

## COMBATING IRON DEFICIENCY

### 1. Editorial Introduction

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Anaemia may be defined as a state in which the quality and/or quantity of circulating red cells are reduced below a normal level. Different biological groups have different cut-off points for haemoglobin (Hb) levels below which an individual is classified as anaemic (1). Iron-deficiency anaemia is by far the most widely prevalent nutritional deficiency in the world, with serious consequences for individuals and populations.

#### Prevalence of Anaemia in Sri Lanka

In Sri Lanka, too, anaemia is a major problem, the main cause being iron deficiency. A survey carried out in 1973 (2,3) showed a prevalence of 38% in men, 68% women, 70% in primary school children and 52% in pre-school children. A more recent study by the Medical Research Institute, in the Gampaha District, indicated a prevalence of about 60% among pregnant women, 30% of whom were mildly anaemic, 28% moderately anaemic and 1% severely anaemic (Hb level < 70 g/L). The plasma transferrin saturation in the Gampaha study was less than 15% in 47% of the study population. In the study sample, 47% had blood folate levels < 3 mg/dL, suggesting folate deficiency associated with iron deficiency. Anaemia occurs despite the national programme in which iron and folate tablets are distributed to all pregnant women at Maternal and Child Health (MCH) Clinics. Several other studies on small groups of subjects (4,5,6,7,8) all indicate that iron deficiency is a health problem that needs urgent attention.

In order to obtain nationally representative data on the prevalence of anaemia, the Ministry of Finance, Planning, Ethnic Affairs and National Integration (MFPEANI) included haemoglobin

measurements in the Third National Nutrition and Health Survey, which was conducted between October 1994 and January 1995. A report of the survey appears in this issue of the Journal (9). Anaemia was most prevalent among primary school children (5 to 10.9 y) and pre-schoolers (3 to 59 mo). One in three adolescents and nearly one in two non-pregnant women were also anaemic.

#### Deleterious Effects of Anaemia and Iron Deficiency

**Brain development.** During the past two decades an increasing number of reports (10,11,12) have confirmed the results of the first clinical study, in 1976, that iron supplementation of diets of adolescents improved their cognitive performance. Where iron deficiency occurs in infancy and is moderate to severe, there is likely to be permanent neurological damage that cannot be corrected by subsequent iron supplementation (13). The effects of mild deficiency, at least after infancy, are detectable but appear to be reversible. Iron deficiency has adverse effects on concentration and school performance of children.

**Infection.** Iron deficiency anaemia is generally believed to increase an individual's susceptibility to infection. There is, however, no firm evidence to support this view (14). The complexity of the interaction between the infective agents and the host makes proof extremely difficult. There is, however, suggestive but not conclusive evidence of an increased susceptibility to infection in iron deficient subjects (15). The mechanisms identified include lowered response to lymphocyte stimulation, fewer natural killer cells and reduced interferon production, and impaired phagocytic killing power (16).

**Pregnancy.** Severe anaemia during pregnancy is associated with an increased risk of maternal and foetal morbidity and mortality (17,18,19). Even mild anaemia has been shown to be associated with an increased risk of premature delivery (20), low birth weight (21), placental hypertrophy (22) and reduced oestriol excretion (20).

**Work capacity.** Work capacity has been shown in a number of studies to be related to Hb concentration and to be decreased even in mildly anaemic subjects (23, 24, 25, 26). Work output is significantly less in iron deficiency in rubber tappers (27) and in tea pluckers (28, 29). In some of these studies, work output increased significantly following iron administration to correct the anaemia. These reports indicate that even moderate degrees of iron deficiency anaemia may have far reaching socio-economic consequences.

**Other effects.** There is evidence that iron deficiency may affect many other bodily functions. Abnormalities such as decreased gastric juice secretion (30), reduced activity of intestinal cell enzymes (31) and structural abnormalities such as mitochondrial enlargement (32, 33) have been reported. Growth rate in children is associated with the degree of anaemia, with apparent beneficial effects of iron therapy (34). However, this effect may be due to a reduction in physical activity, and anorexia resulting in reduced food intake, caused by iron deficiency.

### Interventions

The two principal forms of intervention adopted in Sri Lanka have been

- i. **nutrition education**, stressing the need for iron, the problems regarding absorption of non-haem iron, the usefulness of enhancers of non-haem iron absorption such as ascorbic acid and the meat-fish-poultry foods (which, in addition, are good sources of iron) and avoidance of taking inhibitors of iron absorption such as tannin in tea, with or immediately after a meal.

