Editorial: Our Nevin (1918-2013) -
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Noel W Solomons

Growth, hematological, iron and inflammatory status in Guatemalan children with end-stage renal failure
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EDITORIAL The Nevin Scrimshaw International Nutrition Foundation at thirty
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See you at EB 2013 in Boston
On January 20, 1918, Nevin Stewart Scrimshaw, PhD, MD, MPH drew his first breath in Madison, Wisconsin in the USA. On the corresponding date in 2013, he completed 95 years of one of the most transcendental and importantly contributory careers in the history of science and for Central America. On February 8th of the same year, he drew his final breath in Plymouth, New Hampshire. He left a family including his wife of 70 years, Mary, his daughter Susan, and his sons Norman, Nevin, Stephen, and Nathaniel, along with a host of grandchildren, and at least one great granddaughter.

Nevin Scrimshaw drew his first breath of Guatemalan air in late 1940s on airplane stopovers en route between the United States and Panama, where he was serving as a physician, specialist in obstetrics and gynecology, at an American hospital in the Canal Zone. When the Pan American Health Organization sought leadership for its incipient Institute of Nutrition of Central America and Panama (INCAP) in Guatemala, they found great appeal in the combination of a biochemistry degree from Harvard University and a medical degree from the University of Rochester on which to base a grand adventure in science and service in the center of the Hemisphere. And did they ever make the right choice!! Thus, on September 14, 1949, the day before Guatemala and all of Central America would celebrate the 128th anniversary of Central American Independence from Spain, INCAP was founded in Guatemala City with 31-year-old Nevin S. Scrimshaw as its founding Director.

As much as it is politically correct to attribute the ills of the world to “systems” and to seek to advance society based on egalitarian collective agencies, the truth of the matter is that the force and ingenuity of individuals confronting the challenges of their time make the major impact on history. This is true of Washington, Newton, Lincoln, Pasteur, von Bismarck, Einstein, Churchill, Patton and others. They appraised the nature of the situation, adopted the mantel of leadership, and altered the course of a pivotal situation or changed the current of thought (or both). When it comes to the challenges of malnutrition and food in the 20th Century, no single individual impacted the course more than Nevin Scrimshaw.

There is no contesting the proposition that without Dr. Scrimshaw’s influence in institution building, in advancing scientific thought and in teaching and mentoring, I would not be living where I have been for three and one-half decades doing what I do and basing it within the Center for Studies of Sensory Impairment, Aging and Metabolism (CeSSIAM). Nevin’s hand has had generic and particular agency all along the way and all across the board.

The Scientific Heritage for Better Health and Nutrition

The message from the trajectory of INCAP and the legacy of Scrimshaw, himself, is to look to what needs to be studied and apply the evolving concepts and tools for investigation. That is, not to recline on the narrow laurels of what you and your laboratory do well and repeatedly. In his scientific and policy life, he was like a player in a carnival arcade, taking aim at every target that popped up – and generally hitting the bull’s eye with every toss of the ball.

Scrimshaw is known for his leadership in issues of protein. But, it was iodine and endemic goiter that the INCAP team would first address in Guatemala. As a highland country, the prevalence of iodine deficiency and goiter was high in 1949. The local salt was coarse and humid. The conventional salt for iodizing salt – potassium iodide – was poorly compatible with this class of salt. Through a series of technological innovations, laboratory tests and human studies, the team found that an alternative compound – potassium iodate – was far more stable in salt and could improve the iodine nutrition of deficient individuals just as well as iodide. This set the stage to conquer the goiter problem throughout the isthmus.

Scrimshaw’s interest in protein arose from the large prevalence of acute malnutrition (marasmus and kwashiorkor). This was termed protein – calorie malnutrition (PEM). Aided by a Guatemalan pediatrician, Moise Behar, Scrimshaw innovated with the treatment regimens to speed the rehabilitation of the children. A protein-rich diet was found to resolve the symptoms of acute PEM and lead to recovery. But his biochemistry background led him to work with his colleague, Guillermo Arroyave, to characterize the biochemical and metabolic abnormalities of kwashiorkor. From this interest in the clinical profile of protein deficiency, Scrimshaw and Behar extended the epidemiological metaphor to that of an ice-berg, in an article in 1961 in the prestigious journal, Science. It viewed the clinical syndromes of marasmus and kwashiorkor as the visible tip of the ice-berg; below the waterline of disadvantage populations would be many more individuals with inadequate quantity and quality of protein in their diets.

The thinking conceived of a continuum of impaired protein nutrition would bring out the food technology and solution-building side of Nevin to the fore. Working with Ricardo Bressani, a Guatemalan food scientist, Scrimshaw at INCAP explored a series of plant-based mixtures to develop a high-protein supplement that would prevent protein undernutrition across a population. The mixture that would become INCAParina emerged from these studies in 1958. It highlighted, moreover, how legumes (cotton seed) and cereal (maize) could complement one another to produce a composite protein with the physiological value of animal protein.
In 1953, the INCAP team published the results of a curious experiment of feeding aureomycin to village children on the hypothesis that antibiotics would improve the growth of poorly-growing juveniles as it had been shown to do in poultry and livestock. Although the findings showed no significant trophic effect of antibiotic administration, the notion of infection and the microbial environment playing a role in the stunting in Guatemala would persist. After a decade of experience in Guatemala, Nevin Scrimshaw went to Boston to obtain a Masters of Public Health at Harvard in 1959. The product of the thesis would be the concept “Interaction of Nutrition and Infection”, eventually published as a WHO Monograph of the same name in 1968. In this treatise, he documented how poor nutrition decreases resistance to infection, while infection impairs nutritional status. He also indicates, in a minority of instances, that poor nutrition can confer protection of the host against infection, presumably by depriving the pathogen of the needed nutrient.

