Reemerging Nutritional Rickets

A Historical Perspective

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Recent case reports highlight the resurgence of rickets in certain groups of breastfed infants. Infants residing in the North, irrespective of skin color, and dark-skinned African American infants residing anywhere in the United States are most vulnerable to nutritional rickets if they are exclusively breastfed past age 6 months without vitamin D supplementation. At the turn of the 20th century, rickets was nearly universal among African American infants living in the North. The discovery of vitamin D, the initiation of public health campaigns to fortify infant foods with vitamin D, and the supplementation of vitamin D to breastfed infants were responsible for overcoming the rickets scourge. We review a classic nutritional study by Alfred F. Hess, one of the greatest clinical nutritional researchers of the early 20th century, in the context of the resurgence of rickets, especially among dark-skinned infants. The Columbus Hill district, a black community of New York, NY, served as the setting for the study. Sixty-five infants (aged 1-17 months) entered a 6-month open-label trial of daily cod liver oil therapy. Participants were assessed for signs of rickets at recruitment and at 2, 4, and 6 months. Cod liver oil prevented the development of rickets in 34 (92%) of 37 infants treated for 6 months and in 7 (58%) of 12 treated for 4 months. Of the 16 infants who did not take the prescribed treatment, rickets progressed unremittingly in 15. Hess translated his success into a public health campaign leading to the development of the first rickets clinic in 1917. This was the first step in the conquest of the rickets epidemic of the early 20th century.

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Nutritional rickets, an apparently vanquished disease in the United States, is back in the limelight and has resurfaced as a public health issue. In 2003, in response to the problem of reemerging rickets, the American Academy of Pediatrics revised its policy on vitamin D supplementation to infants and children. Several recently reported case series have highlighted the vulnerability of the breastfed African American infant to the development of nutritional rickets. The common theme among the recently reported cases of nutritional rickets in North America and the United Kingdom is that most affected infants are dark skinned (African American, Afro-Caribbean, or Asian descent) or residents of northern latitudes who had been exclusively breastfed beyond 6 months of age without vitamin D supplementation. Several of the reports were from North Carolina and Georgia, relatively sunny southern states considered to be at low risk for seasonal hypovitaminosis D. In the context of the reemergence of nutritional rickets, we review a classic nutritional study by Alfred Hess that explores the prophylactic role of cod liver oil in the eradication of nutritional rickets in African American infants.

VITAMIN D PHOTOSYNTHESIS AND THE HISTORY OF RICKETS

The propensity for dark-skinned breastfed infants to develop rickets stems from
the fact that people mostly meet their vitamin D needs from exposure to sunlight and that breast milk per se is a poor source of vitamin D. Vitamin D, the sunshine vitamin, is a hormone. On exposure to UV-B rays (290-315 nm), 7-dehydrocholesterol, the vitamin D precursor in the skin, gets photolyzed to previtamin D3. Previtamin D3 is thermally isomerized to vitamin D3 (cholecalciferol). Vitamin D3 undergoes further hydroxylation in the liver and kidney to become the active form of vitamin D (1,25-dihydroxyvitamin D or calcitriol). Endogenous vitamin D production in the skin is affected by the geographic latitude of residence, the degree of skin pigmentation, the season of the year, clothing, atmospheric pollution, and the application of sunscreen.

ROLE OF BREASTFEEDING AND SUNLIGHT

The reemergence of rickets has coincided with the resurgence of breastfeeding. The promotion of breastfeeding without emphasizing the need for vitamin D supplementation for the prevention of rickets has led to the resurgence of this nutritional disorder in a vulnerable population. Most recently reported cases of rickets occurred in breastfed African American infants. Despite the increased prevalence of nutritional rickets among African American infants, rickets is a color-blind disease. Breast milk is a poor source of vitamin D. In the phase of no vitamin D supplementation, all breastfed infants are vulnerable to the development of rickets if they cannot photosynthesize their required levels of vitamin D. The public health message that infants younger than 6 months not be exposed to any direct sunlight to reduce their eventual risk of skin cancer, and the use of sunscreens and protective clothing among older infants to avoid exposure to direct sunlight, are also relevant factors in the resurgence of rickets. The risk of developing rickets is much greater among dark-skinned infants because they require a 6-fold greater exposure to sunlight to elevate their vitamin D levels to the same degree as seen in white infants. Cultural practices that limit exposure to sunlight also exacerbate the vulnerability to vitamin D deficiency.

