Chapter III: Iron Deficiency Anemia

Definition

Anemia is a disorder in which relative tissue hypoxia is caused by inadequate oxygen uptake, transport, distribution, and/or delivery.

Burden

- The commonest nutritional disorder in the world.
- Has a serious impact on school children and working males.
- Occurs frequently in:
  - Pregnancy;
  - Infancy;
  - Growing children and teens;
  - Women of child-bearing ages; and
  - The elderly.

Causes

- One or a combination of:
  - Inadequate diet;
  - Impaired absorption;
  - Blood loss; and/or
  - Repeated pregnancies.
- For adults, increased menstrual bleeding and hemorrhage from the alimentary canal.
- In an adult man or a postmenopausal woman, due to blood loss.
- In pregnancy, most commonly caused by bleeding.

Diagnosis

Laboratory tests should be used to diagnose anemia and determine its severity.

- Hypochromia and microcytosis of the red blood cells
- Diminished serum iron concentration.
- Augmented iron-binding capacity.
- Free protoporphyrin level of the erythrocytes is increased
- The ferritin content of the serum is diminished.

Treatment

- Adequate therapy must not only correct the deficiency but also treat its cause.
- The daily dose of iron ideally should be sufficient to support maximum hemoglobin increase
- Relatively large amounts of ascorbic acid given with ferrous sulfate increase absorption of iron.
- For children:

  A satisfactory schedule is to give half the adult dose to children who weigh from 15-35 kg, and the full dose to those heavier than 35 kg.
- Oral therapy must be continued for 6-12 months if stores are to be repleted.
- Parenteral iron administration (Imferon): for subjects who are unable to tolerate or absorb orally administrated iron.
- Blood transfusions: for patients who have serious complications demanding immediate correction of the anemia.

Prevention of Iron Deficiency Anemia

- Three strategies are implemented together to prevent the occurrence of Iron Deficiency Anaemia:
  - Iron supplementation.
  - Dietary education.
  - Parasitic disease control.

Definition of anemia

- A major conceptual problem is seen in both the definition of anemia and the selection of an adequate indicator. Internationally, there is no common, generally accepted definition of anemia.

A. Functional Definition

- Anemia is a medical condition characterized by abnormal decrease of blood capability for gas and nutrient exchange.
- Very few functional definitions of anemia exist in the literature.
- One is that it is a disorder in which the patient suffers from tissue hypoxia, the consequence of the low oxygen-carrying capacity of the blood.
- Although functional definitions have the advantage of more flexibly covering the expressions of anemia, here again they are limited to the quality of the oxygen-carrying capacity of the erythrocytes.
- In addition to the transport of oxygen, erythrocytes may have other functional tasks in the body. If this is the case, an insufficient quantity and quality of red cells could consequently have several additional effects on the body's metabolism beyond the simple oxygen supply for tissue metabolism. As a consequence, anemia would have side effects that are not fully consistent with the effect of inadequate hemoglobin.[(1)]

B. Structural Definition

- Those most commonly used are structural descriptions, related to the qualitative and quantitative characterization of erythrocytes in the bloodstream.
- Anemia is the state in which the quality and/or quantity of circulating red cells is reduced below normal level.
- Other structural definitions consider the hemoglobin as a reference point; however, they do not mention the functional role of red cells and their effect related to anemia.[(2)]
    - Both definitions are driven by the concept that anemia is caused by an inadequate quantity and quality of red cells. Thus, the authors of the definitions conclude that a hemoglobin concentration below that normally seen in healthy populations best characterizes anemia.
    - Because the different mechanisms responsible for an adequate oxygen supply are interrelated, it may well be that the body tissues receive a sufficient amount of oxygen despite a hemoglobin level that is below normal. In such cases, iron supplementation is less effective than in cases of lower hemoglobin levels showing less effective compensatory mechanisms.
    - Consequently, the following definition is suggested:
      Anemia is a disorder in which relative tissue hypoxia is caused by inadequate oxygen uptake, transport, distribution, and/or delivery. [(3)]

Burden

- Iron deficiency is the commonest nutritional disorder in the world and affects over one billion people.

