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Blue Balls

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Letters to the Editor

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Blue Balls

To the Editor.—

We read with interest the case report and discussion on "blue balls."[1] We agree with the authors' conclusions that "a greater awareness and discussion of this entity would benefit both physicians and their patients." The condition described, what the urologists often term "epididymal hypertension," and some have labeled "deadly sperm buildup" or "DSB," has many other manifestations of which physicians and their caretakers ought to be aware. Other common presentations of this condition include an altered sensorium, thought to be the result of increased cerebrospinal fluid turbidity levels; and decreased visual acuity secondary to cloudiness of the fluid in the anterior chamber of the eye. The latter condition can be diagnosed by the finding of an anterior chamber meniscus.

In the discussion of treatment, however, we wonder whether the authors' suggestion that "straining to move a very heavy object" is the first choice "simple maneuver [that] could bring immediate relief." As this condition is coming to light in a highly respected pediatric journal, perhaps we should resurrect the advice of former Surgeon General Jocelyn Elders and teach masturbation in the schools. This novel idea, which led to her removal from office, should have been implemented yesterday.

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REFERENCE

1. Chalett JM, Nerenberg LT. Blue balls: a diagnostic consideration in testiculoscrotal pain in young adults: a case report and discussion. *Pediatrics.* 2000;106:843–844

To the Editor.—

We read with great interest the case report of acute testiculoscrotal pain after unsatisfied sexual arousal.[1] The authors perform a great service for the field of adolescent medicine by exposing this condition for the true medical problem it is. Countless young men have, no doubt, suffered unnecessarily, as effective treatments are available. However, we believe that the report leaves some ambiguities unresolved:

1. The authors suggest that sexual release is an effective treatment. What are the ethical implications of such a statement? Will young men demand sexual satisfaction of their partners as essential medical therapy? Do the authors condone self-treatment? What about potential adverse effects of treatment, such as blindness and palmar hypertrichosis (personal communications, our mothers)?
2. What are the ethical and/or medical responsibilities for the health care team in treating young men in an urgent care setting? And if treatment is rendered, are there appropriate diagnostic and treatment codes for billing purposes?

We applaud the audacity of the authors to initiate a rational, scientific discussion on this subject that will, we fervently hope, put an end to this dreaded affliction. In the meantime, perhaps the old adage should be amended: "Abstinence makes the gems grow bluer."

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1. Chalett JM, Nerenberg LT. Blue balls: a diagnostic consideration in testiculoscrotal pain in young adults: a case report and discussion. *Pediatrics* 2000;106:843–844

In Reply.—

We thank Drs Rockney and Alario as well as Drs Weinzimer and Thornton for their insightful and amusing letters. It's clear to us that blue balls really exists, and that it is a humorous as well as legitimate topic for medical discussion. The *News Tribune* of Tacoma presented an article (October 2, 2000) about our case report and discussion that, like the letter-writers, balanced information and levity.

A 70-year-old retired college professor told us anecdotally that in Los Angeles public schools in the 1940s a practicing physician taught him and his fellow eighth-graders about sexuality, including "lover's nuts." The doctor told them that masturbation was at times a legitimate medical treatment. As Drs Rockney and Alario point out, Dr Jocelyn Elders lost her job for suggesting the same.

Dr Dean Edell received numerous live phone calls on his national radio program after the October issue of *Pediatrics* was published and later interviewed Dr Chalett on the air. He too stressed the relevance of teaching ourselves and our patients as much about everyday issues (nutrition, stress, human sexuality) as we do about exotic and complicated diseases. He too was candid about how many complaints he would receive for even saying "masturbation" on the air, even if he did not advocate it.

Blue balls is real, yet the condition has been overlooked in the medical literature, adding unnecessary mystique and charge to a common condition. In no way should the pain of blue balls be an excuse to inappropriately advance a sexual relationship. As part of sexual education, we might teach that sexual urges are natural, abstinence is a real choice, and sexual decisions ought never to be based on coercion or exploitation.

We are not advocating any particular treatment method but are proposing education and communication. Sexual release will alleviate the pain of blue balls, but if a Valsalva maneuver offers pain relief, this option must also be taught so another nonsexual choice is available.

Drs Weinzimer and Thornton ask about appropriate billing codes for diagnosis and treatment of this entity, and, of course, we must recommend code blue. They "fervently hope" for "an end to this dreaded condition"; about this we can offer assurance—blue balls is real, and a cure is coming.

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Effect of Inhaled Corticosteroids on Growth

To the Editor.—

I read with interest the meta-analysis of Sharek and Bergman[1] regarding the effect of inhaled corticosteroids (ICS) on growth, and felt it was important to address 2 issues in response. First, the authors' analysis of the growth effect seen during treatment with fluticasone propionate (FP) 200 μg/day indicated a small but statistically significant reduction in growth rate compared with placebo. This differs from the nonsignificant *P* value reported in our original paper,[2] and an explanation for this discrepancy is required. Second, the conclusions arrived at by the authors are nevertheless weakened by a failure to review other growth studies in which FP was the active comparator. The result is a message that may be confusing to practitioners caring for children with asthma.

I would like to begin by addressing the different conclusion arrived at by Drs Sharek and Bergman regarding the effect on growth with FP 200 μg/day. As indicated in our study, we compared the effect of FP 100 μg/day and FP 200 μg/day with placebo in prepubescent children.[2] The data for the children who remained prepubertal throughout the study were analyzed by analysis of variance (ANOVA) controlling for investigator. We reported a nonsignificant *P* value of .313, which supported our hypothesis that growth was not significantly impaired after 1-year treatment with FP 100 μg/day or 200 μg/day. I submit that Drs Sharek and Bergman most likely did not have the complete FP data available to them for their meta-analysis. Hence, it appears that the 95% confidence interval reported in their paper was calculated from the raw mean data that we reported along with the sample sizes obtained from Table 1 in our paper, which described the clinical characteristics of the prepubertal children at screening. The number of prepubertal children who actually completed the trial was less than that indicated by Table 1. The numbers of prepubertal children treated with placebo or FP 200 μg/day who completed the study were 57 and 79, respectively. The analysis in our paper used these smaller sample sizes and controlled for investigator interaction effects. Using this same basis for analysis, one would calculate a 95% confidence interval of (−0.86, 0.1). This confidence interval includes the zero value and supports the conclusion of our original paper. To not use the smaller sample sizes increases the probability of committing a type 1 error. In addition, including a parameter (used in the model to calculate *P* values and confidence intervals) for "investigator interaction effects" controls for the potential of asthmatic children with a specific disease severity being recruited at some, but not all, sites. Likewise, as height is measured at each research site, with the data pooled among all sites, the investigator interaction parameter controls for potential inconsistency in stadiometric height measurements by the different study-site coordinators. In their analysis of the data, I do not believe that Drs Sharek and Bergman took this parameter into consideration. Furthermore, as indicated in our paper, we believe that mean change from the baseline growth velocity more accurately assesses the effects of inhaled steroids on growth. As such, we reported no effect of FP 200 μg/day on this parameter, with an overall *P* value of .380 by ANOVA; a pairwise comparison of the prepubertal children who completed the trial and received either placebo or FP 200 μg/day resulted in a *P* value of .223 with a 95% confidence interval of (−0.83, 0.25).

