our study, duplicated samples consistently gave concordant results, and negative controls were consistently negative.[1]

Dr Koletzko suggests that the two separate nested PCR-ELISAs utilised in our study may have doubtful specificity as we did not sequence the products. We agree that amplicon sequencing is desirable not only to ensure specificity but in the present context would also provide additional data on the molecular epidemiology of the *cag*A gene which was detected in these cases. We believe our assays to be specific. For example, the binding of oligonucleotides of 20 or more bases to template DNA at 55°C has been shown to be 100% specific. And in one of our PCR-ELISAs, there were five such interactions.[1] We agree with Dr Koletzko and other workers that it would be valuable to test other tissues from the same patients by the same method.

Regarding our controls, use of these cases is quite appropriate and to illustrate this we include additional relevant data in table 1. Dr Vieth says our controls have had no normal environmental contact, however, five of these eight had spent time in the home environment since birth. Regarding antibiotic treatment, only one control had received antibiotics for more than one day prior to death, and this is the case in which *H. pylori* was detected.

Dr Koletzko states that "the fact that *H. pylori* was not demonstrated in the stomach, trachea or lung by histology in any of the children must raise major concerns that the applied methods were not specific". However, as pointed out by Dr Vieth, haematoxylin and eosin staining, although a routinely used stain in histopathology practice, may not be optimal for microscopic visualisation of *H pylori*.

In response to Dr Vieth's claim that our suggested role for interleukin-1β (IL-1β) in *H pylori* infection is "totally speculative", we would like to point out that these mechanisms have been demonstrated in an animal model.[2 3] Also, proteins of *H pylori* are known to activate macrophages leading to production of IL-1β[4–6] which is known to inhibit acid secretion by parietal cells and may actually be *the* most potent inhibitor of acid secretion discovered to date.[7] IL-1β gene polymorphisms associated with increased IL-1β production have recently been associated with an increased risk of gastric cancer.[8] In addition, systemic and mucosal humoral recognition of the cagA protein has been linked with peptic ulceration,[9 10] duodenal ulcer patients may more frequently harbour *cag*A$^+$ *H. pylori* strains,[6 10] and it has been shown that infection with *cag*A$^+$ as compared with *cag*A$^-$ strains is associated with increased transcription of IL-1β.[6] It is therefore interesting that 25 of 28 cases of *H pylori* associated SIDS in our study had a detectable *cag*A gene in their tissues,[1] which may provide further support for the proposed pathogenesis of *H pylori* in SIDS and a contributory role for IL-1β.[11]

Dr Paul Beggs from Macquarie University in Australia points out the link between dwelling crowding and *H pylori* infection,[12 13] which has been shown to be independent of socioeconomic status,[14] and the need for research on the possible link between dwelling crowding and SIDS. We agree that "given the importance of SIDS and the growing body of evidence suggesting *H pylori* as a cause of SIDS, it would be pertinent for future studies to consider dwelling crowding in more detail".

We feel that Wiklund and colleagues, and MacKay and colleagues (in separate letters) have misunderstood the proposed hypothesis. Wiklund states that total breakdown of ingested urea occurs in all normal infants without ammonia intoxication and that SIDS victims have undigested urea in their faeces. MacKay states that "it is difficult to imagine that an organism specifically adapted to the microaerophilic and acidic conditions of the gastric mucosa thriving well enough in the

Table 1 Information on antibiotic exposure, environmental exposure, and PCR-ELISA testing for H pylori ureC and cagA genes in the stomach, trachea, and lung of control cases used in the study 'An association between sudden infant death syndrome (SIDS) and Helicobacter pylori infection'.[1] Results of PCR-ELISA testing is expressed as optical density. Those specimens with a cut off value greater than or equal to the mean plus two times the standard deviation of these controls (designated negative) are marked with an asterisk

Case No.	Age at death (wks)	Cause of death	Time of diagnosis	Antibiotic exposure	Exposure to the home environment >1 month	*H. pylori ureC gene*			*H. pylori cagA gene*		
						Stomach	Trachea	Lung	Stomach	Trachea	Lung
C1	3	prematurity	AM	−	−	0.100	0.150	0.180	0.120	0.130	0.090
C2	4	prematurity	AM	−	−	NT	0.200	0.090	NT	0.120	0.100
C3	7	ileal perforation	AM	+	−	0.265	*0.298	0.283	*0.414	*0.303	0.317
C4	7	Necrotising enterocolitis	AM	1 day only	+	0.200	0.150	0.180	0.120	0.200	0.150
C5	20	*E. coli* septicaemia	PM	−	+	0.170	0.160	0.177	0.150	0.120	0.160
C6	24	suffocation	PM	−	+	0.210	0.080	NT	0.150	0.090	NT
C7	32	pneumonia	PM	−	+	NT	0.130	0.180	NT	0.150	0.180
C8	44	*Pneumococcal* septicaemia	PM	−	+	0.100	0.140	NT	0.120	0.090	NT
					Mean	0.174	0.163	0.181	0.179	0.150	0.166
					±SD	±0.065	±0.063	±0.060	±0.116	±0.071	±0.080

C1, control case number 1; AM, ante-mortem; PM, post-mortem; NT, not tested.

lung to produce toxic amounts of ammonia in infants that presumably had normal livers". To reiterate, there are two parts to the hypothesis. First, interleukin-1β production in the *H pylori* infected stomach, and second, supply of ammonia to the systemic circulation[11] (and not the hepatic circulation as MacKay implies). Therefore, faecal urea content is irrelevant and so is ammonia produced in the stomach as this will be detoxified by the liver.

Regarding comments in the media, these are clearly not under our control and we have always stated that our findings are preliminary and require confirmation.

In conclusion, we would encourage researchers to repeat our studies and those of Pattison and colleagues[15–17] in order to clarify the proposed role of *H pylori* in SIDS. In the meantime, we re-emphasise accepted measures to reduce mortality from SIDS and suggest the following additional precautions, all of which constitute good personal hygiene and are therefore advisable even in the absence of such a link. **First**, to prevent the transfer of saliva from the mouths of carers to babies. **Second**, prompt disposal of vomitus, decontamination of soiled surfaces, and washing of soiled clothes/bedclothes, followed by hand washing, in order to minimise transmission to the baby via the gastro-oral route. **Third**, good general hand and personal hygiene. In addition, parents should be reassured that they do not need to do anything more than the above at present.

