Letters to the Editor

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Letters should be submitted in duplicate in double-spaced typing on plain white paper with name and address of sender(s) on the letter. Send them to Jerold F. Lucey, MD, Editor, Pediatrics Editorial Office, Fletcher Allen Health Care, Burlington, VT 05401.

Child Sexual Abuse and Human Papillomavirus Infection

To the Editor.—

Stevens-Simon et al are to be commended for their study in what remains probably among the most persistent controversies in child sexual abuse research: the significance of genital human papillomavirus (HPV) infection.[1] Their study showed that HPV DNA was detected in 5 (16%) of the 31 girls with confirmed or suspected sexual abuse and none of the 9 girls found to not have been abused. However, the statement in the results of this article ("$P < .05$, Fisher's exact test") is in error; this difference did not approach statistical significance, possibly because of the small number of nonabused children (uncorrected $\chi^2 = 1.66$, $P = .1198$; Fisher's exact test, 1-tailed $P = .258$; 2-tailed $P = .570$; see Fig 1).[2] Given the difference in rates of detection of HPV DNA, at least 25 nonabused girls with no HPV DNA detectable would have to have been enrolled to achieve a statistically significant difference. This underscores one of the challenges of this type of analysis: enrolling a sufficient number of nonabused children in a study that includes vaginal lavage and perineal swabs.

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In Reply.—

We appreciate the comments by Dr Beck-Sague and regret that the statistical test as noted in the abstract and results of our paper are in fact incorrect. Thus, the difference we noted in detection of genital HPV in abused versus nonabused girls (5 of 16, 16%, vs 0 of 9) can only be described as a "trend" rather than a statistically significant difference. We agree with her conclusion that acceptable approaches to obtaining genital samples from control children remains a problematic methodologic barrier to performing more definitive studies of genital HPV infection in sexually abused children. Thank you for your letter regarding this issue.

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Child-Friendly Healthcare Initiative

To the Editor.—

I was deeply moved by Fig 1 in the article by Southall et al entitled "The Child-Friendly Healthcare Initiative (CFHI): Healthcare Provision in Accordance With the UN Convention on the Rights of the Child" (*Pediatrics*. 2000;106:1054–1064) that shows a child with neuroblastoma from an unnamed impoverished country. The small body is lying on a small metal cot. Even in the shadows, one can see that the sheets are threadbare, and the upper face is sheathed in some type of surgical bandage. The left arm appears to be splinted, perhaps to some sort of intravenous infusion. The legend mentions that some (palliative?) surgery had been undertaken, but there was inadequate chemotherapy and analgesia.

I was reading this issue of *Pediatrics* in my usual fashion—skimming it at midnight. I wept out loud when I saw this bleak image. No child should have to suffer. No child should have to die in pain, unable to see or to be held.

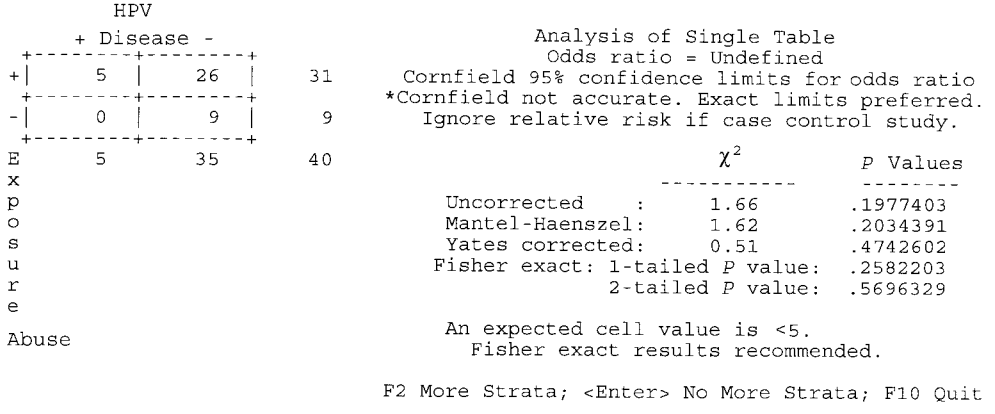

Fig 1. Genital HPV infection (disease) among children with and without evidence of abuse (exposure).

Although I experienced sorrow, I felt proud to be a member of a the American Academy of Pediatrics, whose journal published the photo. This is a specialty that has its heart in the right place.

In March 1996, *Pediatrics* published a poem, "We Pray for Children," by Ina J. Hughes, that concluded Marian Edelman's book, *The Measure of Our Success: A Letter to My Children and Yours* (Beacon Press, Boston, MA, 1992). It has become a prayer that I keep posted near my desk and have distributed to others. Again, I thank the leadership of this journal for giving its readers the opportunity to be touched.

When I wrote this letter, a presidential election was being held. One party spouted the slogan, "compassionate conservatism," which has been implemented as conservative compassion. Those who expressed this slogan should see this photo and read this poem. Our compassion for the sick and poor children of the entire world should be unfettered and boundless.

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We pray for children
who sneak popsicles before supper,
who erase holes in math workbooks,
who can never find their shoes.
And we pray for those
who stare at photographers from behind barbed wire,
who can't bound down the street in a new pair of sneakers,
who never "counted potatoes,"
who are born in places we wouldn't be caught dead,
who never go to the circus,
who live in an X-rated world.
We pray for children who bring us sticky kisses and fistfuls of dandelions,
who hug us in a hurry and forget their lunch money.
And we pray for those
who never get dessert,
who have no safe blankets to drag behind them,
who watch their parents watch them die,
who can't find any bread to steal,
who don't have any rooms to clean up,
whose pictures aren't on anybody's dresser,
whose monsters are real.
We pray for children
who spend all their allowance before Tuesday,
who throw tantrums in the grocery store and pick at their food,
who like ghost stories,
who shove dirty clothes under the bed, and never rinse out the tub,
who get visits from the tooth fairy,
who don't like to be kissed in front of the carpool,
who squirm in church or temple and scream in the phone,
whose tears we sometimes laugh at and whose smiles can make us cry.
And we pray for those
whose nightmares come in the daytime,
who will eat anything,
who have never seen a dentist,
who aren't spoiled by anybody,
who go to bed hungry and cry themselves to sleep,
who live and move, but have no being.
We pray for children
who want to be carried
and for those who must,
for those we never give up on and for those
who don't get a second chance.
For those we smother . . . and for those who will grab
the hand of anybody kind enough to offer it.
(Please offer your hands to them so that no child is left behind because we did not act.)