- Iron deficiency has a serious impact on school children and working males. If uncorrected it leads to anemia of increasing severity, reduced work capacity, diminished learning ability, increased susceptibility to infection and greater risk of death associated with pregnancy and childbirth.
- Iron Deficiency anemia occurs frequently in:
  (a) Pregnancy;
  (b) Infancy (at birth, infant requires enough stored iron for 3-6 months, making it important to feed iron-fortified cereals);
  (c) Growing children and teens (due to an increased blood volume);
  (d) Women of child-bearing ages (due to monthly menstrual losses); and
  (e) The elderly (due to poor dietary intake).
- In Egypt, anemia is reported to be the most common nutritional problem among women of childbearing age, nursing mothers, and children between birth and two years of life.
- Many nutrients are involved in the formation of blood: iron, folic acid, vitamin B12, pyridoxine, ascorbic acid, and vitamin E. So, anemias commonly occur with nutritional deficiencies. Other deficiencies, which can play a role in the development of anemia, include niacin, thiamin, riboflavin, pantothenic acid, biotin, copper, and cobalt. Anemia can also occur with a diet deficient in protein, and anemias are best treated with an adequate intake of high-quality protein.
- 95% of the cases of nutritional anemia are due to Iron Deficiency Anemia (IDA).[4]
- Egypt conducted several surveys to investigate the nutritional status among infants, preschool, school-age children, and women (Appendix). Some were at the national level, such as the National Nutrition Survey, 1978[5], the Health Examination Survey of the Health Profile of Egypt (HES-HPE, 1984)[6], the Demographic and Health Survey (DHS, 1988)[7] and the National Survey for Assessment of Vitamin A, 1995.[8] Others were conducted in different areas like the Nutrition Status Survey II, 1980 [9], the Cairo University and MIT survey, 1978[10], the Collaborative Research Support Program (CRSP), 1985[11] and the Follow-up Nutrition Survey, 1986.[12] Although there were many national surveys, updated population-based data are lacking.

Causes

- Iron deficiency results from one or a combination of the following:
  - inadequate diet;
  - impaired absorption;
  - blood loss; and/or
  - repeated pregnancies.
- If an individual reaches adult weight with normal body stores of iron, deficiency caused solely by poor diet or poor absorption takes years to develop, in the absence of blood loss or pregnancy, because iron excretion is limited.
- The two most common causes of iron deficiency among adults are increased menstrual bleeding and hemorrhage from the alimentary canal.
- The development of iron deficiency in an adult man or a postmenopausal woman should be assumed to be due to blood loss until proved otherwise.
- Except for pregnancy, large losses of iron are most commonly caused by bleeding:

- Hemorrhage from wounds, from the nose or mouth, genitourinary tract, and from hemorrhoids.
- Bleeding from the gastrointestinal canal is often occult; if lost by adults high in the tract, may not cause guaiac-positive stools.
- Hiatus hernia, peptic ulcers, varices, salicylate ingestion, diverticuli, benign or malignant tumors, intestinal parasitic infestation (particularly hookworm disease), and regional enteritis or ulcerative colitis are the most common causes of occult hemorrhage.
- Occult gastrointestinal blood loss may be detected in nearly 50% of affected infants; usually no discrete lesions can be identified.
- Abnormal menstrual loss; menstrual volume may be excessive if:
    - double pads must be worn;
    - duration of periods is greater than 5 days;
    - large clots are passed; and
    - more than 12 pads per period are needed.
- The use of intrauterine devices

o The admirable and necessary donation of blood for transfusions and the collection of large amounts of blood for diagnostic study must be regarded as forms of hemorrhage.

o Iron deficiency as a result of transferrin loss through a nephrotic kidney has been reported but must be rare.

o Under four conditions, iron-deficient erythropoiesis may be found even though body iron is normal or greater than normal:

1) Hereditary absence of transferring;
2) Idiopathic pulmonary hemosiderosis;
3) Paroxysmal nocturnal hemoglobinuria; and
4) Inflammation with inability to mobilize iron from reticuloendothelial cell depots. [13-15]

Specific contributing factors in Egypt

o Food supply in Egypt is influenced by several policies and programs such as the agricultural policy, pattern of investment allocation, food security schemes, and food aid. Undoubtedly, all these policies and programs affect the health and nutrition status of Egyptians either directly like the food security schemes (food ration, subsidies, and aid) or indirectly through the agricultural policy. [16,17]

o Cereals, mainly wheat that is the main staple, rice and corn are the main contributors to dietary energy and protein supply in Egyptian diet. Legumes, mainly faba beans and lentils, are popular substitutes to animal protein. In rural areas, people consume more dairy products, fresh fruits and vegetables and tea, while meat, poultry, fish and eggs constitute regular items in urban diets. [18,19]

o The consumption of animal products is dependent upon the level of income due to the high prices of these items. The level of consumption is also influenced by seasonal changes. [17]

o In Egypt "*baladi*" or unrefined bread (85% extraction) is the most popular. However the presence of phytates and bran in bread inhibits the absorption of dietary iron from plant origin, which may partially explain the widespread prevalence of anemia. [20]

