Serum Tocopherol Levels in Very Preterm Infants After a Single Dose of Vitamin E at Birth

WHAT’S KNOWN ON THIS SUBJECT: Preterm infants are born with low serum levels and low body stores of tocopherol. Serum levels ≥0.5 mg/dL are required for protection against lipid peroxidation. Previous studies have shown good intestinal absorption of vitamin E given intragastrically to preterm infants.

WHAT THIS STUDY ADDS: Serum α-tocopherol increases after a single 50-IU/kg dose of vitamin E as dl-α-tocopheryl acetate given intragastrically to very preterm infants soon after birth; however, 30% of infants still have serum α-tocopherol level <0.5 mg/dL 24 hours after dosing.

OBJECTIVE: Our aim was to examine the impact of a single enteral dose of vitamin E on serum tocopherol levels. The study was undertaken to see whether a single dose of vitamin E soon after birth can rapidly increase the low α-tocopherol levels seen in very preterm infants. If so, this intervention could be tested as a means of reducing the risk of intracranial hemorrhage.

METHODS: Ninety-three infants <27 weeks’ gestation and <1000 g were randomly assigned to receive a single dose of vitamin E or placebo by gastric tube within 4 hours of birth. The vitamin E group received 50 IU/kg of vitamin E as dl-α-tocopheryl acetate (Aquasol E). The placebo group received sterile water. Blood samples were taken for measurement of serum tocopherol levels by high-performance liquid chromatography before dosing and 24 hours and 7 days after dosing.

RESULTS: Eighty-eight infants received the study drug and were included in the analyses. The α-tocopherol levels were similar between the groups at baseline but higher in the vitamin E group at 24 hours (median 0.63 mg/dL vs 0.42 mg/dL, P = .003) and 7 days (2.21 mg/dL vs 1.86 mg/dL, P = .04). There were no differences between groups in γ-tocopherol levels. At 24 hours, 30% of vitamin E infants and 62% of placebo infants had α-tocopherol levels <0.5 mg/dL.

CONCLUSIONS: A 50-IU/kg dose of vitamin E raised serum α-tocopherol levels, but to consistently achieve α-tocopherol levels >0.5 mg/dL, a higher dose or several doses of vitamin E may be needed. Pediatrics 2013;132:e1626–e1633

AUTHORS: Edward F. Bell, MD,a Nellie I. Hansen, MPH,b Luc P. Brion, MD,c Richard A. Ehrenkranz, MD,d Kathleen A. Kennedy, MD, MPH,e Michele C. Walsh, MD, MS,f Seetha Shankaran, MD,g Michael J. Acarregui, MD,h Karen J. Johnson, RN, BSN,i Ellen C. Hale, RN, BS, CCRC,j Lynn A. Messina, RPh,k Margaret M. Crawford, CCRP,l Abbot R. Laptokk,m Ronald N. Goldberg, MD,n Krisa P. Van Meurs, MD,o Waldemar A. Carlo, MD,p Brenda B. Poindexter, MD,q Roger G. Faix, MD,r David P. Carlton, MD,s Kristi L. Watterberg, MD,t Dan L. Ellisbury, MD,u Abhik Das, PhD,v and Rosemary D. Higgins, MDw for the Eunice Kennedy Shriver National Institute of Child Health and Human Development Neonatal Research Network

