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REVIEW ARTICLE

Anemia—still a major health problem in many parts of the world!

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Abstract Anemia is a major global health problem, especially in developing countries. This fundamental health issue still has not been solved and continues to exist affecting the health, quality of life, and working capacity in billions of people all over the world. This paper gives a review on the prevalence and major causes of anemia seen on a global scale. Most cases of anemia are due to iron deficiency, which often work in symphony with folate deficiency and/or vitamin B_{12} deficiency as well as with infections. More efforts should be dedicated to tackle this massive problem—we have the tools, and we know the ways. Iron fortification of appropriate food items combined with iron supplements in specific population groups has proven to be efficient. Initially, the efforts should be centered on the specific risk groups for iron deficiency anemia, i.e., young children, adolescent females, women of reproductive age, as well as pregnant women and postpartum lactating mothers.

Keywords Anemia · Anemia, iron deficiency · Developing countries · Folic acid deficiency · Helminthiasis · Malaria · Vitamin B_{12} deficiency

Introduction

The presence of anemia is basically defined as a red blood cell count, which is below the accepted lower level of the normal range [1]. However, in the daily clinical routine, anemia is defined by a hemoglobin concentration, which is below the recommended lower thresholds established by epidemiological population surveys or by the local laboratory. In order to perform useful comparisons between different countries, it is convenient to use the hemoglobin thresholds defined by the World Health Organization (WHO) shown in Table 1 [2, 3].

These threshold values apparently do not overestimate the prevalence of anemia. In Denmark, epidemiological surveys on presumably healthy subjects without iron deficiency have shown that the fifth percentile for men is 134 g/L, for women of reproductive age, 124 g/L [4, 5], and for pregnant women, 110 in the first, 105 in the second, and 110 g/L in the third trimester [6].

The World Health Organization estimates that anemia affects nearly two billion people all over the world, what is nearly one third of the rapidly growing world population of approximately seven billion people [7]. These figures indicate that, in many countries, anemia constitutes a serious health problem in the population as shown in Table 2.

What are the causes of anemia?

There are many different causes of anemia and they often work in symphony, so in the single individual, various nutritional deficiencies and different infections/infestations may all play a role. This may, of course, have influence on the choice of treatment for the anemia and for the planning of future prophylaxis in the population.

Iron

Iron is an essential mineral for man and an important component of metalloproteins involved in oxygen transport

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Table 1 Hemoglobin (Hb) concentration thresholds used to define anemia in subjects living at sea level according to the World Health Organization guidelines [3]

Age or gender group	Hb threshold, g/L
Children (6 months to under 5 years)	110
Children (5 years to under 12 years)	115
Children (12 years to under 15 years)	120
Non-pregnant women (15 years and over)	120
Pregnant women	110
Men (15 years and over)	130

and metabolism. In a well-nourished individual, the body contains approximately 3–4 g of iron. Almost two thirds of the iron is found in hemoglobin, the protein in the red blood cells that carries oxygen to the body's tissues. The most common nutrition deficiency in both developing as well as in developed countries is iron deficiency [7].

Iron is mandatory for the production of hemoglobin in the red blood cell progenitors (the erythroblasts), and if the iron supply to the bone marrow is inadequate, the hemoglobin production fails and the number of red blood cells in the circulation declines. This subsequently leads to development of iron deficiency anemia (IDA) with a low hemoglobin concentration. A characteristic feature is also that IDA can be corrected or cured by treatment with iron, either by the oral route or by intravenous iron therapy.

In the spectrum of anemia, IDA is by far the most important, causing approximately 75–80% of the total burden of anemias [1–3]. Typically, the anemia is microcytic with a low mean red blood cell volume (MCV) and hypochromic with low hemoglobin content in the red blood cells, i.e., low mean corpuscular hemoglobin and low mean corpuscular hemoglobin concentration. Basically, iron deficiency may arise due to an insufficient dietary iron intake. Dietary surveys have shown that, even in developed countries, dietary iron intake is too low in some population groups [8]. For example, Danish women of reproductive age have a mean dietary iron intake of 9 mg/day [8], which means that more than 90% of the women have an intake below the recommended daily allowance of ~18 mg/day [9].

