

## *Editorials*

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### Universal Vitamin A Supplementation Programme in India: The need for a re-look

Vitamin A is an essential nutrient needed in small amounts for normal functioning of the visual system, growth and development, maintenance of epithelial cellular integrity, immune function and reproduction. Severe deficiency of vitamin A is known to produce corneal xerophthalmia or keratomalacia and blindness in children. Vitamin A deficiency is seen mainly in young children in developing countries. The main causes of childhood vitamin A deficiency in the developing world include maternal vitamin A deficiency resulting in low concentrations of vitamin A in breast milk, inadequate dietary intake of vitamin A during and after weaning, and repeated bouts of common infectious illnesses (diarrhoea, measles and acute respiratory infection), which further decrease vitamin A levels. This micronutrient gained public health importance in the mid-1960s because of its ability to prevent nutritional blindness. Subsequently, vitamin A supplementation became the centre of attention because of its reported child survival benefits.<sup>1</sup> Periodic vitamin A supplementation to children over 6 months of age is being implemented in over 70 countries and is considered by many international agencies to be one of the most effective public health interventions ever undertaken.<sup>2</sup> However, this view is being contested by international and Indian scientists who stress that these claims are exaggerated and misleading.<sup>3-7</sup>

#### *Genesis of the universal vitamin A supplementation programme in India*

The National Prophylaxis Programme against Nutritional Blindness was initiated in 1970 as an urgent remedial measure to eliminate the unacceptably high magnitude of xerophthalmic blindness.<sup>8</sup> All 1–5-year-old children were to be administered 200 000 i.u. of vitamin A orally once in 6 months. During the early 1990s this intervention was restricted to children between 9 months and 3 years as clinical deficiency was almost exclusively restricted to this age range.<sup>9</sup> In 2005, an expert group chaired by the Director General, Indian Council of Medical Research endorsed 9 months to 3 years as the target age group for universal vitamin A supplementation (UVAS). However, digressing from this counsel, in 2006 the age group was broadened to include children between 6 months and 5 years after reconsidering recommendations of the WHO, UNICEF and Ministry of Women and Child Development.<sup>10</sup> The stated objective of the UVAS programme in India remains unaltered since inception; however, the current advocacy for intensification and increase in age range primarily pertains to child survival benefit.

#### *Secular trend in clinical vitamin A deficiency: Signal for policy modification*

In under-5 children, clinical vitamin A deficiency including severe xerophthalmia was a major public health problem in the early 1960s. However, in the past 4 decades keratomalacia has almost disappeared and there is a sharp decline in the prevalence of Bitot's spots.<sup>11,12</sup> Recent surveys indicate that the prevalence of Bitot's spots is >0.5% (conventional cut-off to define public health problem) in a few isolated geographical pockets, which are socioeconomically backward with poor health infrastructure.<sup>9,11,12</sup>

This observed decline is largely due to the implementation of relevant developmental and health initiatives in the country. This has led to better food availability, immunization coverage, access to healthcare facilities and management of childhood diseases. The available evidence indicates that this decline cannot be attributed to the UVAS programme. The latest national survey revealed that only 18% of eligible children received vitamin A supplementation.<sup>13</sup> Further, the predominant decline in clinical vitamin A deficiency antedated a functioning UVAS programme.<sup>11</sup> Conversely, an increase in coverage with UVAS in recent years has not been associated with a disappearance or substantial decline of clinical deficiency.

There is no obvious justification for continuing the UVAS programme to eliminate nutritional blindness. The available evidence too does not support a predominant role for this intervention in reducing clinical vitamin A deficiency. The advocacy for continuation and intensification of UVAS is thus now centred upon concerns of rampant subclinical deficiency and the child survival benefits. Subclinical or biochemical vitamin A deficiency is overestimated in our setting because the serum retinol cut-offs are based on western population norms, which pertain to subjects consuming primarily non-vegetarian diets and having relatively lower infectious diseases. Further, in the backdrop of intensely competing health interventions, there can be no justification for a public health programme solely for elevating biochemical parameters; it should be mandatory to unequivocally demonstrate important health or human capital benefits. As there are no obvious benefits of preventive UVAS for common childhood diseases and human capital,<sup>14</sup> this intervention can be justified only for the claim of mortality reduction.