aDepartment of Pediatrics, University of Iowa, Iowa City, Iowa; bSocial, Statistical and Environmental Sciences Unit, RTI International, Research Triangle Park, North Carolina; cDepartment of Pediatrics, University of Texas Southwestern Medical Center, Dallas, Texas; dDepartment of Pediatrics, Yale University School of Medicine, New Haven, Connecticut; eDepartment of Pediatrics, University of Texas Southwestern Medical School at Houston, Houston, Texas; fDepartment of Pediatrics, Rainbow Babies & Children’s Hospital and Case Western Reserve University, Cleveland, Ohio; gDepartment of Pediatrics, Wayne State University, Detroit, Michigan; hDepartment of Pediatrics, Emory University School of Medicine and Children’s Healthcare of Atlanta, Atlanta, Georgia; iMercy Medical Center, Des Moines, Iowa; jSocial, Statistical and Environmental Sciences Unit, RTI International, Rockville, Maryland; kDepartment of Pediatrics, Women & Infants Hospital of Rhode Island and Brown University, Providence, Rhode Island; lDepartment of Pediatrics, Duke University, Durham, North Carolina; mDepartment of Pediatrics, Stanford University School of Medicine and Lucile Packard Children’s Hospital, Palo Alto, California; nDepartment of Pediatrics, University of Alabama at Birmingham, Birmingham, Alabama; oDepartment of Pediatrics, Indiana University School of Medicine, Indianapolis, Indiana; pDepartment of Pediatrics, University of Utah School of Medicine, Salt Lake City, Utah; qDepartment of Pediatrics, University of New Mexico Health Sciences Center, Albuquerque, New Mexico; rCenter for Research, Education, and Quality, Pediatrix Medical Group, Sunset, Florida; and sEunice Kennedy Shriver National Institute of Child Health and Human Development, Bethesda, Maryland

KEY WORDS
vitamin E, preterm infants

ABBREVIATIONS
NICHD—Eunice Kennedy Shriver National Institute of Child Health and Human Development
NRN—Neonatal Research Network

(Continued on last page)
Vitamin E plays an important role in antioxidant protection and has many other functions, mostly beneficial, in humans and animals. Preterm infants are born with sparse body fat and low body stores of fat-soluble vitamins, including vitamin E. In addition, their serum and erythrocyte levels of tocopherol are low at birth, and they are functionally deficient in vitamin E, as demonstrated by elevated erythrocyte hemolysis in the presence of hydrogen peroxide. In the 1980s and early 1990s, when parenteral and enteral nutrition were commonly delayed for days or even weeks in preterm infants, plasma tocopherol levels did not reach protective levels until 1 to 2 weeks after birth. Little is known about the rate of increase in serum tocopherol levels with more vigorous early nutrition as currently practiced. Moreover, little is known about the effect on serum α-tocopherol level of a single dose of vitamin E given soon after birth.

The question of how best to quickly correct the vitamin E deficiency state in preterm infants is of potential clinical importance. Supplemental dosing of vitamin E has been suggested as a potential agent for the prevention of intracranial hemorrhage, a common, serious complication of prematurity with major adverse consequences.

We undertook this current study to examine the impact of a single enteral dose of vitamin E, given as dl-α-tocopheryl acetate soon after birth, on serum α- and γ-tocopherol levels of very preterm infants during the first week of life. We examined whether a 50-IU/kg dose of vitamin E could increase the serum α-tocopherol level within 24 hours in most infants to >1.0 mg/dL with the hope that these higher levels might also help to prevent intracranial hemorrhage in this vulnerable population.

METHODS

Subjects

The subjects were infants born at <27 weeks’ gestation with birth weight <1000 g at 1 of 14 centers of the Eunice Kennedy Shriver National Institute of Child Health and Human Development Neonatal Research Network (NRN). Study enrollment occurred between October 2010 and July 2011. Infants were not eligible for enrollment if they had received supplemental vitamin E (except as a parenteral multivitamin) or if they had any of the following: umbilical cord or blood pH <7.0, major congenital malformation, or decision to limit treatment based on perceived poor prognosis. In addition, infants were excluded from enrollment if parental consent could not be obtained or if there was another reason it was not possible to administer the study drug before age 4 hours. Parental consent was obtained before or shortly after birth. The study was approved by the institutional review board at each participating site.

