Correspondence

Vitamin A Supplementation for Extremely-Low-Birth-Weight Infants

To the Editor: The study by Tyson et al. (June 24 issue),[1] while impressive in design and numbers of infants studied, does not really answer the question of whether vitamin A supplementation reduces the risk of chronic lung disease in premature infants. The main drawback of this study, as well as those published previously,[2] is the definition of chronic lung disease. The best predictor of chronic lung disease is a chest x-ray film,[3] whereas the authors' definition of chronic lung disease, the need for oxygen at 36 weeks' postmenstrual age, has a positive predictive value of only 63 percent.[4]

Although the authors found that fewer infants given vitamin A had chronic lung disease at 36 weeks (by their definition) than was the case in the control group, we question whether the difference is enough to convince a clinician to give 12 intramuscular injections to extremely-low-birth-weight infants, especially when all other measures of chronic lung disease in this study were not different in the two groups. Their argument in favor of vitamin A supplementation would be greatly strengthened by additional follow-up data.

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To the Editor: In considering the implications of the study by Tyson et al., one has to consider whether the degree of vitamin A deficiency in the infants studied was due to maternal deficiency of this vitamin or to metabolic defects in the processing of the vitamin and its products in the infants. Clarification of this point would help to determine the importance of preventing vitamin A deficiency in pregnant women.

The possibility of maternal vitamin A deficiency may well have been increased by a report on the hazards of excessive vitamin A intake in pregnant women.[1] This report may also be contributing to the risk of vitamin D deficiency, because these two vitamins occur together in many foods, including fish oils, liver, and liver pâté, which expectant mothers in the United Kingdom are advised to eat. Vitamin D deficiency increases the risks of certain infections and of low birth weight and alters immune responses.[2,3] Can the authors, therefore, provide information on maternal serum concentrations of retinol and its esters or 25-hydroxyvitamin D? This information would be of value in the continuing debate on the best dietary advice to offer pregnant women.

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INSTRUCTIONS FOR LETTERS TO THE EDITOR

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Dr. Tyson replies:

To the Editor: The best method of diagnosing chronic lung disease in infants is unclear.[1] Bental et al. are critical of the diagnostic criterion used in our study (the administration of oxygen at 36 weeks' postmenstrual age) and assert that radiologic findings are a better predictor of later outcome. However, the study cited to support this assertion had several limitations. Outcome was not determined for 48 percent of the infants studied. Radiographs were not evaluated at a consistent postnatal or postmenstrual age and were not obtained for all infants. All radiographs obtained between 25 and 35 postnatal days were scored by a neonatologist and a radiologist, and the mean value was calculated for each infant. This method of evaluation is not commonly or easily used. The radiographic findings were not much better (more sensitive but less specific) for predicting outcome than was the use of supplemental oxygen at 36 weeks' postmenstrual age.

We considered obtaining radiographs of all infants at 36 weeks. However, we wished to avoid unnecessary exposure to radiation, expense, variability in interpretations by different radiologists, and the logistical problems of obtaining readings by a single radiologist. Finally, radiographs could be misleading if the administration of vitamin A altered the radiographic findings without changing the clinical course of chronic lung disease. For all these reasons, we — like other investigators[1,2] — did not pursue radiologic findings. The need for oxygen at 36 weeks, which we used as a marker of chronic lung disease, has been found to be predictive of later pulmonary and developmental morbidity.[2,3]

Bental et al. also question whether the reduction in the risk of chronic lung disease in our study justifies the intramuscular administration of supplemental vitamin A to extremely-low-birth-weight infants. The vitamin A intake of these infants is limited by prolonged feeding intolerance, poor enteral absorption of vitamin A, and unreliable intravenous delivery in crystalloid solutions. In contrast, intramuscular supplementation with vitamin A was found in our multicenter trial and in a meta-analysis of all prior trials[4] to reduce chronic lung disease as well as biochemical signs of vitamin A deficiency safely.

Although the effect on chronic lung disease is not dramatic, the evidence available supports the clinical use of the regimen we tested. Whether the benefits would be increased by the use of higher doses or by the administration of vitamin A in intravenous fat emulsions remains to be assessed.

