

services. Bihar has implemented vaccination session-site and community monitoring and together with partners provided feedback on 39,051 immunizations sessions monitored and the vaccination status of 310,843 children 0-23 months of age [6]. In a more robust assessment of *Muskaan*, this information would be crucial to better understand the intermediate pathways associated with the uptake of immunization services. Unfortunately, Bihar is just one of a handful of states that has implemented this system of monitoring. Lastly, strategies and intensity of activities required to increase coverage from 30 to 50 percent will not be the same when attempting to raise coverage to 90 percent and above. For this reason, it is also necessary to link budget and expenditure data to aid decisions related to the cost-effectiveness of different interventions.

Over the last several years, Bihar has more than doubled its proportion of fully immunized children while aggressively pursuing polio eradication at a level of intensity rivaled only in Uttar Pradesh. Untangling the mixed effects in National Rural Health Mission (NRHM), *Muskaan*, polio eradication efforts and the role of Government strength and ownership is a complex endeavor that requires robust prospective program evaluation informed by multiple data sources. As well known evaluators have aptly stated, "Evaluations of complex population-level interventions are likely to have

complex answers, but are necessary to improve future programs." [7]

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#### REFERENCES

1. UNICEF Coverage Evaluation Survey. All India Report. New Delhi: UNICEF; 2009.
2. Goel S, Dogra V, Gupta SK, Lakshmi PVM, Varkey S, Pradhan N, *et al.* Effectiveness of Muskaan Ek Abhiyan (The Smile Campaign) for Strengthening Routine Immunization in Bihar, India. *Indian Pediatr* 2012; 49: 103-8.
3. Ng M, Gakidou E, Levin-Rector A, Khera A, Murray CJ, Dandona L. Assessment of population-level effect of Avahan, an HIV-prevention initiative in India. *Lancet*. 2011;378:1643-52.
4. Victora CG, Black RE, Boerma T, Bryce J. Measuring impact in the Millennium Development Goal era and beyond: a new approach to large-scale effectiveness evaluations. *The Lancet*. 2011;377:85-95.
5. Sagar KS. Improving UIP Coverage in India, concept note. New Delhi: Maternal and Child Health Integrated Program (MCHIP); 2011.
6. National Polio Surveillance Project. Routine Immunization Monitoring database. New Delhi: NPSP, WHO: 2010-2011.
7. Boerma T, d Zoysa I. Beyond accountability: learning from large-scale evaluations. *The Lancet*. 2011;378:1610-1.

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## Low Serum Magnesium and Obesity – Causal Role or Diet Biomarker?

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**T**he association between a low magnesium (Mg) status, and insulin resistance and the metabolic syndrome has been shown repeatedly in adults [1], and higher Mg intakes have been shown to have a protective role [2]. This leads to the tantalizing conclusion of a mechanistic involvement of Mg in weight gain and insulin resistance through its critical role as a co-factor in several enzymes in carbohydrate metabolism [1]. However, the  $K_m$  of Mg for these enzymes is close to its intracellular concentration, which does not decline easily on Mg deficient diets [3]. The effect is also subtle: the adjusted risk for diabetes with quite low (<1.7 mg/dL) serum Mg levels have been shown to increase modestly by about 1.5 fold [4]. Furthermore, reverse causality is also possible: diabetes is known to increase renal Mg

excretion, and insulin resistance decreases Mg uptake. Therefore, the theoretical framework that links low Mg status to obesity and insulin resistance is not simple.

The relation between obesity and Mg is also not clear. Several studies have assessed the association between body mass index and Mg intake or status in adults, but the results are still controversial [2,5]. This may be because the associations of low serum Mg with obesity related outcomes are subtle and subject to type 2 errors. In this issue of *Indian Pediatrics*, Jose, *et al.* [6] have found that serum Mg was lower in obese Indian children, but this counter-intuitively occurred with apparently higher Mg intakes. The authors are careful not to imply any mechanistic linkage either way, but speculate that the

aggravation of the insulin resistant state with low serum Mg could start early in childhood.