Study Intervention

Subjects were stratified based on whether their mothers received a full course of antenatal corticosteroid (2 doses of betamethasone or 4 doses of dexamethasone) and randomized in a 2:1 ratio to receive either a vitamin E preparation or placebo by orogastric or nasogastric tube within 4 hours of birth. A permuted block design with randomly varied block sizes and allocation ratio of 2:1 (vitamin E to placebo) was used to generate the random allocation sequence within each of the 2 strata defined by antenatal corticosteroid exposure. The allocation sequence was generated by a statistician at the NRN data-coordinating center at RTI International. The infants randomized to receive vitamin E received a 50-IU/kg (1.0-mL/kg) dose as dl-α-tocopheryl acetate (Aquasol E drops, Hospira, Lake Forest, IL) diluted with an equal volume (1 mL/kg) of sterile water. The placebo infants received a 2.0-mL/kg dose of sterile water. Treatment assignments were made by an automated telephone-based randomization system operated by the data coordinating center. For each enrolled infant, the study site research coordinator called the randomization system to obtain a randomization number and letter. This letter was given to the research pharmacist at the site, who used a key linking study letter and treatment assignment to determine whether the infant should receive vitamin E or placebo. Study site personnel who were involved in care of the infants or in data collection for the study were blinded to treatment assignment, as were workers at the laboratory where the serum tocopherol analyses were performed.

Data Collection

Blood samples (0.5 mL) for analysis of serum tocopherol levels were collected in serum separator tubes before the dose of study drug was given and 24 hours and 7 days after the dose. Blood samples were not collected for the 5 infants who were randomized but did not receive the study drug. The samples were centrifuged, and the serum removed and frozen in amber tubes to protect it from light until shipped on dry ice to a central laboratory (ARUP Laboratories, Salt Lake City, UT), where they were analyzed by high-performance liquid chromatography for α- and γ-tocopherol. No vitamin E was given after the initial dose of study drug except for that received from the standard parenteral nutrition regimens at each site and from milk or infant formula. The clinical protocol for administration of parenteral multivitamins at each site was recorded.

The nutritional sources received (parenteral nutrition, human milk, infant formula) were collected for the first
week of life. Information was prospectively collected during the first 14 days of life on the occurrence of death, necrotizing enterocolitis, spontaneous intestinal perforation, late-onset sepsis, and severe (grade 3 or 4 by criteria of Papile\textsuperscript{21}) intraventricular hemorrhage. These were monitored as potential adverse effects of the enteral dose of vitamin E, although the study was not powered to detect significant differences in these outcomes.

**Sample Size**

The sample size for this study was determined as the number needed to provide a 95% confidence interval of \( \pm 10\% \) around the percentage of \( \alpha \)-tocopherol levels within the range 1 to 3 mg/dL for the infants who received vitamin E. Assuming that 80\% of the \( \alpha \)-tocopherol levels are within the target range of 1 to 3 mg/dL, a sample of 62 infants provides the desired 95\% confidence bound from 70\% to 90\%. Given this required sample size in the vitamin E arm and the plan for a 2:1 randomization ratio between the vitamin E and placebo groups (because vitamin E was the primary focus of the study), the total sample size for this study was 93, with 62 infants randomized to receive vitamin E and 31 to receive placebo.

**Data Analysis**

Serum \( \alpha \)-tocopherol levels were compared between infants who received vitamin E and those who received placebo. The levels were analyzed both as continuous variables and as categorical variables using the following categories: \( <0.50, \ 0.50 \text{ to } 0.99, \ 1.00 \text{ to } 3.00, \ 3.01 \text{ to } 3.50, \text{ and } >3.50 \text{ mg/dL}. \)

Statistical significance for differences in patient characteristics and \( \alpha \)-tocopherol level between vitamin E and placebo groups was determined using the nonparametric Wilcoxon test for continuous variables and the Fisher’s exact test for categorical variables. Increase in \( \alpha \)-tocopherol level from baseline to 24 hours was calculated for each infant who had both measures, and this value was compared between vitamin E and placebo groups using the Wilcoxon test. Comparisons of adverse events experienced by infants in the vitamin E and placebo groups were adjusted for antenatal corticosteroid stratum and tested for significance using the Mantel-Haenszel \( \chi^2 \) test.

The study was registered with clinicaltrials.gov (NCT01193270) and was conducted under Federal Drug Administration Investigational New Drug Application 105988.