Dr. Boucher raises interesting questions. However, our study was not designed to assess vitamin intake in pregnancy, and we did not measure serum retinol, retinyl esters, or 25-hydroxyvitamin D in the mothers.

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Maternal Viral Load and the Risk of Perinatal Transmission of HIV-1

To the Editor: In the August 5 issue, Mofenson et al.[1] conclude that antiretroviral therapy "should be recommended to all infected pregnant women regardless of their HIV-1 [human immunodeficiency virus type 1] RNA levels," and Garcia et al.[2] conclude that zidovudine therapy has "demonstrated efficacy in reducing the risk of transmission regardless of the maternal HIV-1 RNA levels." Neither study provides sufficient evidence to support these statements.

We updated the results of a meta-analysis of the predictive value of viral load for perinatal HIV-1 transmission[3] with data presented by Garcia et al. Among 10 studies of pregnant women in the United States and Europe, none have shown that women with RNA levels of less than 1000 copies per milliliter have a lower rate of transmission with treatment than without treatment. Pooled data show an overall transmission rate of 3.9 percent in both untreated women (6 of 153) and treated women (5 of 127) with such low RNA levels. By contrast, transmission rates obtained with pooled data are clinically and statistically significantly higher for untreated than for treated women both in the category of 1000 to 10,000 RNA copies per milliliter (16.2 percent [60 of 370 women] vs. 7.8 percent [22 of 283 women]) and in the category of more than 10,000 copies per milliliter (34.5 percent [158 of 458 women] vs. 23.3 percent [44 of 189 women]).

We drew similar inferences when we combined study-specific rates or odds ratios for transmission rates among treated as compared with untreated women with fixed- or random-effects models (data not shown). Data on individual patients according to HIV-1 RNA levels (less than 1000, 1000 to 10,000, and more than 10,000 copies per milliliter) were not presented by Mofenson et al. but would shed more light on this issue. They did not include untreated women, thus prohibiting direct comparisons. Nevertheless, if the transmission rate for women with RNA levels of less than 1000 copies per milliliter is 0 in this study (as was reported for women with levels of less than 500 copies per milliliter), the pooled transmission rate for treated women in this RNA category among all studies would be closer to 2 percent.

Lack of randomization in the comparison of treated and untreated groups unavoidably leads to selection bias. Further bias may stem from the use of different assays for measuring viral load, different ways of storing specimens, measurement error (especially with single measurements), and variable therapeutic regimens.[3] More data are needed to support the conclusion that a clinically relevant difference in transmission rates results from the use of antiretroviral therapy in pregnant women with RNA levels of less than 1000 copies per milliliter. This point is important, because women who were doing very well may have deferred initiation of antiretroviral therapy before pregnancy and may have been reluctant to commit to treatment with zidovudine or combination regimens.[4]

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1. Mofenson LM, Lambert JS, Stiehm ER, et al. Risk factors for perinatal transmission of human immunodeficiency virus type 1 in women treated with zidovudine. N Engl J Med 1999;341:385-93.

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4. Ioannidis JP, O'Brien TR, Goedert JJ. Evaluation of guidelines for initiation of highly active antiretroviral therapy in a longitudinal cohort of HIV-infected individuals. AIDS 1998;12:2417-23.

The authors reply:

To the Editor: As we noted, current Public Health Service guidelines recommend zidovudine prophylaxis to reduce the risk of perinatal HIV-1 transmission regardless of maternal HIV-1 RNA level.[1] Drs. Ioannidis and Contopoulos-Ioannidis correctly point out the lack of data that could definitively demonstrate that zidovudine lowers the rate of perinatal transmission in the subgroup of HIV-1–infected pregnant women with RNA levels of less than 1000 copies per milliliter. Data on HIV-1 RNA levels among untreated women are limited, because HIV-1 RNA assays were not generally available before 1994 and because since 1994, most HIV-1–infected women receiving prenatal care in the United States have received zidovudine prophylaxis. Furthermore, when transmission rates are low (as they appear to be in women with low HIV-1 RNA levels), large numbers of patients are required for a study to have the power to detect an effect of treatment on transmission. For example, if the transmission rate is assumed to be 5 percent among untreated women with HIV-1 RNA levels of less than 1000 copies per milliliter, approximately 1700 mother–infant pairs (850 per group) would be required for a study to establish that zidovudine reduces the transmission rate by 50 percent (with a power of 80 percent and a one-sided alpha of 0.05).