**Social and Cultural Impact on the Science in Central America**

Scrimshaw was a man of inclusion. He recognized and respected cultures and cultural individualism. As a matter of fact both his wife and his daughter were anthropologists, and he supported and embraced the dimension of culture in nutritional beliefs. While respecting culture, he acted in ways to assure that there was no discrimination or exclusion of any cultures, and that they be blended in research: both at the level of those doing the studying and those being studied. In terms of his investigative staff at CeSSIAM, he drew from all of Central America. Along with Guatemalans, figuring prominently in his early staff were Salvadorians and Costa Ricans. INCAP even had a Mexican co-Director for some years in the 1950s. He reached beyond Mesoamerica as well, establishing collaborations and visiting with scientists from North America and Europe. The authorships of the early papers read like a potpourri of origins for the surnames of the contributors. The sponsoring organization, the Pan American Health Organization of INCAP had become part of the newly created United Nations, and Scrimshaw worked to see that a “united nations” was reflected in those working at the Institute.

This influence, to internationalize science in Guatemala continued even after his departure in 1961 to take the post of Head for the Department of Nutrition and Food Science at the Massachusetts Institute of Technology. In 1969, he began to engage with Central America by organizing an International Summer Course for professionals. These continued through the next decade. However, with the founding of the United Nations University in Tokyo, Nevin accepted to head its World Hunger Programme, founded in 1976. This included an exchange-program of UNU fellows. And soon the INCAP campus was being enriched by fellows from Chile, Argentina, Brazil and as far away as India and Malaysia.

His inclusive attitude, moreover, extended to the “nations” within Guatemala. The early photos of Scrimshaw picture him in short sleeves in the Guatemalan countryside examining indigenous children for enlarged thyroids or interviewing a Mayan woman with a malnourished infant in a rebozo on her back. His upbringing in Wisconsin never taught him that the Mayans of Guatemala were in any way an inferior class. As such he could bring resources to their plight that some else might not have been inspired to do. With my own ethnic heritage and social experience in the civil rights struggle, I consider myself a “barometer,” who can testify that racism of any sort was not part of the make-up of the man. He was exemplarily egalitarian.

Finally, his social legacy was, moreover, to give aspiring students and scientists his time and attention, even as his own agenda was incredibly over-full. That included accepting to mentor a Harvard undergraduate student on his thesis project in 1966 and open the eyes of young Noel Solomons to the wonders of international nutrition.

Whereas many of Guatemala’s institutions are supremely national, and even exclusive to a certain ethnic and social class, INCAP represented the true spirit of united nations working with people from across the globe to benefit the most disadvantaged and marginalized within Central America. This model, along with the dignity and value of the scientific career projected to professionals in Guatemala, paved the way culturally speaking, for the establishment of a research center like CeSSIAM in 1985. The model developed by the early development of INCAP paved the road that led this American expatriate to find a home in Guatemalan science and to create a home for an international flock of students and scientist at CeSSIAM.

It is disconcerting to imagine what scientific knowledge, scientific culture or professional fulfillment would have been if Nevin Scrimshaw had not come to Central America in 1949. But, with his passing, 64 years latter, we do not have to make that speculation. Our job is to celebrate the legacy he has left, and to extend it to ever wider and deeper capacity building and scientific discovery in the region that formed his initial home as a leader of nutrition for better health.

*Noel W Solomons, MD*

Scientific Director, CESSIAM
Inflammation is a part of the immune response. The acute form has been recognized for millennia, since Roman times in fact where the four characteristics were enunciated in Latin: calor (heat); rubor (redness); dolor (pain) and tumor (swelling). We also know of situations of chronic inflammation, with rheumatoid arthritis being a classic example. But indolent infections such as tuberculosis and deep tissue fungal infections (mycoses) also produce chronic inflammation. End-stage renal disease has recently been recognized as another situation of severe and chronic inflammation. The past decades have revealed much about the mediation of inflammation at the hormonal and molecular level.

Guatemala is a country with a host of factors that predispose to undernutrition in the poorest members of its population. This manifests as impaired growth as well as nutrient deficiencies such as iron deficiency and anemia. Guatemala has the highest prevalence of chronic undernutrition in the Americas, with a 54% rate of stunting in children under five years of age in the most recent national survey. This group also had an anemia prevalence of 48%. This represents a background of malnutrition for the nation.

The juvenile population of Guatemala is suffering from a growing epidemic of renal afflictions, leading to end-stage renal failure (ESRD). The only therapies are the palliative remedy of extracorporeal dialysis (either hemodialysis (HD) or peritoneal dialysis (PD)) or the curative treatment of renal transplant. With respect to nutritional status, the ESRD patients have the effects of their renal disorders, those of the dialysis, and the background of the Guatemalan diet and environment. In order to investigate some basic aspects of this interaction we enrolled 27 patients on HD and 27 patients on PD and explored aspects of linear growth, hematological status, iron status and metabolism and inflammatory status. Anthropometric evaluation consisted of height and weight. A complete hemogram was performed, extracting the hemoglobin, hematocrit and white cell count. A micro erythrocyte sedimentation rate (ESR) was performed on anticoagulated whole blood. A series of iron-status biomarkers included serum iron, transferring saturation and soluble transferring receptor. Ferritin and hepcidin were also measured. These are both inflammatory and iron-status markers at the same time. A selection of two pro-inflammatory cytokines (interleukin-6 and tumor necrosis factor-alpha) and one anti-inflammatory cytokine (interleukin-10) were measured in serum. Analyses were performed, variously in the Sanatorio Nuestra Señora del Pilar in Guatemala City, the Raboud University in Nijmegen, and the University of Innsbruck.

