

# ZINC *Protects!*

## The Role of Zinc in Child Health

Mary Penny

Instituto de Investigacion Nutricional, Peru



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The beneficial properties of zinc have been appreciated for many years, generations of mothers have applied zinc cream to cure nappy rash and it is common knowledge that zinc helps heal wounds. More than ten years ago the importance of dietary zinc supplements in the recovery from severe malnutrition was documented in Jamaica<sup>1</sup> and more than 35 years ago it was recognized that severe zinc deficiency was responsible for dwarfism and failure to mature in young Iranian and Egyptian youths eating a diet consisting largely of whole meal bread<sup>2</sup>. Now we have realized that lesser degrees of zinc deficiency are more common than was appreciated and the subclinical deficiency of zinc contributes to an increased incidence and severity of common but important infections such as diarrhoea and pneumonia.

Diarrhoea is one of the clinical manifestations of zinc deficiency in humans and animals. The syndrome Acrodermatitis enteropatica received its name because diarrhoea was a cardinal feature<sup>3</sup>. In this inherited congenital condition there is an abnormality in the intestinal absorption of zinc. This can be overcome by giving large oral doses of the mineral which result in the rapid disappearance of all symptoms including the diarrhoea. In a clinical study in Bangladesh, children who were hospitalized with persistent diarrhoea had less diarrhoea and showed improvements in mucosal permeability after supplements of zinc were administered<sup>4</sup>. Diarrhoea is associated with an increased loss of zinc in faeces so that one would expect that children with diarrhoea would be at an increased risk of zinc deficiency<sup>5</sup>.

In recent years a number of other studies have corroborated these preliminary findings in children with both acute and persistent diarrhoea.

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One of the first of these studies, in India, found that children with acute diarrhoea got better faster when they received a zinc supplement<sup>6</sup>. This trial in New Delhi compared vitamin supplements with and without 20 mg elemental zinc administered daily to 937 children with acute diarrhoea. The children who received zinc recovered more quickly and they had 23% less chance of continuing diarrhoea on any day after starting the zinc supplement. The children receiving zinc also had fewer loose stools so that in this study the zinc reduced the severity of the

diarrhoea as well as hastening recovery. Other trials from different parts of the world from Papua New Guinea to Peru have shown similar benefits. The data from these studies has been pooled and the results demonstrate a consistent, significant and clinically important benefit of supplements containing oral zinc (usually 20 mg elemental zinc) in children aged under five years who present acute diarrhoea. Children had a 15% faster recovery with zinc<sup>7</sup>. Similar results have been found in studies of children with persistent diarrhoea. A community based study undertaken by the Instituto de Investigacion Nutricional in Lima found that children who received zinc as opposed to placebo recovered more rapidly from their diarrhoea<sup>8</sup>. The combined results of 4 studies of children with persistent diarrhoea showed a 29% faster recovery. In these diarrhoea studies the positive response to zinc was not limited to malnourished children although children with low plasma zinc levels suggestive of zinc deficiency were more likely to benefit. These findings suggest that zinc supplements may represent an important therapeutic





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advance complementing the oral rehydration therapy which is currently recommended to prevent dehydration but which does not reduce the duration of the diarrhea.

If zinc supplements are of benefit in treating diarrhea especially in children with low blood zinc levels it is logical to think that prevention of deficiency by regular supplementation might reduce the burden of illness in populations subject to zinc deficiency. How commonly does this occur?

Despite the widespread presence of zinc in common foods, dietary deficiency is common because bioavailability of zinc is reduced by the coexistence of inhibitory substances such as fiber and phytates in food of vegetable origin<sup>9</sup>. These substances inhibit the absorption of zinc. The diets of the poorest populations are a poor source of zinc being largely made up of vegetable staples with little content of animal products, especially flesh foods such as meat, fish and offal which are the richest sources of easily assimilated zinc. Children in these communities do not manifest obvious signs of zinc deficiency but have often been found to have low plasma zinc levels compatible with subclinical zinc deficiency. Thanks to recent investigations we now believe that this deficiency may be contributing to the high illness rates which are typical of these populations.