Edelman M. *The Measure of Our Success: A Letter to My Children and Yours.* Boston, MA: Beacon Press; 1992

In Reply.—

The letter from Dr Lin is moving and reveals compassion common to most health care workers attempting to address the needs of sick and injured children worldwide. A perennial problem for disadvantaged countries is not just how to stop such tragedies but how to communicate their predicament to others. In some respects unless one has actually seen the conditions in which three quarters of the world's children are cared for when seriously ill, it is difficult to understand the size and nature of the problem. Almost every health care giver who has worked in a resource-poor, disadvantaged country comes back a "different person." Words are rarely enough to describe the extent of deprivation in so many hospitals caring for children in poor countries; yet the problem is not merely one of resources. Examples of "child-unfriendly" practices abound in rich countries, too, for example, unnecessary restrictions on parental visiting and inadequate attention to pain relief.

We agree with Dr Lin that *Pediatrics* and the American Academy of Pediatrics have taken a brave and vital step in publishing our paper. The constraints of space made it difficult to demonstrate many other unacceptable and unethical practices prevalent in hospitals around the world, but additional examples are published on our Web site: www.childfriendlyhealthcare.org. We urge your readers to look at this Web site and do everything they can to persuade those who control the world's wealth to redistribute it in the interest of providing a standard of care compatible with the internationally agreed rights of children.

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Possible Steroid-Induced Recurrent Patent Ductus Arteriosus After Device Closure

To the Editor.—

We wish to alert those who treat infants and children with steroids of the possible adverse effects that may occur in patients who have had vascular occlusion devices placed.

We treated and closed by catheter device (Gianturco-Grifka vascular occlusion device [GGVOD], Cook Laboratories) a moderately large patent ductus arteriosus (PDA) in a 4-month-old girl. Angiography, subsequently reviewed by Dr R. G. Grifka, showed the device in proper position with the ductus closed. PDA is a common congenital vascular defect that now can often be closed by catheterization techniques with different devices.[1–3] The closure of the PDA with virtually all present devices consists both of mechanical closure/obstruction and obstruction to flow by throm-

bus formation. In animal studies, the different devices have cellular covering of the aortic and pulmonary aspects of the ductus by approximately 6 weeks.[4,5] The in-growth and complete transformation of the thrombus in the ductus proper varies depending on implanted material but occurs within 4 months in dogs with the GGVOD,[3] and within 6 months or less in implants with stainless steel, nickel/titanium coil, and polyvinylalcohol foam plug in lambs.[5] There are no reports of PDA recurrence in humans or animals after GGVOD placement and ductal closure in the absence of the device moving (R. G. Grifka, personal communication, August 5, 2000).

Within 4 weeks the infant started steroid therapy for newly diagnosed infantile spasms, and the ductus was subsequently reopened clinically in three weeks. By echocardiographic Doppler studies, there were at least 2 and probably 4 different areas around the device that were leaking, but the device remained in proper position. MRI studies were not performed because of concern that the device was not fixed in place cellularly. After 1 month off steroids, the ductal leakage was diminished, and 1 year later the infant has a trivial residual leak around the device.

Patients who undergo device closure of a ductus should probably avoid treatment with relatively high-dose steroids for 6 months when possible. The complete healing and tissue organization at the ductal site takes at least 4 weeks and may take up to 6 months after device placement. The use of prednisolone and adrenocorticotropic hormone in this infant within a month of device closure with subsequent reopening of the PDA is suggestive that steroid treatment may interfere with the cellular responses at the ductus site and the device(s) closing the ductus.

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Systematic Review of Treatments for Infant Colic

To the Editor.—

Garrison and Christakis[1] justify their systematic review by pointing at some presumed methodologic shortcomings of our systematic review, published in 1998.[2] In fact, the conclusion of their review differs only slightly from ours, and we wonder if these differences can only be attributed to flaws in ours. We therefore would like to comment on the reasons why our review (according to the introduction of Garrison and Christakis' review) was thought to be inappropriate.

First, one can always argue whether studies are sufficiently homogeneous to be pooled; however, we don't agree that we actually pooled inhomogeneous studies and ask reader to compare. Second, we did pool different outcome measures, using effect sizes. Given the lack of uniformity in outcome measures, we considered this the most informative approach. Although we agree that effect sizes are difficult to translate to the clinical setting, they are often used in systematic reviews and are also described in the handbook of the Cochrane Collaboration, the leading organization in this field.[3] Finally, after checking the studies reviewed by Garrison and Christakis,[1] we actually don't see any study that we missed, as they suggested. From a methodologic point of view, we would like to make a few comments on Garrison and Christakis' review. First, they did not search the Embase database, which includes many European-language journals not indexed by Medline.[4] Second, the authors did not evaluate trial quality using an independent assessment, nor did they use a validated scale.[5] Third, the numbers needed to treat (NNT), presented in Table 3, are provided without confidence intervals, thus hindering objective interpretation by the reader. In addition, presenting NNT based on different definitions of "cure" actually is the same sort of standardization that they reject in our use of effect sizes.