The robustness of the conclusions of Drs Sharek and Bergman with respect to FP is undermined by the paucity of the data presented. In their search strategy, the authors excluded trials with nonsteroid control arms. This eliminates head-to-head comparisons of ICS that provide the practitioner with relevant information regarding potential for adverse growth effects. Although active control studies could not be included in the meta-analysis based on the authors' selection criteria, they could have been included in the discussion for comparative purposes. The studies of de Benedictis et al[3] (FP vs beclomethasone), Ferguson et al[4] (FP vs budesonide), and Price and colleagues[5] (FP vs cromolyn) demonstrate that FP has significantly less effect on growth than beclomethasone[3] or budesonide[4] at clinically equivalent doses, and a similar effect when compared to cromolyn.[5] This reduced effect of FP on growth could have been clearly illustrated in Figure 1 of the article, but the weighted mean difference (WMD) for FP 200 μg/day was inexplicably excluded from this figure.

When considering potential systemic effects of ICS, it is important to keep in perspective the relative benefits and risks of ICS therapy for asthma. The recently published prospective study by Agertoft and Pedersen[6] demonstrated that the administration of inhaled budesonide to asthmatic children had no effect on these children attaining final adult height, which was similar to asthmatic children who did not receive inhaled steroids, as well as healthy children. Furthermore, Suissa et al[7] recently showed that the regular use of low-dose ICS is associated with a decreased risk of death from asthma. In their study, the rate of death from asthma among users of ICS decreased by 21% for every additional canister used during the previous year and by 54% for every canister used in the previous 6 months. In both children and adults, the risk of systemic effects of ICS, already markedly reduced compared with oral corticosteroids, can be minimized by titrating to the lowest effective dose.

Although the methodology is admirable, the authors' emphasis on meta-analytical technique obscures the central message of their manuscript. Many paragraphs describing statistical tests assure the reader that the proper route to a meta-analysis has been followed. However, the results do not allow for any generalization nor do they provide the medical professional with any clear sense of differences among ICS or differences among doses. Consequently, this meta-analysis does not fulfill its potential to enhance the full picture of ICS and their use in pediatric asthma.

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REFERENCES

1. Sharek PJ, Bergman DA. The effect of inhaled steroids on the linear growth of children with asthma: a meta-analysis. *Pediatrics.* 2000;106(1). Available at: http://www.pediatrics.org/cgi/content/full/106/1/e8
2. Allen DB, Bronsky EA, LaForce CF, Nathan RA. Growth in asthmatic children treated with fluticasone propionate. *J Pediatr*. 1998;132:472–477
3. de Benedictis FM, Medley HV, Williams L. Long-term study to compare safety and efficacy of fluticasone propionate (FP) with beclomethasone dipropionate (BDP) in asthmatic children. *Eur Respir J.* 1998;12(suppl); 142S
4. Ferguson AC, Spier S, Manja A, Versteegh GA, Mark S, Zhang P. Efficacy and safety of high-dose inhaled steroids in children with asthma: a comparison of fluticasone propionate with budesonide. *J Pediatr.* 1999;134:422–427
5. Price JF, Russell G, Hindmarsh PC, Weller P, Heaf DP, Williams J. Growth during one year treatment with fluticasone propionate or sodium cromoglycate in children with asthma. *Pediatr Pulmonol.* 1997;24: 178–186
6. Agertoft L, Pedersen S. Effect of long-term treatment with inhaled budesonide on adult height in children with asthma. *N Engl J Med.* 2000;343:1064–1069
7. Suissa S, Ernst P, Benayoun S, Baltzan M, Cai B. Low-dose inhaled corticosteroids and the prevention of death from asthma. *N Engl J Med.* 2000;343:332–336

In Reply.—

Thank you for the opportunity to reply to the letter to the editor by Dr Allen. Below, we address these concerns in the order presented by Dr Allen.

The first major concern expressed by Dr Allen is the difference in statistical significance we obtained for the randomized, controlled clinical trial of Allen et al[1] included in our meta-analysis.[2] As described in our work, we only included studies that provided the direct outcome of linear growth velocity or data convertible to linear growth velocity as an outcome. One purpose, and a major strength of the meta-analysis technique, is to combine similar data to provide a larger number of study participants yielding a more accurate estimate of effect size. This approach combines linear growth velocity (cm per year) data from each study included in the analysis. In Dr Allen's study, the control and intervention groups were effectively randomized. Participants from each group were similar in demographics, clinical characteristics, concurrent asthma medications, oral steroid usage during the study, and compliance rates. The assumption that occurs in a randomized trial is that control and intervention subjects are similar with respect to unknown confounders as well. This assumption is valid if randomization was performed effectively. Given the method of randomization used, use of an off-site envelope, we believed this to be true. Data from Dr Allen's study was therefore directly abstracted and entered into the Review Manager Version 3.1 statistical package (Cochrane Collaboration, Oxford, England) used by the Cochrane Collaboration,[3] revealing a significant difference between the participants using fluticasone propionate 200 μg/day and placebo. Efforts to contact the statistician involved in the Allen et al study to discuss some of these issues were unsuccessful.