Dietary iron consists of heme iron and non-heme iron. Heme iron has a good bioavailability leading to favorable gastrointestinal iron absorption, whereas non-heme iron has a poor bioavailability indicating low iron absorption.

Table 2 Public health significance of different prevalences of anemia according to the World Health Organization [3]

Prevalence of anemia (%)	Public health significance
≤4.9	No public health problem
5.0–19.9	Mild public health problem
20.0–39.9	Moderate public health problem
≥40	Severe public health problem

Heme iron is present in food products of animal origin (meat, poultry, fish), while non-heme iron predominantly is found in food products of plant origin (vegetables, cereals, grains, legumes). In addition, meat contains the so-called “meat factor” which enhances absorption of non-heme iron. Therefore, individuals who regularly consume foods of animal origin are at a lower risk of iron deficiency than individuals who exclusively consume foods of plant origin.

Ongoing, continuing blood losses predominantly from the gastrointestinal tract due to infections, intestinal parasites, and/or inflammatory bowel disease may contribute to IDA in many parts of the world.

Furthermore, women with heavy blood losses at their menstrual periods or by recurrent uterine bleeding due to gynecological disease have a highly increased risk of developing IDA.

Vitamin deficiencies

A number of vitamin deficiencies are associated with the development of anemia such as vitamin A deficiency [10] and vitamin D deficiency [11]. Vitamin C deficiency may contribute to iron deficiency and IDA due to impaired iron absorption and profuse bleeding from the gastrointestinal tract [12].

Folate

The most common vitamin deficiency producing anemia is folate deficiency [13, 14]. So far, folate status in various populations has not been as intensively investigated as iron deficiency and IDA, so further studies are needed before we shall have clearer picture of the prevalence of folate deficiency in many populations. Folate deficiency causes a specific form of anemia termed megaloblastic anemia with high MCV. It has been estimated that, in developing countries, folate deficiency occurs in as many as 25% to 72% of women of reproductive age [13, 14].

In the fetus and newborn baby, folate deficiency is associated with a high risk of neural tube defects as well as other organ defects [13].

Folate is present in food of plant origin, e.g., green leafy vegetables, grains, etc. However, the problem is that food preparation procedures (cooking, frying, milling, baking) actually destroy a high percentage of the folate content in the food.

Vitamin B_{12}

Vitamin B_{12} deficiency is probably the second most common vitamin deficiency causing anemia, which is a megaloblastic anemia with high MCV and typical morphological features such as hyperlobulation of the nuclei of the granulocytes [1]. In developing countries, vitamin B_{12} deficiency constitutes a significant problem [13], and studies from Lebanon and Turkey have revealed that ~40% of women of reproductive age have vitamin B_{12} deficiency [14, 15] which, in addition to insufficient dietary vitamin B_{12} intake, may be due to the food cobalamin malabsorption syndrome or pernicious anemia [14].

In addition to anemia, vitamin B_{12} deficiency causes neuropathy with pronounced neurological symptoms. In the fetus and newborn baby, vitamin B_{12} deficiency has been associated with an increased risk of neural tube defects [16].

Vitamin B_{12} is present in food of animal origin, which means that subjects consuming food of predominantly plant origin, e.g., vegetarians are not getting enough vitamin B_{12} and therefore are at high risk of deficiency.

Infection/infestations

Both acute and chronic infections/infestations are associated with anemia [1]. Intestinal parasites, including hookworms, which are prevalent in many tropical/subtropical regions, play a major cause in the high prevalence of anemia in many countries [17]. Anemia caused by intestinal parasites is mainly due to iron deficiency but is often combined with vitamin B_{12} deficiency as well as folate deficiency.

In areas where malaria is endemic, anemia is quite common, and antimalarial programs have proven to be effective in reducing the prevalence of anemia [18].

Hemoglobinopathies

In many tropical and subtropical countries, the high prevalence of genetic hemoglobinopathies, e.g., thalassemia, sickle cell disorders, etc., plays a significant role in the prevalence of anemia. Geographically, the thalassemia belt includes the Mediterranean passing through West and Central Asian countries like Turkey, Iran, Afghanistan onto Pakistan, and India and passes on to the South-East Asian countries like Indonesia, Burma and Thailand, Vietnam, and Cambodia. This makes it most common in African, Greek, Italian, Middle Eastern, and Southern Asian populations. In some of these regions, as many as 30% may be carriers of the gene defect [19, 20]. For example, in Southern Thailand, 27% of women of reproductive age are carriers of the thalassemia trait [21].

