

# The Carotenoids and Retinoid Interaction Group (CARIG) Conference Meets in Boston

## Noel W Solomons

Center for Studies of Sensory Impairment, Aging and Metabolism (CeSSIAM), Guatemala City, Guatemala

The Hynes Convention Center in Boston, MA, USA, was the setting for the 2018 CARIG Conference. This year's topic was "Carotenoids and Retinoids Throughout the Lifespan." The event was chaired by Dr Elizabeth Johnson of Tufts University and co-chaired by Dr Nancy Engelmann Moran of the Baylor College of Medicine's Children's Nutrition Research Center. On a sad note, the assembled acknowledged, with a moment of silent meditation, the abrupt passing earlier in 2018 of Dr Phyllis E. Bowen, a founding member of the CARIG and a staunch supporter of its development and activities.

The 17<sup>th</sup> annual James Allen Olson Memorial Perspectives on Carotenoids Lecture was delivered by Prof. Keith West, Jr., of the Center for Human Nutrition of the Bloomberg School of Public Health at Johns Hopkins University in Baltimore. His provocative and far-reaching discourse was entitled: "Vitamin A, carotenoids, health and survival by person, place and time." The overall message ranged widely and the full lecture will be published in a forthcoming issue of *Sight and Life* magazine. Suffice it to say, the conference for 2018 was enlivened and enriched by the elements of discussion brought in by Prof. West and his experiences from Nepal and Bangladesh.

**Dr Corrine Hanson** of the University of Nebraska Medical Center delivered a presentation entitled: "Infants: vitamin A and related compounds in maternal-infant pairs, breast milk and formula; serum retinol in women of childbearing age in the US." Although the headline word is *infant*, the first year of the lifespan, the title entails a wide-ranging swath of keywords of individuals and biomarkers. The presentation was based on analysis of venous blood from the mother and cord blood from the infant from a group of 180 maternal-infant dyads deliv-

ered at the University of NE Medical Center in Omaha, NE. The ethnic composition included 12% African-American and 15% Hispanic-American participants. Eighty-four percent were non-smokers.

The Biomarker Research Institute at the Harvard School of Public Health in Boston analyzed a wide battery of fat-soluble nutrients and compounds. In the first instance, an analysis was made of vitamin A status based on circulating retinol. With respect to the cut-off for insufficient vitamin A status of <20 µg/dL, 51% of the mothers' retinol concentrations fell into this zone, and 10% overall were deficient, with a level of <10 µg/dL. Black mothers had twice the probability of whites to have an abnormal vitamin A concentration. Of the data reported for infants, the subjects of an early-life focus, there was a significant correlation between maternal and cord-blood retinols, and 80% of infants had a retinol concentration of <10 µg/dL. It should be noted that criteria for vitamin A status in newborns have not been firmly established.

The investigators received a whole gamut of carotenoid analyses from the same paired blood specimens in the 180-dyad sample. The initial focus was on lycopene, the total circulating pigment and its *cis* and *trans* isomers. Maternal concentrations of total and *cis*-lycopene were positively associated with infant birth weight, length and head circumference after adjustment for relevant confounders. Lower maternal levels of *cis*-lycopene were associated with development of respiratory distress syndrome (RDS) and admission to the newborn intensive care unit (NICU). By contrast, higher cord blood (infant) concentrations of *trans*-lycopene were associated with RDS and NICU admission risk. Accepting a causal assumption – i.e., that total and *cis*-lycopene were responsible for the better growth and health outcomes – the reverse-causality hypothesis is that better-educated and motivated mothers, who would provide better self and infant care, would display a more diverse and balanced diet.



© Liz Johnson

CARIG Symposium reception poster winners and judges. From left: Elizabeth Johnson, PhD (CARIG Chair, Tufts University, poster judge); Zhi Chai (Penn State, third place); Jelena Mustra Rakic (Tufts University, second place); Jirayu Tanprasertsuk (Tufts University, first place); Nancy Engelmann Moran, PhD (CARIG Chair-elect, Baylor College of Medicine, poster judge).

.....

“Having higher or lower circulating levels of carotenoids depends on dietary exposure, which in turn relies on the cultural practices and market or household availability of carotenoid-rich foods”

.....

The Omaha–Boston research axis has reached out to rural northwest Nigeria for blood samples for similar lipid analyses. This is a population with a large and diverse consumption of edible plants; the array of carotenoid pigments in the Midwestern women is *pallid* (both literally and figuratively) as compared to their West African counterparts. Since having higher or lower circulating levels of carotenoids depends on dietary exposure, which in turn relies on the cultural practices and market or household availability of carotenoid-rich foods, variation was not unsurprising. Equally unsurprising is the fact that women consuming the typical meat- and grain-based dietary fare of the US Midwest have a less vibrant array of carotenoid compounds than women on traditional vegetable- and herb-rich repasts

in rural Nigeria. That the blood mimics the dietary exposure is an accepted truism. Only supplementation or major dietary modification would move the Omaha pattern to that of Nigerian women. This line of intervention would also tend to resolve the issue of causality versus simply association in the health-related relationships.