JR KERR
JP BURNIE
AJ BARSON
Infectious Diseases Research Group, The University of Manchester, Clinical Sciences Building, Manchester Royal Infirmary, Oxford Road, Manchester M13 9WL, UK
jonathankerr@hotmail.com

1 Kerr JR, Al-Khattaf A, Barson AJ, *et al*. An association between sudden infant death syndrome (SIDS) and *Helicobacter pylori* infection. *Arch Dis Child* 2000;**83**:429–34.
2 Pattison CP, Marshall BJ, Scott LW, *et al*. Proposed link between *Helicobacter pylori* and sudden infant death syndrome (SIDS): possible pathogenic mechanisms in an animal model. I. Effects of intratracheal urease. *Gastroenterology* 1998;**114**(4):G3689.
3 Pattison CP, Scott LW, Herndon B, *et al*. Proposed link between *Helicobacter pylori* and SIDS: possible pathogenic mechanisms in an animal model. II. Effects of intratracheal urease after pretreatment with intravenous IL-1 beta. *Gastroenterology* 1998;**114**(4):G3690.
4 Noach LA, Bosma B, Jansen J, *et al*. Mucosal tumour necrosis factor-α, interleukin-1β, and interleukin-8 production in patients with *Helicobacter pylori* infection. *Scand J Gastroenterol* 1994;**29**:425–9.
5 Yamaoka Y, Kita M, Kodama T, *et al*. Expression of cytokine mRNA in gastric mucosa with *Helicobacter pylori* infection. *Scand J Gastroenterology* 1995;**30**:1153–9.
6 Peek RM, Miller GG, Tham KT, *et al*. Heightened inflammatory response and cytokine expression in vivo to *cagA*$^+$ *Helicobacter pylori* strains. *Lab Invest* 1995;**73**:742–5.
7 Wallace JL, Cucala M, Mugridge K, *et al*. Secretagogue-specific effects of interleukin-1 on gastric acid secretion. *Am J Physiol* 1991; **261**:G559–64.
8 El-Omar EM, Carrington M, Chow WH, *et al*. Interleukin-1 polymorphisms associated with increased risk of gastric cancer. *Nature* 2000; **404**:398–402.
9 Crabtree JE, Taylor JD, Wyatt JI, *et al*. Mucosal IgA recognition of *Helicobacter pylori* 120 kDa protein, peptic ulceration and gastric pathology. *Lancet* 1991;**338**:332–5.
10 Cover TL, Glupczynski Y, Lage AP, *et al*. Serologic detection of infection with *cagA*$^+$ *Helicobacter pylori* infections. *J Clin Microbiol* 1995; **33**:1496–500.
11 Pattison CP, Marshall BJ. Proposed link between *Helicobacter pylori* and sudden infant death syndrome. *Med Hypotheses* 1997:**49**:365–9.
12 Fall CHD, Goggin PM, Hawtin P, *et al*. Growth in infancy, infant feeding, childhood living conditions, and *Helicobacter pylori* infection at age 70. *Arch Dis Child* 1997;77:310–14.
13 Webb PM, Knoght T, Greaves S, *et al*. Relation between infection with *Helicobacter pylori* and living conditions in childhood: evidence for person to person transmission in early life. *Br Med J* 1994;**308**:750–4.
14 Elitsur Y, Short JP, Neace C. Prevalence of *Helicobacter pylori* infection in children from urban and rural West Virginia. *Dig Dis Sci* 1998;**43**:773–8.
15 Pattison CP, Marshall BJ, Young TW, *et al*. Is *Helicobacter pylori* the missing link for sudden infant death syndrome? *Gastroenterology* 1997; **112**(4SS):A254.
16 Pattison CP, Vergara GG, Young TW, *et al*. Prevalence of *Helicobacter pylori* in sudden infant death syndrome. *Gastroenterology* 1998; **114**(4):G3688.
17 Pattison CP, Smoot DT, Ashtorab H, *et al*. Confirmation of *Helicobacter pylori* by PCR in sudden infant death syndrome. *Gastroenterology* 1998;**114**(4):G3686.

The need for further evidence for the proposed role of *Helicobacter pylori* in SIDS

EDITOR,—We read with interest the article by Kerr *et al*. While the proportion of samples positive for *H pylori* DNA were significantly higher in the SIDS group compared with the control group, the findings need to be interpreted with caution.

PCR is a useful tool for detection of DNA. It is, however, evidence that the DNA of the organism is present, not evidence that the organisms were alive or caused disease. Culture, microscopy, serological evidence or histological evidence of inflammatory or immune responses are needed to support the hypothesis that the bacteria were involved with pathological processes, not just transient contamination of the infant with DNA from non-viable bacteria.

There are several points that detract from the paper:

In relation to the findings reported:

1. Only the PCR assays provided positive evidence. In contrast to other studies reported as abstracts, microscopic examination of the stained sections did not find any evidence of *H pylori*. This discrepancy needs to be explained. There were no serological data to support the PCR findings and no data from histological examinations to provide evidence that the bacteria were causing infection or that inflammatory responses had been elicited.
2. The proportion of PCR positive samples among SIDS infants (88%) was significantly larger than that among controls (12.5%). The possibility of contamination was not addressed for SIDS or the positive control case. There was no demonstration by molecular methods that the DNA detected was from different strains. *H pylori* strains show great genetic variability and previous studies demonstrated that most individuals carry unique strains. Isolates from different individuals that appear to be genetically identical are those obtained only from close contacts, usually within a family.

The interpretation of the epidemiological data for *H pylori* and socioeconomic factors was not assessed in relation to incidence of SIDS among different ethnic groups. In Britain, white families in lower socioeconomic groups have more evidence of *H pylori* infections and more SIDS. If the data for incidence of infections with *H pylori* is assessed for ethnic groups and SIDS, this parallel breaks down. The incidence of seropositivity for *H pylori* among Bangladeshi women in the UK ranges from 66% among women born abroad to 81% among women born in the UK[1]; however, the incidence of SIDS in Bangladeshi families was the lowest in Britain (0.3%).[2] A similar trend was observed in the United States; seropositivity for *H pylori* is 61% among Hispanics and 26.2% among non-Hispanic whites.[3] In the paper quoted in the manuscript, the incidence of seropositivity was similar for Hispanic and black groups and both were significantly higher than that of non-Hispanic whites.[4] The SIDS rates per 100 000 for US populations were 5.1 for blacks, 1.3 for Hispanics, and 1.2 for non-Hispanic whites.[5] This evidence questions the assumptions made by the authors.

While there is increasing evidence for other hypotheses that SIDS might be triggered by inflammatory responses to infection,[6–8] there is no physiological or histological evidence to support the hypothesis that urease in the lung of the infants is causing increased levels of ammonia in the blood (see detailed assessment of pathology of SIDS in relation to this hypothesis below). Animal models[9 10] do not reflect the combination of genetic, environmental, and developmental factors associated with SIDS, and results from animal studies must be interpreted with extreme caution when extrapolated to the human infant. *H pylori* infection does not fit the common bacterial hypothesis, a mathematical model which accurately predicted the age range for SIDS.[11] According to the model, 50% of infants should acquire the bacteria during the first 50 days of life. While 19% of Gambian children were positive for the C13 urea breath test by 3 months of age,[12] in industrialised countries the evidence is that *H pylori* infection in infants under 1 year of age is much lower. Among 67 Belgian children born to seropositive mothers, only 1 (1.5%) had a positive breath test by the age of 12–15 months.[13] Among Finnish children 10.6% had IgG to *H pylori* at birth, but the antibodies disappeared in all but one child before the age of 7 months and there were no seroconversions in these children. The Finnish study concluded that maternal seropositivity is not a straight forward risk factor for acquiring *H pylori* infection.[14]

The oral/oral route of transmission is suggested to be the route by which infants acquire *H pylori*, mainly by vomit.[15] *H pylori* has been cultured from one of four vomit samples from children and detected by PCR in two of four culture negative samples. There is much stronger direct (culture) evidence for transmission from mother to child of other bacterial species implicated in SIDS.[16]

The pathogenic mechanism proposed for the role of ammonia cannot be substantiated by the available evidence:

1. There are no acute changes in the upper respiratory tree or lungs consistent with inflammatory responses to *H pylori*.
2. The presence of ammonia in the lower respiratory tree would initiate a bronchospasm which should produce clinical features such as wheezing which has not been reported by parents of SIDS infants.