- One dietary habit widespread among Egyptians regardless of age or social class is the drinking of strong tea, particularly after meals. Tea contains tannic acid, which inhibits the absorption of dietary iron from plants. As most of the dietary iron consumed by Egyptians is of plant origin, the habit of drinking tea after meals is clearly problematic for adequate iron intake. [18-20]
- With lower levels of education of the family head, there is lowered quantity and quality of the diet. This, associated with the high level of illiteracy for men (37.8%) and women (61.8%), clarifies the inadequacy of Egyptian diet for a significant sector of the population.[21]
- With smaller family size the per capita intake of both energy and animal protein is higher than in larger families. In all cases, the ever increasing food prices in relation to incomes is resulting in reduction in quality and quantity of diets which may explain why the nutritional status is not improving in spite of the several government interventions in this regard. [17]
- Intra-familial food distribution in Egyptian villages: the father got 32.9% of total iron intake while according to RDA for iron, he should have got only 15.4%. Oppositely, the mother got 29.1% while according to her RDA, adapted for local bioavailability of iron, she should have got 48.8%. This discrepancy may be attributed to the documented fact that the father in the Egyptian rural setting is privileged with the high quality expensive nutritious food items available at home. [22,23]
- The prevalence of household food insecurity ranged from 4.7% in Ismailia to 21.6% in Dakahlia in spite of adequate average per capita food supply.[24]

Diagnosis

Severe iron-deficiency anemia is characterized by:

- Hypochromia and microcytosis of the red blood cells; the cells are small and pale when observed on the blood smear. Also, they vary greatly in size and shape.
- Diminished serum iron concentration.
- Augmented iron-binding capacity.
- The saturation of the iron-binding protein (transferrin) is reduced; generally less than 16% of the available iron-binding sites are saturated.
- Free protoporphyrin level of the erythrocytes is increased.
- The ferritin content of the serum is diminished.
- Examination of the bone marrow generally reveals:
    - decrease in the amount of storage iron in reticuloendothelial cells. An exception of this rule is encountered in individuals who have been transfused within the previous few months or who have been given parenteral iron preparations.
    - diminished number of sideroblasts, red cell precursors containing stainable iron.

***Mild iron-deficiency anemia*:**

- May be difficult to diagnose.
- Patients do not manifest the microcytic hypochromic cells, which are characteristic of the severe iron-deficiency state.

- Normal plasma iron level, iron binding capacity, and normal saturation of transferrin.
- Diminished serum ferritin level.
- Free protoporphyrin level of the erythrocytes is increased.
- The bone marrow iron stores are depleted with the exception of patients who have been given blood transfusions or parenteral iron therapy.

It is important to differentiate iron-deficiency anemia from other anemias, particularly hypochromic anemias that may simulate it.

- β Thalassemia minor is characterized by increased levels of hemoglobin A2.
- α- Thalassemia is characterized by the presence of hemoglobin H.
- Hereditary or acquired sideroblastic anemia; has ample bone marrow iron stores, the level of plasma iron is normal or increased, and that of iron binding capacity is usually normal or diminished.

Diagnosis of iron-deficiency anemia is never complete until the cause for the deficiency is recognized. [13-15]

Clinical manifestations

- It often assumed that the manifestations of iron-deficiency anemia result from the lowering of the hemoglobin concentration of the blood. A number of clinical observations suggest that that this is not the case:
    1. The severity of symptoms is not closely correlated with the degree of anemia.
    2. Response to treatment often seems to precede rise in the hemoglobin concentration of the blood.
    3. Certain clinical manifestations such as koilonychias and esophageal webs cannot be accounted for on the basis of anemia alone.
    4. Iron deficiency might produce symptoms in the absence of any anemia at all.
- Some patients with iron-deficiency anemia are unaware of being in ill health. Symptoms are usually so insidious in onset that their duration cannot be dated with accuracy.
- The signs and symptoms of anemia, pallor of the skin and of the conjunctiva, fatigue, shortness of the breath, lack of appetite, are nonspecific and difficult to detect.
- Indeed, the clinical detection of anemia is influenced by so many variables, such as skin thickness and pigmentation. Hence, it is unreliable unless anemia is very severe. [13-15]

Laboratory Tests

- Laboratory tests should be used to diagnose anemia and determine its severity. Such tests are useful in individuals in whom anemia is suspected, especially those from known high-risk groups. They can be repeated over time to monitor the effectiveness of treatment.
- Laboratory tests can also be used to determine the prevalence and severity of anemia in a population as well as to single out the groups that are most affected.