Health and nutrition education of the public through all channels, including schools, ante-natal and post-natal clinics and at every doctor-patient encounter, must be organized and carried out continuously. Education of doctors, nurses, village health workers, health planners and politicians must also be included in any programme aimed at counteracting problems such as energy-protein undernutrition or vitamin A and iron deficiency among the population.

- ii. **Distribution of haematinic supplements** (iron and /or folate) in tablet or liquid forms

The use of pharmacological supplements is the only way of meeting the iron needs during pregnancy and of treating the most severely anaemic in areas of high prevalence. Iron supplementation programmes are influenced by a variety of factors such as the nature of the diet, the type of iron in the supplement used, the organization of primary care services and the prevalence of parasitic infestations, particularly ankylostomiasis. All readily soluble ferrous iron compounds suitable for oral administration are, in general, equally well absorbed and produce the same type of side effects with similar frequency (35). Ferrous sulphate is one of the cheapest available compounds and is the form used in Sri Lanka in community programmes. However, supplementation can reach only selected persons and will leave out those who do not attend clinics. It requires an adequate and expensive delivery system. Further, lack of compliance with tablet intake is a serious problem. Recent studies indicate that iron supplementation weekly (36) or thrice a week (37) is as effective as daily supplementation in improving the iron status of individuals with moderate anaemia. There is an urgent need for similar studies on different groups at risk.

A third intervention which is not currently implemented in Sri Lanka is **food fortification**, where a haematinic is supplied through foods commonly consumed by the community. Several

factors have to be considered when planning a fortification programme:

- i. a suitable vehicle has to be chosen to which the iron could be added. The vehicle should be one that is already consumed in adequate amounts by the general population. It should be processed at relatively few centres where the iron can be added, so that quality can be monitored. After fortification, the vehicle and products made from it should not deteriorate in quality over the normal shelf-life of the foods and under the conditions of storage (temperature, humidity) encountered throughout the island.

Vehicles that have been used include;

- a. Cereal foods such as wheat flour, maize flour and rice in countries where these grains are processed through centralised milling operations. Although rice is the cereal that is consumed by nearly all persons in Sri Lanka (and consumed in quantity), paddy is milled at many centres throughout the island, in addition to being pounded in many households, making it inappropriate as a vehicle for iron.
- b. Common salt is consumed by all persons, but its use as a vehicle for iron sulphate is limited because iron discolours salt, resulting in poor acceptance. Further, salt consumption is low (about 10 g per day per adult), necessitating a high concentration of the fortificant in the vehicle, making its presence difficult to disguise. However, salt has been successfully fortified with ferric orthophosphate together with sodium hydrogen sulphate (38) or ascorbic acid (39), but data on its efficacy to control iron deficiency anaemia in a community setting are not available. Large scale production of salt fortified with iodine and iron has been reported recently (40).
- c. Sugar, widely consumed at a level of between 40 and 100 g/day and processed in a few refineries has been tested as a vehicle for iron (41). A major disadvantage to sugar fortification with iron in Sri Lanka is that

sugar is mainly consumed with tea and the iron added could be precipitated by the tannins in tea. Iron complexed with tannin is not available for intestinal absorption.

- d. Other vehicles that have been tested include fish sauce in Thailand (42) and curry powder (43) in South Africa. Curry powder is used only by people of Indian origin in South Africa so that those of African origin would not be affected by the fortificant in curry powder. Curry powder is suitable from several points of view. It is highly coloured and spiced so that the fortificant would not produce an obvious change in its appearance and taste. It is used uniformly by the entire population. Curry powder by itself appears to have a positive effect on the bioavailability of non-haem iron in food, probably due, in part at least, to its ability to stimulate gastric acid secretion (43). Unfortunately in Sri Lanka, as in other countries, curry powder is processed and packeted at a number of centres and, very often, the different ingredients are mixed in various proportions by the housewife herself.

- ii. When considering iron compounds that could be used as fortificants their chemical properties must be kept in mind.

e.g. Ferrous salts may be oxidised to yellow-green, or black ferric oxide.

Iron salts may react with phenolic compounds, such as tannins, to form blue black colours, or react with sulphur to produce a black colour.