Anemia caused by thalassemia is a purely genetic disorder/disease, but may of course be associated and thus aggravated by anemia due to nutritional deficiencies and/or infections/infestations (see above).

Who are the major risk groups for anemia?

It appears from many surveys that the major risk groups for IDA are young children and, after childhood, individuals of female gender, i.e., adolescent females who grow rapidly and in addition have their first menstruations with iron losses, women of reproductive age who lose iron with their menstrual periods, pregnant women with an increased need for iron, and lactating women (Tables 3 and 4).

Anemia in apparently healthy well-nourished individuals is not very frequent [4, 5]. In Denmark, epidemiological population surveys have shown that the frequency of anemia in men 30 to 60 years of age is ~1% [4] and in women of reproductive age ~4% [5]. Denmark has a balanced social welfare structure, which gives all residents almost equal access to obtain good nutrition and health services. Consequently, the high prevalence of anemia on a global scale is predominantly due to the extremely high frequency in developing countries as well as in developed countries with large social differences between population groups, as, for example, in the USA [22].

In both developing and developed countries, the prevalence of anemia has a social imbalance. It is more prevalent in the lower social strata, in the lower income groups, and in the least educated fraction of a population [7]. This is an important point when it comes to treatment and prophylaxis of anemia.

Newborn infants and young children

It appears from Table 3 that children 0.5–5 years of age on a global scale actually have the highest estimated prevalence of anemia, i.e., 47%. In Europe, the prevalence of anemia is estimated to be 17% [3] which indicates that the prevalence must be extremely high in other regions, such as Africa, which unfortunately is on the top of the list with a prevalence of anemia of 65% [3].

Overall, the fetus' and newborn infant's iron status depend on the iron status of the pregnant woman and therefore, iron deficiency in the mother-to-be means that the

Table 3 Global prevalence of anemia and estimated number of individuals affected [3]

Gender or age group	Anemia[a] (%)	Population affected (millions)
Children, preschool-age	47	293
Children, school-age	25	305
Men	13	260
Non-pregnant women	30	468
Pregnant women	42	56
Elderly men and women	24	164

[a] According to hemoglobin thresholds in Table 1

Table 4 Global prevalence of anemia in non-pregnant women and pregnant women by World Health Organization (WHO) region (data collected 1993–2005) [3]

WHO region	Non-pregnant women (%)	Pregnant women (%)
Africa	47.5 (43.4–51.6)[a]	57.1 (52.8–61.3)
Americas	17.8 (12.9–22.7)	24.1 (17.3–30.8)
South-East Asia	45.7 (41.9–49.4)	48.2 (43.9–52.5)
Europe	19.0 (14.7–23.3)	25.1 (18.6–31.6)
Eastern Mediterranean	32.4 (29.2–35.6)	44.2 (38.2–50.3)
Western Pacific	21.5 (20.8–22.2)	30.7 (28.8–32.7)
Global	30.2 (28.7–31.6)	41.8 (39.9–43.8)

Non-pregnant women: 15 to <50 years of age. Pregnant women: no age range indicated

[a] 95% confidence interval

growing fetus probably will be iron-deficient as well. Iron is an element which is essential for normal growth and development of most organs in the fetus, especially for the hematopoietic organs and what is very important, also for the normal development of the brain. Studies have shown that infants and children born to iron-deficient mothers have a poorer cognitive development of the brain functions and a lower intelligence quotient than infants and children born to iron-replete mothers. These findings may have profound implications for the later development and social functions of the growing child. If iron deficiency is very prevalent in the female population, it may therefore affect the health profile as well as the social structure of the society in a negative direction.

It is therefore a serious and frequent problem in childhood anemia that many children are born to mothers who have IDA and, therefore, already from their birth, start out in life with iron deficiency and maybe even with IDA. Congenital iron deficiency may later be aggravated by insufficient nutrition both qualitatively and quantitatively.