Studies in Vietnam<sup>10</sup>, Mexico<sup>11</sup>, Guatemala<sup>12</sup>, India<sup>13,14,15</sup>, Jamaica<sup>16</sup>, Indonesia<sup>17</sup>, Papua New Guinea<sup>18</sup> and Peru<sup>8</sup> have evaluated the impact of daily oral zinc supplements given to small children. These studies in general demonstrate not only substantial benefits in diarrhea - a reduction in the severity and duration of episodes of diarrhea, fewer episodes of persistent diarrhea and dysentery and lower prevalence of days with fever and anorexia - but importantly, they also demonstrate fewer episodes of respiratory illness, notably less pneumonia, the primary cause of infant deaths in most developing countries. For instance one study in India<sup>15</sup> documented a reduction of 45% in the risk of pneumonia when daily supplements containing 10 mg elemental zinc were given to young children. These data have been contributed to a pooled analysis which will provide more information on the extent of the benefits which can be expected from daily zinc supplementation<sup>7</sup>.

Diarrhea and pneumonia are almost universal, responsible for much infant morbidity and mortality and of enormous public health importance. Other diseases such as malaria cause millions of preventable adult and child deaths in many parts of the world. A study in a community in Papua New Guinea<sup>18</sup> compared children receiving either zinc supplements or placebo and found that those receiving zinc had 40% less visits to the health centre for malaria attacks, especially those due to *Plasmodium falciparum*. If these findings are confirmed by other studies in different countries, this could provide a much needed weapon in the fight against malaria. Zinc has also been reported to be of benefit in a wide variety of other conditions varying from prostatism to acne and the common cold and these are the subject of current investigation.

How can these widespread and apparently dramatic benefits of zinc supplementation be explained? Zinc is essential for more than 300 enzymes, structural proteins and hormones. It is needed for diverse physiological processes and metabolic functions including many aspects of the immune system<sup>19</sup>. Lack of zinc is associated with atrophy of the thymus, a gland which has a role in the maturation of lymphocytes, and the function of "T" lymphocytes is especially vulnerable to deficiency of this mineral. Zinc deficiency is associated with a reduction in delayed type hypersensitivity<sup>20</sup>, and other immune responses mediated by T cells. In zinc deficiency there is an imbalance in the production of T helper cells with different functions; there is a shift from T cells (Th1) which have a predominately cellular

function and are important in the defense against viral and intracellular pathogens in favour of T cells (Th2) which are involved in the production of antibodies<sup>21</sup>. On the other hand in experimentally induced zinc deficiency in animals there is also a reduction in the production of antibodies and in the function of natural killer cells. Further studies will elucidate the role of zinc in the immune system and increase our understanding of how and when this mineral can be best used to prevent and treat infection.

Zinc is also needed for cell replication and is thus essential for the regeneration of the intestinal mucosa, the healing of wounds and the turnover of epithelial cells necessary to maintain healthy skin. The combination of these essential functions explains why zinc plays such an important part in the protection against infections.

As investigation continues and our understanding of biology increases, potent drugs, lifesaving procedures and hitherto humble nutrients are discovered or rediscovered and provide the means for reducing disease and prolonging life. Not all these promising advances can be adopted, especially in countries where resources are inadequate to meet even basic needs and choices have to be made. Possible public health interventions have to be considered in the context of their relative benefit, cost and feasibility. Nevertheless preliminary estimates based on published results of the potential benefits of zinc supplementation compared with other dietary interventions, vaccines, vitamin supplements, and hygiene interventions<sup>22</sup> suggest that zinc supplementation of high risk populations has considerable potential and the search for simple economic options to counteract zinc deficiency should be given priority.

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