- The best laboratory tests for the diagnosis of anemia involve measuring the packed volume of red cells (haematocrit) or the concentration of hemoglobin in circulating blood. Both determinations can be made on either capillary blood obtained by the skin puncture or venous blood obtained by venepuncture.
- Results obtained from capillary blood specimens are less reliable than those from venous blood.
- There are no sharp cut-off points for hemoglobin concentrations below which anemia can be stated as present. However, standards below which anemia is likely to be present at sea level have been set out by WHO and the Centers for Disease Control and Prevention (CDC):
  - In adults:
    - Men, <13 g/dL
    - Menstruating women, <12 g/dL.[1]
  - In infancy and childhood:
    - 0.5-4.9 years, <11 g/dL
    - 5.0-11.9 years, <11.5 mg/dL
  - In pregnancy:
    - First and third trimesters, <11 g/dL
    - Second trimester, <10.5 g/dL.[25-27]

Treatment

- Adequate therapy must not only correct the deficiency but also treat its cause. Increased menstrual flow, occult loss of blood from the urinary or gastrointestinal tracts or defective absorption must be detected and corrected if possible.
- Appropriate selection of a therapeutic agent requires understanding of the maximum expected hematologic response, the amount of iron required to produce this maximum effect and the absorption that can be expected from a given iron compound.
- The physician should observe the patient to make certain that a response is obtained: a satisfactory rise in the hemoglobin level attributable to the iron therapy constitutes final proof of the correctness of the diagnosis. [14,15,28-30]

Hematologic Response and Amount of Iron Required for Maximum Effect

- About 7-10 days after therapy is initiated, the reticulocyte level begins to rise, reaches a peak between 12-16 days and then falls to normal levels during the next 2 weeks. The height of the reticulocyte peak is inversely proportional to the original hemoglobin value and may exceed 20% in severely anemic patients.
- The hemoglobin begins to increase after about 10-14 days; it rises at a rate of 0.2 to 0.3 gm per 100 ml per day when the anemia is severe and at 0.1 to 0.2 gm per 100 ml when the initial hemoglobin level is greater than 7.5 gm per 100 ml.
- As the hemoglobin concentration approaches normal, the rate of increase slows; from 4-8 weeks are required before normal values are attained.
- Return of the plasma iron to normal may take another 1-2 months.
- The response in children is somewhat more rapid than that of adults.

- After intravenous infusion of iron dextran, a substantial change in the hemoglobin concentration may be observed even after 1 week.
- The daily dose of iron ideally should be sufficient to support maximum hemoglobin increase:
  - For adults: on average, 0.3 gm per 100 ml per day or 15 gm of new circulating hemoglobin in a patient with a blood volume of 5 liters. 50 mg of absorbed iron is a reasonable average quantity to provide for adults. The exact amount obviously varies with the blood volume.
  - For children: the amount varies with body weight and can be calculated by estimating the blood volume to be 70 ml per kg body weight.
- The total amount of iron that must be absorbed or injected to correct the deficiency can also be estimated. For example, for woman with severe iron deficiency anemia has a hematocrit of only 15%, each 1,000 ml blood is deficient approximately 300 ml of packed red cells (N.B. normal hematocrit 45%):
  - If the patient's blood volume is 4 liters, enough iron must be supplied to provide 4 times as many red cells, i.e. 1,200 ml.
  - Since each ml of red cells contains about 1 mg of iron, 1.2 gm of iron are needed to restore the red cell mass to normal.
  - In addition, 0.5 to 1 gm of iron should be provided to replete the stores.
  - The total amount needed to correct the deficiency would be 1.7 to 2.2 gm.

Oral therapy

- Ideal iron preparation for oral therapy should be:
  - Well absorbed;
  - Well tolerated by the gastrointestinal tract in therapeutic doses; and
  - Inexpensive.
- Relatively large amounts of ascorbic acid given with ferrous sulfate increase absorption of iron.
- Each of the preparations listed in the table below is entirely acceptable.