Adolescent females

The prepubertal growth spurt puts great demands on iron nutrition both in males and females. In a Danish epidemiological survey of 16-17-year-old adolescents, 0% of males and 23% of females had small iron stores and 0% of males and 10% of females had iron deficiency [23]. In Denmark, adolescent males have a higher intake of different kinds of meat than females, who are more reluctant to consume what they often term “dead animals”. In addition, adolescent females have their menarche and start to lose iron by their upcoming menstrual periods. The combination of these three factors, growth, iron losses, and dietary habits make them more vulnerable to develop iron deficiency and IDA.

Women of reproductive age

In Europe, the prevalence of anemia among women of reproductive age is 15% [3]. In Denmark, among apparently healthy women of reproductive age, ~40% have low iron status (serum ferritin<30 μg/L); 10% have iron deficiency (serum ferritin<16 μg/L), and ~3% IDA [5].

Due to the regular blood and iron losses at their menstrual periods, women of reproductive age a priori face a difficult situation concerning their iron balance. The amount of iron lost by menstruation varies from woman to woman but is quite constant in the individual woman [24]. Natural mechanisms in women have not compensated for these iron losses. In general, both in developed and especially in developing countries, women of reproductive age consume a diet containing an insufficient amount of iron to cover their needs, in part, due to the sedentary lifestyle and, consequently, lower energy intake. Furthermore, the dietary iron they consume is predominantly non-heme iron, which has a very low bioavailability. In other words, their consumption of meat, poultry, and fish is inadequate.

On a worldwide scale, more than 468 million non-pregnant women suffer from anemia; of these women, ~80 millions live in Europe and the Americas and the remaining 388 million in more or less developed regions of the world (Table 4) [3].

Pregnant women

When an iron-deficient woman becomes pregnant, her need for iron will increase dramatically. Pregnancy is a setting where the normal physiological demands for iron display an extraordinary increase of such a magnitude, which has not been recognized in other physiological situations [6]. When iron-deficient women or women with IDA become pregnant, both the prevalence and the severity of IDA may increase markedly during pregnancy unless prophylaxis or treatment is brought into action.

The prevalence of anemia in pregnancy display marked variation from region to region. The lowest prevalence of ~25% is found in Europe and the Americas, whereas South-East Asia and Africa present high prevalences of 48% and 57%, respectively [3]. In Denmark, pregnant women who do not take iron supplements have a prevalence of anemia of ~25% [25]; in contrast, the prevalence of anemia in women taking 40 mg ferrous iron daily is below 5% [26].

In general, more than 56 million pregnant women all over the world suffer from anemia; of these women, ~7 million live in Europe and the Americas and the remaining 49 million in more or less developed countries [3].

IDA has severe implications both for the mother-to-be and for the growing fetus and newborn infant. The women may have general symptoms of anemia including fatigue, weakness, dizziness, headache, palpitations, reduced physical working capacity, feeling of poor health, and, in addition, specific symptoms of iron deficiency such as reduced cognitive abilities, emotional instability, depression, and restless legs.

Experiences from developing countries and the lower social classes in USA have furthermore shown that IDA in pregnant women has a significant negative influence of the outcome of pregnancy. It causes a higher risk of complications at delivery, a higher risk of early and preterm deliveries, and a higher risk of delivering premature children and children with a low birth weight for their gestational age [22].

Postpartum lactating women

There is a direct link from IDA in pregnant women to IDA postpartum. If left untreated, anemia in late pregnancy will inevitably continue after delivery into postpartum anemia, which will even be aggravated due to the blood losses at delivery. Therefore, preventing postpartum anemia means definitely preventing or treating prepartum anemia.

The lactating mother needs to have good nutrition and an adequate intake of vitamins and minerals in order to be physically fit to take proper care of her newborn baby and in order to produce breastmilk of a good quality. Breastmilk is the main nutritional source for the baby for several months, and the quality and quantity of the breastmilk rely on a proper nutritional status of the mother.

The prevalence of postpartum anemia has not been studied as extensively as prepartum anemia. However, we may extrapolate from the prevalence of anemia in pregnant women (see above) to the prevalence in postpartum women, assuming that the figures may be even higher postpartum due to blood losses at delivery. Therefore, in many regions of the world, postpartum anemia is undoubtedly a very significant but partly unrecognized problem.