**Dr Sherry A. Tanumihardjo** of the University of Wisconsin–Madison addressed the issues of childhood with a provocative flare entitled: “Children: biofortification of food and possible vitamin A toxicity.” Dr Tanumihardjo has borne a singular focus on how well – or how poorly – different putative biomarkers indicate human vitamin A status, which she has shared in writing and at previous CARIG conferences. She expresses concern about circulating retinol levels being unreliable in reflecting the two poles of concern of vitamin A status: vitamin A deficiency and vitamin A excess. In this discourse, she went so far as to use the terminology of ‘possible vitamin A toxicity.’

Eighty percent of total-body vitamin A is generally located as reserves in the liver. In agreement with most colleagues, Dr Tanumihardjo feels that the hepatic vitamin A content is the most faithful arbiter of nutritional status, conceding that access to this datum comes only through post-mortem exam or opportunities for liver biopsy. A concentration of >300 µg per gram of hepatic tissue is considered excessive. Less invasive marker studies such as the modified retinol dose response and stable-

isotope-labeled retinol dilution tests can provide more refined diagnoses extending from the deficient through the normal to the excessive range. Such expanse is necessary for population research, since some data cited showed that, in the USA, one can find 22% of individuals with vitamin A deficiency (VAD), whereas 4% have hepatic evidence of excessive content and fat-globule vacuoles on histological examination.

Admitting that VAD is more rampant in low-income countries, Dr Tanumihardjo warned of a downside of excessive exposure from the intervention programs arrayed against it. These include periodic supplementation and fortification of foods such as edible oils and table sugar, and the newest development: biofortification. Varieties of carrots, sweet potatoes and maize have been hybridized to augment their concentration of provitamin A carotenoids such as  $\beta$ - and  $\alpha$ -carotene. Systematic feeding with these biofortified foods in Zambia resulted in orange-colored pigmentation of the palms of the hands, a condition known as carotenodermia. Known to dermatology for decades, this condition has been considered to be benign and harmless. Based on our current knowledge of molecular mechanism, carotene oxidase action in converting dietary provitamin A to retinaldehyde suppresses bioconversion at a normal (adequate) vitamin A reserve status. This was posited as a biological guarantee against hepatic excess of active retinoids. Consistent with the title of the presentation, Dr Tanumihardjo concluded with preliminary biomarker evidence for an escape from regulatory control and vitamin A excess in chronic consumers of biofortified provitamin A sources.

As an editorial comment, a field study is commencing in Guatemala, a nation with a sugar-fortification program, to examine the tissue concentrations and histology of the livers of individuals experiencing sudden death from accidents or violence; this will help clarify the relationships of exposure and adverse effect, if albeit not in the context of biofortification, but in the setting of one of the most successful public health interventions against VAD.

**Dr Randy Hammond** of the University of Georgia took on a process emerging into later adulthood: “The influence of the macular carotenoids on auditory and visual-motor thresholds.” The term macular carotenoids refers to zeaxanthin and lutein, which are selectively deposited in the fovea (macula) of the retina and whose density is believed to represent protection of this essential structure for vision. The former compound is primarily derived from corn and named for the botanical term, *Zea mays*; notably, egg yolk and orange bell pepper are rich in zeaxanthin as well. Corn is also a leading source of dietary lutein, with important contributions from squashes, spinach and orange juice. The mechanism of action and protection has been considered a direct interaction with, and absorption of, damaging light. An internal, potentially nerve-tissue-based role

for these two carotenoids in other sensory functions was the revelation of Dr Hammond’s innovative thesis about these compounds being ‘neural pigments’ and having a role in what he termed ‘neural efficiency.’

From the standpoint of feasibility and construct validity, Dr Hammond noted that xanthophilic cells, with affinity for this class of carotenoids, have been known in the brain since discovered by Craft in 2003. He reviewed findings from his groups and others regarding an association between amnesia (memory loss) and cognitive function in older individuals and the density of the macular pigments in the brain tissue itself. In this presentation, Dr Hammond brought evidence and insights for how these pigments might exert these cerebral-level effects. His focus was on the auditory system (hearing loss) and associations between consumption of the carotenoid pigments and better auditory acuity. He attributed this to their improving the neuronal efficiency to filter auditory signals of interpretive interest from background noise. However, in the presence of hearing-adverse factors, such as tobacco smoking, the improvement of audition with consumption of macular carotenoids was not demonstrated. The conclusion was that the speed and fidelity of auditory stimuli are improved with higher exposures of lutein and zeaxanthin by effects of CNS neurons.