Recommended Oral Iron preparation

Preparation	**gm/tablet**	**Iron Content**		**Acceptable Adult Dose**
		%	*mg Fe / tablet*	*Tablets/day*
Ferrous sulfate	0.32	20	60	4
Ferrous gluconate	0.32	12	40	4 or 5
Ferrous fumarate	0.2	33	66	4
Ferroglycine sulfate	0.25	16	40	5

- An iron deficient patient will absorb approximately 20% of the iron in these tablets. Since the recommended daily dose provides roughly 200 to 240 mg of iron, the desired 40 or 50 mg should be absorbed.

- In those patients who complain of severe epigastric distress, reducing the dose to 1 tablet per day and then gradually adding 1 tablet per day until the full therapeutic dose is reached can frequently induce tolerance. Alternatively, other preparations may be tried until one is found that can be tolerated.
- For children:
  - children tend to have less gastrointestinal distress from iron therapy than do adults.
  - A satisfactory schedule is to give half the adult dose to children who weigh from 15-35 kg, and the full dose to those heavier than 35 kg. For smaller children, and those unable to take tablets, liquid preparations are available.
- A common error is to discontinue iron therapy after 2 or 3 months required for correction of the anemia. Replenishment of iron stores occurs slowly when iron is given orally because absorption falls off as the hemoglobin rises toward normal; consequently, oral therapy must be continued for 6-12 months if stores are to be repleted.
- If the chronic bleeding responsible for iron deficiency cannot be corrected or controlled, continuous iron therapy is required.
- Oral iron therapy may fail in patients with malabsorption syndromes or with diarrhea, or in those who have had a gastrectomy.

Parenteral Therapy

- Parenteral administration should be reserved for those subjects who are unable to tolerate or absorb orally administrated iron:
  - patients with ulcerative colitis, regional enterititis, intestinal shunts, colostomy or ileostomy;
  - patients with malabsorption syndromes;
  - the rare person who is unable or unwilling to cooperate or who has severe intolerance to oral therapy;
  - patients in whom the rare blood loss is so rapid that it is desirable both to introduce large amounts of iron into the body quickly and to re-establish iron stores.
- The most widely used and most satisfactory parenteral iron preparation is iron dextran (Imferon). This preparation may be given either intramuscularly or intravenously.
- The possibility of an anaphylactoid response may be slightly greater when iron dextran is given by the intravenous route.
- Intravenous administration has certain advantages:
  - It is possible to infuse a large dose, even the total dose required, at one time.
  - Intramuscular administration of iron produces staining of the skin and may also result in local discomfort.
- The total dose should be calculated to correct the hemoglobin deficit and to provide at least additional 1,000 mg for storage.
- Intramuscular injections should be given via a zigzag needle tract to minimize unslightly staining of the skin.
- Systemic reactions are unusual but may be severe: headache, fever, arthralgia, back pain and, rarely, peripheral vascular collapse.
- Rates of hemoglobin increase do not differ significantly from those produced by proper oral therapy.

Blood transfusions

- They are rarely necessary in the treatment of iron-deficiency anemia and should generally be reserved for patients who have serious complications demanding immediate correction of the anemia: angina, congestive heart failure or severe pneumonia.
- The patient's clinical status, not the numerical value of the hemoglobin, should be given primary consideration in reaching a decision regarding the advisability of blood transfusion.
- Patients with active bleeding who are iron deficient must sometimes be transfused. In these instances, however, the purpose of transfusion is not primarily to correct anemia but rather to restore a falling blood volume to normal, thus avoiding the development of hemorrhagic shock.

Prolonged Iron Therapy

- In rare instances, the prolonged administration of iron to patients who did not need it has been responsible for iron overload.
- Iron balance is determined by the body's iron stores, iron absorption, and iron loss. At least two-thirds of body iron is functional iron, mostly hemoglobin within circulating red blood cells, with some as myoglobin in muscle cells and parts of iron-containing enzymes. Most of the remaining body iron is storage iron (existing as ferritin and haemosiderin), which serves as a deposit to be mobilized when needed.
- The amount of iron-absorbed seems to be modified by the amount of storage iron. As the fraction of iron absorbed decreases and the amount excreted increases, an equilibrium is established at a level of body iron, which depends upon the dose given.