How can we reduce the prevalence of anemia?

Iron deficiency

How can we approach the widespread endemic of iron deficiency? There are a number of options which can be brought into action, and it is important to emphasize that these options may vary from region to region and from country to country. Within a specific country, prophylactic options could even vary between different population subgroups.

Prophylactic measures should aim at restoring and maintaining an adequate iron status in the groups at highest risk of iron deficiency, i.e., preschool children, adolescent females, women of reproductive age, pregnant women, and postpartum lactating women.

Dietary measures

Ideally, the most natural way of getting enough iron is through a diet with adequate iron content and a good bioavailability of the iron. However, even in Northern Europe, including Denmark, dietary iron intake in women of reproductive age is too low to maintain a good iron status in ~40% of the women and in ~80% of pregnant women [6]. In contrast, Danish men have an adequate iron status and even a high prevalence of slight to moderate iron overload [4].

In general, women consume less food of animal origin than men [8]. Furthermore, due to our sedentary lifestyle in the Western countries, energy intake is relatively low, and we know that the total dietary iron intake is dependent on the energy intake [8]. The mean dietary iron intake in Danish women of reproductive age is 9 mg/day with a bioavailability of 15–20% [8]. This is well below the recommended food iron intake of 18 mg/day [9].

Women do not, to a significant extent, change their dietary habits once they become pregnant, and their needs for food iron increase to ~27 mg/day in order to maintain an adequate iron status [6].

In many developing countries, the diet is composed mainly of foods of plant origin, which per se has low iron content, consisting of non-heme iron. Furthermore, this non-heme iron has a low bioavailability, and diets rich in cereal grains also contain strong inhibitors of iron absorption including phytates. The widespread consumption in some regions of the world of various kinds of teas, which is even taken at meals, will likewise contribute to impaired iron absorption.

It is therefore apparent that nutritional measures against iron deficiency in the risk groups would imply drastic and unrealistic changes in dietary habits, which most likely cannot be implemented in the populations.

Iron fortification of foods

Many Western countries have previously used iron fortification of bread flour. In Denmark, flour was for many years fortified with 30 mg carbonyl iron per kilogram flour. This fortification was stopped in 1987 according to the regulations of the European Union. A follow-up analysis of iron status in the Danish population was performed 10 years after the abolition of the food iron fortification. The results showed that women of reproductive age had unchanged iron status [5], whereas iron status had increased significantly in men, despite the absence of iron fortification [4]!

It has been discussed whether iron fortification should be reintroduced, due to the high prevalence of low iron status in women of reproductive age. However, a general food iron fortification would probably increase the prevalence of the already established iron overload in the male population. In addition, it may have deleterious effect on subjects with genetic iron overload, i.e., the hereditary forms of hemochromatosis, especially *HFE* hemochromatosis, which is quite frequent in populations of Northern European descent [27, 28]. Subjects with hereditary hemochromatosis have abnormally high intestinal iron absorption and certainly do not need extra iron in their diet [28].

Therefore, in the Western countries, we should not rely on food iron fortification but on specific iron prophylaxis in the risk groups.

However, the situation is different in other parts of the world. In South-East Asia, as many as 46% of women of reproductive age have anemia, mainly IDA, which indicates that probably at least 90% of the female population are iron-deficient. Furthermore, genetic iron overload is infrequent in this region. In such a setting, iron fortification of appropriate food items seems justified.

In South-East Asian countries, regular consumption of NaFeEDTA-fortified fish sauce improves iron status and reduces the prevalence of anemia in anemic women [29]. Furthermore, several South-East Asian countries are planning to introduce iron-fortified flour.

In Africa, where the prevalence of anemia is 48% in women of reproductive age, food iron fortification should be balanced against the prevalence of infections, especially malaria, which possibly may be aggravated by the presence of ample iron [30]. However, prospective controlled human studies on the interaction between iron status and malaria have not yet been performed, but a Cochrane review on oral iron supplementation for anemia in children in malaria-endemic areas did not demonstrate any significant change in the prevalence of malaria in iron-supplemented children [31].