Dr Allen is also concerned that we "most likely did not have the complete fluticasone propionate data available." This is true, as many important study details were not provided in his article. We were able to estimate the number of participants remaining in the placebo control and fluticasone propionate 200 μg/day groups using the numbers presented and the text. The correct numbers of patients completed in the control group (57) and the fluticasone propionate 200 μg/day group (79) were estimated correctly and used in our calculations. We were not able to control for "investigator interaction effects" as described. The technique of meta-analysis, if viewed as a trial whose subjects are the articles included, should balance out such parameters when the studies included are of large enough numbers. Clearly, because Dr Allen's study was the only one evaluating fluticasone propionate that passed our strict inclusion/exclusion criteria, this assumption is not necessarily a safe one.

Dr Allen states "the robustness of the conclusions of Dr Sharek and Bergman with respect to [fluticasone propionate] is undermined by the paucity of the data presented." We disagree. Regarding robustness, we clearly stated in the first paragraph of the discussion section: "Caution must be used when generalizing about fluticasone, however, because only one study was incorporated and the magnitude of effect was smaller that that of beclomethasone." In addition, we stated in the first paragraph of the conclusion section: "It would be inappropriate to judge the effect of moderate doses of inhaled fluticasone based on the 1 included study." Regarding the paucity of data, our search strategy revealed only one study that had the degree of scientific rigor we felt necessary to draw appropriate conclusions. Researchers who conduct meta-analysis believe one well-done study provides more valid conclusions than do many poorly done studies.

Dr Allen conveys disappointment in our disinterest in comparing 1 inhaled steroid to another to provide relevant information for potential for adverse growth effects. This, however, was beyond the scope of our meta-analysis. As described in the objective section of our abstract, we wished "to determine whether inhaled steroid therapy causes delayed linear growth in children with asthma." Given the persistent uncertainty in the literature and in practice as to whether inhaled steroids do decrease linear growth, we felt it important to first attempt to answer this more basic question comparing an inhaled steroid to a nonsteroidal control. One study cited by Dr Allen, by Price and colleagues,[4] was reviewed for potential inclusion in our meta-analysis but did not meet the inclusion criteria (many of the patients randomized to the cromolyn arm were switched to the fluticasone propionate arm midway through the study). The other 2 studies cited[5,6] compared 2 different inhaled steroids without a nonsteroidal control group and therefore were removed from consideration based on our inclusion/exclusion criteria. Because we believe we conclusively showed moderate doses of beclomethasone and fluticasone do decrease linear growth velocity in the first year of use, it would therefore appear that direct comparisons are important to determine which inhaled steroid has the smallest growth effect. In our opinion, this question requires a different study design and wouldn't lend itself well to a meta-analysis design. Finally, we chose not to include the fluticasone propionate study in Figure 1 of the article (a weighted mean difference graph) because we suspected, a priori, that each inhaled steroid affects linear growth differently. We therefore subgrouped our results based on the inhaled steroid used and presented in Figure 1 ("inhaled beclomethasone in children with asthma") the data from the beclomethasone subgroup.

Dr Allen suggests that "it is important to keep in perspective the relative benefits and risks of inhaled corticosteroid therapy for asthma." We fully agree. In our conclusion section we state: "The negative effect on linear growth velocity needs to be weighed against the known positive effects of inhaled steroids on such outcomes as quality of life, symptom days, severity of exacerbations, decreased lung architectural changes, and health care utilization before clinical significance is clear." We did not suggest that inhaled steroids should be eliminated from the list of useful medications for childhood asthma but rather that caution should be exercised, doses should be minimized to the lowest effective dose, and height should be followed when they are used. We stated that the effects of inhaled steroids when given for more than 54 weeks, or the effects on adult height, remain unknown. Data published since our meta-analysis was published have shed additional light on the effect of inhaled steroids on adult height.[7] Interestingly, this same data showed decreases in linear growth velocity in the first few years of the trial of inhaled steroids before catchup growth was displayed. This is consistent with our findings, and, if valid, this adult data is reassuring.

Dr Allen believes our publication focused on showing "the proper route to a meta-analysis was followed," which resulted in "an obscuring of the central message." We did discuss in necessary detail the methods of the meta-analysis, as we wished to provide strong evidence that the results obtained were valid. Regarding Dr Allen's concerns that our "results do not allow for any generalization nor do they provide the medical professional with any clear sense of differences among inhaled corticosteroids or differences among doses," we suggest that we have clearly shown beclomethasone in moderate doses decreases linear growth velocity for at least 54 weeks in children with asthma. We sacrificed generalizability to ensure internal validity. Before our meta-analysis was published, we believe this question was not answered conclusively.

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REFERENCES

1. Allen DB, Bronsky EA, LaForce CF, et al. Growth in asthmatic children treated with fluticasone propionate. *J Pediatr.* 1998;132:472–477
2. Sharek PJ, Bergman DA. Inhaled steroids and growth in children with asthma: a meta-analysis. *Pediatrics.* 2000;106(1). Available at: http://www.pediatrics.org/cgi/content/full/106/1/e8
3. Mulrow CD, Oxman AD, ed. *Cochrane Collaboration Handbook* [updated March 1, 1997]. In: The Cochrane Library [database on disk and CDROM]. The Cochrane Collaboration. Oxford: Update Software; 1996. Updated quarterly
4. Price JF, Russell G, Hindmarsh PC, Weller P, Heaf DP, Williams J. Growth during one year treatment with fluticasone propionate or sodium cromoglycate in children with asthma. *Pediatr Pulmonol.* 1997;24:178–186
5. De Benedictis FM, Medley HV, Williams L. Long term study to compare safety and efficacy of fluticasone propionate with beclomethasone dipropionate in asthmatic children. *Eur Respir J.* 1998;12(suppl):142S
6. Ferguson AC, Spier S, Manja A, Versteegh GA, Mark S, Zhang P. Efficacy and safety of high-dose inhaled steroids in children with

asthma: a comparison of fluticasone propionate with budesonide. *J Pediatr.* 1999;134:422–427
7. Agertoft L, Pedersen S. Effect of long-term treatment with inhaled budesonide on adult height in children with asthma. *N Engl J Med* 2000;343:1064–1069

Alternating Antipyretics: Is This an Alternative?