Systematic reviews are considered the best evidence available. Therefore, we should aim at concordance between reviews. We propose to collaborate on a joint updated review for the Cochrane Collaboration, resolving the discordance in methods and results.[6]

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In Reply.—

We appreciate the comments of Lucassen and Assendelft in response to our systematic review of treatments for infant colic.

Regarding the issue of homogeneity, we respectfully disagree with the authors' contention that heterogeneous studies were not pooled in their meta-analysis.[1] In fact, the meta-analysis by Lucassen et al appeared to have problems with heterogeneity on several levels. This issue, among others, was originally raised in a letter to the editor after publication of the meta-analysis.[2] The meta-analysis pooled data from studies concerning heterogeneous interventions, such as hypoallergenic formulas and dietary modifications in breastfeeding mothers. Second, data concerning heterogeneous outcomes (such as duration of crying and presence of colic) were pooled using effect sizes, without detailing which outcomes were selected for analysis from each study and why. This is problematic because it further hinders interpretation of the effect sizes. Additionally, meta-analyses commonly include statistical tests to determine whether statistically significant heterogeneity is present in the data before pooling; their article did not state if such tests were performed. Although the authors used a random-effects model in their meta-analysis, there remains considerable controversy as to whether this statistical method can adequately compensate for heterogeneity among the data of pooled studies.[3,4]

We are pleased that the authors agree that effect sizes lack clinical applicability, despite being adequate tests of statistical significance. Perhaps authors of future studies will take this into account when performing meta-analyses. The primary goal of our review was to provide clinically relevant data for practitioners; hence, we did not consider effect sizes to be useful or informative. Although our NNT are calculated based on differing outcomes, these are clearly stated in the article, as is the fact that the NNT cannot therefore be directly compared.

The differences between the studies included in their meta-analysis and our systematic review are as follows: there were 3 articles that appeared in our analysis but not in theirs,[5–7] and 8 articles that appeared in theirs but did not meet our inclusion criteria.[8–15] The additional articles in our analysis were all published in 1997 or later, and were likely not included in their

literature search. However, these articles do contain 2 interventions not studied in the meta-analysis: sucrose[5,7] and intensive parental counseling.[6] There were 2 articles[8,11] that appeared in their article but not in our literature search; neither article is included in the Medline or Embase databases. Of the 6 remaining articles that appeared in their article but not in ours, 2 were in a language other than English,[14,15] 2 were comparative trials without placebo controls,[10,12] and 2 were not adequately randomized.[9,13] A posthoc search of Embase using the same search criteria discovered no additional articles that would have met our inclusion criteria.

We did, in fact, limit our search to the English language, because of resource limitations, and acknowledge this as a potential weakness of our review, although it must also be noted that colic is a culturally defined phenomenon and studies from non-English language countries may or may not have applicability elsewhere. Contrary to the authors' assertion, however, the articles included in our review had indeed passed a quality review, utilizing the criteria for randomized controlled trials presented in *JAMA*'s "Users' guides to the medical literature."[16] We did not employ quality scores in our review, as the utility of these scales is considered questionable.[4,17]

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The Unnecessary Epidemic of Folic Acid-Preventable Spina Bifida and Anencephaly

To the Editor.—

The commentary by Brent et al in the October 2000 issue of *Pediatrics* has a title that should invoke no disagreement: "The Unnecessary Epidemic of Folic Acid-Preventable Spina Bifida and Anencephaly." The authors allowed for the association of valproic acid exposure and maternal insulin-dependent diabetes making up a portion of the neural tube defects, but the vast majority were attributable to folic acid deficiency. Or, at least, prevention was associated with folic acid intake. The folic acid issue seems to be: "How much and in what form?"

Supplementation was evaluated with varying reliability, from a telephone survey to data from countries with higher compliance rates than could be expected in this country. Whether a study was based on intake from natural folic acid sources, suboptimal supplementation, the accepted standard of 400 μg/day, enrichment of flour with 200 versus 400 μg, or whether supplementation was started before conception or during the first trimester, confounding variables are rampant in such studies. How can we evaluate the intake from natural sources or the absolute intake from the ingestion of supplemented white flour?

My disagreement is with the authors' stance that commonly eaten foods should be fortified so that "prevention occurs without the need for a behavior change." If neural tube defects are attributed to maternal elevated homocysteine levels, as are strokes and heart disease, as the authors state, we should think of all the "big 3 Bs"—folic acid, B12, and pyridoxine. The first two enhance methylation in the conversion of homocysteine to methionine, while pyridoxine enhances sulfuration to reduce homocysteine levels (as in the treatment for the pediatric disease homocysteinuria. My thought is that we should encourage the intake of these B vitamins plus the antioxidants and bioflavonoids found in folic acid-rich foods. In the face of the appalling rise of the incidence of childhood obesity and noninsulin-dependent diabetes, we *must* think of changing the behavior of children and young adults by encouraging them to exchange some of their favorite deficient foods, such as white flour and pop, for nutrient-dense foods.

Isolating a nutrient from a whole food that is responsible for a nutritional deficiency disease and incorporating it into a food that is a staple in the diet is not the same as leaving a healthy food unadulterated and educating people of its value and of how to prepare it in an attractive form. If this goal can't be met, answer the authors' plea, and throw some money into the equation that could supply supplementation along with nutrition education. But certainly we should not encourage the consumption of high-glycemic-index "enriched flour."

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In Reply.—

We very much appreciated Dr Campbell's thoughtful letter concerning our commentary[1] entitled "The Unnecessary Epidemic of Folic Acid-Preventable Spina Bifida and Anencephaly." Your letter is evidence of your broad interest in the problems of children. If we had written a commentary about *Haemophilus influenzae* meningitis 10 years after the vaccine was approved complaining that the vaccine was not being administered, we would probably have received 200 angry letters from pediatricians demanding that a program should be initiated that would enable every child to be vaccinated. Apparently, the epidemic of neural tube defects does not evoke an angry response from our colleagues. We believe that support for higher folic acid supplementation from the pediatric community could significantly reduce the frequency of neural tube defects.