**RESULTS**

Of the 494 infants screened for eligibility, 180 met all criteria for eligibility, 255 were ineligible, and information needed to determine eligibility was not available for 59 (Fig 1). For 60\% of those screened, the parents were approached for consent before birth. Thus, some infants for whom consent was obtained and who were expected to meet inclusion criteria were determined to be ineligible at birth due to gestational age \( \geq 27 \) weeks (68 infants) and/or birth weight \( \geq 1000 \) g (34 infants). The most common reason for ineligibility was inability to give the study medication by 4 hours of age (96 infants). The other reasons for ineligibility were plan for limited treatment based on poor prognosis (58 infants), pH \( \leq 7.0 \) (20 infants), major congenital malformation (4 infants), had already received supplemental vitamin E (3 infants), and born in an outside hospital (1 infant). The sum of the numbers for each exclusion criterion exceeds 255 because some infants met \( >1 \) criterion. Of the 180 infants who met all eligibility criteria, consent was obtained from the parents of 94; 1 of these infants died soon after birth, and the other 93 were randomly assigned to receive vitamin E (62) or placebo (31).

Five of these infants (3 vitamin E and 2 placebo) did not receive the study drug; 3 of these infants were withdrawn from the study by a treating physician, 1 died before the drug could be given, and 1 infant did not receive the drug because a research pharmacist was not available. Thus, of the 88 infants receiving study drug, 59 received vitamin E and 29 received placebo.

The 93 randomized infants were born at 22 to 26 weeks’ gestation and weighed 400 to 990 g at birth (Table 1). The vitamin E infants were less likely to be small for gestational age (3\% vs 16\%, \( P = .04 \)). Nearly all infants were exposed to antenatal corticosteroids to promote fetal maturation: 92\% of vitamin E infants and 94\% of placebo infants. The patient characteristics were similar for the 88 infants who received the study drug (vitamin E or placebo). On each of the first 7 days of life, the fraction of infants who received parenteral nutritional solutions, parenteral multivitamins, human milk, and formula did not differ significantly between the vitamin E and placebo groups.

For the 88 infants who received the study drug, 83 had blood samples collected at each of the 3 expected points: before dosing, 24 hours after dosing, and 7 days after dosing. Overall, 257 of the expected 264 blood samples were collected; 32 samples were not analyzed because of technical problems or inadequate sample volume, and for 2 samples, the quantity was sufficient for analysis of serum \( \alpha \)-tocopherol level but not \( \gamma \)-tocopherol. The results described here were based on \( \alpha \)-tocopherol levels from 225 samples and \( \gamma \)-tocopherol levels from 223 samples.

The median serum \( \alpha \)-tocopherol level was similar at baseline in the vitamin E and placebo groups, 0.31 mg/dL and 0.33 mg/dL, respectively (Table 2). The \( \alpha \)-tocopherol level was higher in the vitamin E group than the placebo group 24 hours after dosing (0.63 vs 0.42 mg/dL, \( P = .003 \)).
and at 7 days (2.21 vs 1.86 mg/dL, \(P = .04\)). At 24 hours, only 30% (15 of 49) of infants who received vitamin E had serum \(\alpha\)-tocopherol levels <0.50 mg/dL (\(P = .01\); Fig 2), the lower limit of vitamin E sufficiency. At 24 hours, 33 of 50 (66%) of the vitamin E infants and 10 of 26 (38%) of the placebo infants had \(\alpha\)-tocopherol levels between 0.5 and 3.5 mg/dL (\(P = .03\)). At 24 hours, 7 of 50 (14%) of the vitamin E infants and 3 of 26 (12%) of the placebo infants had \(\alpha\)-tocopherol levels between 1.0 and 3.0 mg/dL.