Prevention of Iron Deficiency Anemia

- Three strategies are implemented together to prevent the occurrence of Iron Deficiency anemia; supplementation, dietary education and parasitic disease control. [31-35]

I. Iron Supplementation

A. For pregnant and lactating women

- Universal iron supplementation for pregnant women (60 mg of elemental iron + 250 ug of folic acid, once or twice daily) to be taken throughout the second half of pregnancy;
- In 1995, the UNICEF/WHO Joint Committee on Health Policy (JCHP) endorsed iron/folate supplementation as the strategy of choice and recommended that where the prevalence of Iron Deficiency Anemia in pregnant women exceeds 30%, countries should implement universal supplementation through antenatal clinics, regardless of women's individual hemoglobin status.
- In December 1997 the Essential Drugs Committee of WHO approved increasing the folic acid content of the iron/folate tablet used in the program to 400 ug.
- An authoritative meta-analysis of the efficacy of intermittent iron supplementation was completed in 1999. The major findings were that:

(1) Both daily and weekly iron supplementation are efficacious, but weekly supplementation is likely to be less effective than daily administration, except in situations where weekly but not daily supervision is feasible;
(2) Weekly supplementation may be particularly disadvantageous during pregnancy and in situations where the baseline prevalence of anemia is high;
(3) Unless ways are found to greatly improve compliance, neither daily nor weekly supplementation is likely to be an effective approach to preventing and controlling anemia in developing countries, and
(4) Regardless of the degree of supervision that can be arranged, weekly iron administration instead of daily is not recommended for pregnancy.

B. For infants and children

- For infants, breast milk should be adequate for the first six months, but in low birth weight infants' supplementation may be required from two months onwards.
- From six months, supplementation may also be widely necessary. Full-term healthy infants who are exclusively breastfed until about six months of age are not at high risk of developing anemia.
- From six months onward, the infant's iron needs must be met by the family diet. Rapid growth during this period increases the need for iron.
- In older children, supplementation is less widely needed and screening may be advised.
- The JCHP called for preventive iron supplementation for all infants and young children in situations where the prevalence of Iron Deficiency Anemia in pregnant women exceeds 30%.
    - Children aged 6-9m: 12.5 mg oral iron per day unless there is strong evidence that children's diets contain adequate available iron.
    - In older children, supplementation dosage depends on the child's age and weight: 20-30 mg elemental iron daily for children aged 2-5y; 30-60 mg for children aged 6-11y; and 60 mg for adolescents.
- Periodic cycles of daily iron supplements and treatment of those already anemic, plus periodic de-worming, are recommended by WHO.

II. Dietary Education

- The longer-term solution to the problem of iron deficiency is dietary modification. Improvement in supply, consumption and bioavailability of iron in food is an important strategy to improve the iron status of populations.
- Encourage all individuals to consume a diet with sufficient iron to prevent iron deficiency.
- The main types of iron available in foods are: haem iron which is present in meat and its products and is well-absorbed; and non-haem iron which is present from food of vegetable sources, generally of low bioavailability.
- Iron is also provided by other animal products, such as milk, with intermediate absorption.
- Haem iron from meat is highly bioavailable - around 20 to 30 percent being absorbed; whereas non-haem iron from cereals, pulses, fruits, vegetables, etc. has much lower bioavailability - ranging from 1 to 8 percent.

- The absorption of non-haem iron is highly variable and depends on the nature of the meal. Vitamin C importantly enhances iron absorption.
- Factors that inhibit iron absorption include decreased gastric acidity, *H. pylori* infection, tannins (tea), polyphenols (coffee, herbal teas and cocoa containing beverages – taken within one hour of the meal), phytates (legumes, grains, rice) and calcium and phosphate (antacids and calcium tablets).
- Factors that enhance iron absorption are: presence of meat, citrus juices, vitamin C (e.g. from broccoli, strawberries, tomato, spinach, citrus fruit), and EDTA fortification of foods.

III. Other Anemia Control Programes

- Malaria and intestinal parasites (especially hookworm) are important contributors to anemia in endemic areas; the role of anthelmintics and micronutrient supplements in the control of iron deficiency anemia.
- Vitamin A deficiency also contributes to anemia; national policies ensuring vitamin A supplementation of children. Women are routinely provided with a high-dose vitamin A supplement soon after delivery.
- In many countries, AIDS is also a major contributor to anemia, particularly severe anaemia, and AIDS control programmes may be expected to play a part in anaemia reduction.