We agree with Dr Campbell that we should encourage healthy diets for children and adults alike. We also think that no child should be born with folic acid-preventable spina bifida and anencephaly. The best evidence we have today suggests that we would make very substantial strides to the total prevention of these birth defects if all women of the world consumed 400 μg of synthetic folic acid daily above whatever natural folate they consume. Adding *enough* folic acid to commonly eaten foods would be a very effective way to achieve this goal. We do not encourage individ-

uals to eat more foods with enriched flour. We suggested that enriched flour should contain more folic acid.

The March of Dimes has been very active in publicizing the importance of taking folic acid as part of their national campaign to prevent birth defects. Part of their campaign has included surveying the population to determine whether their message is reaching the public. There has been a steady but slow improvement of awareness over the past 5 years. But the following information tells us that more education is needed. In 2000, 75% of the population have heard of folic acid; 14% know that it prevents birth defects; 10% know that folic acid must be taken before a woman becomes pregnant; 32% consume folic acid on a daily basis; 54% have heard about folic acid from the media; and 20% have heard about folic acid from their health care provider.

Since we wrote our commentary, the National Center for Health Statistics has published data showing that the current fortification of enriched grains had made a remarkable increase in the median serum folate among American women of reproductive age.[2] The median increased from 4.8 to 14.5 ng/mL.[1] In the United States we must determine whether or not to add more folic acid to grains. In countries that have not fortified grains with enough folic acid, the unnecessary epidemic of folic acid-preventable birth defects continues unabated. We note in closing that the Institute of Medicine in 1998 recommended that those over 50 consume 2.4 μg of synthetic vitamin B12. We remain puzzled as to why the Food and Drug Administration has not moved to add vitamin B12 to enriched grains. It seems long overdue to us.

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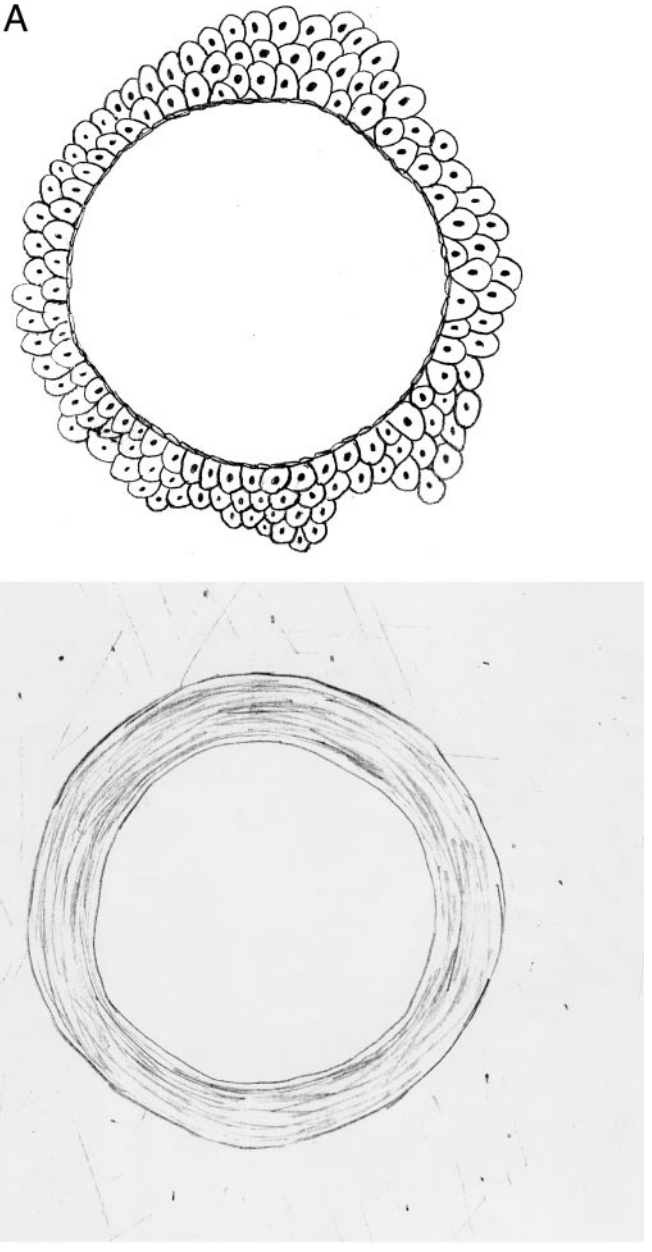

Fig 1. A, Blood vessel in the germinal matrix of a premature infant. The vascular lumen is lined by a single layer of flat endothelial cells surrounded by plump neuroblasts of the germinal matrix. B, Adult artery. In contrast, the vascular lumen and thin endothelial layer are surrounded by a tough layer of smooth muscle and connective tissue in the glial matrix.

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The Structure of Blood Vessels in the Germinal Matrix and the Autoregulation of Cerebral Blood Flow in Premature Infants

To the Editor.—

The recent article by Tsuji et al[1] is very important and illustrates the absence of adequate autoregulation of cerebral blood flow by premature infants. However, the authors fail to stress an important anatomic cause for this lack of autoregulation.