BACKGROUND

Nearly 85 years ago, Alfred F. Hess (Figure 1), in collaboration with Lester Unger, pioneered a community-based clinical study to evaluate the effectiveness of cod liver oil as a remedy in the preventive treatment of rickets. Until then, cod liver oil had been used only as a therapeutic agent in individual cases of infantile rickets. Having been aware that the rickets burden was highest among black infants, Hess and Unger chose the Columbus Hill district, a black community of New York, NY, to conduct their research. At the time of this study, rickets was pervasive among black infants. Hess and Unger observed: “It may be safely stated that 90% of colored babies have rickets, and that even a majority of those that breastfed show signs of this disorder.”

The Henry Street Settlement (Figure 2) and the National League for the Study of the Urban Conditions of...
the Negro identified the Columbus Hill district as a needy neighborhood in terms of health disparities and economic woes.\textsuperscript{33,34} Hess and Unger summarized their plight as follows: “People pay high rents, earn low wages, and unfortunately have had but meager educational opportunities.”\textsuperscript{33(p487)} The infant mortality statistics reflect the extent of the health burden faced by the residents of Columbus Hill. In 1915, when the infant mortality rate was 96 per 1000 in the white population and 202 per 1000 in the Negro infants of New York City, the Columbus Hill district’s infant mortality rate was 314 per 1000. Most infant deaths were due to respiratory illnesses such as pulmonary tuberculosis, whooping cough, and pneumonia, and rickets predisposed an infant to increased morbidity from such respiratory illnesses. Therefore, Hess and Unger proposed that the reduction of rickets could indirectly reduce the high infant mortality rate among Negro infants.

**METHODS**

Sixty-five infants, 1 to 17 months of age, were studied for a 6-month period between December 1916 and June 1917. A visiting nurse familiar with the community helped the researchers access recruited patients in their homes throughout the study (Figure 3). Most of the enrolled infants had siblings with rickets at the time of recruitment. Patients were clinically assessed for rickets at the beginning of the study based on the presence or absence of craniotabes, rickety rosary, and epiphyseal widening, and the signs of rickets were divided into 4 grades of intensity (+ to ++++). Enrolled patients began daily therapy with cod liver oil for 6 months. Infants younger than 6 months were prescribed $\frac{1}{2}$ teaspoon (2.5 mL) of cod liver oil 3 times a day, and older infants were asked to take twice as much. Although cod liver oil was initially delivered to the homes of the infants, prescription refills were provided at a neighborhood settlement house each morning and 1 evening of the week. At recruitment, the mode of infant feeding (breastfeeding vs artificial feeding) and the dietary intake of the mothers were reviewed. Data regarding the time the family has spent in the North and the family’s socioeconomic strata were collected. The investigators evaluated the clinical status of rickets among the enrolled patients at 2, 4, and 6 months. The visiting nurse and the researchers frequently visited the families to monitor the health of the enrolled infants and assure themselves of the compliance with the prescribed treatment.

**RESULTS**

At the end of 6 months, the eligible patients were categorized into 3 treatment groups and 1 control group. The group categorization was based on the average cumulative amount of cod liver oil ingested by each infant in the group and the duration of therapy. Treatment group
1 (n=32) was compliant for 6 months, and each infant had an average cumulative total of 54 oz (1620 mL) of cod liver oil. Although treatment group 2 (n=5) was also compliant for 6 months, the average cumulative intake of cod liver oil per infant was lower (23 oz [690 mL]). Infants belonging to treatment group 3 (n=12) were compliant for only 4 months, and the average cumulative intake of cod liver per infant was 21 oz (630 mL). The control group comprised the 16 noncompliant infants who took no cod liver oil at all.

