Editorial

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Nutrition and hearing loss: a neglected cause and global health burden[1]

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Hearing loss is a neglected public health problem that affects an estimated 360 (1) to 554 (2) million adults and children in the world. Although the difference in magnitude depends in part on the hearing threshold adopted, available estimates ignore milder, yet consequential, hearing loss. The estimates, however, reveal a disability that appears early in life, increases several-fold over the life span, and affects all societies. The prevalence of hearing loss is disproportionately high in low-resource settings, especially in South Asia and sub-Saharan Africa (2), the reasons for which remain uncertain.

Hearing loss has profound health, social, and economic consequences (3). Affected children are likely to experience speech, language, and cognitive delays and poor school performance (4), whereas adults face higher risks of unemployment or low earnings (3), cognitive decline, and dementia (5). Social isolation accompanies daily life of the hearing impaired (6). Major causes of this burden vary across the life stages and include congenital disorders; otitis media; vaccine-preventable infections such as measles, mumps, and rubella; noise exposure; ototoxic drugs; and age (1). Surprisingly, only severe prenatal iodine deficiency (7) is listed by the WHO as a nutritional cause of hearing loss (1), leaving the broad roles of diet and nutrition within its complex set of etiologies yet to be defined.

In high-income countries, large-population studies in adults have reported protective risk ratios against hearing loss with higher dietary intakes of fish, long-chain PUFAs, folate, β-carotene, and vitamins A, E, and C. Although findings across studies are inconsistent, animal evidence exists to support roles for each of these studied nutrients in regulating redox stress, protecting cochlear function, and enabling hearing. Interestingly, dietary exposure to potentially ototoxic heavy metals (e.g., cadmium, lead), a high BMI and waist circumference (i.e., obesity), and reduced physical activity have also been linked to hearing loss (8), which implies that systemic stress from a chronically unhealthy diet, lifestyle, and environment may carry consequences for ear health and hearing. In low-income countries, where undernutrition remains widespread, limited research has identified micronutrient deficiencies (e.g., of vitamin A and zinc) as risk factors for otitis media (9), the leading acquired cause of childhood hearing loss (10). In one trial cohort, preschool vitamin A supplementation was shown to reduce hearing loss attributed to childhood purulent ear infection (11). Animal evidence suggests that vitamin A deficiency may also lead to hearing loss through an entirely separate, developmental pathway (12). Nonetheless, few studies have reported other nutritionally sensitive mechanisms to explain the high prevalence of hearing loss in low-income countries (9), which reveals a formidable research gap to define roles for malnutrition in the etiology of this global disability.

In this issue of the Journal, studies by Curhan et al. (13) and Choudhury et al. (14) reinforce the likely importance of micronutrient imbalance or deficiency as determinants of hearing loss for 2 very different life stages, populations, environments, and causal pathways: the Nurses' Health Study cohort in the United States (13) and a study in infants born at $\geq$34 wk of gestation in New Delhi, India (14). Curhan et al. prospectively assessed diets of 65,521 nurses by a validated food-frequency questionnaire every 4 y from 1991 to 2009, at the end of which the occurrence and year of onset of a hearing problem, inferred as hearing loss, was obtained by self-report. Although no effect of vitamin A was observed, perhaps reflecting its homeostatic control in a well-nourished population, the authors reported higher intakes of β-carotene, β-cryptoxanthin, and folate to be protective against incident hearing loss. Oxidative stress and impaired homocysteine metabolism appear to contribute to inner-ear dysfunction, effects that adequate carotenoid and folate nutriture may attenuate by postulated scavenging of free radicals (13) and maintenance of antioxidant enzyme homeostasis (15), respectively, although other mechanisms likely exist. Paradoxically, the risk of hearing loss was increased in subjects who reported an increased intake of vitamin C, also an established antioxidant, at amounts that exceeded the Recommended Dietary Allowance (i.e., >75–90 mg/d) but that fell well below the Tolerable Upper Intake Level (<2000 mg/d) of the Dietary Reference Intakes, suggesting that poorly understood, organ-specific nutrient interactions may exist.

A limitation of the Nurses' Health Study was its reliance on self-report of incident hearing loss, because audiometric testing is necessary to quantify severity and extent of hearing loss and to differentiate sensorineural, or inner-ear, from conductive or middle-ear pathologies. Conventional audiometry has required permanent equipment in a sound-proof room. In the United States, NHANES overcame this limitation by using audiometric booths fit onto

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mobile units. However, accurate, reliable, and far less costly portable devices will soon enable quantitative audiometry in field settings to facilitate population-based hearing assessment.

The nutritional origins of hearing loss likely differ substantially in chronically undernourished settings where etiologies of premature dysfunction may start in utero. In India, Choudhury et al. (14) screened newborn hearing via the auditory brainstem response, a well-accepted measure of auditory maturation. Delayed interpeak latencies and wave V latency, as observed in newborns with latent iron deficiency (i.e., cord plasma serum ferritin $\leq$75 ng/mL), is highly suggestive of abnormal myelination of the auditory pathway. Multiple facets of intracellular iron metabolism support oligodendrocyte signaling pathways, proliferation, energetics, and formation of myelin, which are critical for auditory neurotransmission (16). In one small study, disturbed myelination in infancy, approximated by auditory brainstem response, was associated with auditory abnormalities later in childhood (17). As the roles and timing of iron in myelin growth and maturation become better understood, it will be essential to explore the efficacy of iron supplementation to iron-deficient mothers during gestation or their infants in normalizing auditory function.