To the Editor.—

We read with interest the article by Mayoral et al.[1] We would like to describe a case of acute renal failure that may add to the general discussion regarding alternating antipyretics. A 14-month-old previously healthy girl was admitted to Bryn Mawr Hospital for febrile status epilepticus. Initial laboratory studies revealed a normal head computed tomography scan, normal cerebrospinal (CSF) studies, and negative bacterial cultures of the blood, urine, and CSF. Initial electrolytes were normal, and initial blood urea nitrogen (BUN) and creatinine were 16 mg/dL and 0.5 mg/dL, respectively. The patient received the following anticonvulsants: lorazepam, phenytoin, and phenobarbital. After initial control of the seizures, the patient was maintained on phenobarbital without additional seizure activity. The only other drug initially administered was ceftriaxone, which was continued for 72 hours pending negative bacterial cultures. The patient's initial course was one of general improvement, but she continued to have fever. On hospital day 6 the patient spiked a temperature to 105.0, and additional evaluation was undertaken but was unrevealing. At this same time, given the height of the fever, the patient received an alternating regimen of acetaminophen and ibuprofen. The patient had some loose stools during this same interval, but did not receive parenteral fluids. On day 8 of hospitalization the patient had further laboratory evaluation that revealed a BUN of 63 mg/dL and creatinine of 3.4 mg/dL. The patient had an extensive renal evaluation, including a pediatric nephrology consultation, without discovering a definite cause for the acute renal failure. The patient had no features of hemolytic-uremic syndrome, systemic lupus, obstructive uropathy, or sickle cell disease. The patient was treated with careful medical management and she gradually recovered. She was discharged on hospital day 15 with a BUN of 15 mg/dL and creatinine of 0.9 mg/dL. She has gone on to have a full recovery. We believe that the acute renal failure was attributable to the additive and synergistic renal toxicities of acetaminophen and ibuprofen, in a patient who was moderately dehydrated. McIntire et al[2] pointed out that acetaminophen and nonsteroidal anti-inflammatory drugs (NSAIDs) may cause renal failure synergistically by oxidative metabolites of acetaminophen accumulating in the renal medulla during renal ischemia, which can be caused by NSAIDs. We would like to suggest an additional mechanism for toxicity from the combination of acetaminophen and ibuprofen. Eguia and Materson[3] point out that acetaminophen inhibits urinary prostaglandin synthesis, just as NSAIDs do. Thus, you have an additive effect of this toxicity. In the normal participants, this decrease in prostaglandin synthesis does not seem to be clinically relevant, but in impaired individuals can lead to renal injury. We suggest that the synergistic and additive toxicities of acetaminophen and ibuprofen in a mildly to moderately dehydrated child can lead to acute renal failure. Although the clinical event of acute renal failure may be quite rare in the above circumstances, we believe it should be taken into account before prescribing the combination of these antipyretics.

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REFERENCES

1. Mayoral C, Marino R, Rosenfeld W, Greensher J. Alternating antipyretics: is this an alternative? *Pediatrics.* 2000;105:1009–1012
2. McIntire S, Rubenstein R, Gartner J, Gilboa N, Ellis D. Acute flank pain and reversible renal dysfunction associated with nonsteroidal anti-inflammatory drug use. *Pediatrics.* 1993;92:459–460
3. Eguia L, Materson B. Acetaminophen-related acute renal failure without fulminant liver failure. *Pharmacotherapy.* 1997;17:363–370

To the Editor.—

In support of the recent article by Mayoral on "Alternating Antipyretics: Is This an Alternative?"[1] I would add emphasis to their statement that:

> "There is presently no scientific evidence that this combination [acetaminophen and ibuprofen] is safe or achieves faster antipyresis than either agent alone." It has been postulated that they may even "act synergistically and produce tubular toxicity."

Back in 1991, within a 2-year time frame after the approval of prescription ibuprofen for children in the United States, Robert J. Walker wrote in the article "Paracetamol [acetaminophen], Nonsteroidal Anti-inflammatory Drugs (NSAIDs) and Nephrotoxicity"[2] as follows:

> "Renal metabolism . . . is related to generation of nontoxic and toxic paracetamol metabolites . . . The accumulation of paracetamol in the medulla is important in the subsequent generation of chronic nephrotoxicity."
>
> "Under conditions of . . . intravascular volume depletion, paracetamol concentrations will increase in the inner medulla."
>
> "NSAIDs may have a synergistic effect with paracetamol in producing cell toxicity by the reduction in renal blood flow particularly into the medulla. The reduced oxygen gradient that already exists in the renal medulla would be further compromised and hence increase the risk of cellular damage. These potential interactions await experimental confirmation."

Subsequently, in 1993 McIntire and colleagues[3] from Children's Hospital of Pittsburgh reported that:

> ". . . concomitant acetaminophen use [with an NSAID] was present in both cases and its role is more problematic. Acetaminophen accumulates in the renal medulla . . . Oxidative metabolites of acetaminophen can result in medullary cellular necrosis in the absence of reduced glutathione, the production of which is inhibited by agents that inhibit renal prostaglandin synthesis."
>
> "Thus, the tubular toxicity of NSAIDs and acetaminophen are, at least theoretically, synergistic . . . The practice of alternating doses of acetaminophen and NSAIDs for fever control theoretically increases the risk of nephrotoxicity."

In view of the preceding comments and observations, it appears prudent to avoid alternating or simultaneous administration of acetaminophen with ibuprofen. Engaging in wishful thinking may tempt possibly synergistic adverse events.

The individual utility of ibuprofen or of acetaminophen, *separately*, for fever control and associated improved comfort of children, is well-known. The safety record of each is a matter of record, and I would refer colleagues to my letter on ibuprofen safety published in *Pediatrics* in January 1992.[4]

Alternating or combining the two medications is not recommended.

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REFERENCES

1. Mayoral CE, Marino RV, Rosenfeld W, Greensher J. Alternating antipyretics: is this an alternative? *Pediatrics.* 2000;105:1009–1012
2. Walker RJ. Paracetamol, nonsteroidal anti-inflammatory drugs and nephrotoxicity. *N Z Med J.* 1991;182–183
3. McIntire SC, Rubenstein RC, Gartner JC, Gilboa N, Ellis D. Acute flank pain and reversible renal dysfunction associated with nonsteroidal anti-inflammatory drug use. *Pediatrics.* 1993;92:459–460
4. Rosefsky JB. Ibuprofen safety [letter]. *Pediatrics.* 1992;166–167

In Reply.—

We welcome Dr Rosefsky's support of our admonition against the use of combination therapy for the management of fever in children.

Despite the lack of scientific knowledge regarding the use of acetaminophen and ibuprofen in combination or in an alternating regime, physicians have not been dissuaded from practicing this method of antipyresis.