The colour and flavour of the iron compound itself may be undesirable.

A high-density product such as reduced iron may require special measures to achieve a stable and uniform distribution.

In addition, iron is a pro-oxidant and iron compounds may catalyse the development of oxidative reactions.

A large number of iron compounds, have been and are used as fortificants. Among the soluble compounds are ferrous sulphate, citrate, fumarate, gluconate, lactate, and tartrate. Ferrous sulphate is the cheapest. Of the ionizable ferric

compounds, ferric sulphate and chloride are the cheapest. Elemental iron, reduced either by hydrogen or by electrolysis, have been widely used and are of high bioavailability. Sodium ferric EDTA is the most absorbable iron compound available. Unfortunately it is also the most expensive. It was used in fortifying curry powder and found to be acceptable and highly bioavailable (43).

#### **Iron Fortification of Wheat Flour Project**

A wheat fortification trial is presently underway in Sri Lanka, with the assistance of USAID. USAID has been actively involved in food and nutrition programmes in Sri Lanka for nearly three decades. Until recently, USAID was the principal provider of wheat flour to the island. The idea of fortifying wheat flour with iron was first raised at the Sessions of the Nutrition Society of Sri Lanka, held in November, 1976, the theme of the Sessions being "Nutrition and National Development". This was picked up by a USAID consultant in 1982, who proposed that flour be fortified with vitamin A, iodine and iron. The government of Sri Lanka did not pursue this suggestion due to the costs involved. About 10 years later the suggestion was again raised by another USAID consultant; the focus this time was on iron. By then the milling of all imported wheat and distribution of flour was being handled by Prima Ceylon Limited, based in Trincomalee. There was also widespread recognition that anaemia is a serious health problem in the country. The Iron Fortification of Wheat Flour Project began in 1994, jointly sponsored by the Government of Sri Lanka, USAID/Sri Lanka and USAID/Washington.

The project has been arbitrarily divided into three phases. Phase I was designated as the initial evaluation of feasibility and need, Phase II as the period for evaluating the effectiveness and acceptability of iron fortified wheat flour, and Phase III as the implementing, scaling-up and advocacy portion.

The report on Phase I has been published by the MFPEANI. During this Phase several critical,

simultaneous activities were carried out. The most appropriate iron compound for fortifying wheat flour was selected, the level of fortificant and the method of incorporating the fortificant into the flour were identified. Both the fortified flour and the products from that flour (bread, string-hoppers, roti and "hulang viscotu") were evaluated after storage. Prima Ceylon Ltd., was responsible for fortifying the flour and the Ceylon Institute of Scientific and Industrial Research (CISIR) was responsible for preparing and evaluating the fortified test products. A report on the work done by the CISIR is published in this number of the Journal (44). Prima Ceylon Ltd. also conducted tests on the physical properties of fortified bread.

Two equally important activities during Phase I were establishing the extent and severity of anaemia, based on haemoglobin levels, and patterns of wheat flour consumption. The Nutrition Division of the Medical Research Institute was responsible for collecting the recipe data needed for determining wheat flour consumption levels. A report of this study appears in the Journal (45). Data on both the prevalence of anaemia and the pattern of wheat flour consumption was obtained during the Third National Nutrition and Health Survey carried out by the MFPEANI at the end of 1994 (9).

Preparation for Phase II activities began in 1995. Both the flour distribution system within the market and the processes of business and managerial control influenced how the project established the required monitoring and control components in the field trial. After considering a number of alternatives, it was decided that the field trial would be carried out in the estate sector. The mechanics of adding the selected iron compounds will be refined and scaled up during the early period of Phase II.

Flour will be fortified at a level of 66 ppm, so that the risk of iron overload is negligible. However, this aspect of iron metabolism is also being monitored by estimation of serum ferritin levels

in healthy adult males. The benefit of such a supplementation programme should be a slight improvement in the iron status of the population as a whole. Pharmacological iron supplements for pregnant women and for those severely anaemic will have to be continued. Their needs cannot be met with iron-fortified foods alone.

The benefits of the iron fortification programme relative to its cost will depend on the results of Phase II. While the unit cost of fortification (cost per kg) is small and the cost is recoverable through very small price adjustments, the volume multiple is large and relies on foreign exchange. The benefits accruing to the costs must be identified and measured. The data will be used in the public debate, which will precede any policy change.