Limited data on the association of HIV-1 RNA levels, zidovudine use, and the risk of transmission are available from the original placebo-controlled trial (Pediatric AIDS Clinical Trials Group Protocol 076).[2] The transmission rates for patients with HIV-1 RNA levels of less than 1730 copies per milliliter (the lowest quartile according to the results of the reverse-transcription HIV-1 RNA polymerase-chain-reaction assay) were 2.5 percent in the zidovudine group and 7.5 percent in the placebo group.[2] As we also noted, our results can only be used to address transmission rates among women receiving zidovudine and cannot be used specifically to address whether zidovudine is effective in lowering the rate among women with HIV-1 RNA levels of less than 1000 copies per milliliter. In our study, 1 of 135 women with RNA levels of less than 1000 copies per milliliter (0.7 percent), 6 of 149 women with RNA levels of 1000 to 10,000 copies per milliliter (4.0 percent), and 17 of 195 women with RNA levels of more than 10,000 copies per milliliter (8.7 percent) had infected infants. If one pools our data with the data provided by Drs. Ioannidis and Contopoulos-Ioannidis, the transmission rate was 41 percent lower among zidovudine-treated women (2.3 percent among 262 treated women, as compared with 3.9 percent among 153 untreated women).

The mechanism of zidovudine efficacy is most likely multifactorial and involves both lowering of the maternal viral load and pre- and postexposure prophylaxis in the infant. The importance of pre- and postexposure prophylaxis for preventing perinatal transmission is demonstrated by the recent results of a Ugandan study showing the efficacy of a two-dose intrapartum–postpartum regimen of nevirapine in lowering the risk of perinatal transmission.[3]

The risk of transmission among untreated women with HIV-1 RNA levels of less than 1000 copies per milliliter is low but not zero. For women with low viral loads who wish to reduce the risk of transmission of HIV-1 infection to their infants even further, potential interventions include zidovudine prophylaxis and, for those who do not wish to expose the fetus to antiretroviral drugs during pregnancy, intrapartum–postpartum nevirapine or elective cesarean delivery.[4]

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1. Public Health Service Task Force recommendations for the use of antiretroviral drugs in pregnant women infected with HIV-1 for maternal health and for reducing perinatal HIV-1 transmission in the United States. MMWR Morb Mortal Wkly Rep 1998;47(RR-2):1-30. [Errata, MMWR Morb Mortal Wkly Rep 1998;47:287, 315.]
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To the Editor: We agree with Drs. Ioannidis and Contopoulos-Ioannidis that our data do not prove that zidovudine therapy reduces the rate of perinatal transmission of HIV-1 among the select and somewhat arbitrarily defined subgroup of women with HIV-1 RNA levels below 1000 copies per milliliter. The small size of this subgroup in our study as well as in the pooled data that Ioannidis and Contopoulos-Ioannidis used precludes the detection of differences in transmission rates with respect to treatment, since the transmission rates are low. The frequencies both of the condition and the event are low, and there are ethical problems with placebo-controlled trials once the efficacy of affordable and easily administered chemoprophylaxis has been demonstrated.[1,2] Hence, it is unlikely that we will ever know definitively whether any intervention is better than no intervention for pregnant women with low levels of plasma HIV-1 RNA.

Our recommendation that women be offered zidovudine prophylaxis regardless of their HIV-1 RNA level, in accordance with Public Health Service guidelines,[3] is supported by several observations. Perinatal transmission is multifactorial, and our multivariate analysis clearly demonstrates the independent effect of zidovudine therapy on transmission. Sperling et al.[4] point out that the protection against

transmission offered by zidovudine appears to be due only in part to its ability to decrease viral load. The recently demonstrated efficacy of peripartum antiretroviral prophylaxis[2] suggests a mechanism more closely related to prophylactic treatment of the fetus than to a reduction of maternal viral load. Despite our finding that there was no transmission among women with HIV-1 RNA levels of less than 1000 copies per milliliter, there are multiple reports of transmission at this level, including one study in which 16 of 132 women with such RNA levels transmitted HIV-1 infection to their infants.[5] We would therefore caution readers that translating population-level risks to the assessment of individual risks for purposes of clinical management is potentially hazardous. Measurement of maternal plasma HIV-1 RNA has inherent biologic and technical variability that makes establishing an individual threshold value difficult, not to mention the practical issues associated with monitoring and management decisions when time is so critical.

