

# Commentary: Is vitamin A playing a hidden role in children's lung function?

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Kassaye *et al.*<sup>1</sup> have evaluated for the first time the relationship between vitamin A status and respiratory function in children. Previous studies in adults suffering from chronic diseases, which affect respiratory function, have shown a beneficial effect of short-term vitamin A supplementation on forced expiratory volume (FEV<sub>1</sub>) and/or forced vital capacity (FVC). Because vitamin A deficiency is associated with keratinizing metaplasia of the respiratory tract in children, the authors hypothesized that the differential vitamin A status of malnourished children could be related to differential FEV<sub>1</sub> and FVC values.

Measurement of FEV<sub>1</sub> and FVC in children is difficult because it requires good co-operation from each child and the authors enrolled children of 6–9 years. Moreover, FEV<sub>1</sub> and FVC depend not only on permeability of airways but also on other anatomical characteristics and physiological events. Lung size, diameters of the airways, previous physical activity, and emotional involvement during the test could modify the results. However, it can be assumed that these features had been distributed evenly in the sample because of the random selection of children from Wukro wereda, Tigray region in Northern Ethiopia.

Unadjusted analysis showed lower FEV<sub>1</sub> values in vitamin A deficient children as assessed by Modified Relative Dose Response (MRDR). This is believed to be a better reflection of actual vitamin A stores than simple serum levels.<sup>2</sup> Low FEV<sub>1</sub> values were also found in girls, underweight and stunted children. Higher FEV<sub>1</sub> values were related to increases in height, weight, age, history of previous measles episode, and cough during the month prior to FEV<sub>1</sub> test. The authors' speculation that a prior measles episode may be protective against asthma, based on this unadjusted analysis, is not convincing to this commentator. In contrast to this theory, it has recently been reported that respiratory infections during the first 2 years of life are related to the subsequent development of childhood asthma.<sup>3</sup> More prospective studies are required to address this interesting question.

Surprisingly, adjusted analysis by age-gender-height reduced the difference in the FEV<sub>1</sub> values between vitamin A deficient children and children with normal vitamin A reserves. When more variables were included in the adjusted analysis, there was no difference in FEV<sub>1</sub> values according to vitamin A reserve status. However, height and body mass index (BMI) were directly associated with FEV<sub>1</sub> values when vitamin A status and other personnel and health variables were controlled. This finding apparently diminishes the importance of vitamin A in explaining the lung function. Global nutritional status as

indicated by height appears to be the main explanatory factor. However, since vitamin A deficiency and nutritional status are linked, it is possible that vitamin A status may be indirectly linked to lung function via its effects on growth.

Height seems to be influenced by vitamin A through growth hormone production.<sup>4</sup> In endemic vitamin A deficient areas, where food is lacking, the growth response to vitamin A supplements is affected by respiratory infections.<sup>5</sup> Acute infection is associated with increased metabolism, micronutrient loss, and protein consumption.<sup>6</sup> These findings suggest that vitamin A is required for optimal growth, but the potential beneficial effect of vitamin A supplements demands a good supply of other nutrients implicated in the growth process, such as zinc.<sup>7</sup> Therefore, marginal vitamin A replenishment may not be enough to sustain the growth rhythms in chronically malnourished populations.

Because height is a good predictor of lung function it is crucial to prevent infections which are linked to the loss of critical nutrients that are the building blocks for growth. Paradoxically, the same vitamin A that is so easily lost during infections may prevent recurrent infectious episodes in children. We have found, in a study carried out in Ecuador in collaboration with Griffiths at Tufts University, that weekly low-dose vitamin A supplements prevent acute lower respiratory infections (ALRI, or pneumonia) in underweight and stunted children.<sup>8</sup> The beneficial effect of vitamin A supplements on the prevention of severe diarrhoea was also documented.<sup>8,9</sup>

Ideally underweight and/or stunted children should be given sufficient protein and calories on a daily basis with food supplies. But, in reality, many developing countries cannot guarantee food security, and thus require feasible short- and medium-term strategies to manage nutritional problems in order to have healthy populations of children. New perspectives are developing on the roles of micronutrients and vitamins in promoting growth and fighting infections. Zinc supplements, for example, improve linear growth, and prevent pneumonia in malnourished children.<sup>7,10,11</sup> Research to test the potential of both vitamin A and zinc, or other micronutrient combinations, on growth and the prevention of diarrhoea and acute respiratory infections seems to be required.

In spite of the conclusion of the authors that vitamin A plays a minor role in determining FEV<sub>1</sub> level even in an area endemic to vitamin A deficiency, I am not sure this is the case. It must be emphasized that the critical role vitamin A plays in growth and immunity is integrated in a complex process of reciprocal interactions with other crucial micronutrients. Outside of this framework the important piece of knowledge advanced by Kassaye *et al.* would become lost.

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## References

- <sup>1</sup> Kassaye T, Becklake MR, Receveur O, Hanley JA, Johns T. Association between vitamin A status and lung function level in children aged 6–9 years in Wukro wereda, Northern Ethiopia. *Int J Epidemiol* 2001;**30**: 457–464.
- <sup>2</sup> Tanumihardjo SA, Permaesih D, Muherdiyantiningsih RE *et al*. Vitamin A status of Indonesian children infected with *Ascaris lumbricoides* after dosing with vitamin A supplements and albendazole. *J Nutr* 1996;**126**:451–57.
- <sup>3</sup> Nafstad P, Magnus P, Jaakola JJ. Early respiratory infections and childhood asthma. *Pediatrics* 2000;**106**:e38.
- <sup>4</sup> Evain-Brion D, Porquet D, Thérond P, *et al*. Vitamin A deficiency and nocturnal growth hormone secretion in short children. *Lancet* 1994;**343**:87–88.
- <sup>5</sup> Hamam H, Stoltzfus RJ, Moulton LH, Dibley MJ, Wets KP. Respiratory infections reduce the growth response to vitamin A supplementation in a randomized controlled trial. *Int J Epidemiol* 1999;**28**:874–81.
- <sup>6</sup> Keusch GT. Malnutrition, infection, and immune function. In: Suskind RM, Lewinter-Suskind L (eds). *The Malnourished Child*. Nestlé Nutrition Workshop Series, Vol. 19, 1990, pp.37–59.
- <sup>7</sup> Umeta M, West CE, Haidar J, Deurenberg P, Hautvast JG. Zinc supplementation and stunted infants in Ethiopia: a randomized controlled trial. *Lancet* 2000;**355**:2021–26.
- <sup>8</sup> Sempértegui F, Estrella B, Camaniero V *et al*. The beneficial effects of weekly low-dose vitamin A supplementation on acute lower respiratory infections and diarrhea in Ecuadorian children. *Pediatrics* 1999;**104**:e1.
- <sup>9</sup> Barreto ML, Santos LMP, Assis AMO *et al*. Effect of vitamin A supplementation on diarrhea and acute lower-respiratory tract infections in young children in Brazil. *Lancet* 1994;**344**:228–31.
- <sup>10</sup> Sazawal S, Black RE, Jalla S, Mazumdar S, Sinha A, Bhan MK. Zinc supplementation reduces the incidence of acute lower respiratory infections in infants and preschool children: a double blind controlled trial. *Pediatrics* 1998;**102**:1–5.
- <sup>11</sup> Ninh NX, Thissen JP, Collete L, Gerard G, Khoi HH, Ketelslegers JM. Zinc supplementation increases growth and circulating insulin-like growth factor I (IGF-I) in growth-retarded Vietnamese children. *Am J Clin Nutr* 1996;**63**:514–19.