Acetaminophen and ibuprofen act via similar mechanism: they both inhibit cyclooxygenase activity and therefore the formation and release of prostaglandin.[1] In certain settings, such as hypovolemia, inhibition of prostaglandin synthesis may impair renal perfusion.[2] McIntire et al present two cases where patients developed acute flank pain and reversible renal dysfunction after use of nonsteroidal anti-inflammatory agents. In both cases, acetaminophen was also ingested. McIntire suggests that in states of renal ischemia, acetaminophen metabolites may accumulate in the renal medulla and lead to medullary cellular necrosis. Theoretically these two products may act synergistically and cause tubular toxicity.[2]

Dr Del Vecchio and Dr Sundel provide the first documentation of acute renal failure in a patient who also received combination therapy for fever management. This example adds support to our concerns about the safety of this method of antipyresis. There is presently no scientific evidence that the use of this combination achieves faster antipyresis or has greater efficacy than either agent used alone. Because of the lack of evidence regarding the safety of this combination and until properly controlled studies have assessed the risk of combining or alternating these 2 products, we believe it would be prudent for physicians to advise parents to use one single agent during the management of the febrile child.

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REFERENCES

1. Gilman AG, Rall TW. *Goodman and Gilman's the Pharmacologic Basis of Therapeutics.* 8th ed. New York, NY: Pergamon Press; 1990
2. McIntire SC, Rubenstein RC, Gartner JC, Gilboa N, Ellis D. Acute flank pain and irreversible renal dysfunction associated with nonsteroidal anti-inflammatory Drug use. *Pediatrics.* 1993;92:459

Distinguishing SIDS From Child Abuse Fatalities

To the Editor.—

Currently, nearly 3000 children die each year in the United States from sudden infant death syndrome (SIDS).[1] It is therefore important for health care providers to understand this clinical entity and know how to differentiate it from other conditions, including child abuse. The recent position statement from the AAP's Committee on Child Abuse and Neglect[2] updates a previous position statement by this committee[3] on this topic. Although the committee's recommendations are laudable, they now advocate for "examination of the dead infant at a hospital emergency department by a child maltreatment specialist" but do not specify what qualifications a "child maltreatment specialist" must hold. The American Board of Pediatrics does not offer a subspecialty certificate in child abuse (W. W. Tunnessen, Jr, Senior Vice President, American Board of Pediatrics, personal communication, April 2001). The committee should explain and qualify its statement.

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REFERENCES

1. MacDorman MF, Atkinson JO. Infant Mortality Statistics from the 1997 Period Linked Birth/Infant Death Data Set. *National Vital Statistics Reports from the Centers for Disease Control and Prevention.* July 30, 1999; 47:
2. American Academy of Pediatrics, Committee on Child Abuse and Neglect. Distinguishing sudden infant death syndrome from child abuse fatalities. *Pediatrics.* 2001;107:437–441
3. American Academy of Pediatrics, Committee on Child Abuse and Neglect. Distinguishing sudden infant death syndrome from child abuse fatalities. *Pediatrics.* 1994;94:124–126

Day Care and Asthma?

To the Editor.—

I wish to add the following comment to the article by Lanphear et al.[1]

It has been well-established that the prevalence of asthma is increasing, both in the United States and worldwide, with the most rapid increase being in the pediatric population. The reason(s) for this increased prevalence is not known, but clearly risk factors such as environmental tobacco smoke (ETS) and indoor allergens play a role. Other factors such as urbanization, access to health care, diesel particles, and race are involved. Unfortunately, there remains a huge gap in our understanding of this most disruptive disease.

The article by Lanphear et al reviews over 8000 children who participated in the Third National Health and Nutrition Examination Survey (NHANES III). As is true of other reviews, their results highlight the incredible correlation between atopy and asthma, both allergy in the patient and in family members. ETS also shows up as a significant risk factor. The authors then incriminate a gas stove or oven in the home, which barely met significance ($P = .04$), but had nothing to say about the greatly increased risk of a child attending day care ($P = .01$). They failed to mention day care attendance in their abstract, and there is only a transient reference to it at one point in the discussion.

Martinez et al have published a number of articles, both in pediatric journals as well as allergy journals, following a group of children in Arizona. They clearly show an increased prevalence of asthma in children who have had "wheezy illnesses" as youngsters. Surely the association between day care attendance and frequent infections plays a role that needs to be addressed.

The fact that the authors have downplayed day care is clearly a bias on their part (I guess it is not politically correct anymore to suggest that mothers stay home and take care of their children). Instead, they manipulate the discussion to bring out poor housing, subclinical lead toxicity (whatever that is), and fatal injuries—none of which have any correlation to asthma or NHANES III. This bias should have been addressed before publication of the article.

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REFERENCE

1. Lanphear BP, Aligne CA, Auinger P, Weitzman M, Byrd RS. Residential exposures associated with asthma in US children. *Pediatrics.* 2001;107:505–511

Inadequate Internet Resources Cited

To the Editor.—

We applaud the American Academy of Pediatrics for recognizing the need for, and publishing, their guidelines on counseling families about using complementary and alternative medicine (CAM) for their children.[1] Your stated goals of advising pediatricians to evaluate the scientific merits of CAM approaches, identify potential risks, and provide families with information on a range of treatment options are laudable. However, we believe you fall short in your additional call "to guard against bias" in your choices of "Helpful Resources on the Internet" in Appendix I.

Unfortunately, the otherwise excellent information on the University of Texas Center for Alternative Medicine Research's Web site has not been updated since 1998, and a notice published on its home page states, "UT-CAM is no longer operational." In any event, the information on that site is solely about alternative cancer treatments.

Your reference to the Office of Alternative Medicine is likewise dated. The OAM was renamed the National Center for Complementary and Alternative Medicine (NCCAM) in 1998, with an expanded mission and budget. The clinical information on NCCAM's Web site is limited and is unlikely to be of much use for specific decisions on CAM therapies. Their correct URL is http://nccam.nih.gov/.

Of most concern to us are your choices of the Consumer Federation of America (Quackwatch) and the National Council for Reliable Health Information (the National Council Against Health Fraud). Both Web sites are the work of 1 person, Stephen Barrett, MD. Dr Barrett has for many years vociferously campaigned against any and all uses of CAM. The information on these sites is limited to his editorial viewpoint and, in our opinion, is highly biased and not representative of the evidence-based information on CAM that has been published in the medical literature.