This type of reaction should be demonstrable histologically by muscular, glandular and secretory changes identified by microscopy.
3. If ammonia is present in excess in the blood as a proximate cause of death, this should be demonstrable in blood samples and vitreous fluid, and there is no evidence for this.
4. The liver in SIDS cases shows no abnormality and had it been acutely affected by an influx of ammonia, there should be changes.
5. Ammonia in excess leads to cerebral changes of an acute type and none have been demonstrated.
6. If the ammonia is postulated as a cause of petechiae in the lungs due to local damage, this does not account for the presence of petechiae in the thymus and pericardium.

There is evidence to explain how risk factors could contribute to susceptibility of infants to infectious agents to triggering the series of events leading to SIDS[17]; however, that presented for *H pylori* needs to be substantiated by more than one method and testable hypotheses proposed to explain how these bacteria might contribute to the series of events that lead to SIDS.

C C BLACKWELL
D M WEIR
A BUSUTTIL
University of Edinburgh, Teviot Place, Edinburgh
Caroline.Blackwell@ed.ac.uk

1 Banatvala N, Clements L, Abdi Y, *et al*. Migration and Helicobacter pylori seroprevalence: Bangladeshi migrants in the UK. *J Infect* 1995;**31**:133–5.
2 Balarajan R, Raleigh VS, Botting B. Sudden infant death syndrome and post neonatal mortality in immigrants in England and Wales. *BMJ* 1989;**298**:716–20.
3 Everhart JE, Kruszon-Moran D, Perez-Perez GI, *et al*. Seroprevalence and ethnic differences in Helicobacter pylori infection among adults in the United States. *J Infect Dis* 2000;**181**: 1359–63.
4 Malaty HM, Evans DG, Evans DJ, *et al*. Helicobacter pylori in Hispanics: comparison with blacks and whites of similar age and socioeconomic class. *Gastroenterology* 1992;**103**:813–16.
5 Nelson T. Sudden infant death syndrome and child care practices. Hong Kong: Lammar Offset Printing, Ltd., 1996.
6 Vege A, Rognum TO. Inflammatory responses in sudden infant death syndrome: past and present views. *FEMS Immunol Med Microbiol* 1999;**25**:67–78.
7 Raza MW, Blackwell CC. Sudden infant death syndrome: virus infections and cytokines. *FEMS Immunol Med Microbiol* 1999;**25**:85-96. *Gastroenterology* 1998;**114**:G3690.
8 Forsyth KD. Immune and inflammatory responses in sudden infant death syndrome. *FEMS Immunol Med Microbiol* 1999;**25**:79–84.
9 Pattison CP, Marshall BJ, Scott LW, *et al*. Proposed link between Helicobacter pylori and sudden infant death syndrome (SIDS): possible pathogenic mechanisms in an animal model. I. Effects of intratracheal urease. *Gastroenterology* 1998;**114**:G3689.
10 Pattison CP, Scott LW, Herndon B, *et al*. Proposed link between Helicobacer pylori and SIDS: possible pathogenic mechanisms in an animal model. II. Effects of intratracheal urease after pretreatment with intravenous IL-1b. Ibid.
11 Morris JA. The common bacterial toxins hypothesis of sudden infant death syndrome. *FEMS Immunol Med Microbiol* 1999;**25**:11–18.
12 Thomas JF, Dale A, Harding M, *et al*. Helicobacter pylori colonization in early life. *Pediatric Res* 1999;**45**:218–23.
13 Blecker U, Lanciers S, Keppens E, *et al*. Evolution of Helicobacter pylori positivity in infants born from positive mothers. *J Pediatr Gastorenterol Nutr* 1994;**19**:87–90.
14 Ashorn M, Miettinen A, Ruuska T, *et al*. Seroepidemiological study of Helicobacter pylori infection in infancy. *Arch Dis Child Fetal Neonatal Ed* 1996;F141–2.
15 Leung WK, Siu KL, Kwok CK, *et al*. Isolation of Helicobacter pylori from vomitus in children and its implication in gastro-oral transmission. *Am J Gastroenterol* 1999;**94**:2881–4.
16 Blackwell CC, Mackenzie DAC, James VS, *et al*. Toxigenic bacteria and SIDS: nasopharyngeal flora in the first year of life. *FEMS Immunol Med Microbiol* 1999;**25**:51–8.
17 Blackwell CC, Weir DM, Busuttil A. Infection, inflammation and sleep: more pieces to the puzzle of sudden infant death syndrome (SIDS). *APMIS* 1999;**107**:455–73.

Controls not matched

EDITOR,—The paper by Kerr *et al* reported an association between *H pylori* and sudden infant death syndrome (SIDS). We have reviewed their data and believe that the methods used may have led to incorrect conclusions.

Kerr *et al* examined retrospective material from 32 cases of SIDS infants and 8 non-SIDS controls. They used nested PCR followed by an ELISA detection step which would have made their method exquisitely sensitive. Consistent with this, no other method was able to confirm that *H pylori* was actually present. Instead, Kerr *et al* used a relative increase of "*H pylori* signal" above that of the mean +2SD for a control group, as an indicator of *H pylori* presence. This prompted us to more carefully consider the appropriateness of their control and patient groups.

Since ethnicity and socioeconomic details of the SIDS infants were not given, we could not confirm that these matched the control infants. We also noted important clinical details of the controls which could make them inappropriate. It appears that most of the controls would have had very little bacterial contamination of the PCR specimens because they died in hospital while on antibiotic therapy for sepsis, or were deceased very soon after premature birth. In addition, they might have been transferred to refrigeration very soon after death. SIDS infants however, probably died at home, many hours before being refrigerated.

Finally, as *H pylori* is a gastric organism, it was surprising to find the bacterium in lung or trachea of eight patients (ureC gene) or six patients (cagA gene) in whom gastric specimens were negative.

Since Kerr's paper was widely reported in the media, we believe that it needs to be stated that the case for *H pylori* as a cause of SIDS is certainly unproven and is in quite considerable doubt.

BARRY J MARSHALL
GRACE Y HO
H pylori Research Laboratory, Department of Microbiology, University of Western Australia, Australia
bmarshall@hpylori.com.au

No association in a Chinese population

EDITOR,—We read with great interest the paper by *Kerr et al* on the association between *H pylori* infection and SIDS. However, we cannot agree with the speculation the authors made.

Recently, we performed a similar retrospective analysis of nine cases of SIDS and eight controls collected in our hospital over the past two years. Controls were selected from infants with known cause of death, including congenital malformation, infection, metabolic disease, and drug intoxication (see table).