FIGURE 1
Patient flow through screening, enrollment, randomization, and study drug administration. Some study candidates failed to meet \(\geq 1\) criterion for eligibility. AN, antenatal; BW, birth weight; DR, delivery room; GA, gestational age.
There were few infants with 7-day \( \alpha \)-tocopherol level \( >3.5\) mg/dL were at 3 centers where the smallest infants received higher than the recommended vitamin E dose of 2.8 IU/kg per day. The rise in serum \( \alpha \)-tocopherol level from baseline to 24 hours was larger in the vitamin E group than the placebo group (median 0.25 vs 0.08 mg/dL, \( P < .001 \)) (Table 2).

There were no differences in serum \( \gamma \)-tocopherol levels between the vitamin E and placebo groups at any time before or after the dose of \( dl \)-\( \alpha \)-tocopheryl acetate was given (Table 2), which was not surprising given that the administered vitamin E product contained no \( \gamma \)-tocopherol. The serum concentrations of \( \alpha \)-tocopherol and \( \gamma \)-tocopherol increased during the first 7 days in both the vitamin E and placebo groups.

There was no significant difference between vitamin E and placebo groups in the incidence of death, necrotizing enterocolitis, spontaneous intestinal perforation, late-onset sepsis, or severe (grade 3 or 4) intraventricular hemorrhage.

### DISCUSSION

A single 50-IU/kg enteral dose of vitamin E as \( dl \)-\( \alpha \)-tocopheryl acetate, given within the first 4 hours after birth, allowed more rapid correction of the low serum \( \alpha \)-tocopherol levels seen at birth in preterm infants. Two-thirds of infants who received vitamin E had 24-hour \( \alpha \)-tocopherol levels between 0.5 and 3.5 mg/dL, the range that is thought to be both adequate and safe.\(^{1, 8, 16, 22} \)

However, this single dose of vitamin E left nearly one-third of infants with \( \alpha \)-tocopherol levels still below the critical threshold of 0.5 mg/dL 24 hours after dosing and only 14% with levels within the targeted range of 1.0 to 3.0 mg/dL. There were few infants with \( \alpha \)-tocopherol levels \( >3.5\) mg/dL; most of these were in several centers where the doses of parenteral multivitamin given were higher than recommended.\(^{23–25} \) Serum levels of \( \alpha \)-tocopherol \( >3.5\) mg/dL have been associated with increased risks of sepsis and necrotizing enterocolitis.\(^{16, 26, 27} \)

If the goal of vitamin E administration at birth is to normalize the serum \( \alpha \)-tocopherol level in nearly all infants, it seems that several doses or a larger single dose will be required to accomplish this. It is not known whether rapidly improving vitamin E status on the day of birth will help to reduce intracranial hemorrhage. This question can only be answered through larger trials.

The rise in serum \( \alpha \)-tocopherol level after a vitamin E dose of 50-IU/kg was less than expected based on previous work with somewhat larger preterm infants.\(^{26–30} \) This may indicate that gastrointestinal absorption of the vitamin E was reduced or delayed in these very preterm infants.

The serum \( \gamma \)-tocopherol levels seen in our infants are similar to those reported previously for preterm infants.\(^{31, 32} \)

The rise in \( \gamma \)-tocopherol seen in our patients over the first week of life is similar to that reported by Kaempf and Linderkamp\(^{31} \) and presumably resulted from dietary sources of \( \gamma \)-tocopherol.\(^{33} \)

The low serum and whole-body levels of tocopherol in preterm infants at birth are, at least in part, the result of their low body fat stores,\(^{34–36} \) which indirectly lead to a lower requirement of vitamin E to prevent lipid peroxidation in cell membranes.\(^{35, 37} \) If vitamin E helps to protect the preterm infant against intracranial hemorrhage,\(^{10–16} \) the mechanism of protection is not known; therefore, the importance of the serum tocopherol level and the tocopherol/lipid ratio in plasma and tissues for this protection is not known.

Administration of supplemental vitamin E to the mother has been considered as a method of protecting the preterm infant from intracranial hemorrhage,\(^{38} \) but this approach seems to hold little potential for protecting the fetus from the consequences of vitamin E insufficiency because placental transfer of tocopherols is quite limited.\(^{36, 39} \)
The question remains whether a single dose or several doses of vitamin E given soon after birth can reduce the risk of intracranial hemorrhage in preterm infants. It is possible that rapid correction of the deficiency of vitamin E at birth could confer benefit to the infant, as occurs with administration of vitamin K, another fat-soluble vitamin.

