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. 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

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

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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 child1 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 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.

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Control your controls and conclusions

EDITOR,—In a retrospective study, Kerr and coworkers investigated formalin fixed, parafin embedded tissues (stomach, trachea, and lung) of 32 infants who had died of SIDS, and eight control cases. 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 13C-urea breath test corrected for estimated individual CO2 production rate.6 Although a quarter of the children have at least one positive serology test, 7 none of the children have positive tests during the first six months 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 public health action.

M STEPHEN MURPHY
Associate Editor

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 who 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.

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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.

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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.

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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 \( H\), pylori like organisms. A Warthin-Starry-silver stain, modified Giemsa or immunocytochemistry 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 observed. 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 a high level of \( H\), 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 be a direct 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.

There are likely to be many causes of dwelling crowding. It has been shown that this is associated with low socioeconomic status, but the study by Eliot et al 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 time.

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. 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.

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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 23 (of
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 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, 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 this is the case in which infection and subsequent aspiration into the lungs of control cases used in the study ‘An association between sudden infant death syndrome (SIDS) and Helicobacter pylori infection’.

**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’. 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.

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Age at death (wks)</th>
<th>Cause of death</th>
<th>Time of diagnosis</th>
<th>Antibiotic exposure</th>
<th>Exposure to home environment</th>
<th><em>H pylori</em> ureC gene</th>
<th><em>H pylori</em> cagA gene</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Stomach</td>
<td>Trachea</td>
</tr>
<tr>
<td>C1</td>
<td>3</td>
<td>prematurity</td>
<td>AM</td>
<td>–</td>
<td>–</td>
<td>0.100</td>
<td>0.150</td>
</tr>
<tr>
<td>C2</td>
<td>4</td>
<td>prematurity</td>
<td>AM</td>
<td>–</td>
<td>–</td>
<td>0.120</td>
<td>0.090</td>
</tr>
<tr>
<td>C3</td>
<td>7</td>
<td>ileal perforation</td>
<td>AM</td>
<td>+</td>
<td>–</td>
<td>0.265</td>
<td>0.298</td>
</tr>
<tr>
<td>C4</td>
<td>7</td>
<td>Necrotising enterocolitis</td>
<td>AM</td>
<td>1 day only +</td>
<td>–</td>
<td>0.200</td>
<td>0.150</td>
</tr>
<tr>
<td>C5</td>
<td>20</td>
<td><em>E coli</em> septicaemia</td>
<td>PM</td>
<td>–</td>
<td>+</td>
<td>0.170</td>
<td>0.160</td>
</tr>
<tr>
<td>C6</td>
<td>24</td>
<td>suffocation</td>
<td>PM</td>
<td>–</td>
<td>–</td>
<td>0.210</td>
<td>0.090</td>
</tr>
<tr>
<td>C7</td>
<td>32</td>
<td>pneumonia</td>
<td>PM</td>
<td>+</td>
<td>–</td>
<td>0.100</td>
<td>0.140</td>
</tr>
<tr>
<td>C8</td>
<td>44</td>
<td>Pneumococcal septicaemia</td>
<td>PM</td>
<td>+</td>
<td>–</td>
<td>0.178</td>
<td>0.163</td>
</tr>
</tbody>
</table>

C1, control case number 1; AM, ante-mortem; PM, post-mortem; NT, not tested.
lungs to produce toxic amounts of ammonia in infants that presumably had normal livers.\textsuperscript{9} To reiterate, there are two parts to the hypothesis. First, interleukin-1\textsubscript{b} production in the \textit{H pylori} infected stomach, and second, supply of ammonia to the systemic circulation\textsuperscript{10} (and 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\textsuperscript{11,12} in order to clarify the proposed role of \textit{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.

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6 Peek RM, Miller GG, Tham KT, et al. Heightened inflammatory response and cytokine expression in vivo to 
7 Wallace JL, Cucala M, Mugridge K, et al. Secretagogue-specific effects of interleukin-1 on gastric and duodenal absorbate with 
9 Crabtree JE, Taylor JD, Wyatt JI, et al. Mucosal IgA response to \textit{Helicobacter pylori} 120 kDa outer membrane protein and 
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 by triggering the series of events leading to SIDS; 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.

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10 Pafton 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 urogenital tract infection after pretreatment with intravenous IL-1β. Ibid.

.controls not matched

EVIDENCE—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 +2 SD in the 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 that 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 in the home, many hours before being refrigerated.

Finally, as H pylori is a gastric organism, it was surprising to find the bacteria 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.

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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).

The formalin-fixed and paraffin-embedded stomach, trachea, and lung specimens obtained during postmortem examination were retained. 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 gene1 and the cagA gene2 to detect the presence of H pylori DNA in these samples.

Histological examination failed to show any Helicobacter like organism in these specimens. 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.3 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 investigations. Taken together, the significance of H pylori as a cause of SIDS is highly questionable.