*Child survival benefit: Is it likely in the current Indian context?*

The basis for the oft-cited mortality benefits are systematic reviews,<sup>15–17</sup> which suggest a mortality benefit of 23%–30% in children between 6 months and 5 years of age. The data pertain to global trials conducted over 2 decades ago when the magnitude of vitamin A deficiency was much higher. Most of these studies were conducted in areas with rudimentary healthcare facilities and by the same group of investigators from the Johns Hopkins School of Public Health, USA. Robust external validations of these claims by other groups of independent scientists are scarce.

A systematic review of Indian trials concluded that for the prevention of mortality and morbidity, the findings of 'vitamin A trials are not consistent, and there is no evidence as yet in favour or against substantive benefit of universal vitamin A supplementation to children in India'.<sup>18</sup> The De-worming and enhanced vitamin A (DEVTA) trial, done between 1999 and 2004, explored child survival benefits among 1 million children above 6 months of age in underprivileged, rural areas (72 blocks) of Uttar Pradesh, India with a relatively higher prevalence of clinical vitamin A deficiency. This trial with a sample size greater than all earlier global studies pooled in the meta-analyses, failed to document a child survival benefit of vitamin A supplementation.<sup>19</sup> However, allegedly due to pressure by the 'vitamin A lobby' the results have not been published even 6 years after the completion of the study. Nonetheless, these data must be considered while formulating our national policy.

*Potential harms ignored*

Potentially important and serious safety concerns have been ignored while framing policy regarding intensification of UVAS. Overzealous efforts at intensification of vitamin A supplementation were associated with the death of over 30 children in Assam, probably due to micronutrient overdosage.<sup>20</sup> Vested interests labelled this episode as mass hysteria.<sup>21</sup> The explicit warning of this possibility by the Indian Academy of Pediatrics was not heeded to.<sup>22</sup>

Administration of a mega-dose of vitamin A is associated with an increased risk of bulging fontanelle in early infancy due to a transient rise in intracranial pressure (RR 1.53, 95% CI 1.03–2.27, Gogia S and Sachdev HPS, unpublished observations). This may occur in up to 16% of young children.<sup>23</sup> Infancy is a crucial period for development of the brain and the long term adverse consequences of bulging fontanelle on humans are unknown.

Systematic reviews show that vitamin A supplementation results in an increased risk of developing acute respiratory infection,<sup>14,24</sup> which violates the public health principle of causing no harm.

Vitamin A in large doses causes hypercalcaemia due to a direct effect on bone.<sup>25</sup> It intensifies the severity of bone demineralization and inhibits the ability of vitamin D to prevent such demineralization.<sup>26</sup> Excessive dietary intake of vitamin A in adults is associated with reduced bone mineral density and increased risk for hip fracture.<sup>27,28</sup> In the backdrop of high prevalence of adult osteoporosis, we need to unequivocally establish the long term safety of UVAS for bone health in young undernourished children subsisting on low calcium intakes.

Other latent but crucial implications for public health policy deserve greater attention. An intervention that was intended to be an interim 'fire fighting' exercise to control xerophthalmic blindness is now a permanent 'quick fix' due to several reasons including possibly commercial, which have been recently commented upon.<sup>3</sup> Intensification and permanency of such 'quick fixes' is an important barrier to sustainable solutions, the development process and self-sufficiency in India, which is struggling to prioritize competing interventions within the available financial resources. Local evidence and the opinion of national scientists and professional organizations have been repeatedly ignored in preference to international experience and vested interests. These potential negative consequences alone provide enough rationale for discontinuing UVAS.

#### *The way forward*

The current evidence suggests that UVAS cannot be justified as a public health intervention for prevention of xerophthalmic blindness or childhood mortality in India. The continuation and intensification of UVAS despite consistent opposition from Indian scientists is proving detrimental for our public health needs. We suggest a dispassionate, national evidence-based process to examine an appropriate shift in the vitamin A supplementation policy.

#### COMPETING INTERESTS

None

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