Table 1 Characteristics of SIDS cases and controls

	Sex	Age	Diagnosis
Controls			
1	F	4 months	Congenital heart disease
2	F	2 months	Morphione toxicity
3	M	13 hours	Bronchopneumonia
4	M	1 hour	Amniotic fluid aspiration
5	M	6 months	Premature, septicemia
6	M	3 months	Congenital brain tumour
7	M	6 months	Glutaric aciduria type I
8	M	2 months	Extreme premature
Cases			
1	M	3 months	SIDS
2	M	3 months	SIDS
3	M	13 months	SIDS
4	M	7 days	SIDS
5	M	5 days	SIDS
6	F	8 months	SIDS
7	F	2 months	SIDS
8	F	2.5 months	SIDS
9	M	2 months	SIDS

The formalin-fixed and paraffin-embedded stomach, trachea, and lung specimens obtained during postmortem examination were retrieved. Initial histological examination was performed by an experienced pathologist to look for any evidence of *H pylori* colonisation in these specimens. In addition, we used three different PCR assays that amplify two regions of the ureB gene[1 2] and the cagA gene[3] to detect the presence of *H pylori* DNA in these samples.

Histological examination failed to show any *Helicobacter* like organism in these samples. Moreover, despite using three different sensitive PCR assays, we failed to show the presence of *H pylori* DNA in the stomach, lung, or trachea of the SIDS and control patients.

Viable *H pylori* has recently been recovered from the vomitus of infected children and adults.[2] Conceivably, it could lead to silent aspiration of gastric contents into the lung and result in bronchopneumonia. However, the failure to detect the organism in the stomach, trachea, and lung specimens, together with the absence of features to suggest aspiration pneumonia as the cause of death in these infants, argue against the validity of this speculation. With the high prevalence of *H pylori* infection in Chinese, one would expect a parallel high incidence of SIDS in our ethnic group, which does not fit into any epidemiological observations. Taken together, the significance of *H pylori* as a cause of SIDS is highly questionable.

WAI K LEUNG
JUN YU
K F TO
Department of Medicine & Therapeutics and Department of Anatomical & Cellular Pathology Chinese University of Hong Kong Shatin, Hong Kong
wklueng@cuhk.edu.hk

1 Leung WK, Sung JJY, Ling TKW, *et al*. Does the use of chopsticks for eating transmit Helicobacter pylori? *Lancet* 1997;**350**:31.
2 Leung WK, Siu KLK, Kwok CKL, *et al*. Isolation of Helicobacter pylori from vomitus in children and its implication in gastro-oral transmission. *Am J Gastroenterol* 1999;**94**: 2881–4.
3 Yamaoka Y, Kodama T, Kita M, *et al*. Relationship of vacA genotypes of Helicobacter pylori to cagA status, cytotoxin production, and clinical outcome. *Helicobacter* 1998;**3**:241–53.

More on SIDS and *H pylori*—Authors' response

EDITOR,—At present, we do not understand the pathogenesis of sudden infant death syndrome (SIDS), however, it is accepted to be a multifactorial disease for which certain risk factors have been identified. Various theories have been developed to explain the existence of these risk factors.

Blackwell reminds us of the accepted fact that PCR detects DNA from both live and dead organisms, but her phrase "transient contamination of the infant with DNA from non-viable bacteria" seems inappropriate. The detection of *H pylori* DNA in the trachea and lung of such babies is a finding of particular importance both for our understanding of the pathogenesis of SIDS and for our understanding of the pathogenesis and epidemiology of *H pylori* infection in infants.

The study by Kerr *et al*[1] showed *H pylori* DNA in the stomach, trachea, and lung tissues of SIDS cases, but did not visualise bacteria at these sites. As stated in the paper and by several other authors, the study used haematoxylin and eosin staining, a suboptimal methodology for visualisation of gastric bacteria. Other studies have shown inflammatory changes in both antrum and trachea of *H pylori*-PCR positive SIDS cases.[2]

Genetic subtyping would be valuable as suggested, but not essential, as the PCR-ELISA utilised was specific, tests were performed in duplicate and positive and negative controls consistently gave expected results.[1]

Our hypothesis is that *H pylori* infection accounts for a proportion of cases of SIDS. Blackwell cites several epidemiological papers, stating that they argue against this hypothesis, but she does not state how exactly she considers that they do argue against it. Epidemiological data for *H pylori* and socioeconomic factors in various ethnic groups are not clear cut and are incomplete. Such factors as prevalence of bottle feeding, parental smoking, family size, adherence to supine sleep position, etc, may explain differences of SIDS incidence in various ethnic groups. Blackwell's use of data regarding breath testing in children aged 12–15 months is in contrast to the finding of 44% *H pylori* positivity by 13C-urea breath testing of 2 year olds in childcare centres serving low socioeconomic groups in Houston, Texas.[3]

Blackwell reminds us of the accepted fact that animal work is not directly applicable to events in the human infant. But, it is relevant. The proposed hypothesis cannot be verified in the human infant, but this should not be taken as evidence that it does not account for infant mortality.

The common bacterial hypothesis[4] has been useful for studies of other bacteria,[5] but is not a basis for rejection of conflicting data.

While other bacteria may be readily transmitted from mother to infant,[5] none has been consistently linked with SIDS, and transmission efficiency does not equate with pathogenicity in a particular setting.

There are three proposed routes of transmission of *H pylori*; oral-oral, gastro-oral and faecal-oral.[6] Blackwell has misunderstood these, as she refers to transmission by vomit as "oral-oral", when this is actually gastro-oral.[6] The transmission of *H pylori* is more complex than that of other oral bacteria.

The proposed pathogenesis of the involvement of *H pylori* in SIDS is that death may occur as a result of one or both of two events[7] both of which have been demonstrated in a rat model.[8 9] First, *H pylori* produces large amounts of urease, which will be fully active in the neutral pH of the *H pylori*-infected stomach.[10] Therefore, aspiration of this gastric juice may lead to large amounts of urease in the alveolae in close proximity to plasma urea. In this setting, urea hydrolysis may lead to ammonia production and supply directly to the systemic circulation where it cannot be detoxified by the liver[8]; unlike the case of ammonia production within the gastric mucosa. Intravenous administration of ammonia is known to be fatal.[11] Second, IL-1β produced in the *H pylori*-infected gastric mucosa may lead to fever, immune activation and increased deep sleep, which in combination with supply of ammonia to the systemic circulation may be lethal.[9] Increased production of IL-1β alone as a result of gastric *H pylori* infection may predispose to the development of SIDS due to other factors.[12]

Blackwell states that the proposed pathogenesis cannot be substantiated due to the following:

(a) "There is no inflammation in the lungs of SIDS cases". This is not true; mild inflammation of the upper respiratory tract is a recurrent, although not invariable, finding in SIDS.[13]

(b) "Ammonia in the lower respiratory tract would cause bronchospasm and wheezing which has not been reported by SIDS parents". In animal studies (not yet published as a full paper), bronchospasm was suggested by progressively less bronchoalveolar lavage (BAL) fluid return after sequential doses of intratracheal urease.[8] Since parents are invariably absent at the time of death, it would be unlikely that wheezing would be detected. "If bronchospasm occurs, this should be demonstrable histologically". Findings of relevance in SIDS include intrathoracic petechiae, patchy pulmonary oedema, emphysema, and increased muscle mass in pulmonary arteries,[13] although these are not invariable findings.