We concur that further study is needed to determine the specific benefits and risks of prophylactic interventions such as antiretroviral therapy or cesarean delivery for women with low viral loads and their infants. The existence of clinically significant negative maternal consequences of brief exposure to zidovudine or nevirapine is not sufficiently well established to justify deferring perinatal prophylaxis; the risks of such treatment thus do not outweigh its potential benefits.

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Use of the Nicotine Patch by Pregnant Women

To the Editor: Even if women acknowledge the perinatal risks of cigarette smoking and wish to quit the habit, many women continue to smoke after realizing that they have conceived.[1] The transdermal nicotine patch, when combined with counseling, is an effective method of nicotine replacement.[2] However, nicotine has been shown to be teratogenic in animal studies, and it is categorized by the Food and Drug Administration at risk level D, which implies substantial risk to the fetus.[3,4] This has led clinicians and pharmaceutical companies to hesitate and largely to ignore the potential opportunity offered by the transdermal nicotine patch for helping pregnant women protect their unborn children.

We hypothesized that use of the transdermal nicotine patch by pregnant women would prevent exposure of the fetus to the scores of other toxins besides nicotine that are present in tobacco smoke, such as carbon monoxide, cyanide, and thiosulfate. However, to justify this approach, it must be ensured that women are exposed to less nicotine than they would be from continued smoking.

In a pilot phase of a randomized, placebo-controlled trial of use of the transdermal nicotine patch during pregnancy, we measured serum and salivary levels of nicotine and cotinine at base line and after use of the patch for one week in a group of women who smoked. Serum cotinine levels decreased in six of the seven pregnant women studied and remained unchanged in one. The mean serum cotinine level decreased from 247.6±96.9 ng per milliliter at base line to 163.7±72.9 ng per milliliter after use of the patch ($P=0.003$ by the two-tailed t-test). Salivary cotinine levels showed a similar trend (449.4±233.4 ng per milliliter at base line and 197.7±114.2 ng per milliliter after use of the patch for one week, $P=0.02$). Because of the relatively long elimination half-life of cotinine (approximately 20 hours), weekly monitoring of cotinine levels can ensure that systemic exposure of the fetus to this xenobiotic remains lower than it would have been with continued smoking. To ensure fetal safety further, the use of a 16-hour patch can mimic the use of cigarettes on a typical day followed by 8 hours of sleep, so that nicotine levels at night will be no higher than would be the case with smoking.

If cotinine levels increase while a woman is using the transdermal nicotine patch, its dose can be decreased, and studies should be performed to verify whether and how much the woman is smoking. Measurement of thiosulfate and carbon monoxide levels can distinguish smoking from use of the transdermal nicotine patch.

The ethical and practical challenge is to help women who are unable to stop smoking during pregnancy to do so with use of the nicotine patch, without encouraging the use of the patch by women who are able to stop smoking on their own. The method we propose overcomes the chief hurdle blocking use of the transdermal nicotine patch during pregnancy and may lead to a decrease in the perinatal morbidity and mortality caused by smoking tobacco during pregnancy.

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A Comparison of Botulinum Toxin and Nitroglycerin Ointment for Chronic Anal Fissure

To the Editor: Brisinda et al. (July 8 issue)[1] report that healing of chronic anal fissure occurred in 22 of the 25 patients in the group receiving botulinum-toxin injections and in 10 of the 25 patients treated with topical nitroglycerin ointment. In addition, symptomatic improvement, defined by the authors as the absence of symptoms despite the persistence of the fissure, occurred in 2 of the 3 remaining patients in the botulinum-toxin group and 8 of the remaining 15 patients in the nitroglycerin group. These results indicate that healing of fissure and resolution of symptoms should not be equated. The authors did not report the rate of symptomatic improvement in the patients with healed fissures. Did only two thirds of the fissures healed with the use of botulinum toxin result in symptomatic improvement? If so, then perhaps a multimodal approach, aimed at both healing and symptomatic improvement, would be more efficacious therapy for patients with chronic anal fissure.