Autoregulation of cerebral blood flow depends in large part on control of the caliber of small cerebral arteries. To control the diameter of these arteries, smooth muscle in the media of these vessels must contract or relax to maintain constant cerebral blood flow while systemic blood pressure varies. This system is thought to be under sympathetic nervous system control.[2]

An important reason for the reported lack of autoregulation of cerebral blood flow in premature infants is the lack of smooth muscle in the walls of arteries in the germinal matrix. The histology of the blood vessels in the germinal matrix of premature infants was first described by Haruda and Blanc in 1981.[3] Microscopic examination of autopsy specimens revealed that the vascular structures supplying the germinal matrix consist of simple endothelial lined channels (see Fig 1). No structure is present to control the caliber of these vascular channels, even larger ones such as Huebner's artery. There is no smooth muscle, elastin, or connective tissue.

The structure of normal adult arteries resembles automobile tires, tough and elastic. In contrast, the vessels of the germinal matrix of prematures resembles an inner tube, with no surrounding rubber tread or steel cord. Their microscopic appearance implies that any surge in blood pressure could cause rupture and hemorrhage. Without the autoregulation described by the authors to prevent pressure surges, these vascular channels are disasters waiting to happen. Germinal matrix and intraventricular hemorrhages resulting from ruptures of these channels are frequently catastrophic and a major cause of neonatal mortality and major disability in survivors. This is why exquisite blood pressure control in the neonatal intensive care unit is crucial and, without autoregulation, is like walking a tightrope in a hurricane.

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In Reply.—

Dr Haruda addresses a potential anatomical basis for the impairment of cerebrovascular autoregulation identified by us in sick premature infants studied by near-infrared spectroscopy.[1] He cites his 1981 abstract that describes a lack of smooth muscle in arteries of the germinal matrix.[2] We have cited this work in relation to the pathogenesis of germinal matrix-intraventricular hemorrhage many times, including very recently.[3] The work of others has shown that this lack of muscularis includes virtually all arterial vessels penetrating the cerebral parenchyma in the third trimester of human gestation.[4] Thus, it is tempting to conclude that a pressure-passive state of the cerebral circulation in the sick premature infant relates simply to this expression of vascular underdevelopment.

Although it is likely that the vascular anatomic factors are important in the pathogenesis of a pressure-passive cerebral circulation, it is not likely to be "the whole story." For example, there is good evidence that in some premature infants there is a degree of intact cerebrovascular autoregulation (see reference 3). This finding is not unexpected because elegant studies in dogs show that large cerebral arteries in the subarachnoid space proximal to penetration of the cerebral parenchyma account for 20% to 50% of the changes in cerebrovascular resistance that occur in response to alterations in blood pressure and blood gases.[5–8] It is likely that in the healthy premature infant the status of cerebrovascular autoregulation is similar to that in certain immature animals: the autoregulatory range is relatively narrow, and the resting mean arterial blood pressure is dangerously close to the lower limit of the autoregulatory plateau.[9–10] Because of the propensity of autoregulation to disturbance by modest hypoxemia, hypercarbia, disturbances in such endothelial-derived signals as nitric oxide and endothelin-1, and probably many factors to be determined, it is perhaps not surprising that the sick premature infant is so likely to develop a pressure-passive cerebral circulation. The challenge is to define the causes of this cerebrovascular abnormality and the means of correction or at least amelioration. The use of continuous near-infrared spectroscopic measurements of the cerebral circulation at least gives us a start by identifying those infants with the abnormality and therefore with the high risk for ischemic and hemorrhagic injury.

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Immunization Status of Internationally Adopted Children

To the Editor.—

Many internationally adopted children arrive in the United States with incomplete or uncertain vaccination status. Some have suggested that even children who have received adequate numbers of vaccines for tetanus and polio have inadequate titers, resulting from poor immunogenicity of the vaccines, impaired immune responses (possibly attributable to malnutrition), or incorrect records.[1,2] Some physicians recommend revaccinating all international adoptees at arrival in the United States.[3] We reviewed the vaccination status and titers of 70 newly arrived internationally adoptees to assess the adequacy of vaccines given in the children's birth countries, and related the results to assessment of their nutritional status at arrival in the United States. We also

	Tetanus	Diphtheria	Pertussis	Polio-1	Polio-2	Polio-3	Measles	Mumps	Rubella
Immune	61%	88	50	58	65	62	90	66	79
Borderline	33	9	0	0	0	0	0	14	4
Not immune	3	3	50	42	35	38	10	19	16

analyzed whether vaccines administered in the orphanage or community differed in immunogenicity.

The children (41 boys, 29 girls) were from Russia (17), China (13), Romania (9), Lithuania (8), Phillipines (6), Kazakhstan (5), Colombia (3), India (3), Guatemala (2), Lebanon (1), Moldova (1), Latvia (1), and Bulgaria (1). The age at arrival in the United States was 38.2 months ± 24.07 months (range: 9 months to 10 years). Age at evaluation was 42.6 months ± 23.6 months (range: 10 months to 10 years 1 month). Sixty-five percent of children had resided entirely in institutional care before adoption. Nutritional status of the children was similar to other populations of international adoptees. *Z* scores for height, weight, and head circumference were −1.53 ± 1.34; −1.10 ± 1.20; and −1.10 ± 1.28, respectively. Many children had associated medical problems including parasites (25%), infections (25%), rickets (11%), birth defects (9%), reactive purified protein derivative (9%), severe anemia (5%), hepatitis B or C (5%), elevated lead levels (3.5%), uncertain age (3.5%), and hemophilia (1.7%).

Titers (enzyme-linked immunosorbent assay/neutralizing antibodies) were obtained in children who had received ≥3 diphtheria, pertussis, and tetanus, or polio vaccines, or vaccination against measles, mumps, or rubella. No child had received vaccines in the United States at the time samples were collected. Percent of children with adequate immunity for each disease is shown:

No relation was found between immunity and the age, nutritional status, or associated medical problems of the child, or the site of vaccine administration (community versus orphanage).