(c) "If ammonia accounts for death, this should be demonstrable in blood and vitreous". Our hypothesis is supported by intratracheal urease adminisatration to rats which caused increased ammonia in BAL fluid although this was not accompanied by significantly increased serum ammonia.[8] The physiological effects of pre-treatment with IL-1β could not be clearly defined.[9]

(d) "The liver should be affected by hyperammonaemia and it is not in SIDS". Blackwell has misunderstood our hypothesis. First, interleukin-1β production in the *H pylori*-infected stomach, and second, aspiration of urease into the lung and supply of ammonia to the systemic circulation (and not the hepatic circulation as Blackwell implies).

(e) "The brain should be affected by hyperammonaemia and it is not in SIDS". If our hypothesis is correct, then the terminal event, involving hyperammonaemia in the systemic circulation is an acute and rapidly fatal occurrence, which may not result in brain pathology.

(f) We do not understand this point.

Marshall's views on controls used in the original paper[1] do not take account of further information provided at the request of other authors[14] which show that of eight controls used, five had an exposure to the home environment of more than one month.

Marshall states that *H pylori* is a gastric organism and that it is surprising to find evidence of infection in lung and trachea. However, *H pylori* has been detected at other sites, for example, the respiratory tract of intubated adults,[15] and in the liver of patients with primarysclerosing cholangitis and primary biliary cirrhosis.[17]

The pathogenesis of SIDS is accepted to be multifactorial, and therefore, small studies with a negative association between *H pylori* and SIDS, such as that of Leung and colleagues, are to be expected.

Emotion aside, the fact remains that three groups have found *H pylori* in some cases of SIDS, and all three groups have detected the organism in the lung.[1 2 17]

JONATHAN R KERR
Infectious Diseases Research Group, University of Manchester, Manchester, UK
jonathankerr@hotmail.com

C PHILLIP PATTISON
Department of Medicine, University of Missouri at Kansas City School of Medicine, Kansas City, Missouri, USA

1 Kerr JR, Al-Khattaf A, Barson AJ, *et al*. An association between sudden infant death syndrome (SIDS) and *Helicobacter pylori* infection. *Arch Dis Child* 2000;**83**:429–34.
2 Pattison CP, Smoot DT, Ashtorab H, *et al*. Confirmation of Helicobacter pylori by PCR in sudden infant death syndrome. *Gastroenterology* 1998;**114**(4):G3686.
3 Malaty HM, Bousylman JE, Graham DY. Helicobacter pylori infection in day care centers [Abstract]. *Gut* 1996;**39**(suppl2):A85.
4 Morris JA. The common bacterial toxins hypothesis of sudden infant death syndrome. *FEMS Immunol Med Microbiol* 1999;**25**:11–17.
5 Blackwell CC, Mackenzie DAC, James VS, *et al*. Toxigenic bacteria and SIDS: nasopharyngeal flora in the first year of life. *FEMS Immunol Med Microbiol* 1999;**25**:51–8.
6 Feldman RA, Eccersley AJP, Hardie JM. Epidemiology of Helicobacter pylori: acquisition, transmission, population prevalence and disease-to-infection ratio. *Br Med Bull* 1998;54: 39–53.
7 Pattison CP, Marshall BJ, Young TW, *et al*. Is Helicobacter pylori the missing link for sudden infant death syndrome? *Gastroenterology* 1997; **112**(4SS):A254.
8 Pattison CP, Marshall BJ, Scott LW, *et al*. Proposed link between Helicobacter pylori and sudden infant death syndrome (SIDS): possible pathogenic mechanisms in an animal model. I. Effects of intratracheal urease. *Gastroenterology* 1998;**114**(4):G3689.
9 Pattison CP, Scott LW, Herndon B, *et al*. Proposed link between Helicobacter pylori and SIDS: possible pathogenic mechanisms in an animal model. II. Effects of intratracheal urease after pretreatment with intravenous IL-1 beta. *Gastroenterology* 1998;**114**(4):G3690.
10 Mobley HL, Cortesia JM, Josenthal LE, *et al*. Characterisation of urease from Campylobacter pylori. *J Clin Microbiol* 1988;**26**:831–6.
11 Fitzgerald O, Murphy P. Studies on the physiological chamistry and clinical significance of urease and urea with special reference to the stomach. *Ir J Med Sci* 1950;**292**:96–159.
12 Kerr JR. Sudden infant death syndrome, long QT interval and *Helicobacter pylori*. *J Clin Pathol* 1998;**332**:943–4.
13 Guntheroth WG. Cribdeath—the sudden infant death syndrome. Armonk, NY: Futura, 1995: 91.
14 Kerr JR, Barson AJ, Burnie JP. Further information on an association between sudden infant death syndrome (SIDS) and Helicobacter pylori infection. *Arch Dis Child* 2001 (in press).
15 Mitz HS, Farber SS. Demonstration of Helicobacter pylori in tracheal secretions. *J Am Osteopath Assoc* 1993;**93**:87–91.
16 Nilsson HO, Taneera J, Castedal M, *et al*. Identification of Helicobacter pylori and other Helicobacter species by PCR, hybridisation and partial DNA sequencing in human liver samples from patients with primary sclerosing cholangitis and primary biliary cirrhosis. *J Clin Microbiol* 1999;**38**:1072–6.

17 Elitsur Y, Btriest W, Sabet Z, *et al*. Is sudden infant death syndrome associated with Helicobacter pylori infection in children? Helicobacter 2000;5:227–31.

Growth hormone in Turner syndrome

EDITOR,—The recent interesting and valuable article by Johnston and colleagues[1] describing the outcome of a trial of recombinant growth hormone (GH) and low dose oestrogen in girls with Turner syndrome (TS) concluded that low dose oestrogen before planned induction of puberty was not beneficial for adult height. However, they extend their conclusions by the cautious word that although the majority of girls might benefit from GH treatment, a "realistic appraisal" suggests "modest" benefit. Although evidence to the contrary is fully discussed in their paper, this generalisation might lead the reader to doubt the efficacy of GH in TS.

The best known of the trials of GH in TS is that of Rosenfeld and colleagues[2] who followed their patients until the age of 17–18 years (near final height). Although they started this trial with a randomised untreated control arm who grew at a rate of 3.8 cm per year in contrast to girls in the treatment arms who grew more rapidly, the former were placed in a treatment arm of the study. Therefore historical controls were needed for comparison of near final height. The historical controls achieved an adult height of 142.2 (6.0) cm, comparable with their original projected adult of 142.2 (6.1) cm. The group treated with GH alone gained 8.4 (4.5) cm height and the group treated with GH and oxandrolone gained 10.3 (4.7) cm over their projected heights. The benefit from GH treatment seemed to be more than modest, so why the discrepancy between the US results and those of Johnston *et al*? There could be a number of reasons but a striking contrast is in the use of oestrogen; Rosenfeld and colleagues did not induce puberty until a minimum age of 14 years and at least three years of GH treatment. Johnston *et al* induced puberty at 12 years and many of the girls had already had low dose oestrogen for some years, the very purpose and design of the study.

Chernausek and colleagues[3] have thrown light on the timing of the use of oestrogen in girls who received GH treatment. They found that the number of years on GH treatment prior to introduction of oestrogen was a strong predictor of height gained (the equation was given simply: height gain in cm = 2.1 × years on GH before oestrogen; $p < 0.0001$; r^2 41%).