The collaborating institutions are:

The MFPEANI, CISIR, MRI, Universities of Colombo, Peradeniya and Ruhuna, Prima Ceylon Ltd., and OMNI Project/USAID. The Iron Fortification of Wheat Flour Technical Committee consists of members of the MFPEANI, MRI, CISIR, USAID/Sri Lanka, Prima Ceylon Ltd., and Faculties of Medicine of the three Universities.

#### References

1. WHO. Nutritional anaemia. World Health Organization technical report series no. 405. Geneva: World Health Organization, 1968.
2. Sood SK. Assignment report on the control of nutritional anaemia in pregnancy in Ceylon. New Delhi: WHO 1972; 12pp.
3. de Mel BV, Sood SK. Consultation on nutritional anaemia. New Delhi; SEARO 009.06, 1973.
4. Atukorala TMS, Sheriff MHR. Effect of supplementation on iron status of geriatric subjects. Ceylon Medical Journal 1986; 31: 15-20.
5. Atukorala TMS, Ranjini LPP, Sheriff MHR. Nutritional status of institutionalised elderly with special reference to iron. Ceylon Journal of Medical Science 1988; 31:7-17.
6. Atukorala TMS, de Silva LDR. Iron status of adolescent females in three schools in an urban area of Sri Lanka. Journal of Tropical Paediatrics 1990; 36: 316-321.
7. Atukorala TMS, de Silva LDR, Dechering WHJC, Dassenaik TS de C, Perera RS. Evaluation of the effectiveness of iron folate supplementation and anthelmintic therapy against anaemia in pregnancy: a study in the plantation sector of Sri Lanka. American Journal of Clinical Nutrition 1994; 60: 286-292.
8. de Silva LDR, Atukorala TMS. Micronutrient status of plantation workers in Sri Lanka during pregnancy and post partum. Journal of Obstetrics and Gynaecological Research 1986; 24: 239-246.
9. Mudalige R, Nestel P. Prevalence of Anaemia in Sri Lanka. Ceylon Journal of Medical Science 1996; 39: 9-16
10. Garn SM, Smith NJ. More on haemoglobin levels: relation to growth performance. Journal of Paediatrics 1973; 8: 346-348.
11. Webb TE, Oski FA. The effect of iron deficiency anaemia on scholastic achievement, behavioural stability and perceptual sensitivity of adolescents. Paediatric Research 1973; 82: 827-830.
12. Muhilal, Sumarno I, Komari. Review of surveys and supplementation studies of anaemia in Indonesia. Food and Nutrition Bulletin 1996; 17: 3-6.
13. Scrimshaw N. Malnutrition, brain development and behaviour. 20th Kamala Puri Sabharwal Memorial Lecture at Lady Irwin College, New Delhi, 23rd November 1993.
14. Elwood PC. Some epidemiological aspects of iron deficiency relevant to its evaluation. Proceedings of the Royal Society of Medicine 1970; 63: 1230-1231.