Descriptive statistics for demography and anthropometry for ESRD patients are given in (Table 2). Most were linear growth retarded with a median height-for-age Z-score of −2.77 and a stunting prevalence of 74%, as shown in the high rates of stunting and severe stunting in both dialysis modes, with HD more dramatically affected (Figure 1). The distribution of the 25 male patients on the 2006 WHO reference growth is shown in Figure 2; the females showed a comparable pattern (data not shown). Stunting is more extreme than the national average.

In terms of hematological status, Hb concentration means were 9.0±1.9 g/dL in HD and 9.9±2.7 g/dL in PD (p=0.17). Only 6 of the 54 subjects were not anemic, considering an altitude-adjusted criterion for low hemoglobin concentration.

The data for conventional and sophisticated biomarkers of iron status are shown in the upper panel of Table 2 by range and central tendency, with only ferritin differing between HD and PD. Inflammatory biomarkers are presented in the same manner in the lower panel without statistical comparison. Among HD patients, 11 had elevations for three or more inflammatory biomarkers, whereas the maximum was 2 elevations in PD. Curiously, ferritin correlated significantly with hepcidin-25 in PD (r=0.72; p<0.001), but not in HD (r=0.04; p=0.82).

We confirm that growth failure is a consistent component of ESRD, and it is superimposed on a background of short stature in the population at large. The total body stores of iron are likely elevated, consistent with the iron administration to the patients and indicated by the robust ferritin increases. Hepcidin is increased by inflammation and represents and appropriate response to limiting iron transport in the face of tissue overload. The anemia a consequence of the lack of erythropoietin and the hepcidin-limited iron transport to pro-erythrocytes to form hemoglobin. The hepcidin levels are marked elevated in juvenile ESRD, as compared to Dutch adults with the same disease and treatments and derived from the same analytical laboratory in Nijmegen, the Netherlands [1]. Factors of younger age, more aggressive iron administration and poorer environmental hygiene could factor into the stronger hepcidin response.

References:
Table 1. Characteristic of the subjects

<table>
<thead>
<tr>
<th></th>
<th>Hemodialysis (n = 27)</th>
<th>Peritoneal dialysis (n = 27)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male (%)</td>
<td>52</td>
<td>41</td>
<td>--</td>
</tr>
<tr>
<td>Age (years)</td>
<td>12±2</td>
<td>13±3</td>
<td>0.499</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>27±8</td>
<td>29±8</td>
<td>0.532</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>126 [96 – 160]</td>
<td>138 [110 – 157]</td>
<td>0.433</td>
</tr>
<tr>
<td>Height-for-age (z-score)</td>
<td>-2.8 [-5.9 - -0.1]</td>
<td>-2.3 [-5.7 - -0.4]</td>
<td>0.161</td>
</tr>
<tr>
<td>Time on dialysis (mo)</td>
<td>3 [&lt;1 – 42]</td>
<td>13 [1 – 58]</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Figure 1: Height-for-age (HAZ) score in A. Peritoneal dialysis and B. Hemodialysis

A.  

B.  

Figure 2: Height of ESRD patients in relation to an international reference growth curve, differentiated by mode of dialysis

Table 2. Central tendency and variance values for iron status and inflammatory biomarkers in hemodialysis and peritoneal dialysis patients

<table>
<thead>
<tr>
<th>Iron Status Biomarker</th>
<th>Hemodialysis (n = 27)</th>
<th>Peritoneal dialysis (n = 27)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hb (g/dL)</td>
<td>9.0 ± 2.0</td>
<td>9.9 ± 2.7</td>
<td>0.168</td>
</tr>
<tr>
<td>Serum iron (µg/dL)</td>
<td>65 [24 – 148]</td>
<td>65 [30 – 175]</td>
<td>0.291</td>
</tr>
<tr>
<td>TIBC (µg/dL)</td>
<td>282 [143 – 488]</td>
<td>253 [154 – 340]</td>
<td>0.533</td>
</tr>
<tr>
<td>Transferrin (ng/dL)</td>
<td>21 [7 - 63]</td>
<td>28 [12 – 103]</td>
<td>0.229</td>
</tr>
<tr>
<td>Transferrin saturation (%)</td>
<td>21 [7 - 63]</td>
<td>28 [12 – 101]</td>
<td>0.233</td>
</tr>
<tr>
<td>sTfR (mg/dL)</td>
<td>3.4 [1.8 – 6.1]</td>
<td>2.7 [0.3 – 7.1]</td>
<td>0.139</td>
</tr>
<tr>
<td>Ferritin (ng/ML)</td>
<td>602 [193 – 4,113]</td>
<td>458 [17 – 1,506]</td>
<td>0.015*</td>
</tr>
<tr>
<td>Hepcidin-25 (nm)</td>
<td>36 [2 – 131]</td>
<td>43 [0.5 – 140]</td>
<td>0.678</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Inflammatory Biomarker</th>
<th>Hemodialysis (n = 27)</th>
<th>Peritoneal dialysis (n = 27)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>White cell count (10³/L)</td>
<td>5.2 [2.7 - 14.1]</td>
<td>6 [4 – 12]</td>
<td>0.045</td>
</tr>
<tr>
<td>ESR (mm/h)</td>
<td>97 [16 – 145]</td>
<td>75 [2 – 125]</td>
<td>0.032</td>
</tr>
<tr>
<td>C-Reactive Protein (mg/dL)</td>
<td>[&lt; 5 – 70]</td>
<td>[&lt; 5 – 62]</td>
<td>0.029</td>
</tr>
<tr>
<td>Interleukin-6 (pg/mL)</td>
<td>7 [3 – 335]</td>
<td>3 [1 – 13]</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Interleukin-10 (pg/mL)</td>
<td>14 [5 – 690]</td>
<td>6 [2.5 – 65]</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>TNF-alpha (pg/mL)</td>
<td>6.5 [0 – 122]</td>
<td>[0 – 9]</td>
<td>&lt;0.001*</td>
</tr>
</tbody>
</table>