Iron supplementation

In the Western countries with easy access to the health care system, it is easy to identify persons with iron deficiency and IDA by analyzing hemoglobin and serum ferritin. According to the outcome, adequate treatment or prophylaxis with oral iron can be instituted.

In developing countries where the health care is less efficient, especially in the rural districts, hemoglobin is often analyzed with a hemoglobinometer, e.g., Hemocue®, but there are no facilities for the analysis of ferritin. In regions with a high prevalence of anemia, there is a definite need to establish the ferritin analysis on a broader scale and to use it routinely in association with the analysis of hemoglobin. There is also a need for a simple ferritin analysis, which can be performed under field conditions.

Even if ferritin cannot be analyzed, in regions with a high prevalence of IDA, the finding of anemia should imply generous use of oral iron supplementation in order to benefit the risk groups.

Iron prophylaxis in pregnancy

Due to the drastic increase in the need for iron during pregnancy, the majority of pregnant women have a definite need for iron supplements [6]. This goes both for Western countries and developing countries. Ideally, the iron supplement should be tailored to the individual woman according to her iron status, i.e., serum ferritin concentration [32]. But, so far, a general iron prophylaxis regime including all pregnant women is used in most countries.

In Denmark and USA, pregnant women are recommended oral iron supplements from their first visit to the antenatal clinic at approximately 10 weeks gestation. The general recommendation in Denmark is 40 mg ferrous iron and in USA 30 mg ferrous iron daily taken between meals.

Some studies suggest that in order to be of optimum benefit for the outcome of pregnancy, iron supplements should be started already when the woman decides to become pregnant in order to establish adequate iron reserves during pregnancy and postpartum. This approach is especially important in regions where iron deficiency and IDA are prevalent among women of reproductive age, such as South-East Asia and Africa. Furthermore, this approach is in accordance with the concept of folic acid supplements, which should be started when conception is planned (see below).

In regions where iron deficiency and IDA is highly prevalent, the dose of iron should be higher than in the Western countries. An appropriate dose would be 100 mg ferrous iron/day, preferably taken at bedtime or between meals [32].

Tablets, which combine iron, folic acid, vitamin B_{12}, and vitamin C, will be much easier to administer to women instead of taking the single components in separate tablets.

Iron treatment of iron deficiency anemia

IDA should initially be treated with oral ferrous iron in doses of 100–200 mg/day. It is essential to check the hemoglobin concentration after 2–4 weeks to see if the treatment works and induces an increase in hemoglobin. Iron should be continued for at least 6 months after hemoglobin concentrations have reached normal levels in order to rebuild a minimum of body iron reserves. In profound IDA with hemoglobin <90 g/L, intravenous iron should be considered.

Treatment of iron deficiency anemia in pregnancy

Prophylaxis is better than cure! However, some women have so severe IDA at their first visit to the antenatal clinic that oral ferrous iron in prophylactic doses of 40–50 mg may be inadequate in order to correct the anemia prior to delivery. The Guidelines by the Swiss Society for Gynecology and Obstetrics recommend that if the woman's hemoglobin is <105 g/L, first-line treatment is to increase the dose of oral iron to 200 mg/day. Hemoglobin should be checked after 2 weeks, and if there is an increase of 10 g/L or more, oral iron should be continued throughout pregnancy. In women, who after 2 weeks do not respond to oral iron by an increase in hemoglobin of 10 g/L or more, intravenous iron treatment should be considered [33].

For treatment of IDA in pregnancy, the Network for Advancements of Transfusion Alternatives (NATA) recommends oral ferrous iron 100–200 mg/day in the first and second trimester. If there is no increase in hemoglobin after 2 weeks, intravenous iron therapy should be considered. In the third trimester, intravenous iron is advocated as first-line treatment because oral iron, even in high doses, has too short a time to work in order to correct the anemia before delivery [34].

Studies from the Indian subcontinent have demonstrated that intravenous iron therapy can be very efficient in the correction of IDA in late pregnancy. Intravenous iron can be administered as a single dose infusion, which is convenient for the patient and reduces the costs of the health care system.