There is no doubt that the lack of a prospective randomised control study with an untreated arm until adult height has raised important doubts about the efficacy of GH for improved adult height. These doubts have been increased because of clinicians' experience of treating individual girls subsequent to the licensing of GH for TS. The availability of GH treatment for TS girls led to the treatment of a much older population compared to the US trial, and oestrogens were often introduced close to the onset of GH treatment. The results were "modest" or of no benefit.

To overcome the problem of being unable now to run a study with an untreated arm, Sas and colleagues[4] cleverly devised a randomised dose response study. The lowest dose of GH was 4 IU/m^2/day in a group of girls who started GH at 7.9 (0.9) years, oestrogen at 12.7 (0.6) years, and completed 93.3 (8.5) months of GH treatment. For this standard dose group their projected heights were 146.2 (7.5) cm and their achieved last heights were 158.8 (7.1) cm. The group receiving 8 IU/m^2/day had significantly greater gains over projected heights and greater latest heights. This seems to be good evidence that there is a GH effect and that the gains are clinically useful.

What then should be our "best" practice in 2001? Based on the evidence of the thorough trials discussed above, we feel that it is justified to make efforts to diagnose girls with TS early so that they can receive at least four years of oestrogen free GH treatment with a standard dose. The issues involved in the timing of pubertal induction are complex and not just related to height as an outcome, but one should be aware of Chernausek's analysis of the relationship of oestrogen free years and height gained.

However, although cohorts of TS girls may incur significant benefit in adult height, there remains considerable variability in response, both in the short and long term, between individuals. A reasonable approach would be for the child and the parents to be given an estimate of the expected response in the first and subsequent years, and should there be a serious shortfall in achieved response, then issues of treatment adherence, tissue resistance, and other incidental diseases need investigation. Ranke and colleagues[5] have shown that a major predictor of growth response in the second, third, and fourth years of GH is the first year response, and therefore the end of the first year of GH treatment is an appropriate time for reassessment of likely long term benefit. If the factors inhibiting first year response cannot be satisfactorily addressed, it is unlikely that there will be more than a modest effect on adult height, and then the patient, parents, and doctor may agree on cessation of treatment.

D A PRICE
Royal Manchester Children's Hospital, Hospital Road, Pendlebury, Manchester M27 4HA, UK

M B RANKE
University Children's Hospital, Tübuingen, D-72076, Germany

1 Johnston DJ, Betts P, Dunger D, *et al*. A multicentre trial of recombinant growth hormone and low dose oestrogen in Turner syndrome: near final height analysis. *Arch Dis Child* 2001; **84**:76–81.
2 Rosenfeld RG, Attie KM, Frane J, *et al*. Growth hormone therapy of Turner's syndrome: beneficial effect on adult height. *J Pediatr* 1998; **132**:319–24.
3 Chernausek SD, Attie KM, Cara JF, *et al*. Growth hormone therapy of Turner's syndrome: the impact of age of estrogen replacement on final height. *J Clin Endocrinol Metab* 2000;**85**:2439–45.
4 Sas TC, de Muinck Keizer-Schrama SMPF, Stijner T, *et al*. Normalisation of height in girls with Turner syndrome after long-term growth hormone treatment: results of a randomised dose-response trial. *J Clin Endocrinol Metab* 1999;**84**:4607–12.
5 Ranke MB, Lindberg A, Chatelain P, *et al*. Prediction of long-term response to recombinant human growth hormone in Turner syndrome: development and validation of mathematical models. *J Clin Endocrinol Metab* 2000;**85**:4212–18.

Bronchodilator responsiveness testing in young children

EDITOR,—There is some concern that asthma may be misdiagnosed when reported symptoms only are considered.[1] In Britain, asthma is usually diagnosed without any lung function testing whereas in the USA, measurement of bronchodilator responsiveness (BDR) is recommended.[2] Perhaps routine spirometry is perceived as impractical. If lung function testing is to be recommended for the diagnosis of asthma, the method used must be easy.

Measurement of BDR using spirometry in children over 7 years has been reported feasible in children.[3] We have shown that in 55% (49/89) of 5–7 year olds and 30% (14/47) of 7–10 year olds, BDR could not be measured because a satisfactory FEV_1 could not be obtained. These were children with respiratory symptoms who were attending the laboratory for the first time and so had no previous practice. Of the 63 with unusable spirometry, in 48 the effort for forced expiration was submaximal or they did not breathe in to total lung capacity (TLC) before the expiration, nine coughed, and three did not blow for one second. Three refused the test. Modern spirometers have expiratory incentive devices, but inspiratory incentive displays are still needed to encourage children to reach TLC before a forced expiration.

Using the interrupter technique (R_{int}), all but three could successfully undertake BDR testing. This test is no more difficult from a technical viewpoint and takes no more time than spirometry. We have shown that R_{int} can detect BDR in preschool children with previous wheeze but not wheezy at the time of test, with 80% specificity and 76% sensitivity.[4] If the specificity and sensitivity profile for BDR is acceptable in older children using R_{int}, we suggest that this method is preferred to spirometry.

P D BRIDGE
S A MCKENZIE
Department of Child Health, The Royal London Hospital, Whitechapel, London E1 1BB, UK

1 Cane RS, Ranganathan SC, McKenzie SA. What do parents understand by "wheeze"? *Arch Dis Child* 2000;**82**:327–32.
2 National Asthma Education and Prevention Programme. *Guidelines for the diagnosis and management of asthma. 2*. Bethesda: National Institutes of Health, 1997:15–17.
3 Dales RE, Spitzer WO, Tousignant P, *et al*. Clinical interpretation of airway response to a bronchodilator. Epidemiologic considerations. *Am Rev Respir Dis* 1988;**138**:317–20.
4 McKenzie SA, Bridge PD, Healy MJR. Airways resistance in pre-school children with wheeze and cough. *Eur Respir J* 1999;**15**:533–8.

BOOK REVIEWS

Improving newborn infant health development in developing countries. Edited by Costello AJ and Manandhar D. Imperial College Press. (Pp 570, hardback; £99.00) UK: Imperial College Press. ISBN 1 86094 097 8

Improving neonatal care, as with improving any service in any part of the world, would require two main components; (a) good quality information and (b) co-ordination to deliver this service to the client. The information required would have to be specific to that region's demographic, geographic, cultural, economic, characteristics, as well as encompass evidence based appropriate technical and scientific information.

Costello and Manadhar's book on improving newborn care in developing countries arose from a workshop held in Kathmandu, Nepal in 1997. As with all books produced this way there are specific strengths and weaknesses with a bias towards areas of specific interest. This book's bias appears to be towards the provision of good quality information. The contributors, most of whom have worked in developing countries, come from a variety of professional backgrounds and include epidemiologists, health planners, scientists, paediatricians, obstetricians, and anthropologists.

They have made a serious effort at putting together all the available information on neonatal care, and the problems encountered with its delivery in the developing world. Three of the five sections deal with the current state of maternal and neonatal care and the relatively low technology-high efficacy interventions that would improve it. Of note are the chapters addressing birth asphyxia, effective neonatal resuscitation, and neonatal hypothermia. As birth asphyxia accounts for over 40% of the 7.6 million annual perinatal deaths, I felt the studies were well reported that introduced face mask to mouth resuscitation delivered by trained traditional birth attendants and room air versus 100% oxygen for neonatal resuscitation were well reported.