Values or mean±SD or median and [minimum-maximum]. *High significant difference between groups, ** Range of values

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Randall Lou is the head of the Pediatric Neurology Service of the Roosevelt Hospital
Noel W Solomons is the scientific director of CeSSIAM
Guenter Weiss is professor at the Medical University of Innsbruck
Dorine Swinkels is professor at the Nijmegen Medical Centre of the Radboud University
Klaus Schümann is professor in the Universitaet Technische Munchen
In Central America, maize represents three quarters of the total cereal consumption. This staple food is part of the culture and traditions of the Latin American region, especially in Guatemala, where it represents an important food source for the population. (1,2)

In January 2012, the newly elected Guatemalan government created the Ministry of Development, which established a series of strategic programs focused on fighting malnutrition and poverty in Guatemala. One of these programs was entitled “The Super Tortilla”, and consisted on the distribution of fortified maize flour with protein and micronutrients, to nutritionally vulnerable populations. It is expected that the recipients of this product will substitute maize and prepare tortillas and other traditional maize-based products with maize flour instead. Unfortunately, there are no reliable data on the consumption of these products which would allow estimating the impact of this sort of government strategy.

This information gap evidences the need to explore the anthropology of the use and consumption of maize flours, tortillas, tamalitos, gruels and other maize-based products in rural Guatemala. The knowledge of the intra-family consumption distribution of tortillas will provide with important information on which members of the family are consuming more maize products (i.e. adult men), an important matter to consider when evaluating safety issues for certain micronutrients. Furthermore, this will allow designing strategies targeted to certain vulnerable groups within the family, through the use of maize-based products such as gruels and soups, which are mainly consumed by women and children.

In order to explore the habitual consumption practices of tortillas and other potential uses for fortified maize flours, we conducted a study in rural, peri-urban and urban communities in Quetzaltenango, Guatemala, which aimed to determine the forms in which women could use this product and their habitual consumption patterns. Validated face-to-face interviews with a total of 150 women with children under 2 y were used for this purpose. The study had two components:

1. Interviews: To assess the consumption distribution of maize products within the family members, as well as the use and preparation of maize products, face-to-face interviews were conducted in the study population. To quantify maize flour consumption as tortillas, we converted the grams of tortilla to grams of maize flour using the preparation instructions of the product’s label.

2. Recipe preparation: Two groups of women were recruited for this phase: 10 from the urban area and 10 from the rural. We gave them 1 kg of flour and asked them to prepare the following foods: tortillas, tamalitos, gruel and a free recipe. We requested them to record the recipe and take a sample of the food to the study site the next day. Information of consumption distribution and demographic data were collected as well.

Figure 1 and Table 1 show the types of preparations and maize products prepared freely by these women. Urban women preferred fried preparations, whereas rural women chose a larger selection of cooked recipes. This could be associated to better economic conditions in the urban area that allows them to acquire a larger selection of ingredients, compared to the urban females.

Table 2 shows the consumption of maize flour tortillas and its equivalent to grams of maize flour throughout the 3 study areas. There were no significant differences between the 3 sites. Interestingly, the consumption between the males and females in this study did not differ as much as expected. This study revealed that there is a wide variety of forms and preparations of maize flour products which can easily substitute the maize traditionally used in these areas. The consumption patterns of this product could allow its use as a vehicle for fortification targeted to nutritionally vulnerable families in Guatemala.

References:

Mónica Orozco is head of “Safety and Efficacy of Iron Program” at CeSSIAM
Rosario García, Déborah Fuentes and Marta Lucia Escobar are Research Nutritionist at CeSSIAM-Quetzaltenango
Figure 1 Types of commonly prepared recipes by study area