We urge physicians and other health care providers to make better use of up-to-date and unbiased sources of information, and to critically evaluate the primary literature for themselves. To that end, two Internet resources may be of value.

1. PubMed is the National Library of Medicine's user-friendly Internet search engine for its Medline database. http://www.ncbi.nlm.nih.gov/PubMed/
2. NCCAM's CAM on PubMed allows one to limit a literature search to those journals that report primarily on CAM research. http://www.nlm.nih.gov/nccam/camonpubmed.html

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REFERENCE

1. American Academy of Pediatrics, Committee on Children with Disabilities. Counseling families who choose complementary and alternative medicine for their child with chronic illness or disability. *Pediatrics.* 2001;107:598–601

Apparently Severe Late-Onset Neutropenia in Two Very Low Birth Weight Infants

To the Editor.—

In 2000, Omar et al[1] reported for the first time late-onset neutropenia in very low birth weight (VLBW) infants. The authors showed an incidence rate of late-onset neutropenia (defined as absolute neutrophil count lower than 1500/mm^3 after 3 weeks of life) as high as 22%. The average nadir of the neutrophil in the neutropenic infants was 1067 ± 44/mm^3. Severe late-onset neutropenia has to our knowledge not yet been described.

We report 2 cases of premature infants who developed apparently severe late-onset neutropenia.

Case 1 was born at 29 weeks of a bichorial biamniotic pregnancy (birth weight = 1.285 kg). The child required artificial ventilation for 2 days and had by then a normal evolution. She received rHuEpo 3 times a week (250 IU/kg) from day 7 to day 40. However, the child required transfusion on day 69. On day 69, a complete blood count performed before the transfusion showed an absolute neutrophil blood count of 423/mm^3. White blood cells were 4700/mm^3, hemoglobin 8.5 mg/dL, and blood platelets 333 000/mm^3. The child was asymptomatic and, as no specific cause was found, no specific treatment was performed. A blood count performed on day 76 showed an absolute neutrophil blood count of 1211/mm^3. The child was discharged on day 77.

Case 2 was born at 28 weeks (birth weight = 1.280 kg) after having developed chronic intrauterine transfusion syndrome that caused the intrauterine death of her twin. She required artificial ventilation for 4 days and had by then a normal evolution. She received rHuEpo 3 times a week (250 IU/kg) from day 7 to day 39. She developed a progressive neutropenia with a nadir of 532/mm^3 on day 69. Hemoglobin was then 9.2 g/dL and blood platelets 353 000/mm^3. The absolute neutrophil blood count slowly increased and the child was discharged on day 75. On day 82, the neutrophil blood count was 1350/mm^3. By then, she had a normal evolution.

Our patients developed late-onset neutropenia as defined by Omar et al, but we think that the decreasing absolute neutrophil blood count could have been worsened by the rHuEpo administration, as reported by Latini et al for non-neutropenic infants.[2] However, the dose of rHuEpo received by our patient was lower than the ones who developed neutropenia in the report of Latini et al (750 IU/kg/week vs 1200 IU/kg/week) and was given 3 times a week rather than 1 time a week.

Omar et al[1] recommend avoiding institution of agressive therapy such as granulocyte colony-stimulating factor (G-CSF) for late-onset neutropenia. However, Christensen et al[3] recommend G-CSF when the absolute neutrophil count is below 500/mm^3 for 2 or 3 days, regardless of the cause.

We believe that additional reports and studies are required before recommending agressive and expensive therapy of late-onset neutropenia, even when the absolute neutrophil blood count is around 500/mm^3.

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REFERENCES

1. Omar SA, Salhadar A, Wooliever DE, Alsgaard PK. Late-onset neutropenia in very low birth weight infants. *Pediatrics* 2000;106(4). Available at: http:www.pediatrics.org/cgi/content/full/106/e55
2. Latini G, Rosati E. Transient neutropenia may be a risk of treating preterm neonates with high doses of recombinant erythopoietin. *Eur J Pediatr.* 1998;157:443–444
3. Christensen RD, Calhoun DA, Rimsza LM. A practical approach to evaluating and treating neutropenia in the neonatal intensive care unit. *Clin Perinatol.* 2000;27:577–601

In Reply.—

I appreciate the opportunity to respond to the letter from Servais et al regarding apparently severe late-onset neutropenia in VLBW infants. The incidence of late-onset neutropenia in our study was 22% (51/225 infants),[1] and the nadir absolute neutrophil count (ANC) in the neutropenic infants was 1067 ± 44/mm^3. Apparently severe late-onset neutropenia, defined as ANC <750/mm^3, was detected in 10 of the infants in our study (4.4%). The mean gestational age of infants with apparently severe late-onset neutropenia was 28 ± 1 weeks (range: 25–32 weeks), and mean birth weight was 1056 ± 96 g (range: 726–1430 g). The nadir ANC was 577 ± 43/mm^3 (range: 279–720/mm^3) with a concomitant hemoglobin of 9.8 ± 0.4 g/dL (range: 6.7–11.1 g/dL), reticulocyte count of 7.5% ± 1.6% (range: 4.2%–14.6%), and platelet count of 339 ± 38 $\times 10^3$/mm^3 (range: 139–497 $\times 10^3$/mm^3). The mean ANC subsequent to the nadir ANC was 1901 ± 351/mm^3 (range: 1044–3180/mm^3). The mean postnatal age at onset was 6 ± 1 weeks (range: 4–10 weeks). This apparently severe late-onset neutropenia was transient and lasted for 1 week in 9 infants and 2 weeks in 1 infant. The lowest ANC of 294 and 444/mm^3 were detected in 2 infants with subsequent increase of ANC to 1125 and 1776/mm^3, respectively. All 10 infants with apparently severe late-onset neutropenia were stable, growing in full oral feeding. In contrast to the 2 infants reported by Sarvais et al, none of the infants in our study received erythropoietin. Late-onset neutropenia is a phenomenon that occurs in VLBW infants with anemia of prematurity and marked reticulocytosis.[1] It seems that neutropenia detected in premature infants treated with erythropoietin[2,3] has a similar mechanism and is secondary to marked reticulocytosis rather than to erythropoietin therapy. We agree with Servais et al and continue to recommend avoiding aggressive and expensive therapy such as G-CSF for late-onset neutropenia, even when ANC is around 500/mm³. Additional studies are needed to examine the incidence of nosocomial infection in stable, growing VLBW infants with late-onset neutropenia. In contrast, G-CSF may be a reasonable therapy for VLBW infants with persistent early-onset neutropenia during the first 3 weeks of life. VLBW infants with early-onset neutropenia are usually sick with multiple foreign bodies, such as central lines, peripheral intravenous lines, and endotracheal tubes, which increase their susceptibility to sepsis. Multiple studies have shown a possible beneficial effect of G-CSF in premature infants with early-onset neutropenia.[4–8]