This survey confirms that immune responses to vaccines administered by sending countries to international adoptees are incomplete, and that a significant percentage of children lack adequate immunity despite satisfactory vaccination records. We conclude that international adoptees should be tested for titers to vaccine-preventable diseases to ascertain their immune status on arrival and to guide decisions about revaccination.

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End-of-Life Care

To the Editor.—

Recently, the care that pediatricians provide to dying children has begun to attract attention.[1] Numerous specialty boards and organizations, including the American Academy of Pediatrics, have developed professional standards on end-of-life care for their members.[2,3] Although it may not be accurate to attribute inadequate end-of-life care to a single factor, insufficient training of clinicians in palliative care methods is undoubtedly a major contributor to the problem.[4] Certainly, the textbooks used to train pediatricians must share some of the blame. Our previous research has revealed grossly deficient coverage of end-of-life content in 50 best-selling medical textbooks, including 4 top pediatrics textbooks.[5] Although some of the pediatrics textbooks did include chapters devoted to end-of-life care, the amount of clinically useful content throughout these texts was limited. As a group, the pediatrics textbooks only contained helpful information for an average of 23.5% of expected end-of-life care content. These pediatrics texts were entirely lacking in information for 60.7% of expected end-of-life care content.

Confronted with this scarcity, we have undertaken efforts to encourage publishers, editors, and authors to improve their textbooks' end-of-life content, including adding or enhancing book chapters, cross-referencing, and indexing.[6] As a follow-up to these efforts, we recently surveyed textbook publishers and editors to assess their progress in revising their books.

We have been welcomed by an encouraging initial response. To date, 23 editors (including editors from 2 of the 3 pediatrics textbooks) and 19 publishers of the 50 top-selling textbooks reviewed have responded to the follow-up survey. They report planned or completed expansion of end-of-life content in the next editions of 22 textbooks, including 17 textbooks with new end-of-life care chapters, 17 with revised indexes, and 11 with expanded cross-referencing. In the group of 50 textbooks, more than one third are expanding end-of-life care content in their next editions. Finally, we have received supportive letters from 6 editors and publishers, including a poignant one from a textbook editor dying of metastatic melanoma at the time he wrote us.

Recently, the Robert Wood Johnson Foundation presented awards to honor the textbook publishers, editors, and authors who have been working to make these important changes. On February 21, 2001, at a ceremony at the Last Acts Project National Meeting, the authors presented awards to 1 medical textbook publisher (Lippincott, Williams & Wilkins) and to the editors of 3 textbooks (*Nelson Textbook of Pediatrics,* 16th edition, editors: Richard Behrman, Robert Kliegman, and Hal Jenson; *Textbook of Primary Care Medicine,* 3rd edition, senior editor: John Noble; and *Emergency Medicine,* 5th edition, editor-in-chief: Judith Tintinalli).

Unfortunately, our work is far from completion. Many best-selling textbooks have not yet responded to their specialty boards' suggestions, their readers' needs, or their patients' and parents' demands to improve the care children receive at the end of life. We are committed to monitoring these textbooks over the next several years, and the Robert Wood Johnson Foundation will continue offering awards to those publishers, editors, and authors who improve the end-of-life content of their books. It is essential that the current knowledge about providing excellent palliative care to dying children and that ongoing research about how to do so published in this journal quickly finds its way into the best-selling pediatrics textbooks.

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Methodologic Flaws, Wrong Answers, and Right Questions: Pediatric Office Emergencies

To the Editor.—

In their study of the frequency of medical emergencies in pediatric offices in a small, rural state, Heath et al[1] reached a questionable conclusion that may potentially harm pediatricians and their patients. Their statement that "serious medical emergencies are rare events in the primary care pediatric office" goes beyond their data and appears to reflect several methodologic and analytic flaws:

1. In the retrospective portion of the study, the authors did not identify what was defined as an emergency in the survey of participants. Was an emergency self-identified by the clinician, one of several predefined diagnostic categories (such as status asthmaticus or shock), or based on other criteria? Clearly, how an emergency is defined can lead to substantially different findings and conclusions, but we are never told what definition the authors chose.
2. In the retrospective study phase, there is a distinct possibility of recall bias in asking pediatricians to remember office emergencies that occurred up to 1 year ago. Recall (or anamnestic) bias is a well-known phenomenon in which inaccuracies frequently occur in the recall of distant events.[2]
3. Regarding the prospective study component, assessing the frequency of office emergencies based on "the need to use the emergency kit" is fundamentally flawed. As the authors themselves report (Table 2), most office practices already had many of the equipment and medication items in the kit, so they probably used their own items, rather than opening the kit. Basing emergency frequency on kit use would thus result in an falsely low estimate.
4. In the "Methods" section, another fatal flaw is evident in the prospective study component. The authors define an office medical emergency as "an event that required equipment and intervention beyond the usual and customary scope of pediatric office practice." This is a classic tautology: the emergency by definition must be rare (*not* usual or customary), and the authors indeed find that emergencies *are* rare! It would seem that the definition of office emergencies should be determined by office pediatricians or diagnostic categories, as other researchers[3,4] (including myself[5]) have concluded. Use of such more realistic definitions might have avoided Heath et al's dubious finding (Table 3) that only 10 asthma office emergencies occurred in 1 year in the whole state of Vermont.
5. The external validity of the study findings is questionable. Somehow the authors lose sight of Vermont being "a small, rural state" (to use words from their title), whose situation may not apply to many other regions of the country. The authors suddenly extrapolate their findings to the nation, concluding that "serious medical emergencies are rare events in the primary care pediatric office." This contradicts findings from all other studies[3–6] on the prevalence of pediatric office emergencies, which should have alerted the authors to flaws in their study design. In addition, this conclusion gives the impression that the authors have "shot themselves in their own foot," because, if the emergencies were so rare in Vermont, why did they bother performing their extensive educational intervention?