CONCLUSIONS

We have shown that enteral administration of a single 50 IU/kg dose of vitamin E to preterm infants at birth raises the serum α-tocopherol level above the critical threshold of 0.5 mg/dL in most but not all infants. A different dosing strategy will be required to quickly and reliably achieve α-tocopherol levels in the physiologic range, 1 to 3 mg/dL, for all infants. Additional study is needed to identify the best dosing regimen and to test the efficacy of vitamin E at birth in reducing the preterm infant’s risk of intracranial hemorrhage.

ACKNOWLEDGMENTS

The National Institutes of Health, the Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD), the National Center for Research Resources, and the National Center for Advancing Translational Sciences provided grant support for the NRN’s Vitamin E pilot trial.

Data collected at participating sites of the NICHD NRN were transmitted to RTI International, the data-coordinating center (DCC) for the network, which stored, managed, and analyzed the data for this study. On behalf of the NRN, Drs Abhik Das (DCC Principal Investigator) and Nellie Hansen (DCC Statistician) had full access to all the data in the study and take responsibility for the integrity of the data and accuracy of the data analysis. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

We are indebted to our medical and nursing colleagues and the infants and their parents who agreed to take part in this study. The following investigators, in addition to those listed as authors, participated in this study: NRN Steering Committee Chairs: Richard A. Polin, MD, Division of Neonatology, College of Physicians and Surgeons, Columbia University, (2011–present) Alpert Medical School of Brown University and Women & Infants Hospital of Rhode Island (grant U10 HD27904): Angelita M. Hensman, RN, BSN; Kristin M. Basso, BSN, MA; Michael R. Muller, PharmD

Case Western Reserve University, Rainbow Babies and Children’s Hospital (grant U10 HD21364): Nancy S. Newman, RN; Arlene Zadell, RN; Bonnie S. Siner, RN; Michael Banchy, RPH

Duke University School of Medicine, University Hospital, University of North Carolina, Alamance Regional Medical Center, and Durham Regional Hospital (grants U10 HD40492, UL1 RR24128, UL1 RR25747): Ronald N. Goldberg, MD; C. Michael Cotten, MD, MHS; Matthew M. Laughon, MD, MPH; Kimberley A. Fisher, PhD, FNP-BC, IBCLC, Sandra Grimes, RN, BSN, Joanne Finkle, RN, JD

Emory University, Children’s Healthcare of Atlanta, Grady Memorial Hospital, and Emory University Hospital Midtown (grants U10 HD27851, UL1 RR25008): Barbara J. Stoll, MD; Yvonne C. Loggins, RN, BSN; Diane I. Bottcher, RN, MSN

NICHD: Stephanie Wilson Archer, MA

Indiana University, University Hospital, Methodist Hospital, Riley Hospital for Children, and Wishard Health Services (grant U10 HD27856): Gregory M. Sokol, MD; Leslie D. Wilson, BSN, CCRC

RTI International (grant U10 HD36790): Dennis Wallace, PhD; Jeanette O’Donnell Auman, BS; Jenna Gabri, BS; David LeBlond, BS; Carolyn Petrie Huitema, MS; Kristin M. Zaterka-Baxter, RN, BSN

Stanford University, Lucile Packard Children’s Hospital (grants U10 HD27880, UL1 RR25744): David K. Stevenson, MD; M. Bethany Ball, BS, CCRC; Melinda S. Proud, RCP; Steven R. Chinn, PharmD

University of Alabama at Birmingham Health System and Children’s Hospital of Alabama (grant U10 HD34216): Namavivayam Ambalavanan, MD; Monica V. Collins, RN, BSN, MaEd; Shirley S. Cosby, RN, BSN; Rebecca J. Quinn, PharmD
REFERENCES