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1. Brisinda G, Maria G, Bentivoglio AR, Cassetta E, Gui D, Albanese A. A comparison of injections of botulinum toxin and topical nitroglycerin ointment for the treatment of chronic anal fissure. N Engl J Med 1999;341:65-9.

To the Editor: Although a six-week treatment with 0.2 percent nitroglycerin ointment will cost no more than 10 to 15 Swiss francs (equivalent to $6 to $10), a single injection of 20 U of botulinum toxin, taken from a vial containing 100 U, currently costs 357 Swiss francs ($238). Assuming that the lack of response to an initial treatment of topical nitroglycerin varies between a maximum of 40 percent (as reported by Brisinda et al.) and a minimum of 12 percent (as reported by others[1,2]) and that these patients would have to be offered an injection of botulinum toxin later, the resulting overall costs of the treatment of 100 patients would be considerably lower with an initial treatment of nitroglycerin ointment than with a single injection of botulinum toxin. Initial treatment with nitroglycerin should therefore be favored in patients with chronic anal fissures, and botulinum-toxin injections should be reserved for patients without an adequate response after six weeks.

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The authors reply:

To the Editor: Symptomatic improvement, defined in our study as the persistence of fissure and the absence of post-defecatory pain, occurred in less than 10 percent of the patients in the botulinum-toxin group because of that group's higher rate of complete healing, which was defined as the healing of the fissure and the disappearance of symptoms. We believe that the combination of both treatments is less helpful; complete healing and symptomatic relief can be achieved with botulinum-toxin injections alone. Nitrates have a short duration of action; thus, frequent application is mandatory. Side effects, such as headaches and tachyphylaxis, limit their utility.[1] Nitroglycerin ointment causes headaches more often than it treats symptoms of anal fissure.[2] In addition, higher doses of nitroglycerin are not more effective than lower doses in inducing healing.[3]

In patients with posterior anal fissure, we found a healing rate of 96 percent when botulinum toxin was injected anteriorly into the internal sphincter. The different injection site induces a greater decrease in resting pressure and improves the clinical outcome. This effect should be related to the fibrosis of the internal sphincter, which is more prominent at the site of the fissure than at other sites in the smooth muscle.[4] The fibrosis may reduce the compliance of the internal sphincter and limit the diffusion of the toxin. Moreover, botulinum toxin is more effective than nitroglycerin in alleviating sphincter hypertonia.[5]

Kaiser states that in order to reduce the costs of treatment, nitroglycerin ointment should be used initially in patients with chronic anal fissure and botulinum-toxin injections should be reserved for patients with unhealed fissures. Nevertheless, we found that botulinum toxin was more effective and safe in inducing healing than nitrate therapy; the efficacy is not related to the patient's willingness to complete treatment. Although treatment with botulinum toxin is more costly than treatment with nitroglycerin ointment, denying patients a more effective treatment for this reason makes little sense.

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1. Hasler WL. The expanding spectrum of clinical uses for botulinum toxin: healing of chronic anal fissures. Gastroenterology 1999;116:221-3.
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Musculoskeletal Tumors of Childhood

To the Editor: The review by Arndt and Crist (July 29 issue)[1] underplays the role of stem-cell transplantation in the treatment of Ewing's sarcoma. Our group has worked on stem-cell transplantation in Ewing's sarcoma since the early 1980s and has published data demonstrating a two-

year survival rate of approximately 70 percent among patients presenting with metastasis, large lesions (those more than 8 cm), or both, at diagnosis.[2] Follow-up data since 1990 show 60 percent survival at 1 to 11 years among 40 such high-risk patients. These results should be considered promising.

Several developments, however, suggest that stem-cell transplantation may become an even better option in the future. These include improved methods to reduce the amount of tumor-cell contamination in autologous cells at the time of reinfusion, a known risk factor for relapse after transplantation.[3] One such method is the use of peripheral-blood stem cells rather than marrow stem cells, a standard practice in most transplantation centers already.