References

1. Erslev A.J. (1990): Clinical Manifestations and Classification of Erythrocyte Disorders. In: Williams W.J., Beutler E., Erslev A.J., and Lichtman M.A. (Eds.): Hematology. 4th ed., New York: McGraw-Hill, pp. 423-9.
2. DeMaeyer E.M., and Adiels-Tegman M. (1985): The Prevalence of Anemia in the World. World Health Statistics Q; 38: 302-16.
3. Gross R., Gliwitzki M., Gross P., and Frank K. (1996): Anaemia and Haemoglobin Status: A New Concept and A New Method of Assessment. Food and Nutrition Bulletin Volume 17, Number 1.
4. FAO, Food Agriculture Organization (1993): Summery of the International Conference on Nutrition ICN country papers, for selected countries in the Near East Region. FAO Regional Office for the Near East RNEA, Cairo, Egypt.
5. AID, Agency for International Development (1978): ARE National Nutrition Survey. Office of Nutrition, Washington D.C., USA
6. Moussa W.A. (1987): Health Profile of Egypt, The Health Interview Survey, Final Report, Dietary Habits. Publication No. 3615, ARE, Ministry of Health, ARE.
7. Sayed H.A., Osman M.I., El-Zanaty F., and Way A.A. (1989): Egypt Demographic and Health Survey (DHS), 1988. Egypt National Population Council, Cairo, Egypt and Institute for Resource Development/Macro Systems Inc.
8. Moussa W.A., Nahry F.I., and Abdel Gelil A. (1995): National Survey for Assessment of Vitamin A Status in Egypt, Final Report. Nutrition Institute & UNICEF, Egypt.
9. AID, Agency for International Development (1980): ARE National Nutrition Survey II. Office of Nutrition, Washington D.C., USA.
10. El-Lozy M., Field J.O., Ropes G., and Burkhart R. (1980): Childhood Malnutrition in Rural Egypt-Results of the Ministry of Health-Weighing Exercise. Cairo University & MIT Technological Planning Program Monograph 4- TAP Report 90-11.
11. Central Bank of Egypt, Several Reports Cairo, ARE (1987): Collaborative Research Support Program on Food Intake and Human Function-Final Report. Egypt.
12. Hussein M.A., Hanan H.A., Noor E.F., and El-Shafie M. (1989): Nutritional Assessment of Preschool Children in Egypt. Gaz.Egypt Ped. Ass. 37:25-27.
13. Goodhart R.S., and Shils M.E. (1980): Modern Nutrition in Health and Disease. 6th ed., Philadelphia: Lea and Febiger Company.
14. Barrett B.J., Fenton S.S., Ferguson B., Halligan P., Langlois S., and McCready W.G. (1999): Clinical Practice Guidelines for the Management of Anemia Coexistent with Chronic Renal Failure. Canadian Society of Nephrology. J Am Soc Nephrol.; 10 Suppl 13: S292-S296.
15. British Columbia Medical Association (2002): Investigation and Management of Iron Deficiency. Guidelines and Protocols Advisory Committee. www. healthservices. gov. bc. ca/msp/
16. NARP, National Agricultural Research Project (1995): Development of Food Consumption Monitoring System-Egypt-Final Report. Submitted to the US Department of Agriculture and the Egyptian Ministry of Agriculture.
17. Nassar H., Moussa W., Kamel A., and Miniawi A. (1993): Review of Trends, Policies and Programs Affecting Nutrition and Health in Egypt (1970-1990). UN ACC/SCN country case study for the XV Congress of the International Union of Nutritional Sciences, Sep. 26-Oct. 1, Adelaide.
18. Aly H.E., Dakroury A., Said A.K., Moussa W.A., Shaheen F., Ghoneme F.M., Hussanein M.A., Hathout M., Shehata M., and Gomaa H. (1981): ARE National Food