The final presentation was from **Jirayu Tanprasertsuk** of Tufts University closing the upward tour of the lifespan with a talk entitled: “Oldest of the old: metabolomics, brain carotenoids and pathology and cognition in centenarians.” The background information was the epidemiological evidence, in older individuals, that risk of cognitive deterioration was mitigated by higher vegetable consumption in some populations or by higher combined fruit and vegetable consumption in others. A legitimate hypothesis would be an effect of exposure to carotenoid pigments from the diet. B-carotene is the predominant pigment in most Western diets and in the human circulation, but lutein is the dominant carotenoid in cerebral tissue, suggesting a selective uptake of the latter.

An interesting insight comes in a potential interaction with essential fatty acids in the effects of carotenoids on human cognition. In one study reported in this presentation, the performance on four cognitive tests by elderly subjects was evaluated after oral supplementation with four treatments: **1)** placebo; **2)** lutein alone; **3)** docosahexaenoic acid (DHA); and **4)** lutein plus DHA. The only group to have superior performance on all four cognitive tests was the combined treatment.

Except with biopsy or autopsy study, the pigment density of the cerebral tissue cannot be directly quantified, but Jirayu Tanprasertsuk advanced the premise that macular-pigment optical density (MPOD) in the fovea of the eye was a faithful surrogate for the condition of the brain behind the eyes. Feeding studies comparing enhanced intakes of the macular carotenoids from

avocados and low intakes derived from potatoes and chickpeas showed a reflection in the MPOD in both Alzheimer’s disease patients and more cognitively intact elders.

The speaker’s own research may allow circulating levels of certain lipid biomarkers in data derived from immediate post-mortem specimens of blood and brain (frontal and temporal cortex) in 47 recently deceased participants in the Georgia Centenarian Study. After adjustments, no significant association between circulating and cerebral-tissue content was identified for retinol, total saturated fatty acid, total monounsaturated fatty acid and trans-fatty acid levels. On the other hand, strong associations were found for serum carotenoids (lutein, zeaxanthin, cryptoxanthin, β-carotene) along with tocopherols, total n-3 PU-FAs and n-6/n-3 PUFA ratio.

So, the presentations on carotenoid effects on health revisit the time-honored question on the ‘essentiality’ of nutritional compounds that vary so widely from culture to culture and across agriculture and foraging situations of abundance and availability of sources.

.....  
**“The presentations on carotenoid effects on health revisit the time-honored question on the ‘essentiality’ of nutritional compounds that vary so widely from culture to culture”**  
 .....

Later, the CARIG reception, with its annual poster competition, was held. A jury of three senior CARIG members selected the best free-paper science among the posters in two categories: 2018 CARIG Reception Poster Competition and 2018 CARIG Emerging Leaders Poster Competition. The winners and the titles of the reports are below.

**2018 CARIG Reception Poster Competition Winners**

.....  
**1<sup>st</sup> Place**

Jirayu Tanprasertsuk, Tufts University  
 Brain fat-soluble nutrient pattern is related to pre-mortem cognition among non-demented centenarians

.....  
**2<sup>nd</sup> Place**

Jelena Mustra Rakic, Tufts University  
 Dietary lycopene feeding inhibits cigarette-smoke-induced

COPD and lung preneoplastic lesions in ferret model

.....  
**3<sup>rd</sup> Place**

Zhi Chai, Pennsylvania State University  
 Differential expression and coexpression analyses on transcriptional profiles of lower small intestine suggest key pathways regulated by vitamin A

.....  
**2018 CARIG Emerging Leaders Poster Competition Winners**

.....  
**1<sup>st</sup> Place (joint)**

Minkyung Bae, University of Connecticut  
 Hepatic stellate cells exposed to astaxanthin during activation exhibit a distinct metabotype from quiescent and activated hepatic stellate cells

.....  
**1<sup>st</sup> Place (joint)**

Jelena Mustra Rakic, Tufts University  
 Dietary lycopene feeding inhibits cigarette-smoke-induced COPD and lung preneoplastic lesions in ferret model

Next year, the CARIG conference heads for the vitamin A in oysters and the carotenoids in crabs when NUTRITION 2019 convenes in Baltimore, MD.

.....  
**Correspondence: Noel W. Solomons,**

*Executive and Scientific Director, Center for Studies of Sensory Impairment, Aging and Metabolism, CeSSIAM in Guatemala, P.O Box 02-5339, Section 3163/Guatemala, Miami, FL 33102-5339, USA*

**Email:** [cessiam@cessiam.org.gt](mailto:cessiam@cessiam.org.gt)  
 .....