Given these 5 serious methodologic and analytic issues, it becomes clear why this study has the potential to do great harm to pediatricians and their patients. Because of methodologic flaws, Heath et al have obtained the "wrong answer" to the right question. The erroneous conclusion that "serious medical emergencies are rare events in the primary care pediatric office, occurring less than once per office per year" may produce a false complacency in the office pediatrician, leading him or her to be unequipped and unprepared for common, serious events. For example, we found that there was a median of 24 emergencies per pediatric office practice annually in Fairfield County, including at least 1 emergency monthly in 82% of practices, at least 50 emergencies annually in 25% of practices, and >100 emergencies per year in 1 of 8 practices.[5] Pediatric office emergencies should not be dismissed as "rarities" based on a single, flawed study that ignores the findings of all other studies.[3–6] We owe it to the children we care for to be prepared for their life-threatening office emergencies and to make clinical decisions based on rigorous data.

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In Reply.—

We appreciate the comments offered by Dr Flores.

We began our study believing that medical emergencies in the pediatric office setting were common events, and that most pediatric offices were not well-equipped to manage them. Our multidisciplinary educational program and equipment donation was an attempt to help pediatricians in Vermont offer more uniform care to their patients with serious medical emergencies.

Defining a medical emergency was problematic when we began our study and remains so today. There is no uniform consensus in the medical community or the insurance industry as to what constitutes a medical emergency. The American Academy of Pediatrics' Committee on Pediatric Emergency Medicine comments on the lack of universal understanding and application of a definition of "emergency"; the lack of third-party use of the prudent layperson standard for definition of emergency; and the retroactive denial of third-party payment when diagnostic signs and/or symptoms suggest an emergent condition, but final diagnosis (often after treatment) is "nonemergent."[1]

In our retrospective study we specifically did not offer a menu of diagnoses to define an emergency. We asked our participants to use their own definition. As "beauty is in the eye of the beholder," we wanted to understand what the practicing pediatrician considered a medical emergency without the bias of how emergencies were defined in the literature. The recall bias that Dr Flores appropriately points out can be applied to any retrospective study of this type, including the literature on pediatric office emergencies.[2–6] We undertook our prospective study to eliminate this reporting bias. In his own study, Dr Flores noted that there may have been interpractice variability in the estimates of office emergencies because of differences in definitions of emergent and nonemergent cases.[6] It is interesting to note that our study group's retrospective estimates of the frequency of office emergencies, 0.9 per office per year, is very close to our prospective study's result of 0.8 emergencies per office per year.

Our kits were uniform and available in every office. Four practices consolidated our equipment with existing resuscitation kits. Study participants used the donated or consolidated kits for all medical emergencies. There was no unreported use of the resuscitation kits. Dr Flores's speculation concerning unreported use of emergency drugs or equipment is unwarranted.

The retrospective literature on the frequency of pediatric office emergencies offers a wide range in the estimate of medical emergencies per office per year—from a low of 1.2 emergencies per office per year[3] to a high of 38 emergencies per office per year.[5] We would disagree that our findings of approximately 1 emergency per office per year "contradicts finding from all other studies."

We believe that our definition of an emergency as "an event that requires equipment and intervention beyond the usual and customary scope of office practice" is accurate and useful. Pediatric offices are not emergency departments. Office visits in pedi-

TABLE 1. Background, Data Entry, and Outcome Variables for Massage Therapy Studies

	Field et al, 1986		Scafidi et al, 1990		Moyer-Mileur et al, 1995		Current	
	Control	Massage	Control	Massage	Control	Massage	Control	Massage
Birth weight	1268 (199)	1280 (249)	1180 (176)	1173 (176)	1240 (182)	1207 (172)	1426 (375)	1343 (422)
Gestational age	31 (2.8)	31 (2.2)	30 (2.0)	30 (2.1)	29 (1.5)	28 (1.3)	30 (2.2)	30 (2.8)
Weight at Entry	1385 (131)	1393 (114)	1303 (122)	1322 (76)	1207 (130)	1166 (188)	1755 (117)	1773 (192)
M weight gain	17 (6.7)	25 (6)	28.4 (5.5)	33.6 (5.4)	13.4 (2.8)	17.8 (2.8)	34.9 (11.9)	31.6 (11.4)
	47% ↑		21% ↑		33% ↑		No significant change	

atric practices fall into 3 major categories: health supervision, acute illnesses, and chronic problems, both medical and behavioral. Most pediatricians would classify medical emergencies as a subset of acute illness visits. The interpractice variability in the estimates of office emergencies attributable to differences in definitions was eliminated in our study design. During the study period many children in Vermont were treated for asthma. It was practicing pediatricians who determined if their patient's exacerbation of asthma constituted a medical emergency.

Vermont is a small, rural state. Our study represents a unique scope of participation over an entire geographic area. We offer the first prospective look at medical emergencies in the pediatric office setting. We would hope that our findings could be confirmed or refuted by a larger prospective study.

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Evidence-Based Medicine and Massage

To the Editor.—

Over the past 20 years, randomized, controlled studies have evaluated tactile/kinesthetic stimulation effects (more popularly referred to as massage therapy) for preterm infants residing in neonatal intensive care units. The protocol in these studies typically involves administering 30 to 45 minutes of daily stroking and flexion and extension of extremities to medically stable preterm infants. The massage therapy is provided in 10- to 15-minute sessions, 3 times a day, for 2 to 4 weeks.