Consumption Study, Final Report. Nutrition Institute, Ministry of Health, Cairo, ARE.
19. Moussa W.A. (1988): Food Sources of Energy. Proceedings of the CRSP Policy workshop, Nutrition Institute, Cairo, Egypt.
20. Galal O., Kirksey A., Harrison R., Jerome N., Dokrouny A., Moussa W., and Shaheen F. (1987): The Collaborative Research Support Programs (CRSP) on Food Intake and Human Function- Final Report. Grant No. Dan-1309-G-SS-1070-00, USAID.
21. Velez H., Restrepo A., Vitale J.J., and Hellerstein E.E. (1966): Folic Acid Deficiency Secondary to Iron Deficiency in Man: Remission with Iron Therapy and A Diet Low in Folic Acid. American Journal of Clinical Nutrition; 19: 27-36.
22. Nkrumah F.K., Nathoo K.J., and Sanders D.M. (1988): Iron, Folate and Vitamin B12 in Severe Protein-Energy Malnutrition. Central African Journal of Medicine; 34: 39-43.
23. ACC/SCN (Subcommittee of Nutrition of the Administrative Committee on Coordination of the United Nations) (1992): Second Report on the World Nutrition situation. Vol. 1. Geneva.
24. Fleming A.F. (1981): Anemia in Tropical Countries. Medical Digest; 7: 5-19.
25. Fleming A.F. (1989): Tropical Obstetrics and Gynecology. I.: Anemia in Pregnancy in Tropical Africa. Transactions of the Royal Society of Tropical Medicine and Hygiene; 83: 441-448.
26. Baker S.J. (1981): Nutritional Anemias. Part 2: Tropical Asia. Clinical Hematology; 10: 843-871.
27. WHO, World Health Organization (1975): Control of Nutritional Anemia with Special Reference to Iron Deficiency. WHO technical report series, No. 580.
28. Goddard A.F., McIntyre A.S., and Scott B.B. (2000): Guidelines for the Management of Iron Deficiency Anaemia. British Society of Gastroenterology. Gut.; 46(Suppl 3-4): IV1-IV5.
29. Gordon S., Bensen S., and Smith R. (1996): Long-Term Follow-Up of Older Patients with Iron Deficiency Anemia after a Negative GI Evaluation. Am J Gastroenterol.; 91: 885-889.
30. Brigden M.L. (1997): Iron Deficiency Anemia. In: Rakel R.E. (Ed.): Conn's Current Therapy. Philadelphia: W. B. Saunders.
31. Recommendations to Prevent and Control Iron Deficiency in the United States. MMWR –Morbidity & Mortality Weekly Report 47[RR-3], 1-36. 4-3-1998. http://www.cdc.gov/mmwr/PDF/RR/RR4703.pdf
32. Bothwell T.H. (2000): Iron Requirements in Pregnancy and Strategies to Meet Them. Am J Clin Nutr.; 72: 257S-264S.
33. Sawchuk P., Rauliuk M., and Kotaska A. (1998): Infant Nutrition Program Effectively Prevents Iron-Deficiency Anemia in a First Nations Community. Int J Circumpolar Health; 57 Suppl 1: 189-193.
34. Kaltwasser J.P., Werner E., Schalk K., Hansen C., Gottschalk R., and Seidl C. (1998): Clinical Trial on the Effect of Regular Tea Drinking on Iron Accumulation in Genetic Haemochromatosis. Gut; 43: 699-704.
35. Hurrell R.F., Reddy M., and Cook J.D. (1999): Inhibition of Non-Haem Iron Absorption in Man by Polyphenolic- Containing Beverages. Br J Nutr.; 81: 289-295.

APPENDIX

National Surveys on anemia in Egypt (1978-1995)

Survey	Conductor	Sample size	Age	Time	Area
National Nutrition Survey, 1978	Nutrition Institute, CDC, UNICEF	9794	6-71 Months	Early January-mid April	330 samples, 11 universes by using Geopolitical and Population Criteria
Cairo University & MIT Weighting Exercise	Cairo University & MIT	4327	0-5 Years	April 1978	17 Rural Health Centers in Different Governorates in Upper and Lower Egypt
Nutrition Status Survey II	Nutrition Institute & The center for Disease Control, Atlanta, Georgia, USA	1783	6-71 Months	August and September 1980	Two Universes: Lower Egypt: Damietta Kafr El-Sheikh & Upper Egypt: Giza, Fayoum, Ben Sueif, Mineya
The Health Examination Survey (HES) of the Health Profile of Egypt (HPE)	Health Profile of Egypt (HPE), Ministry of Health (MOH)	2482	< 6 years	November 1979 to March 1984	National
The Collaborative Research Support Program (CRSP)	Nutrition Institute & USA	321 House-holds	Toddlers 18-29 Months	October 1982 to December 1985	Village of Kalama Kalyoubia Governorate
Follow-up Nutrition Survey , 1989	Nutrition Institute	1020	6-71 Months	Summer 1986	34 sites previously surveyed in 1978 belonging to 6 Governorates: 23 sites from small villages & 9 sites from large villages
Demographic and Health Survey (DHS) , 1989	Egypt National Population Council & Institute Resource Development Macro System Inc.	1907	3-36 Months	November 1988 till Mid January 1989	21 Governorates
National Survey for Assessment of Vitamin A Status, 1995	Nutrition Institute & UNICEF	1613	< 6 Mon. Children & Non-pregnant Mothers		National, 5 Geographic Areas (Metropolitan, coastal, Canal, Lower and Upper Egypt