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Table 1 Characteristics of SIDS cases and controls

<table>
<thead>
<tr>
<th>Sex</th>
<th>Age</th>
<th>Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>F</td>
<td>4 months</td>
<td>Congenital heart disease</td>
</tr>
<tr>
<td>F</td>
<td>2 months</td>
<td>Morphone toxicity</td>
</tr>
<tr>
<td>M</td>
<td>13 hours</td>
<td>Bronchopneumonia</td>
</tr>
<tr>
<td>M</td>
<td>1 hour</td>
<td>Amniotic fluid aspiration</td>
</tr>
<tr>
<td>M</td>
<td>6 months</td>
<td>Premature, septicaemia</td>
</tr>
<tr>
<td>M</td>
<td>3 months</td>
<td>Congenital brain tumor</td>
</tr>
<tr>
<td>M</td>
<td>6 months</td>
<td>Glutaric aciduria type I</td>
</tr>
<tr>
<td>M</td>
<td>2 months</td>
<td>Extreme premature</td>
</tr>
</tbody>
</table>

Cases

| M   | 3 months | SIDS               |
| M   | 3 months | SIDS               |
| M   | 13 months | SIDS              |
| M   | 7 days   | SIDS               |
| M   | 5 days   | SIDS               |
| F   | 8 months | SIDS               |
| F   | 2 months | SIDS               |
| F   | 2.5 months | SIDS         |
| M   | 2 months | SIDS               |

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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 lungs 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. 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.1

(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 ammonia after substantial doses of intratracheal urease.3 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 inchohlorotic perichondrial patches, pulmonary oedema, emphysema, and increased muscle mass in pulmonary arteries,4 although these are not invariably findings.

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

(d) “The liver should be affected by hyperammonaemia and it is not in SIDS”. Blackwell has misunderstood our hypothesis. First, interleukin-1 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 paper2 do not take account of further information provided at the request of other authors3 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,4 and in the liver of patients with primary sclerosing cholangitis and primary biliary cirrhosis.5

The pathogenesis of SIDS is accepted to be multifactorial, and therefore, small studies with a negative association between \( H \) pylori and SIDS data 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.6

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References


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Growth hormone in Turner syndrome

EDITOR,—The recent interesting and valuable article by Johnston and colleagues1 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 outcome of TS.

The best known of the trials of GH in TS is that of Rosenfeld and colleagues2 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 84 (4.5) cm height and the group treated with GH and oxandrolone gained 103 (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 who had already had low dose oestrogen for some years, the very purpose and design of the study. Charnessauk and colleagues3 have shown that major predictors of growth response in the second, third, and fourth years of GH is the first year response, and that of Rosenfeld and colleagues2 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 outcome of TS.

However, though 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 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 medical conditions need investigation. Ranke and colleagues 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, then it is likely 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.

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Bromocholductor 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 bromocholductor 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 FEV1 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 those with measurable spirometry, in 48 the effort for forced expiration was submaximal or they did not breathe 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 interpretation of the maximum criteria, BDR testing is no more difficult from a technical viewpoint and takes no more time than spirometry. We have shown that Rrs, the bronchodilator response ratio of TS girls in 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 Charnessauk’s analysis of the relationship of oestrogen free years and height gained.

However, though 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 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 medical conditions need investigation. Ranke and colleagues 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, then it is likely 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.

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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, scientist, paediatricians, obstetricians, and anthropologists.

They have made a serious effort at putting together as much as possible of 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 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 umbilical cord clamping were well reported. It is depressing that hierarchical monocratic 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 across 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 under-reported. In addition, the experience of some regions of developing countries that have managed to establish an effective referral system within their geographic regions is not called upon.

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


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, related to adult 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”. As the professionals will know, one of the requirements 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 GPs for whom could be usefully 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 there.

With the advent of the “quality protects initiative” to improve the care of children in public care, this book is a timely reminder of the need 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 under-reported. In addition, the experience of some regions of developing countries that have managed to establish an effective referral system within their geographic regions is not called upon.

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SUREKHA PRABHU CLIONA NI BHROLCHAIN Northampton General Hospital UK


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 “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 Magriner’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 have particular 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 behaviours change and in 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 chimpanzees 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 Groener’s review, titled “Crying, hurt, pain or response 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 be spread to the 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 infant-generated “expression of responsiveness” as a cause of prolonged.

www.archdischild.com
The importance of this formulation lies in avoiding the expectation that a crying baby will be difficult at later ages, and in operation- alising 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 depth to interest clinical and academic audiences are either a strength or weakness. Its price of £45 does not seem designed to encourage indi-
viduals 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
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London


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 fol-
lowed 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 write many letters to counsel, 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 treat-
ment and so patients were not referred. Edu-
cation, a few brilliant diagnoses and not a few medico-legal cases changed all of that, but the unspoken bargain that was entered into by the majority of those involved is still in operation—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 books for 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 journal, which is an increasingly discussed effec-
tively. 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


This is a handsome book, with hand, 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 cov-
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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, apart from one specific chapter on practical procedures, such as insertion of chest drains, abdominal paracent-
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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 guidance on what he would want to know whether surgery has anything to add to the treatment of spinal tuberculosis; what are the reasons for using lormaram rather than diąsarep in the manage-
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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 recogn-
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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, func-
tional 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


Many doctors have difficulty with medical writing. There is a crying need for concise, clear text whether it be for papers, grant appli-
cations, book chapters, or CVs. Further-
more, 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 poor and 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 alpha-
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