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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Environmental Exposures and Childhood Cancer

GAURI KAPOOR
Pediatric Hematology Oncology, Rajiv Gandhi Cancer Institute & Research Center, Sec -V, Rohini, Delhi-110085.
gauri_kapoor2000@yahoo.com

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

report its presence in the bone marrow of 7/34 children residing in these areas including 6 who had leukemia.

The authors themselves point out that this study does not in any way prove that endosulfan is a cause of leukemia. As of date, there are no available epidemiological studies linking endosulfan exposure specifically to cancer in humans. It is important to understand that an association between an exposure and cancer does not necessarily mean that the exposure causes cancer. Most importantly, other possible explanations of the observed association must be ruled out. The consistency of an association is to be considered, and the association must be temporally correct meaning that we must be sure that the exposure actually preceded the development of the disease, which in this case would include events taking place before birth, during conception, embryogenesis and early postnatal life. Another important aspect in such a study is the sample size and whether it is truly representative of the population. As acknowledged by the authors, the small sample size, other compounding factors like genetic susceptibility, exposure to other carcinogens and their effects, are the limitations of this study.

Endosulfan, an off patent organochlorine insecticide and acaricide was developed in the early 1950s and has been used globally in agriculture to control insect pests. Although industrialized nations have restricted or banned many organochlorine pesticides, some of these chemicals (like endosulfans) are still used, on the assumption that they pose little threat to the environment, wildlife, or human health.

It has long been recognized that leukemia is a heterogenous disease with a multifactorial and multistep pathogenesis with a fetal origin being postulated by some [3,5]. Epidemiological evidence suggests that ionizing radiation, certain chemicals (such as benzene), viruses (human T-cell leukemia/lymphoma virus type I, Epstein-Barr virus), and bacteria *(Helicobacter pylori)* may play a part in the development of some subtypes of leukemia and lymphoma in adults and children.

Finding causes of any disease is usually a long, slow process. No one study is likely to prove that a particular exposure definitely causes a particular cancer. However, each well designed and well executed study with adequate sample size will bring us closer to understanding the causes of these cancers within populations of children.

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