Critical findings from 3 studies indicate a 21% to 47% greater weight gain for the massage therapy versus the standard care control group. Other findings of interest include greater bone mineralization,[1] earlier hospital discharge,[2,3] and more optimal behavioral and motor responses for the massage therapy group.[2,3] These findings and a meta-analysis of 19 studies indicating that 72% of infants receiving massage therapy did better than controls support the view that massage therapy improves the clinical and developmental course of preterm infants.[4]

In a more recent study, we were unable to replicate the weight gain findings when the massage therapy was performed on medically stable preterm infants who were within 7 to 10 days of discharge from a neonatal intermediate care unit (Table 1). A closer inspection of the data revealed that the preterm weight at time of entry for the current study was approximately 468 g greater (*M* entry weight = 1764) than that of the earlier studies (*M* entry weight = 1296). Massage therapy apparently facilitates weight gain only if the intervention is started when the preterm infant weighs between 1100 and 1300 g.

Given that the percent of preterm births rose to 11.8% over the past decade[5] and weight gain is a critical measure for evaluating growth and well-being in the preterm infant, interventions, such as massage therapy, that promote weight gain should be of interest to the neonatologist and should be implemented at a time when they yield the most benefit. Underlying-mechanism studies are currently underway to examine massage therapy effects on IGF-1, oxytocin, and gastric motility with preterm infants weighing between 1100 and 1300 g at entry.

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Sedation for Electroencephalograms

To the Editor.—

Olson et al,[1] in a retrospective review, report their experience regarding electroencephalograms (EEGs) in 2855 children, of which 513 received sedation. The authors are to be complimented for describing methods that allowed successful completion of most EEG examinations while avoiding the need for sedating medications. This is particularly stunning considering that the percentage of sedated children dropped from 32% in 1995 to 2% in 1998. The patients were monitored in accordance with the American Academy of Pediatrics (AAP) guidelines.[2] But, as with any retrospective study, there are some problems: the data are only as good as the information recorded on the charts, and there is likely to be some degree of underreporting. Nevertheless, there were 3 complications (desaturations in children at increased risk).

The accompanying commentary by Dr Freeman[3] raises grave concerns. I agree with the hypothesis that any time a child is sedated there is a risk:benefit ratio, and the benefit needs to outweigh the potential risk. I would not, however, rely on the Olson study as providing adequate information to measure this risk. The number of patients is quite small for looking at rare events such as the need to perform positive pressure ventilation, the need for resuscitation, or resultant injury.[4,5] Such severe ad-

verse outcomes are, fortunately, very rare. Five hundred patients is a completely inadequate number to truly estimate risk. I agree with Dr Freeman that overdoses of chloral hydrate or any drug should never occur especially for a purely elective procedure. However, medication errors do occur at the hands of technologists, nurses, and physicians, as well as dentists.[6] That is but one of the important reasons that monitoring guidelines were developed for children undergoing sedation for diagnostic procedures. Dr Freeman has focused only on the patients in the Olson report[1] who received chloral hydrate while ignoring those who received 2 to 4 sedating medications. Several studies have demonstrated increased risk for children receiving 3 or more sedating medications.[7,8] As Olson so nicely described, because an appropriate "safety net" was in use (pulse oximetry and skilled nursing personnel observing the patients), these complications were readily recognized, and the patients were rescued successfully, ie, the events did not progress to severe hypoxemia or worse. Dr Freeman suggests that an EEG technician could be adequately trained to obtain the study, observe the patient at the same time, and then intervene successfully should an adverse outcome occur! The AAP guidelines are not limited to just patient observation during the procedure, but describe a systematic approach to sedation. This includes a careful screening process and physical examination to anticipate those patients who are at greater risk and continued observation after the procedure until the patient has recovered. EEG technicians do not have the skills and training for these important components of care. The reason that a skilled practitioner with resuscitation skills needs to be available was confirmed by the Olson study, even with the small number of patients reported.

Dr Freeman suggests that the guidelines published by the Joint Commission on Accreditation of Healthcare Organizations[9] as well as those of the AAP[2] were developed by anesthesiologists with a "conflict of interest." Although anesthesiologists were consulted in the development of these guidelines, the guidelines were only published after review and approval by all 39 sections of the Academy as well as endorsement by the Executive Board of the AAP. The Academy is made up of over 50 000 members, of which only about 350 are anesthesiologists. The primary responsibilities of anesthesiologists are related to the perioperative care of children. Anesthesiologists are usually only involved in sedation services at the request of hospitals, pediatricians, or other practitioners. Their involvement and consultation in the development of the AAP guidelines is a powerful pediatric safety advocacy supported by the entire Academy membership and not a conflict of interest!

The sarcasm at the end of Dr Freeman's commentary about pulse oximetry and sudden infant death syndrome seems inappropriate and out of place in the context of this discussion. I am greatly disappointed that instead of looking at the positives, Dr Freeman chooses to look at the negatives. The enhanced level of safety for patients that has come from the widespread adoption of the AAP guidelines is a significant advance for children.

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ERRATUM

Two editing errors occurred in a letter to the editor entitled "Circumcisions: Again" by Dr Thomas B. Newman that appeared in the August 2001 issue of *Pediatrics* (2001;108:522–523).

On page 523 in the last paragraph of Dr Newman's letter, the sentence that now reads: "In fact, according to the US Renal Data Service, end-stage renal disease (ESRD) in children younger than 20 years old has an annual incidence of only about ***13 million per year,*** of which only about 2.7% is attributed to chronic pyelonephritis or reflux nephropathy.[6]" That sentence should read: "In fact, according to the US Renal Data Service, end-stage renal disease (ESRD) in children younger than 20 years old has an annual incidence of only about ***13/million/year,*** of which only about 2.7% is attributed to chronic pyelonephritis or reflux nephropathy.[6]"

Likewise, in that same paragraph, the sentence immediately following the one above now reads: "Over the next 25 years the annual incidence rises to ***109 million per year,*** but the proportion attributed to chronic pyelonephritis or reflux nephropathy declines to 0.7%." That sentence should read: "Over the next 25 years the annual incidence rises to ***109/million/year,*** but the proportion attributed to chronic pyelonephritis or reflux nephropathy declines to 0.7%."

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