Table 1 Recipe preparation made with corn or corn flour

<table>
<thead>
<tr>
<th>Food preparation</th>
<th>Ingredients</th>
<th>Image</th>
</tr>
</thead>
<tbody>
<tr>
<td>Empanadas</td>
<td>Corn flour, water, beef, chicken bouillon, salt, tomato, onion, parsley, vegetable oil</td>
<td><img src="image1" alt="Empanadas" /></td>
</tr>
<tr>
<td>Pupusos de chicharron</td>
<td>Corn flour, salt, chicken bouillon, water, onion stalk, vegetable oil</td>
<td><img src="image2" alt="Pupusos de chicharron" /></td>
</tr>
<tr>
<td>Pupusos con queso</td>
<td>Corn flour, water, onion, vegetable oil, salt, cheese</td>
<td><img src="image3" alt="Pupusos con queso" /></td>
</tr>
<tr>
<td>Debidados con queso</td>
<td>Corn flour, water, salt, cheese, vegetable oil, tomatillo</td>
<td><img src="image4" alt="Debidados con queso" /></td>
</tr>
<tr>
<td>Debidados con chicono</td>
<td>Corn flour, water, chicken bouillon, salt, tomato, onion, chicharron, vegetable oil</td>
<td><img src="image5" alt="Debidados con chicono" /></td>
</tr>
<tr>
<td>Tacos</td>
<td>Corn flour, water, salt, chicken, carrots, bay leaves, thyme, chicken bouillon, vegetable oil</td>
<td><img src="image6" alt="Tacos" /></td>
</tr>
<tr>
<td>Chuchitos</td>
<td>Corn flour, water, chicken bouillon, salt, pepper, roasted pumpkin seeds, schilote, garlic salt, onion salt, tomato, onion, chile gorda, chile pico, chicken, vegetable oil, sesame seeds, french bread, corn leaves</td>
<td><img src="image7" alt="Chuchitos" /></td>
</tr>
<tr>
<td>Tortillas</td>
<td>Corn flour and water</td>
<td><img src="image8" alt="Tortillas" /></td>
</tr>
<tr>
<td>Tamalito</td>
<td>Corn flour, lime water, fresh corn leaves</td>
<td><img src="image9" alt="Tamalito" /></td>
</tr>
<tr>
<td>Cambray</td>
<td>Corn flour, baking powder, sugar, margarine, pink sugar, vegetable oil, dry corn leaves</td>
<td><img src="image10" alt="Cambray" /></td>
</tr>
<tr>
<td>Tlayudas</td>
<td>Corn flour, water, vegetable oil, chicken bouillon, salt, fried black beans, cheese, tomato, chile chilito, dry corn leaves</td>
<td><img src="image11" alt="Tlayudas" /></td>
</tr>
<tr>
<td>Tamal</td>
<td>Corn flour, chicken stock, chile guisado, chile pico, sesame seeds, husk tomatoes, onion, garlic, cinnamon, bay leaves, roasted comino seeds, chicken, mahon leaves</td>
<td><img src="image12" alt="Tamal" /></td>
</tr>
</tbody>
</table>

Table 2 Median daily intake of corn tortillas in the household by family members

<table>
<thead>
<tr>
<th></th>
<th>Number of tortillas*</th>
<th>Grams of tortillas*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Father</td>
<td>Mother</td>
</tr>
<tr>
<td>Rural area (n=49)</td>
<td>13.4±7.2</td>
<td>11.0±5.6</td>
</tr>
<tr>
<td></td>
<td>(5 – 35)</td>
<td>(4 – 31)</td>
</tr>
<tr>
<td>Semi-urban area (n=50)</td>
<td>12.5±8.7</td>
<td>9.5±5.8</td>
</tr>
<tr>
<td></td>
<td>(0 – 45)</td>
<td>(0 – 31)</td>
</tr>
<tr>
<td>Urban area (n=47)</td>
<td>9.0±7.2</td>
<td>6.9±5.4</td>
</tr>
<tr>
<td></td>
<td>(0 – 36)</td>
<td>(6 – 20)</td>
</tr>
<tr>
<td>P-value</td>
<td>0.214</td>
<td>0.515</td>
</tr>
</tbody>
</table>

No significant differences in the estimated intakes of tortillas were observed between the study sites (ANOVA, SPSS 15)

* Mean±SD (minimum-maximum)
The traditional diet of Guatemala, based on maize, beans, squash, coffee and limited sources of animal sources of protein, has been implicated in a number of micronutrient deficiencies over the decades. The deficiencies of iodine and vitamin A have been addressed by the public health measures of salt and sugar fortification, respectively. Vitamin D had not been among the micronutrients identified in the mix. Guatemala is a nation located in the tropical zone at 14° N.W of the equator. Although certain foods such as fortified milk and margarine, seafoods, fish liver and fish liver oils are rich sources of vitamin D, their consumption in the Guatemalan diet is exceedingly low.

CeSSIAM was the first research group to examine vitamin D status in Guatemala. Sud et al., in 2010, published findings related to elderly individuals of Mayan ascendancy living at 2300 meters above sea level. They found 46.3% to have a circulating 25-hydroxy vitamin D (25(OH)D) of <20 ng/mL. The analytical collaboration came from the Creighton University in Omaha, Nebraska, USA. In last year's CeSSIAM Bulletin, Hernández et al. reported a 76% prevalence of either insufficient or deficient values for circulating 25(OH)D.

The study was undertaken as part of a larger research project, conducted in a total of 12 small communities in rural areas on the southern coast of Guatemala. Blood samples were drawn in the month of March, 2011, which is the fifth month of the annual dry (non-rainy) season in the Pacific side of the continental divide in Guatemala. The subgroups were constituted of apparently healthy and non-diabetic adult women in the fertile age (18 – 48 y, n=157) and comparable school children (aged 7-11 y, n=60 boys and n=74 girls). Plasma samples were collected, frozen and shipped to the laboratories of the Osteoporosis Division of the Creighton University Medical School in Omaha, Nebraska. 25(OH)D concentrations in the plasma specimens were measured using LIAISON 25 OH Vitamin D TOTAL Assay (DiaSorin). 25(OH)D concentrations >30 ng/mL were classified as adequate. Concentrations between 29.9 and 20 ng/mL were classified as insufficient, whereas those <20 ng/mL were deemed as deficient.

In women, the 25(OH)D levels ranged from 14.1 to 54.0 ng/mL, with a median value of 29.0 ng/mL and a mean of 29.4±7.3 ng/mL; in schoolchildren, the corresponding levels ranged from 9.6 to 60.2 ng/mL, with a median value of 29.9 ng/mL and a mean of 30.7±9.6 ng/mL. The classification among the three categories were distributed as shown in the pie graphs in the Figure.