Prophylactic cod liver oil therapy successfully prevented the onset of rickets or resolved the signs of established rickets in 92% of infants treated for 6 months and in 58% of infants treated for 4 months (Table 1). Of the 16 untreated infants in the control group, 15 (94%) had progressive unremitting rickets (Table 2).

In the control group, the group that received no cod liver oil, rickets progressed in 15 of the 16 infants, and neither breastfeeding nor artificial feeding afforded any protection against rickets.

Hess and Unger concluded that cod liver oil was efficacious in protecting the Negro infant against the development of rickets. Although larger doses of cod liver oil offered more protection (54 vs 23 oz [1620 vs 690 mL]), Hess and Unger stated that it is the regularity and duration of administration (6 vs 4 months) that confers the protection against rickets. Infants who were not given prophylactic therapy invariably had progressive unremitting rickets.

Hess and Unger were aware of the seasonal vulnerability for the occurrence of rickets and chose the “colder season” for conducting their study. Acknowledging the seasonal limitation of their study and their previous experience with rickets, Hess and Unger stated that cod liver oil prophylactic treatment should be considered only during the colder season. Hess and Unger realized that many Negro infants residing in New York were afflicted with rickets and that neither breastfeeding nor artificial feeding offered any protection against the development of rickets. In an attempt to explain this racial predilection, they explored the role of maternal diet, culinary practices, and the immigration history of the residents of Columbus Hill.

The Columbus Hill district was in Manhattan, on west 30th Street and the area around 7th Avenue, and had previously been called San Juan Hill. Most residents of Columbus Hill were migrants from the West Indies, and only a few of them were from the South. In their native West Indies, there was plenty of sunshine and an abundance of fresh vegetables and fruits. In contrast, New York City offered a distinct change in climate and diet. The Columbus Hill resident’s diet lacked fresh fruits, vegetables, and milk and offered plenty of meat. Rickets was rare among infants residing in the tropics. Hess and Unger confirmed directly from several physicians practicing in the West Indies and other parts of the tropics that rickets was rare among the native infants. They ventured to speculate that the contrast in the northern Negro’s mode of life, the change in the climate, and the marked difference in the food could all play a part in their excessive susceptibility to rickets.

In this seminal study, Hess and Unger also demonstrate the successful essentials of recruitment of minori-
ties in research participation and the establishment of effective public health initiatives in overcoming the rickets burden. The National League for the Study of the Urban Conditions of the Negro and the Henry Street Settlement had surveyed the Columbus Hill community to ascertain the socioeconomic conditions responsible for its high infant mortality rate. Lincoln House, a branch of Henry Street Settlement in the Columbus Hill neighborhood, had a reputation for social reform.36,37 Partnering with those organizations was essential for the building of trust between the community and the researchers, which enabled the researchers to gain access to the homes of the participants. The fact that the study nurse had worked in the district for several years previously was also a factor in helping build the trust between the participants and researchers and in gaining access to the homes of the participants.33 Conducting the study in an economically and medically vulnerable community where rickets was highly prevalent was essential for judging the impact of the intervention. The Syphilis Study at Tuskegee (1932-1972) used similar methods to build community trust, namely, hiring a black nurse (Eunice Rivers) to work in the district for several years previously was a leading clinical researcher of the early 20th century. His pioneering work pertains to nutritional science. Hess recommended supplementation of fresh fruit or vegetable juices to infants fed heated milks to prevent scurvy.44

During the study, the dispensing station for cod liver oil evolved into a community-based rickets clinic. As the research progressed, community awareness of rickets increased, and Columbus Hill district mothers began to seek consultation for diagnosis and treatment of rickets at that clinic. Hess and Unger33 proposed setting up such “rickets clinics” in the Negro and Italian districts of large cities because rickets was equally prevalent among Italian infants. The proposed creation of the rickets clinic was modeled after the existing specialized clinics for treating the condition of the poor, established a rickets clinic during the fall of 1917 at the Columbus Hill district’s baby welfare station and to dispense cod liver oil at cost. As envisioned by Hess, the Department of Health, in collaboration with the Association for Improving the Condition of the Poor, established a rickets clinic during the fall of 1917.40 By 1921, the success of the Columbus Hill experiment was adapted by the Mulberry Health Center, located in an Italian neighborhood, and infants younger than 1 year were actively screened and treated for rickets.41 The Columbus Hill clinic emphasized maternal and child care throughout the early years and was accessed by 90% of the community by 1925.41