Dr Bell conceived and led the design of the study, participated in the interpretation of the data, wrote the first and subsequent drafts of the manuscript, and revised it based on feedback from the other authors; Ms Hansen helped to design the analysis plan and was responsible for the data management and analysis, performed the analysis with guidance from Drs Bell and Das, and helped revise the manuscript critically for important intellectual content; Dr Brion participated in the conception and design of the study, participated in the interpretation of the data, and helped revise the manuscript critically for important intellectual content; Ms. Johnson participated in the conception and design of the study, helped to draft the data forms and the manual of operations, and helped revise the manuscript critically for important intellectual content; Drs Laptook, Goldberg, Van Meurs, Carlo, Poindexter, Faix, Carlton, Watterberg, and Ellsbury participated in the design of the study and the interpretation of the data and reviewed the manuscript for important intellectual content; Dr Das participated in the design of the study and the plan for data analysis, was responsible for the data management and participated in the analysis, and helped to revise the manuscript critically for important intellectual content. All authors approved the final version of the manuscript.

This trial has been registered at www.clinicaltrials.gov (identifier NCT01193270).

www.pediatrics.org/cgi/doi/10.1542/peds.2013-1684
doi:10.1542/peds.2013-1684

Accepted for publication Sep 16, 2013

Address correspondence to Edward F. Bell, MD, Department of Pediatrics, University of Iowa, 200 Hawkins Dr, Iowa City, IA 52242. E-mail: edward-bell@uiowa.edu

PEDIATRICS (ISSN Numbers: Print, 0031-4005; Online, 1098-4275).

Copyright © 2013 by the American Academy of Pediatrics

FINANCIAL DISCLOSURE: The authors have indicated they have no financial relationships relevant to this article to disclose.

FUNDING: The National Institutes of Health and the Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD) provided grant support for the Neonatal Research Network's Generic Database Study. Dr Higgins is employed by the NICHD. The institutions of most of the other authors received grant funding from NICHD in support of this study. Funded by the National Institutes of Health (NIH).

POTENTIAL CONFLICT OF INTEREST: The authors have indicated they have no potential conflicts of interest to disclose.
Serum Tocopherol Levels in Very Preterm Infants After a Single Dose of Vitamin E at Birth
Pediatrics 2013;132;e1626
DOI: 10.1542/peds.2013-1684 originally published online November 11, 2013;

Updated Information & Services
including high resolution figures, can be found at:
http://pediatrics.aappublications.org/content/132/6/e1626

References
This article cites 35 articles, 13 of which you can access for free at:
http://pediatrics.aappublications.org/content/132/6/e1626.full#ref-list-1

Subspecialty Collections
This article, along with others on similar topics, appears in the following collection(s):
Fetus/Newborn Infant
http://classic.pediatrics.aappublications.org/cgi/collection/fetus:newborn_infant_sub
Neonatology
http://classic.pediatrics.aappublications.org/cgi/collection/neonatology_sub
Pharmacology
http://classic.pediatrics.aappublications.org/cgi/collection/pharmacology_sub
Toxicology
http://classic.pediatrics.aappublications.org/cgi/collection/toxicology_sub

Permissions & Licensing
Information about reproducing this article in parts (figures, tables) or in its entirety can be found online at:
https://shop.aap.org/licensing-permissions/

Reprints
Information about ordering reprints can be found online:
http://classic.pediatrics.aappublications.org/content/reprints

Pediatrics is the official journal of the American Academy of Pediatrics. A monthly publication, it has been published continuously since 1948. Pediatrics is owned, published, and trademarked by the American Academy of Pediatrics, 141 Northwest Point Boulevard, Elk Grove Village, Illinois, 60007. Copyright © 2013 by the American Academy of Pediatrics. All rights reserved. Print ISSN: .
Serum Tocopherol Levels in Very Preterm Infants After a Single Dose of Vitamin E at Birth

Pediatrics 2013;132:e1626
DOI: 10.1542/peds.2013-1684 originally published online November 11, 2013;

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://pediatrics.aappublications.org/content/132/6/e1626