These findings now add another piece of evidence that vitamin D status is less than ideal and less than optimum in the Guatemalan population. It accompanies the data presented in the following abstract. Of all of the settings studied so far in Guatemala, the southern coast would be the situation with the greatest possibilities of achieving a better vitamin D status. It is close enough to the sea that fish and seafood, the few natural dietary sources of the vitamin, might be of higher consumption than in the highland areas of earlier study. Moreover, the sunny days of the dry season should have induced vitamin synthesis in the skin. Because of the hot temperatures, both adults and children tend to wear light clothing with exposure of arms and legs. Nevertheless, the findings show substantial rates of sub-adequate vitamin D status in both age groups of the population. A mitigating factor might be the pigmentation factor. The ethnic groups of the coast are naturally pigmented, and the sun-exposure produces a chronic tanning. Both of these factors may combine to reduce the efficiency of ultraviolet light reaching the dermal layer of the skin to activate the synthetic chain of endogenous vitamin D.

The fact of low vitamin D status in Guatemala links it with other countries of the Latin American region. As concluded by Alex Brito and collaborators: “There is some indication that vitamin D insufficiency may be a public health problem in Latin America and the Caribbean, but the exact magnitude is currently unknown.” As the revelation of vitamin D problems in this region of the Americas is new and emerging, the consequences of this region-wide sub-adequacy are not yet evident.

References

Figure. Distribution of vitamin D status in women (A) and in schoolchildren (B)
Yet a third experience with the evaluation of vitamin D status in a sub-sample of the Guatemalan population has been obtained at CeSSIAM. This in a group of preschool aged children attending three different day-care centers in the Central Highlands of Guatemala; one in the city of Guatemala, another in the city of Antigua, and a third one located in a rural area at the western edge of the Department of Guatemala some 45 km from the capital. The baseline survey of the 25(OH)D levels was presented in an abstract in volume 22 of the CeSSIAM Bulletin [1]. Surprising to us at the time, but now becoming increasingly common in CeSSIAM studies, was the observation of insufficient or deficient circulating values for vitamin D in almost two-thirds of the 104 preschool children sampled in these centers. The ethical tenets of the study prescribed that subjects found to be abnormally low in vitamin D status were to be supplemented with the vitamin so as to restore a suitable nutritional state. However, when it came time to address the situation posed by the survey, the team of investigators realized that clear guidelines from evidence and experience in this age group, at a public health level, were really not available in the literature. One publication by Holick [2] recommended the administration of 4000 IU (100 µg) of oral vitamin D for a month. Given the proximity of the dosage to the 2500 IU upper tolerable intake level (UL) in this age-range and the luxury of time to affect a supplementation campaign, we opted to provide the same cumulative dosage, and chose to prolong it over twice the period. This would mean 2000 IU (50 µg) over a total of 60 days. One of us was able to offer the assistance of pro bono follow-up 25(OH)D measurements in serum, and it was decided to turn the ethical and humanitarian supplementation into an efficacy trial about the daily dose and duration of this modified regimen.

Ethical approval was extended and a system for supervised delivery was established using institutional or community monitors. Vitamin D3 drops (Optimal Vitamin D drops Seeking Health®, Bellingham, WA, USA), with each dropper delivery providing 2000 IU, was used. The intervention period extended over the end-of-the-year holiday period. If a child was missed on a day, doses could be made up by providing a double dose on the following day or days until the dosage schedule was back on track. Serum samples were obtained at the conclusion of the intervention, at the beginning of the subsequent 2012 school year. Some 76 of the 80 children eligible for the supplementation, based on their survey value, were provided with the total cumulative amount of vitamin D3 contemplated.

Of the 76 subjects with initial 25(OH)D levels below 20 ng/mL, 75 (98.6 %) had values restored into the normal range. They rose from 23.3±4.4 ng/mL to 43.3±10.6 ng/mL (p=0.001). The individual responses are shown in the Figure.

This is an important complement to the central original finding of a ~75% of surveyed individuals with less than adequate circulating concentrations. It provides a preliminary guide to a regimen of supplementation with vitamin D3 in a community setting that can respond to the finding of sub-adequate vitamin D status. What we undertook was based on a cumulative dosage, and was time-limited. In this way it is more “therapeutic” than prophylactic. The cost to treat each child is estimated as $0.02 USD for the medication, and this excludes any expenses to trained personnel to dispense the drops. However, additional safety and logistical consideration impinge upon the reality of community-level dispensing of vitamin D. As dispenser bottles have 900 drops. This is more than is needed by any one child to take a 60-day course, but there are sanitation considerations in transferring the oily syrup to smaller vessels for a specific individual. Moreover, whether an intact bottle – or a measured aliquot – were distributed to the home for administration, the possibility that the subject or a younger or older sibling could access the medication and ingest it all. This could lead to a one-time dose that is 48 or more times the 2500 IU upper tolerable intake level (UL) for a 3 year old child. In the Guatemalan context, the added expense of having a trained monitor provide a course of restorative vitamin D3.

References

Figure. Initial and follow-up 25(OH)D levels

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Stunting rates in infants and toddlers born in metropolitan Quetzaltenango, Guatemala

Marieke Reurings, Marieke Vossenaar, Colleen M Doak, Noel W Solomons

The accumulation of literature over the past three decades has coalesced around the notion that the first 1000 days of life, from conception to the second birthday, represent the most critical period for determining survival, adequate growth and development, and long-term health of an individual born in disadvantaged conditions in the developing world (1). Achieving normal linear growth rates is one of the major challenges of the first 1000 days. Guatemala has the highest prevalence of stunting in the Americas. According to the most recent survey, 54% of children under five years were stunted (2). As a practical matter for designing policy and programs to improve growth outcomes for Guatemalan children, it is important to identify the socio-economic and environmental circumstances most strongly associated with stunting.

The objective of the study was to describe the stunting prevalence and the association with early feeding practices, morbidity patterns and socio-economic status in a sample of infants and toddlers from urban Quetzaltenango.