In this article, we celebrate Hess’s contribution as a clinical researcher and his ability to translate clinical research into public health and preventive medicine. Hess was a leading clinical researcher of the early 20th century. His pioneering work pertains to nutritional sciences. He demonstrated that oxidation of foods results in the loss of vitamin C.42 At the Hebrew Infant Asylum, Hess observed several cases of scurvy among infants fed pasteurized milk when orange juice had been excluded from their diets.43,44 He showed that the feeding of orange juice, raw milk, or potatoes could cure the scurvy.44

The contribution of Hess to the field of vitamin D nutrition is seminal. Besides successfully demonstrating the efficacy of cod liver oil as a prophylactic agent in the prevention of rickets, Hess also showed that infantile rickets could be cured by exposure to sunlight alone while...
the affected infant’s diet remained unchanged. \textsuperscript{33,42,45} Hess established the chemical basis for heliotherapy by demonstrating that the clinical cure of rickets by sunlight was associated with an increase in serum phosphate level, as noted with cod liver oil therapy. \textsuperscript{46} Hess’s greatest discovery came in 1924, when he showed that UV irradiation could render antirachitic function to certain foods. \textsuperscript{27,42} Windaus identified the antirachitic substance in irradiated foods as ergosterol in 1927, and the following year he was awarded the Nobel Prize for this discovery. \textsuperscript{42} Windaus acknowledged the influence of Hess’s work on his discovery in his acceptance speech. \textsuperscript{12}

By the time Hess died in 1933, he had published 227 medical manuscripts and classic monographs on scurvy and rickets. At the time of his death, Hess was a foremost investigator among pediatricians in the United States. \textsuperscript{42} An eminent contemporary pediatrician described Hess as an “out post in the advance of scientific medicine.” \textsuperscript{42} In memory of Hess, Abraham Flexner states that “Hess put forth a whole series of publications of the greatest worth and value. Some of these have been outmoded by time; science has passed beyond them and their importance at the time of their appearance is no longer apparent. Others have great importance today.” \textsuperscript{42(pxxviii)}

Hess’s contribution to child health will always be revered; however, his ability to translate clinical knowledge into successful public health initiatives in the eradication of rickets is what we would like to reflect. We believe that reviewing this classic study by Hess at a time when rickets is reemerging as a disease to contend with among breastfed African American infants will inspire us to find ways to combat this problem.

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Additional Information: Throughout the article, the terms Negro, black, colored, and African American are used interchangeably to reflect the nomenclature during the times in which these terms were used.

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REFERENCES


11. Holick MF. Vitamin D: the underappreciated D-lightful hormone that is important for skeletal and cellular health. Curr Opin Endocrinol Diabetes. 2002;9: 87-98.
Correction

Error in Table. In the article “Impact of the Bienestar School-Based Diabetes Mellitus Prevention Program on Fasting Capillary Glucose Levels: A Randomized Controlled Trial” by Treviño et al published in the September issue of the ARCHIVES (2004;158:911-917), the 95% confidence intervals were incorrectly calculated in Table 3. The correct confidence intervals for Table 3 are given in the following tabulation:

<table>
<thead>
<tr>
<th>Variable</th>
<th>Adjusted Difference (95% Confidence Interval)</th>
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<tbody>
<tr>
<td>Fasting capillary glucose</td>
<td>-2.24 (-4.20 to -0.28)</td>
</tr>
<tr>
<td>Body fat</td>
<td>0.18 (-0.45 to 0.81)</td>
</tr>
<tr>
<td>Physical fitness score</td>
<td>1.87 (0.09 to 3.65)</td>
</tr>
<tr>
<td>Dietary fiber intake</td>
<td>0.99 (0.30 to 1.68)</td>
</tr>
<tr>
<td>Energy intake from saturated fat</td>
<td>-0.68 (-2.01 to 0.65)</td>
</tr>
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