Another is the detection of residual disease through sensitive immunocytochemical techniques, which allows the transplantation to be performed after all tumor cells have been eradicated and permits the exclusion of patients who still have tumor cells despite treatment. Such detection is now possible through an assay developed at several centers, including our own, that can detect as few as 1 Ewing's sarcoma cell per million cells.[4]

A third development is the use of CD34+ selection techniques to purge Ewing's sarcoma cells. In four of our recently treated patients, stem-cell harvests in which this technique was used contained no tumor-cell contamination; three of these four underwent stem-cell transplantation and have been in complete, continuous remission for 76 to 553 days. These three patients are also receiving post-transplantation therapy with interleukin-2, thalidomide, or both as antiangiogenesis therapy. It is not yet known whether these remissions will be sustained and whether they can be replicated in large patient populations.

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The authors reply:

To the Editor: Drs. Mehta and Wingard cite a paper by Marcus et al.[1] that reports 70 percent two-year disease-free survival among "standard-risk patients" without metastatic disease, a result that is expected for similar patients treated conventionally.[2] In fact, only 3 of 10 patients treated on their third high-risk protocol had metastases at presentation. The two patients with lung metastases remained disease-free, and the one with bone metastases had already had no response. Furthermore, only 8 of these 10 "high-risk" patients completed the transplantation portion of the protocol. Cardiotoxicity developed in two before transplantation, and thus they could not undergo the procedure. The two-year follow-up time was too short to permit solid conclusions regarding curative potential, and the small and clinically heterogeneous patient population further complicated the interpretation of the results. Our comments referred to patients with metastatic disease at diagnosis.

Other reports of the potential value of high-dose chemotherapy with stem-cell support have the same limitations. The patient populations evaluated are small and clinically heterogeneous. The European Bone Marrow Transplant Group reported a five-year event-free survival of 32 percent among patients who underwent transplantation during a second complete remission, as compared with 21 percent for those with metastatic disease at presentation who underwent transplantation during a first complete remission.[3] Thus, despite the use of very intensive therapy with stem-cell support, the outcome was not better than that expected with the use of contemporary multimodal therapy.[2,4] In 1997, Atra and colleagues[5] described early results in 18 patients with poor-risk Ewing's sarcoma (including 11 with metastatic disease at presentation) who were treated with high-dose busulfan and melphalan and stem-cell rescue. Six patients with initial metastatic disease survived, with a median follow-up of two years. The small number of patients in this series and the short duration of follow-up limit the conclusions that can be drawn.

We agree with Drs. Mehta and Wingard that tumor-cell contamination of stem-cell products is a potential risk factor for relapse, that new methods of purging tumor cells from autologous stem cells are of interest, and that immune modulation may eventually have a role in the improvement of treatment for patients with high-risk Ewing's sarcoma. Clearly, better therapy for such patients is urgently needed. Our expression of disappointment in the results of recent clinical trials in which high-dose therapy with stem-cell support was used for patients with metastatic Ewing's sarcoma was not intended to discourage such efforts.

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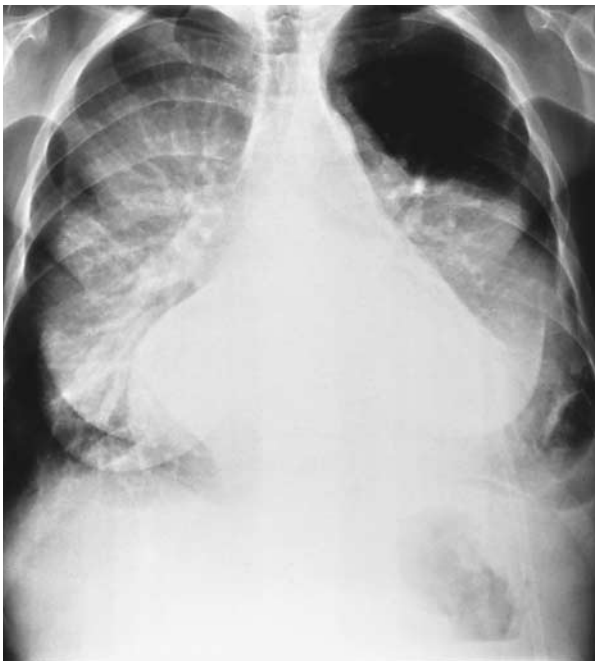
Extramedullary Hematopoiesis: Breathtaking and Hair-Raising