We performed careful, standardized measurements of length in a gender-stratified, convenience sample of 299 young children (149 boys), aged 6-23 mo, recruited at 2 public health clinics in metropolitan area of the Western Highland city of Quetzaltenango. Data on socio-economic status, early feeding practices and morbidity were collected by means of a single face-to-face interview. Recumbent spine length and weight were measured according to standardized procedures and height-for-age (HAZ) Z scores were calculated. HAZ < -2 SD of the WHO 2006 Growth Standards was considered stunting. Multiple logistic regression analysis was used to examine determinants of stunting.

The average HAZ-score for the 299 children included in this study was -1.89 ±1.11, ranging from -4.76 to +3.37. A total of 135 (45%) children were classified as stunted. Children in the following subgroups were significantly shorter than their counterparts: children from the suburban area, aged 12-17 mo, born in a home setting, with mothers with primary schooling or less and of Mayan Indigenous racial descent.

The results of the crude odds ratios showed the following characteristics were strongly and significantly (p<0.05) associated with stunting: place of interview (suburban), being a boy, being 13-18 mo old, being born at home, mother having a low level of education, Mayan (indigenous) ethnicity, maternal shortness and ever having been given iron supplementation. None of the other variables, such as supplement use and morbidity rates, contributed to the predictive model.

We did not observe an association between early feeding practices or morbidity and stunting.

A number of variables (male gender, home birth, parents being married, low maternal education, low birth weight, short maternal height, and having been given iron supplements) were found to contribute to the final predictive model. In the backwards stepwise selection process, mother’s marital status emerged as strongly and significantly associated with stunting after controlling for other covariates. In contrast, the effects of place of interview, child’s age and mother’s ethnicity were attenuated and did not contribute to the predictive model (p<0.10) when controlling for other predictors. The Hosmer and Lemeshow test showed no significant difference in the prevalence of stunted and not-stunted children (p = 0.25), indicating a good fit for the model.

Our findings confirm prior Guatemala-based observations on socio-economic and educational influencing linear growth (3, 4). We validate a role for maternal education mitigating stunting. Ethnicity is a strong risk factor for poor linear growth, presumably related to parental heights. However, this association disappears after controlling for maternal education. The stature of the indigenous women is about 3 cm lower than that of the non-indigenous mothers (data not shown). Lower economic status of the semi-urban community, rather than its ethnic make-up, may be a stronger factor for the higher degree of stunting (3).

The stunting prevalence of 45% exceeds the cut-off of 40% used to indicate very high malnutrition. Even the highest socioeconomic-status group has a stunting prevalence indicating high malnutrition. Low birth weight, being a boy, and having a mother with short stature are most strongly and significantly associated correlates of infant and toddler stunting. These findings demonstrate the importance of child undernutrition in urban Quetzaltenango and the need for intervention in all strata, particularly in the Mayan women with low educational level and short stature.

References:
4. Lee J, Houser RF, Must A, de Fulladolsa PP, Bermudez OL. Disentangling nutritional factors and household characteristics related to child stunting and maternal overweight in Guatemala. Econ Hum Biol 2010;8:188-96.

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The INF works toward a future where the quantity and quality of food consumed does not constrain the achievement of full genetic potential of any individual or the economic and social progress of developing countries.

NSINF Vision Statement

On February 8, 2013, Professor Nevin Scrimshaw passed away peacefully in the State of New Hampshire in the United States. The lead Editorial of this issue of the CeSSIAM Bulletin addresses the influence of this leader on the social, cultural and technical aspects of scientific development in the country of Guatemala, in which he first projected leadership as the founding Director of the Institute of Nutrition of Central America and Panama (INCAP) in 1949. It states that his “model, along with the dignity and value of the scientific career projected to professionals in Guatemala, paved the way culturally speaking for the establishment of a research center like CeSSIAM in 1985.” This is testimony to the impact on the progress of investigation in Guatemala of the organization that we have inherited from Dr. Scrimshaw, and now lead as President and Chairman of the Board, respectively. And indeed, to support the scientific and human development across the emerging regions of Asia, Africa and Latin America was the vision of its founder when it was established on April 11 in 1982. This is captured in its vision statement.

For 30 years, it has been the mission of the Foundation that has given reality to this vision. As enunciated in the statement: “The mission of the INF is to build capacity in developing country individuals and institutions in the areas of nutrition research, policy and programming so they can effectively address issues of food, nutrition and hunger in their countries.” This has had numerous reflections within Guatemala itself, of which we cite a selected few. Consistent with the emphasis on capacity building, the Foundation has given logistical and financial support to the Latin American Nutrition Leadership Program since the first regional workshop was held in Antigua Guatemala in 1997. In individual capacity building, the International Nutrition Foundation – Ellison Medical Foundation (INF-EMF) Fellowship was instrumental in enabling advanced scientific training for many developing-country students. Monica Orozco of the CeSSIAM staff was a recipient of a INF-EMF fellowship to complete her doctoral studies in Human Nutrition and Food Technology at the University of Manitoba in Winnipeg, Canada. She now heads the Program on Iron Safety and Efficacy at the Center. It goes without saying that the institutional capacity of CeSSIAM has been supported for most of its history by the financial management liaison with the Foundation.

The official organ of the Foundation, the Food and Nutrition Bulletin (FNB), had Dr. Ricardo Bressani as its long-term Associate Editor for Food Technology. It is now served by the CeSSIAM Scientific Director and NSINF Director for Central America, Dr. Noel Solomons, as the current Associate Editor for Nutrition Programs. In March, 2011, a Special Supplement on the first fifty years of INCAP in Guatemala filled the pages of the FNB with 16 historical narratives, recruited and edited by that institution’s founding Director, Nevin Scrimshaw.