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REFERENCES

1. Omar SA, Salhadar A, Wooliever DE, Alsgaard PK. Late-onset neutropenia in very low birth weight infants. *Pediatrics.* 2000;106(4). Available at: http://www.pediatrics.org/cgi/content/full/106/4/e55
2. Latini G, Rosati E. Transient neutropenia may be a risk of treating preterm neonates with high doses of recombinant erythropoietin. *Eur J Pediatr.* 1998;157:443–444
3. Halperin DS, Wacker P, Lacount G, et al. Effects of recombinant human erythropoietin in infants with anemia of prematurity. *J Pediatr.* 1990; 116:779–786
4. Russell ARB, Davies EG, Ball SE, Gordon-Smith E. Granulocyte colony-stimulating factor treatment for neonatal neutropenia. *Arch Dis Child.* 1995;72:F53–F54
5. Kocherlakota P, La Gamma EF. Human granulocyte colony-stimulating factor may improve outcome attributable to neonatal sepsis complicated by neutropenia. *Pediatrics.* 1997;100(1). Available at: http://www.pediatrics.org/cgi/content/full/100/1/e6
6. Kocherlakota P, La Gamma EF. Preliminary report: Rh G-CSF may reduce the incidence of neonatal sepsis in prolonged pre-eclampsia associated neutropenia. *Pediatrics.* 1998;102:1107–1111
7. Makhlouf RA, Doron MW, Bose CL, Price WA, Stiles AD. Administration of granulocyte colony-stimulating factor to neutropenic low birth weight infants of mothers with pre-eclampsia. *J Pediatr.* 1995;126: 454–456
8. La Gamma EF, Alpan O, Kocherlakota P. Effect of granulocyte colony-stimulating factor on pre-eclampsia associated neutropenia. *J Pediatr.* 1995;126:457–459

Surprised by Publication

To the Editor.—

Before the 20th century, most infants slept in a bed with their parents. An infant who was suddenly and unexpectedly found dead in such an environment was presumed to have been overlain. More recently, with lack of evidence after a thorough postmortem investigation (autopsy), these deaths have been diagnosed as unexplained or sudden infant death syndrome (SIDS). According to the conclusions of Carroll-Pankhurst and Mortimer,[1] we have apparently come full circle and should attribute the sudden death of younger infants to the proximity of larger parents.

Their study design has some fundamental flaws, not least of which is that the data on which their hypothesis is being tested is the same data from which their hypothesis was generated. The authors' findings were based on 26 co-sleeping SIDS infants further split into 2 groups by maternal pre-gravid weight (using arbitrarily defined cutoffs rather than standardized body mass index). It is highly dubious as to whether parametric testing was appropriate, given such small numbers, but more importantly the study used no controls. Whether maternal weight is associated with co-sleeping in the rest of the Cleveland population is therefore unknown. Breastfeeding women commonly bedshare,[2,3] but larger women who breastfeed tend to stop earlier,[4–6] so one might expect bed-sharing by larger women to be associated primarily with younger infants. The larger mothers in this study also had larger babies. Given that the proportional difference in weight between the average mother and baby is in excess of 10-fold, would an increase in maternal weight really elevate the risk of overlaying? To properly assess this issue in relation to bed-sharing, it would be necessary to examine known overlaying deaths (not presumed) with population controls utilizing maternal body mass index for this last sleep.

The observation that bed-sharing SIDS infants are younger is not new and confirms findings from our UK study that the characteristic 3-month peak age of SIDS is actually bimodal, at around 8 weeks for bed-sharers and 15 weeks for those who died in a crib.[7] This is not surprising, given the higher prevalence of bed-sharing among younger infants.[8–9] What is surprising, if the co-sleeping deaths were attributable to overlaying, is that so few occurred in the first month of life, when bed-sharing is most frequent and the smaller infants presumably were more vulnerable. The authors' criticism of our study was also misplaced; if they had read the references cited,[10] our case ascertainment was 98.3% in a population of 470 000 births.

To conclude, in the absence of any information collected by parental interview or death scene assessment (as strongly recommended recently by the American Academy of Pediatrics in this journal[11]), that these deaths were probably accidental is irresponsible supposition. To further advocate an avoidance of bed-sharing when co-sleeping deaths on a sofa have been included in the analysis and the contribution of known SIDS risk factors (eg, sleeping position, heavy wrapping, etc) have been ignored is tantamount to the same presumptions made a century earlier.

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REFERENCES

1. Carroll-Pankhurst C, Mortimer A. Sudden infant death syndrome, bed-sharing, parental weight, and age at death. *Pediatrics.* 2001;107:530–536
2. Ball HL, Hooker E, Kelly PJ. Where will the baby sleep? Attitudes and practices of new and experienced parents regarding cosleeping with their newborn infants. *Am Anthropol* 1999;101:143–151
3. Clements MS, Mitchell EA, Wright SP, et al. Influences on breastfeeding in southeast England. *Acta Pediatr.* 1997;86:51–56
4. Hilson JA, Rasmussen KM, Kjolhede CL. Maternal obesity and breast-feeding success in a rural population of white women. *Am J Clin Nutr.* 1997;66:1371–1378
5. Rutishauser IHE, Carlin JB. Body mass index and duration of breastfeeding: a survival analysis during the first six months of life. *Breastfeeding Rev.* 1993;2:326–333
6. Donath SM, Amir LH. Does maternal obesity adversely affect breast-feeding initiation and duration? *J Paediatr Child Health* 2000;36:482–486
7. Blair PS, Fleming PJ, Smith IJ, Ward Platt M, Young J, Nadin P, Berry PJ, Golding J and the CESDI SUDI Research Group. Babies sleeping with parents: case-control study of factors influencing the risk of sudden infant death syndrome. *BMJ.* 1999;319:1457–1462
8. Tuony PG, Smale P, Clements M. Ethnic differences in parent/infant co-sleeping practices in New Zealand. *N Z Med J.* 1998;111:364–366
9. Rigda RS, McMillen IC, Buckley P. Bed sharing patterns in a cohort of Australian infants during the first six months after birth. *J Paediatr Child Health.* 2000;36:117–121
10. Leach CEA, Blair PS, Fleming PJ, Smith IJ, Ward Platt M, Berry PJ, Golding J. Sudden unexpected deaths in infancy: similarities and differences in the epidemiology of SIDS and explained deaths. *Pediatrics.*