Although these 2 provocative studies raise many questions, they add to a developing story that adequate and balanced nutrition during pregnancy, infancy, and adulthood may reduce hearing loss globally and across the life span. Needed, and on the horizon, are accurate, faster, and less costly field methods for measuring diet, status for some micronutrients, and hearing to expand investigations of the roles of nutrition on hearing loss. Both under- and overnutrition are likely to be essential aspects of this story. As the UN General Assembly in September 2015 calls for disability-inclusive sustainable development goals, it is time for hearing loss to exit the ranks of neglected public health problems and move toward centrality in the global nutrition community.

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REFERENCES

1. Olusanya BO, Neumann KJ, Saunders JE. The global burden of disabling hearing impairment: a call to action. Bull World Health Organ 2014;92:367–73.
2. Stevens G, Flaxman S, Brunskill E, Mascarenhas M, Mathers CD, Finuncane M; Global Burden of Disease Hearing Loss Expert Group. Global and regional hearing impairment prevalence: an analysis of 42 studies in 29 countries. Eur J Public Health 2013;23:146–52.
3. Emmett SD, Francis HW. The socioeconomic impact of hearing loss in U.S. adults. Otol Neurotol 2015;36:545–50.
4. Wake M, Hughes EK, Poulakis Z, Collins C, Rickards FW. Outcomes of children with mild-profound hearing loss at 7 to 8 years: a population study. Ear Hear 2004;25:1–8.
5. Deal JA, Sharrett AR, Albert MS, Coresh J, Mosley TH, Knopman D, Wruck LM, Lin FR. Hearing impairment and cognitive decline: a pilot study conducted within the Atherosclerosis Risk in Communities Neurocognitive Study. Am J Epidemiol 2015;181:680–90.
6. Schmitz J, Pillion JP, LeClerq SC, Khatry SK, Wu LSF, Prasad R, Karna SL, Shrestha SR, West KP Jr. Prevalence of hearing loss and ear morbidity among adolescents and young adults in rural southern Nepal. Int J Audiol 2010;49:388–94.
7. Melse-Boonstra A, Mackenzie I. Iodine deficiency, thyroid function and hearing deficit: a review. Nutr Res Rev 2013;26:110–7.
8. Shargorodsky J, Curhan SG, Henderson E, Eavey R, Curhan GC. Heavy metals exposure and hearing loss in US adolescents. Arch Otolaryngol Head Neck Surg 2011;137:1183–9.
9. Elemraid MA, Mackenzie IJ, Fraser WD, Brabin BJ. Nutritional factors in the pathogenesis of ear disease in children: a systematic review. Ann Trop Paediatr 2009;29:85–99.
10. Monasta L, Ronfani L, Marchetti F, Montico M, Brumatti LV, Bavcar A, Grasso D, Barbiero C, Tamburlini G. Burden of disease caused by otitis media: systematic review and global estimates. PLoS One 2012; 7:e36226.
11. Schmitz J, West KP Jr., Khatry SK, Wu L, LeClerq SC, Karna SL, Katz J, Sommer A, Pillion J. Vitamin A supplementation in preschool children and risk of hearing loss as adolescents and young adults in rural Nepal: randomized trial cohort follow-up study. BMJ 2012;344:d7962.
12. Emmett SD, West KP Jr. Gestational vitamin A deficiency: a novel cause of sensorineural hearing loss in the developing world? Med Hypotheses 2014;82:6–10.
13. Curhan SG, Stankovic KM, Eavey RD, Wang M, Stampfer MJ, Curhan GC. Carotenoids, vitamin A, vitamin C, vitamin E, and folate and risk of self-reported hearing loss in women. Am J Clin Nutr 2015;102:1167–75.
14. Choudhury V, Amin SB, Agarwal A, Srivastava LM, Soni A, Saluja S. Latent iron deficiency at birth influences auditory neural maturation in late preterm and term infants. Am J Clin Nutr 2015;102: 1030–4.
15. Martínez-Vega R, Garrido F, Partearroyo T, Cediel R, Zeisel SH, Martinez-Alvarez C, Varela-Moreiras G, Varela-Nieto I, Pajares MA. Folic acid deficiency induces premature hearing loss through mechanisms involving cochlear oxidative stress and impairment of homocysteine metabolism. FASEB J 2015;29:418–32.
16. Bakoyiannis I, Gkioka E, Daskalopoulou A, Korou L-M, Perrea D, Pergialiotis V. An explanation of the pathophysiology of adverse neurodevelopmental outcomes in iron deficiency. Rev Neurosci 2015;26: 479–88.
17. Algarín C, Peirano P, Garrido M, Pizarro F, Lozoff B. Iron deficiency anemia in infancy: long-lasting effects on auditory and visual system functioning. Pediatr Res 2003;53:217–23.