Treatment of postpartum iron deficiency anemia

Postpartum anemia is a poorly recognized problem. In many developed countries, including Denmark, the mothers are discharged from the public birth clinics within hours after delivery. So far, it has not been possible to measure hemoglobin at 48 h after delivery in order to estimate the prevalence of postpartum anemia. The prevalence of major maternal bleeding >500 ml in association with delivery is in the range of 5–7%. The Guidelines by the Swiss Society for Gynecology and Obstetrics recommend that if the woman's hemoglobin is 95–120 g/L, first-line treatment is to increase the oral iron to 80–200 mg/day. If hemoglobin has dropped to <95 g/L, intravenous iron 500–1,000 mg is recommended, and at hemoglobin levels <80 g/L, giving recombinant human erythropoietin in addition to intravenous iron should be considered [33].

The Network for Advancements of Transfusion Alternatives recommends intravenous iron at hemoglobin levels 60–95 g/L and blood transfusion at hemoglobin levels <60 g/L [34].

Folate deficiency

In order to prevent neural tube defects in the fetus, it is important to maintain good folate status in women of reproductive age who may become pregnant as well as in pregnant women. The neural tube is formed within approximately 30 days after conception, so it is essential that the woman's folate status is good already prior to conception. This can be obtained by a general folic acid fortification of appropriate food items, usually flour [13] as well as by individual folic acid supplementation. The general recommendation for supplemental folic acid is 400 μg/day [13]. The nutrition authorities in USA have implemented folic acid fortification of flour but, nevertheless, still recommend that women of reproductive age should take additional folic acid supplements of 400 μg/day [35].

Vitamin B_{12} deficiency

Although the recommended daily intake of vitamin B_{12} is ~2.4 μg/day, many elderly persons appear to require much higher supplement doses to achieve optimum vitamin B_{12} status, probably due to a limited gastrointestinal absorption. In order to increase the dietary intake of vitamin B_{12}, the diet should be rich in foods of animal origin. This would, however, be almost impossible for the majority of people in many developing countries due to the high costs of meat and poultry. If the deficiency is caused by malabsorption of vitamin B_{12}, dietary measures would be insufficient and prophylaxis/treatment should rely on oral supplementation of synthetic vitamin B_{12} in adequate doses. The synthetic form of vitamin B_{12} is absorbed much better than the food forms and may, in high doses, bypass the “natural” absorption mechanism [13].

Infections/infestations

In communities where infections/infestations are frequent and contribute significantly to a high prevalence of anemia, treatment and prophylactic eradication of infections are important in order to improve the situation [36].

In areas with high frequencies of parasitic diseases such as malaria and intestinal helminth infestations, antimalarial programs as well as deworming programs should be effectuated [18].

In Africa, ~30 million women living in malaria-endemic areas become pregnant each year. For these women, malaria is a threat both to themselves and to their babies, with up to 200,000 newborn deaths each year as a result of malaria in pregnancy. Pregnant women are particularly vulnerable to malaria as pregnancy reduces a woman's immunity to malaria, the parasites being resident in the placenta, making her more susceptible to malaria infection and increasing the risk of illness, severe anemia, and death. For the unborn child, maternal malaria increases the risk of spontaneous abortion, stillbirth, premature delivery, and low birth weight—and is therefore a leading cause of child mortality [37].

Hemoglobinopathies

The management of the hemoglobinopathy issue relies primarily on genetic counseling in order to limit or avoid the occurrence of severe disease, which demands expensive treatment and is associated with a poor quality of life and a poor survival rate. Systematic follow-up and case management of abnormal newborn screen for hemoglobinopathy can improve the acceptance of genetic counseling [38].

Conclusion

Anemia has been recognized as a major health problem in developing countries for many years: still, this basic problem has not been solved but continues to exist affecting the health, quality of life, and working capacity in billions of people around the world. Most cases of anemia are due to iron deficiency, which often work in symphony with folate and/or vitamin B_{12} deficiency as well as infections/infestations.

The World Health Organization has initiated successful campaigns against a number of infectious diseases—but the battle against anemia is far from being won and more efforts should be concentrated on tackling this massive problem—we have the tools and we know the ways. Initially, the efforts should be centered on the risk groups for iron deficiency anemia, i.e., young children, adolescent females, women of reproductive age as well as pregnant women and postpartum lactating mothers.

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