Measuring Mg status accurately is challenging, since serum Mg is only about 1% of the total body Mg, and most probably reflects its renal handling rather than its dietary intake. A very low Mg diet (<10%) in a human subject in 'excellent health' led to a drop by about 0.4 mg/dL in serum levels, along with negative balances, but no drop in intracellular levels [3]. On the other hand, intracellular Mg depletion has been found with normal serum Mg concentrations [1]. The point is that Mg intake cannot easily be related to serum level or status. Pre-analytical factors, including the effect of prior exercise on serum Mg, are also important.

Nevertheless, given the observation that the obese children had a higher energy adjusted Mg intake [6], the low serum Mg levels are likely to be an 'effect' rather than a cause. The authors' opinion is that the observed differences could have been due to decreased Mg absorption or increased excretion. Both these mechanisms are plausible. The questions relate to how and why. For example, one could enquire whether the obese children had a higher calcium (Ca) intake, since this is known to interfere with Mg absorption. Indeed, dairy products are high in Ca and low in Mg content. The intake of carbonated soft drinks, with higher intakes of phosphorus could also interfere with absorption while caffeine can increase renal Mg excretion [7]. A vegetarian and unprocessed food-based diet, such as with whole grains, nuts, and green leafy vegetables, is high in Mg, which is lost during processing. Therefore, in studies that investigate associations between serum Mg and other outcomes, it is critical to have a close inspection of the dietary environment.

Observational studies such as those by Jose, *et al.* [6] are important in a transitioning society with changing processed food intake; however, longitudinal studies with detailed food intake assessment are required to assign causality or to assess the potential interaction with insulin resistance. Until then, the role of Mg will remain enigmatic, the need for supplements unclear, and serum Mg may simply have to continue to be considered as a biomarker for a particular type of diet.

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#### REFERENCES

1. Barbagallo M, Dominguez LJ. Magnesium metabolism in type 2 diabetes mellitus, metabolic syndrome and insulin resistance. *Arch Biochem Biophys.* 2007;458:40-7.
2. He K, Liu K, Daviglus ML, Morris SJ, Loria CM, Van Horn L, *et al.* Magnesium intake and incidence of metabolic syndrome among young adults. *Circulation.* 2006;113:1675-82.
3. Dunn MJ, Walser M. Magnesium depletion in normal man. *Metabolism.* 1966;15:884-95.
4. Kao WH, Folsom AR, Nieto FJ, Mo JP, Watson RL, Brancati FL. Serum and dietary magnesium and the risk for type 2 diabetes mellitus: The Atherosclerosis Risk in Communities Study. *Arch Intern Med.* 1999;159:2151-9.
5. Song Y, Sesso HD, Manson JE, Cook NR, Buring JE, Liu S. Dietary magnesium intake and risk of incident hypertension among middle-aged and older US women in a 10-year follow-up study. *Am J Cardiol.* 2006;98:1616-21.
6. Jose B, Jain V, Vikram NK, Agarwala A, Saini S. Serum magnesium in overweight children. *Indian Pediatr.* 2012, 49:109-12.
7. Swaminathan R. Magnesium metabolism and its disorders. *Clin Biochem Rev.* 2003;24:47-66.

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## Environmental Exposures and Childhood Cancer

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The link between environmental agents and childhood cancer is not a new concept. Environmental causes of childhood cancer have long been suspected by many scientists but have been difficult to pin down, partly because cancer in children is rare and because it is difficult to identify past exposure levels in children, particularly during potentially important periods such as pregnancy, *in-utero*, or even prior to conception. Hence, many of the

environmental agents hypothesized for childhood leukemia remain speculative [1-3].

In this issue of *Indian Pediatrics*, Rau *et al.* [4] investigated the presence of endosulfan in the bone marrow of children with hematological malignancy residing in areas sprayed with the pesticide (in South India). This is a case-control study in which the authors