It is depressing that hierarchical monocentric systems—that is, government led health care systems, do not work effectively in most developing countries. In addition, it seems that health education delivered on a one to one basis also does not seem to work. So is there a third way? It is this exploration that I found lacking. The co-ordination of health care systems or the lines of communication necessary to deliver health care, or indeed newborn care, in developing countries are notably weak. Studies akin to home based neonatal care as described by Bang *et al* are notably underreported.[1] In addition, the experience of some regions of developing countries that have managed to establish an effective referral system within their geographic constraints are not called upon.[2]

This book does fill the large gap in compiled information on current trends in perinatal care in the developing world. It would probably be invaluable to health professionals working there and should make interesting reading to those paediatric specialist registrars planning to join the VSO scheme of working in the third world.

SHOBHA CHERIAN
Specialist Registrar
St Peter's Hospital
Chertsey, UK

1 Bang AT, Bang RA, Baitule SB, *et al.* Effective home based neonatal care and management of sepsis on neonatal mortality: field trial in rural India. *Lancet* 1999;**354**:1955–61.
2 Anand K, Kant S, Kumar G, *et al.* " Development" is not essential to reduce infant mortality rate in India: experience from the Ballabgarh project. *Epidemiol Community Health* 2000; **54**:247–53.

Doctors for children in public care. M Mather. (£14.95; paperback). British Agencies for Adoption & Fostering, 2000. ISBN 1873868812

This is the first book in recent times to deal with the health services needed for children looked after in public care. We are all aware of the authors' key role in highlighting the plight of this forgotten group of children. The outcome in terms of their current health is a severe indictment of the lack of care they receive. Their risk of mental illness is four times that of their peers. One in six girls that leave care has already been pregnant or become pregnant within a year. Social outcomes are no better. Only one in six go on to higher education, compared with two thirds of their peers. Over a third of young prisoners have been in care.

The book gives a review of the wide ranging issues. For those already working as medical advisers, the information will not be new. However, it provides a valuable resource in one volume to those community paediatricians, in permanent posts and in higher specialist training, who would otherwise have to spend much time accumulating the same information from a variety of sources. It should be essential reading for those embarking on the medical adviser role for the first time.

The book deals with the history of medical advisers, issues relating to adult health and primary care, the diverse health needs of this vulnerable group of children together with chapters on young people's own views and on medical records and confidentiality. For the medical managers amongst us, there are invaluable service specifications and practice standards including model job descriptions for advisers in adoption and "looked after children". A suggestion of the sessional requirement needed to do justice to these roles would have been a useful addition.

The back of the book contains several teaching exercises for medical advisers. They are intended to provide a framework for group discussion. We thought these very helpful for higher specialist trainees as well. Simpler exercises aimed at SHO, "core registrars" and GP principals could usefully be added. Model answers might be helpful for non-specialist trainers although the resources needed (mostly British Association of Adoption and Fostering guidance and practice notes) are listed for each exercise.

With the advent of the "quality protects initiative" to improve the care of children in public care, this book is a timely reminder of what we as paediatricians can do to advocate for this vulnerable group of children. Our SpR will be offered the book as he starts his adoption and fostering module later in the year. We are also likely to use some of the training exercises in our own continuing professional development programme.

The "starfish story" of the late David Baum is an apposite reminder of the plight of children looked after in public care. He presented a starfish to BACCH, as the chairman's badge of office, as a constant reminder of the importance of the individual child in community child health services. The authors have used the story as their frontispiece. Read it when you buy the book.

SUREKHA PRABHU
CLIONA NI BHROLCHAIN
Northampton General Hospital, UK

Crying as a sign, a symptom, and a signal. Edited by Barr RG, Hopkins B, Green JA. (Pp 228, hardback, £45) UK: Cambridge University Press, 2000. ISBN 1 898 6831 2

Unexplained crying in young babies is a common and puzzling phenomenon. Stimulated by this, the last few years have brought paediatricians and developmental psychologists together, with the result that many traditional assumptions have begun to be questioned or overturned. This book is the first to draw this developmental perspective together, so that it is a welcome addition to the literature.

The book's enigmatic title refers to the distinction between crying behaviour as a "sign" of an underlying disease, a "symptom" (which the editors define as a more subjective report or complaint by a patient), and a "signal" which has communicative purposes. Their introductory chapter proposes that crying can serve all three functions, but that distinguishing between them helps to uncover the different starting assumptions which parents, clinicians and researchers may bring to bear.

As well as the editors' introduction and summary, the book contains 10 chapters which examine crying across a broad range of contexts. Three (Poole and Magilner's review of hospital emergency department practice towards crying complaints; Lehtonen, Gormally, and Barr's model of the aetiology and outcome of "early increased" crying, and Blackman's summary of crying in children with disability) are of obvious clinical relevance. Other chapters will be of most immediate interest to researchers. These include Hopkins' analysis of the development of infant crying behaviours, which discusses continuity with fetal behaviour and highlights the question of how cry behaviours originate and change in their function with age. Craig, Gilbert-MacLeod, and Lilley review the findings on infant crying as a sign of pain, pointing both to the advances in understanding and to the conceptual and methodological difficulties which remain. Potegal moves the focus to temper tantrums in toddlers, presenting a model of autonomic reactivity which parallels ideas elsewhere in the book about the aetiology of crying. Bard asks whether the crying "peak" found in western infants at around 6 weeks of age—now widely considered part of normal development—is also found in our evolutionary relatives, chimpanzees. The answer is a partial yes. A peak in maternal soothing of infant chimps was found at a comparable age. However, Bard observed none of the prolonged, unsoothable crying which characterises the situation in human newborns.

The chapters are of a uniformly high standard, but two seem likely to have an especially lasting impact. One is Gustafson, Wood, and Green's review, titled "Can we hear the causes of crying?" They take issue with the conclusion, widely reproduced in textbooks, that young babies produce qualitatively distinct cry types—for example, "hunger", "anger", and "pain" cries, which a sensitive parent can interpret to identify the causes of the crying. The unfortunate corollary is that a parent who cannot work out the cause and resolve the crying is inadequate. As Gustafson *et al* carefully point out, the evidence does not support this "cry type" view. Instead, the cries of young babies are "graded signals" which convey the degree to which a baby is upset, but not the specific cause of the crying. This is an important message, which needs to reach a general audience. An equally important message for researchers is carried by Barr and Gunnar's "transient responsivity" chapter. Prolonged early infant crying (or "colic") has often been attributed to an infant's "difficult temperament". Barr and Gunnar argue that the evidence does not support this, but is consistent with the notion of acute individual differences in infants' "reactivity" or "regulation" of responsiveness as a cause of prolonged

crying. The importance of this formulation lies in avoiding the expectation that a crying baby will be difficult at later ages, and in operationalising the concepts of reactivity and regulation so that they can be tested.

Depending on your point of view, this book's breadth of coverage and desire to interest clinical and academic audiences are either a strength or weakness. Its price of £45 does not seem designed to encourage individuals to buy it. However, because it is part of the "Clinics in Developmental Medicine" series, it is likely to be taken by university and medical school libraries which subscribe to this series. It is worth seeking out.