15. Masawe AEJ, Muindi JM, Swai GBR. Infections in iron deficiency and other types of anaemia in the tropics. *Lancet* 1974; ii: 314-315.
16. Scrimshaw NS. Editorial Introduction. *Food and Nutrition Bulletin* 1996; 17: 1-2.
17. Tasker PWG. Anaemia in Pregnancy. *Medical Journal of Malaya* 1958; 13: 3-6.
18. Mac Gregor MW. Maternal anaemia as a factor in prematurity and perinatal mortality. *Scottish Medical Journal* 1963; 8: 134-136.
19. Llewellyn – Jones D. Severe anaemia in pregnancy in Australia and New Zealand. *Journal of Obstetrics and Gynaecology* 1965; 5: 191-193.
20. Ratten GJ, Beischer NA. The significance of anaemia in an obstetric population in Australia. *Journal of Obstetrics and Gynaecology of the British Commonwealth* 1972; 79: 228-230.
21. Yusufi D, Mathan VI, Baker SJ. Iron, folate and vitamin B<sub>12</sub> nutrition in pregnancy: a study of 1000 women from Southern India. *Bulletin of the World Health Organization* 1973; 48:15-20.
22. Beischer NA, Holsman M, Kitchen WH. Relation of various forms of anaemia to placental weight. *American Journal of Obstetrics and Gynaecology* 1968; 101:801-803.
23. Cifunetes E, Viteri FE. Physical fitness, iron deficiency and anaemia in agricultural labourers of Central America. *Federation Proceedings* 1972; 31:719-722.
24. Davies CTM, Chuk Weumeka AC, Van Haaren JP. Iron deficiency anaemia: its effect on maximum aerobic power and responses to exercise, in African males aged 17-40 years. *Clinical Science* 1973; 44:555-559.
25. Davies VTM, Van Haaren JP. Effect of treatment on physiological responses to exercise in East African industrial workers with iron deficiency anaemia. *British Journal of Industrial Medicine* 1973; 30:335-340.
26. Goonewardene FA. Iron deficiency and its effect on worker productivity and activity patterns. *British Medical Journal* 1970, ii: 1546-1547.
27. Basta S, Churchill A. World Bank Working Paper 175, 1974.
28. Gordner GW, Edgerton VR, Seneviratne B, Bernard RJ, Ohira Y. Physical work capacity and metabolic stress in subjects with iron deficiency. *American Journal of Clinical Nutrition* 1977; 30:910-913.
29. Edgerton VR, Ohira Y, Gordner GU, Seneviratne B. Effects of iron deficiency anaemia on voluntary activity of humans. In: Pollitt E, Leibel RL, eds. *Iron deficiency: Brain biochemistry and behaviour*. New York: Raven Press 1982; pp. 141-160.
30. Davidson AEJ, Markson JL. The gastric mucosa in iron deficiency anaemia. *Lancet* 1955; ii:639-640.
31. Dallman PR, Sunshine P, Leonard Y. Intestinal cytochrome response with repair of iron deficiency. *Paediatrics* 1967; 39:863-865.
32. Jacobs A. Tissue change in iron deficiency. *British Journal of Haematology* 1968; 16:1-3.
33. Dallman PR, Goodman JR. Enlargement of mitochondrial compartment in iron and copper deficiency. *Blood* 1973; 8:346-348.
34. Auket MA, Parksya, Scott PH, Wharton BA. Treatment with iron increase weight gain and psychomotor development. *Archives of Diseases of Childhood* 1986; 61: 849-857.

35. Hallberg L, Ryttinger L, Solvell. Side effects of oral iron therapy. A double blind study of different iron compounds in tablet form. *Acta Medica Scandinavica* 1966; 175 (suppl 459).
  36. Gross R, Schultink W, Juliawati. Treatment of anaemia with weekly iron supplementation. *Lancet* 1994; 344:821.
  37. Goonewardena IMR, Liyanage C. Ante-natal iron supplementation: only thrice a week. *Ceylon Journal of Medical Science* 1996; 39: 41-47.
  38. National Institute of Nutrition, Hyderabad, India: Annual Report 1973; pp. 10-14.
  39. Sayers MH, Lynch SR, Charlton RW, Bothwell TH, Walker RB, Mayer F. The fortification of common salt with ascorbic acid and iron. *British Journal of Haematology* 1974; 28: 483-485.
  40. Ranganathan S, Reddy V, Ramamoorthy P. Large-scale production of salt fortified with iodine and iron. *Food and Nutrition Bulletin* 1996; 17: 73-78.
  41. Layrisse M, Martinez – Torres C, Renzy M, Velez F, Gonzales M. Sugar as a vehicle for iron fortification. *American Journal of Clinical Nutrition* 1976; 29: 8-10.
  42. Garby L, Areekul S. Iron supplementation in Thai fish sauce. *Annals of Tropical Medicine and Parasitology* 1974; 68: 467-470.
  43. Lamperelli RD, Mac Phail AP, Bothwell TH, Ballot D, Danilewitz MD, Mac Farlane BJ, Mayet F, Baynes RD. Curry powder as a vehicle for iron fortification: effects on iron absorption. *American Journal of Clinical Nutrition* 1987; 46: 335-340.
  44. Gooneratne J, Mudalige R, Nestel P, Purvis G. Product evaluation using iron fortified wheat flour. *Ceylon Journal of Medical Science* 1996; 39: 23-34.
  45. Piyasena C, Mudalige R, Nestel P. Wheat consumption patterns in Sri Lanka. *Ceylon Journal of Medical Science* 1996; 39: 17-22.
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