To the Editor: Thoracic masses due to extramedullary hematopoiesis are rare, occurring most often in patients with



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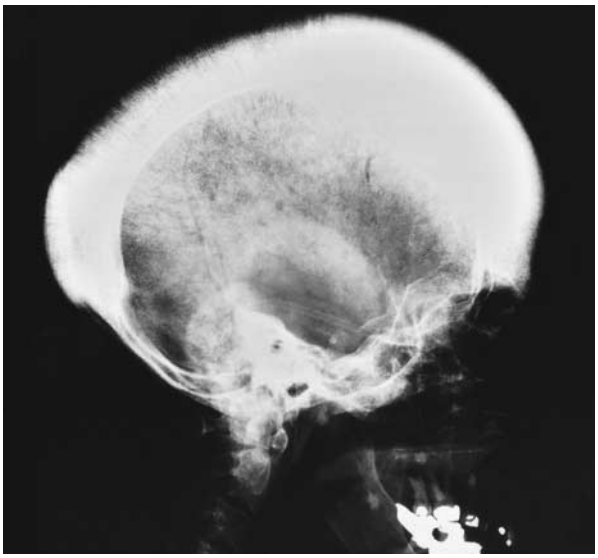

B

Figure 1. Radiographs of the Chest and Skull in a Patient with Congenital Dyserythropoietic Anemia.

A radiograph of the chest (Panel A) shows large paravertebral masses. A lateral radiograph of the skull (Panel B) shows hair-on-end phenomenon.

thalassemia or congenital hemolytic anemia.[1] The masses usually cause no symptoms but can cause pleural effusion or hemothorax. Here, we describe a patient with respiratory insufficiency caused by large, hematopoietic thoracic masses.

A 51-year-old woman with type III congenital dyserythropoietic anemia[2] (diagnosed in 1971, with lifelong anemia) was referred to our clinic in December 1998 because of exertional dyspnea and respiratory insufficiency. In 1980, a routine radiograph of the chest had shown a small, right-sided thoracic mass; biopsy had revealed extramedullary hematopoiesis. In November 1998, the patient had had bilateral pleural effusions and was treated with thoracentesis and pleurodesis.

At referral, when her condition was clinically stable, she had persistent hypercapnia and severely restrictive lung function (forced vital capacity, 0.84 liter; forced expiratory volume in one second, 0.66 liter) Her hemoglobin concentration was 7.6 g per deciliter. Radiographs and computed tomographic (CT) scans of the chest showed large paravertebral masses that deformed and stretched the lower-lobe bronchi in both lungs (Fig. 1A). The right mass measured 17 by 12 cm, and the left 15 by 12 cm. A single-photon-emission CT (SPECT) scan of the bone marrow obtained after injection of technetium-99m sulfur colloid revealed accumulation of the radionuclide in both masses. Superimposition of the SPECT image of the bone marrow on the CT scan of the chest confirmed that the thoracic masses contained hematopoietic cells. The bone marrow scan also showed enlargement of the liver and spleen and accumulation of hematopoietic cells in the extremities, the sternum, the ribs, and the skull. This accumulation caused an extreme "hair-on-end" phenomenon on the radiograph of the skull (Fig. 1B).

Extramedullary hematopoiesis can be treated with frequent blood transfusions to limit the hematopoietic stimulus. In addition, hydroxyurea therapy has been reported to decrease the size of masses of hematopoietic cells and to relieve spinal cord compression,[3] as well as to reduce the size of cutaneous masses.[4] We treated our patient with blood transfusions and hydroxyurea (500 mg twice daily). During a four-month treatment period, her clinical condition gradually improved, her forced vital capacity and forced expiratory volume in one second increased,[4] her blood gas values normalized, and the thoracic masses decreased slightly in size.

Extramedullary hematopoiesis has been reported in an asymptomatic patient with type II congenital dyserythropoietic anemia.[5] Our patient had respiratory insufficiency due to paravertebral extramedullary hematopoiesis, and treatment with blood transfusions and hydroxyurea resulted in a satisfactory clinical, functional, and radiologic response.

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