IAN ST JAMES-ROBERTS
Thomas Coram Research Unit, London

Preventitive management of children with congenital abnormalities and syndromes. GN Wilson and WC Cooley. (Paperback including CD-rom). UK: Cambridge University Press. ISBN 0 521 77673 2

As more and more rare syndromes are described and the clinical features of the common syndromes are enlarged upon, there have been calls for studies on long term follow up, to assess complications and prognosis. For the rare syndromes this had been slow in coming. Patients diagnosed by geneticists are rarely followed up, or seen again by them. They are mostly sent back to the referring paediatrician. This, in part, has arisen because geneticists in the UK had to battle, in the 1960s and 70s to persuade paediatricians and physicians to refer their patients for diagnosis.

There was, at that time, a small set of geneticists who had developed an expertise in dysmorphology and syndrome identification, but their colleagues were frightened that, if they used them, they would lose their patients; or they took the view that there was no need for a diagnosis if there was no treatment and so patients were not referred. Education, a few brilliant diagnoses and not a few medico-legal cases changed all of that, but part of the unspoken bargain that was entered into included the family's return, after diagnosis (or the attempt thereof) back to the referring physician.

Geneticists, have learned what becomes of some patients with rare conditions by reading the literature. This information is important. Faced with a risk of recurrence, most sensible parents will want to know what has happened to other children with their child's condition, what else is in store for them, and who will keep an eye open for the complications.

Drs Wilson and Cooley have written a unique book that fills a gap in the market. They have chosen some of the more common malformation anomalies or syndromes and written about preventative management. "Common" in their terms means those conditions with a frequency of more than 1 in 25 000 births, and by preventative management they mean knowing about and acting upon, complications. To achieve this, the authors have drawn up checklists of what needs to be assessed at every age. There are for instance three tables for cerebral palsy, one from 0–1 years, one for 1–6 years, and finally a checklist for those after 6 years. There are tables for tuberous sclerosis, neurofibromatosis, Noonan syndrome, Ehlers-Danlos, and some 130 other conditions. They list patient groups and summarise clinical and laboratory diagnoses and key management issues. They have not gone back to original references, but refer frequently to Gorlin's textbook "Syndromes of the Head and Neck" for a fuller understanding of some of the differential diagnoses mentioned in this book, but that is in order.

This is an excellent book. One for the shelf of every genetics department and also for easy reach of those following the patient. It comes with a CD-ROM and I can see clinical geneticists, instead of writing long letters to the GP, listing what needs to be checked, and simply printing the table from the CD.

MICHAEL BARAITSER
London

A–Z of medical writing. Albert T. (Paperback) London: BMJ Books. ISBN 0 7279 1487 1

Many doctors have difficulty with medical writing. There is a crying need for concise, clear text whether it be for papers, grant applications, books/book chapters, or CVs. Furthermore, hospital doctors generate more than 40 million letters per year about their outpatients, as part of communication with the primary care team. Unfortunately many of us produce offerings that are full of jargon, lack a clear message, and are too long (even if this is not recognised by the writers!). Sadly most of us have had no teaching on how to write during our medical training and virtually none as part of our continuing medical education.

Tim Albert's book has been created to help with these problems. Paradoxically, electronic publishing is leading to an expansion in the need for written information and—outside of informal email communications—this needs to be of high quality. A large number of topics of relevance to medical writers has been chosen by the author and arranged in alphabetical order, so that the aim is for the reader to be able to dip into various sections as needed. There is good cross referencing between sections and book lists interspersed every few pages but there is no formal index. Although there are other publications on writing for journals, the advantage of this modestly priced paperback is that it covers a wide breadth of writing and publishing. For example, how to write an editorial, systematic review, or writing for a medical magazine are discussed effectively. Many will have experienced "writer's block" and some useful tips are given on how to circumvent this malevolent condition. It is suggested that the condition is not a sign of failure but rather that we are taking the trouble to produce something worthwhile!

Overall, this book is helpful for potential medical writers. Inevitably some subjects are not covered in depth because of insufficient space. However, the text is easy to read with the book designed to dip into, rather than read from cover to cover. It should be useful to both trainees and senior doctors. Often there is a need to write an obituary or grant application at short notice and the practical advice will assist the writer in his task. The alternative is to seek advice from a wily old friend who has been there before.

NICK MANN
Consultant Paediatrician

Manual of tropical pediatrics. Edited by Seear, MD. (Pp 480, hardback, £50.00) UK: Cambridge University Press, 2000. ISBN 0 521 65835 7

This is a handsome book, with hard, thick covers, quality printing, and superb illustrations. It will look just grand on a bookshelf, but how often will it come down from that bookshelf? This manual is a comprehensive textbook of child health. In 480 pages, it covers general paediatrics, as well as infective and nutritional disorders confined to developing countries. The quality of the illustrations is superb, and relative to the text. The *x* rays in particular enhance the teaching message. However, the microbiology illustrations seem designed to relieve the tedium of grey text, rather than adding useful information. The chapter on rashes would benefit from more illustrations but perhaps the cost implications were too high.

The chapter on paediatric emergencies is informative but not easy to access and the readability of the text would be improved by more tables and diagrams. There is not a specific chapter on practical procedures, such as insertion of chest drains, abdominal paracentesis, or subdural taps, yet there is a chapter on laboratory procedures.

The book lacks references. Are these are not considered necessary now that we all have access to electronic journals? Try getting on to Medline from Chad. If this is to be a comprehensive textbook, the reader needs need guidance on where to go next. I would want to know whether surgery has anything to add to the treatment of spinal tuberculosis; what are the reasons for using lorazepam rather than diazepam in the management of status epilepticus; and what advice would you give to a girl with rheumatic mitral valve disease who is about to get married?

Health workers in tropical countries are dividing into two groups: those who are practising in city hospitals with improving facilities, delivering services to a slowly growing affluent population, who are demanding neonatal intensive care, renal dialysis, etc, and the remainder who still deal with poor populations, poor medical resources, coping with recyclable diseases, such as gastroenteritis, malaria, malnutrition, and HIV.

The majority of children in developing countries are treated by health workers who do not have medical degrees. To them, the physiology in this book is largely irrelevant. Most would make diagnoses based on recognition of clinical patterns, as exemplified in the Integrated Management of Childhood Illnesses. They require a portable, cheap book with advice on practical procedures, drug doses, and management of acute conditions. Many will combine curative medicine with primary health. They will see many children with chronic intractable disease, where the disease impinges upon the whole family, such as cerebral palsy, malnutrition, and AIDS. These problems require a whole chapter to themselves, and will vary depending on cultural practices in individual societies. This is not easy to cover in a textbook written for the whole tropics.

I appear to have said little that is positive about this manual, which is written for two audiences with disparate needs. It is neither the authoritative textbook of child health with a tropical flavour, nor the pragmatic, functional pocket book. I suspect it will continue to look handsome sitting on the bookshelf. At £50, much cheaper than some alternatives, it deserves better.

PAUL EUNSON
Consultant Paediatric Neurologist, Royal Hospital for Sick Children, Edinburgh