It is worth our pointing to two recent landmarks this three-decade evolution. On October 4, 2009, in Bangkok, in a solemn ceremony presided over by Her Royal Highness, Crown Princess Maha Chakri Sirindhorn of Thailand, the Foundation was rededicated and renamed as the “Nevin Scrimshaw International Nutrition Foundation” in the honor of its founder. Dr. Scrimshaw became President Emeritus, and its future entrusted to the authors of this Editorial. On April 12, 2012, the current staff and Board of Directors met for a dinner in Boston to commemorate the 30th anniversary of the Foundations establishment. The founder’s failing health found him too ill to attend on this occasion. However, in the international spirit of the founder and the foundation, around the table were persons born not only in the United States but in Chile, India, Japan, Kenya and Honduras. These professionals from law, industry and science constitute the current adherents to and custodians of the vision and mission of the Foundation. If the past three decades represent the grounding of a visionary notion, future multiplication of capacity building in the region will serve as a legacy of the NSINF while the NSINF will continue to seek opportunities to diversify and deepen the support it can provide to the region.

Ricardo Uauy-Dagach, Foundation President
Irwin H Rosenberg, Chairman of the Board of Directors
SUNDAY April 21, 2013

Poster presentations

**Stunting at birth: An under-recognized phenomenon with implications for maternal health and nutrition.** Anne Marie Chomat, Marieke Vossenaar, Elena Maria Diaz Ruiz, Hilary Wren, Kristine G Koski, Marilyn E Scott, Noel W Solomons
Program Number: 618.1, Poster Board Number: D55, Time: 12:45-1:45PM (I)

**Evidence for Functional Sex Dimorphism in the Serum Iron Response to Oral Iron Supplements.** Monica N Orozco, María-Eugenia Romero-Abal, Noel W Solomons, Klaus Schümann
Program Number: 634.5, Poster Board Number: D256, Time: 12:45-1:45PM (I)

**Low retinol levels virtually undetected in coastal Guatemala: Findings from a convenience sample of women and schoolchildren.** María José Soto-Méndez, Raquel Campos, Ana Carolina Martínez, Michelle Detlefsen, Noel W Solomons
Program Number: 620.4, Poster Board Number: D80, Time: 1:45-2:45PM (II)

Oral presentation

**The effect of short-term frozen storage of human milk on the validity of Vitamin A assays using the iCHECKTM rapid analyzer.** Christine Whang, Odilia Bermudez, Anne Marie Chomat, Noel W Solomons
Session Title: Global Nutrition: Biomarkers for Assessing Interventions
Session Time: 8:00 AM - 10:00 AM, Location: Room 153A

MONDAY April 22, 2013

Poster presentations

**Local concepts of infant illness among Mam-Mayan women and impact on feeding practices: a qualitative study in the Western Highlands of Guatemala.** Mariah Kincaid, Odilia I. Bermudez, Anne Marie Chomat, Marta Escobar, Maria Garcia, Rosario Garcia, Marilyn E. Scott, Kristine G. Koski, Noel W. Solomons
Program Number: 841.13, Poster Board Number: D33, Time: 12:45-1:45PM (I)

**Feeding practices during pregnancy and lactation amongst Mam-Mayan women in rural Guatemala: a mixed qualitative and quantitative evaluation.** Olivia Russell, Odilia I. Bermudez, Anne Marie Chomat, Alejandra Maldonado, Rosario Garcia, Hilary Wren, Marilyn E. Scott, Kristine G. Koski, Noel W. Solomons
Program Number: 841.14, Poster Board Number: D34, Time: 1:45-2:45PM (II)

**Adaptation of a compact rapid vitamin A assay device (iCHECKTM) to simulated field conditions and relevant substrates in Guatemala.** Zsofia Magdolna Zambo, Jose David Sanchez-Mena, Monica N Orozco, Noel W Solomons
Program Number: 845.10, Poster Board Number: D94, Time: 1:45-2:45PM (II)

Oral presentations

**Status of Selected Iron-Status Biomarkers in Juvenile End-Stage Renal Disease in a Guatemalan Context: Comparative Aspects by Mode of Dialysis.** Juliana Casimiro, Randall Lou-Meda, Marion Olbert, Günter Weiss, Dorine W Swinkels, Harold Tjalsma, Noel W Solomons, Klaus Schümann
Session Title: Iron, Copper and Chronic Disease
Session Time: 8:00 AM - 10:00 AM, Location: Room 154

**Perceptions surrounding food preferences and avoidances in pregnant and lactating women in the Western Highlands of Guatemala.** María del Rosario García, Marieke Vossenaar, Melissa JL Bonorden, Noel W Solomons
Session Title: Health Promotion and Disparities in Diverse Communities
Session Time: 10:30 AM - 12:30 PM, Location: Room 153B

TUESDAY April 23, 2013

Poster presentations

**Nutritional Deficits in Juvenile End-Stage Renal Disease in a Guatemalan Context.** Juliana Casimiro, Randall Lou-Meda, Noel W Solomons, Klaus Schümann
Program Number: 1060.7, Poster Board Number: D117, Time: 12:45-1:45PM (I)

**Low Omega-3 Fatty Acid Status in Residents of the Guatemalan Pacific Coastal Plain.** Raquel Campos, María José Soto-Méndez, Eileen Bailey, Michelle Detlefsen, Klaus Kraemer, Norman Salem Jr
Program Number: 1072.14, Poster Board Number: D268, Time: 1:45-2:45PM (II)