1999;104(4). Available at: http://www.pediatrics.org/cgi/content/full/104/4/e43
11. American Academy of Pediatrics, Committee on Child Abuse and Neglect. Distinguishing sudden infant death syndrome from child abuse fatalities. *Pediatrics.* 2001;107:437–441

To the Editor.—

I read with great interest the article by Carroll-Pankhurst and Mortimer,[1] and applaud the authors for an outstanding study. I was concerned, however, of a very important issue in the incidence of SIDS as well as the incidence of bedsharing that is not mentioned: the mode of feeding. Mothers who breastfeed tend to bring their babies to bed, and therefore the incidence of bedsharing is higher among breastfeeding mothers. The data on the incidence of SIDS in breastfeeding versus bottle-feeding infants provide the notion that the incidence is less among breastfeeding children. Do the authors have access to this information?

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REFERENCE

1. Carroll-Pankhurst C, Mortimer A. Sudden infant death syndrome, bed-sharing, parental weight, and age at death. *Pediatrics.* 2001;107:530–536

In Reply.—

We appreciate the comments of Blair et al but must disagree with some of them. Our report repeatedly states that we believe bed-sharing to be a cause of only a portion of SIDS-like deaths, and therefore we have not gone full circle as they contend. Rather, our position calls for a compromise between the all-or-none positions that have characterized this debate in the past. If it is correct that our observation explains some undetermined number of such deaths, it may help investigators separate explainable causes from true idiopathic SIDS.

As to the absence of true controls, there have been many classic descriptive epidemiologic studies that demonstrate association and/or causation that did not include controls in the usual sense.[1] Among these are the Framingham studies of precursors of adult cardiovascular disease,[2] the longitudinal British studies of birth cohorts,[3] and the well-known Cleveland family studies.[4] Moreover, each of these developed hypotheses and tested them from the same data.

In relation to the comment about the paucity of SIDS in the first month of life when bed-sharing is most frequent, we do not know the prevalence of that sleeping practice with young infants in Cleveland. Further, if this concern is valid, should it not apply to the prone versus supine problem as well?

We did not suggest that the report of Blair et al[5] suffered from underascertainment; instead, we were concerned about the criteria for explained deaths. Their subsequent report[6] indicates that our concern was unfounded.

Finally, we believe that the bimodal peak age distribution of SIDS (8 weeks for bed-sharers and 15 weeks for crib sleepers) demonstrated in the British studies[5] supports our concern about co-sleeping. Their implication that this distribution might well explain our results ignores the maternal weight finding. As we stated in our report, each of the factors (bed-sharing, age at death, and maternal weight) is meaningless when considered individually. What is important is the combination of the 3 factors, which led to our conclusion and from which we are not dissuaded. The fact that the significance of this difference disappears when the British data are adjusted for fatigue and alcohol use by the bed-sharing adult, overcrowding in the household, and duvet use does not invalidate this finding. The first 3 characteristics are not risk factors for SIDS, but instead may increase the likelihood of bed-sharing. A basic principle of multivariate analysis in epidemiology is that adjustments for potential confounders are made only for other known risk factors.

In short, we believe that the major criticisms of our data and our conclusions are in error. Additionally, we believe that the risk of bed-sharing is demonstrated in the British studies as well.

In response to Lawrence's questions on breastfeeding, bed-sharing, and SIDS, we would note that we do not have prevalence data for the Cleveland population. We have evaluated intent to breastfeed at hospital discharge in our data and found no significant difference between those who were bed-sharing and those who were not (20% vs 17%, respectively). We would also point out that the AAP Task Force on Infant Sleep Position and SIDS, in its most recent assessment of factors thought to protect against SIDS, concluded that although there were contradictory reports, the current evidence was insufficient to conclude that breastfeeding was protective for SIDS.[7]

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REFERENCES

1. Friedman GD. *Primer of Epidemiology.* 2nd ed. New York, NY: McGraw-Hill Book Co; 1980:52
2. Dawber TR. *The Framingham Study: The Epidemiology of Atherosclerotic Disease.* Cambridge, MA: Harvard University Press; 1980
3. Wadsworth MEJ. Follow-up of the first national cohort: findings from the Medical Research Council National Survey of Health and Development. *Paediatr Perinat Epidemiol* 1987;1:95–117
4. Dingle JH, Badger GF, Jordan WS Jr. *Illness in the Home. A Study of 25,000 Illnesses in a Group of Cleveland Families.* Cleveland, OH: The Press of Western Reserve University; 1964
5. Blair JS, Fleming PJ, Smith JJ, et al. Babies sleeping with parents: case-control study of factors influencing the risk of sudden death syndrome. *BMJ.* 1999;319:1457–1462
6. Leach CEA, Blair JS, Fleming PJ, et al. Epidemiology of SIDS and explained sudden infant deaths. *Pediatrics* 1999;104(4). Available at: http://www.pediatrics.org/cgi/content/full/104/4/e43
7. American Academy of Pediatrics, Task Force on Infant Sleep Position and Sudden Infant Death Syndrome. Changing concepts of sudden infant death syndrome: implications for infant sleeping environment and sleep position. *Pediatrics.* 2000;105:650–656

ERRATUM

Some errors occurred in the article entitled "The Timing of Neonatal Discharge: An Example of Unwarranted Variation," which appeared in the January 2001 issue of *Pediatrics.* The corrections are as follows:

1. Michael S. Kornhauser's title should have read: Medical Director, Paidos Health Management Services, Inc, Deerfield, IL, and Department of Pediatrics, Jefferson Medical College, Philadelphia, PA.

2. David B. Nash's title should have read: Office of Health Policy and Clinical Outcomes and Department of Medicine, Jefferson Medical College, Philadelphia, PA.

3. This research was supported in part by a grant from Paidos Health Management Services, Inc awarded to Suzanne M. Touch, MD, and Jay S. Greenspan, MD.

Blue Balls

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