

Iron-Deficiency Anemia: Reexamining the Nature and Magnitude of the Public Health Problem

Defining Iron-Deficiency Anemia in Public Health Terms: A Time for Reflection^{1,2}

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ABSTRACT This paper provides a historical context for this meeting, which aimed to examine critically the way we have defined iron-deficiency anemia as a public health problem. The terms and concepts used to define the problem are reviewed first, followed by estimates of the global prevalence of the problem from 1985 to 2000. It is argued that recent estimates are not credible and that we must redefine the problem in terms that are important, measurable and addressable. This meeting was designed to take first steps toward that goal, namely, to identify the causal factors (e.g., iron deficiency vs. iron-deficiency anemia vs. severe anemia from any cause) that link iron-deficiency anemia to important health outcomes and to estimate the magnitude of their effects in public health terms. *J. Nutr.* 131: 565S–567S, 2001.

KEY WORDS: • iron deficiency • anemia • public health • history

The impetus for this meeting was the conviction that we must define the problem of iron-deficiency anemia in terms of its health consequences in human populations. To do this with clarity, we must look critically at the evidence. First, this meeting must be put in historical context. Where have we come from in defining iron-deficiency anemia as a public health problem? Where do we hope to go?

WHERE HAVE WE COME FROM? TERMS AND CONCEPTS

The initial term and concept was nutritional anemias. Although this term is not commonly used today, it lives on in the name of the International Nutritional Anemia Consultative Group (INACG).³ Nutritional anemia was defined in a 1968 WHO technical report as “a condition in which the hemoglobin content of the blood is lower than normal as a result of a deficiency of one or more essential nutrients, regardless of the cause of such deficiency.”

To determine which nutritional deficiencies were most responsible, WHO coordinated a series of studies in pregnant women in which anemia, serum folate, transferrin saturation

and serum B-12 were assessed. They concluded that “Iron deficiency was present in 40–99% of the pregnant women studied and was undoubtedly responsible for the major proportion of anemia” (WHO 1968).

The evidence that led them to that conclusion is shown in **Figure 1**. Certainly the authors were impressed by the prevalence of iron deficiency, which was ~10 times higher than that of folate deficiency or vitamin B-12 deficiency based on their indicators. However, the relation between anemia prevalence and iron deficiency prevalence is not apparent when the data are compared among populations. Within-population correlation coefficients with hemoglobin were published for the study in Vellore, India. There was a strong correlation between hemoglobin and transferrin saturation ($r = 0.56, P < 0.001$), but the correlation with serum folate was even stronger ($r = 0.82, P < 0.001$). There was no significant correlation between serum vitamin B-12 and hemoglobin (Baker and DeMaeyer 1979).

The singular importance of iron deficiency was restated with more confidence by Baker and DeMaeyer (1979): “The major factor responsible [for nutritional anemia] is a deficiency of iron, with folate deficiency also playing a role in some population groups, especially in pregnant women.”

In 1985, DeMaeyer and Adiels-Tegman published a landmark paper entitled “The Prevalence of Anemia in the World,” in which they compiled global data from reasonably large studies. The data presented in that paper constitute the core of the database used for global prevalence estimates of anemia and iron-deficiency anemia. In that paper, nutritional anemia was considered to be a large component of global anemia prevalence, and iron deficiency was considered the most common cause of nutritional anemia. By making the assumption that the prevalence of anemia in adult men is the

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² This article was commissioned by the World Health Organization (WHO). The views expressed are those of the author alone and do not necessarily reflect those of WHO.

³ Abbreviations: HIV, human immunodeficiency virus; INACG, International Nutritional Anemia Consultative Group; MI, Micronutrients Initiative; UNICEF, United National International Children's Emergency Fund; UNU, United Nations University.

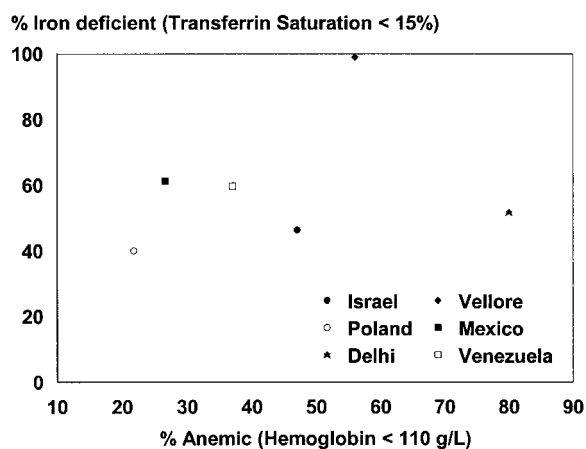


FIGURE 1 Scatterplot of anemia prevalence vs. iron deficiency prevalence in pregnant women, from World Health Organization studies of nutritional anemia (WHO 1968).

amount of anemia not attributable to iron deficiency, the authors tentatively estimated that ~50% of anemia in women and children is attributable to iron deficiency (DeMaeyer and Adiels-Tegman 1985).

The next evolution of concepts is the shift from nutritional anemia (of which iron-deficiency anemia is one important part) to iron-deficiency anemia as the major public health problem. This is reflected in the title of the 1989 WHO monograph, *Preventing and Controlling Iron Deficiency Anaemia Through Primary Health Care*, which states (DeMaeyer et al. 1989), "Iron deficiency anaemia is the most prevalent nutritional disorder in the world today. . . . Iron deficiency is by far the commonest nutritional cause of anaemia; it may be associated with a folate deficiency, especially during pregnancy. Other nutrient deficiencies, such as vitamin B-12, pyridoxine (PN) and copper are of little public health significance because of their infrequency."

In 1993, a WHO/United Nations International Children's Emergency Fund (UNICEF)/United Nations University (UNU) consultation made the next shift in thinking, i.e., from iron-deficiency anemia to iron deficiency as the problem. In the report from that meeting, anemia was considered an indicator of iron deficiency rather than iron deficiency being considered a contributing cause of anemia (WHO/UNICEF/UNU, unpublished). The authors state, "Because anaemia is the most common indicator used to screen for iron deficiency, the terms anaemia, iron deficiency, and iron deficiency anaemia are sometimes used interchangeably. There are, however, mild-to-moderate forms of iron deficiency in which, although anaemia is absent, tissues are still functionally impaired."

However, a more recent meeting in Africa brought the thinking full circle. The lead recommendation from the meeting proceedings reads: "Beyond iron deficiency—focus on anaemia as the principal problem. Even though iron deficiency is a major factor contributing to the anaemia problem in parts of Africa, there are a number of other factors that coexist and contribute to the burden. They include other nutrient deficiencies (e.g., folate, vitamin A), malaria, HIV [human immunodeficiency virus], other infectious diseases, sickle cell disease and other inherited anemias" [Micronutrients Initiative (MI)/UNICEF 1997].

In the past 3 years, there has been a confusing mixture of language, as illustrated by these three recent expert committee statements: 1) "Iron deficiency is not the only cause of anemia, but where anemia is prevalent, iron deficiency is usually the most common cause" (Stoltzfus and Dreyfuss 1998). 2) "Anemia has a multifactorial etiology and the contributions of its determinants vary in many ways. Anemia can be caused by dietary factors, malaria, intestinal parasites, HIV, or certain genetic hemoglobinopathies. . . . Moreover determinants interact" (Gillespie and Johnston 1998). 3) "Although iron deficiency accounts for most of the anaemia in underprivileged environments, there are other causes of anaemia. . . . As iron deficiency prevalence decreases, other causes of anaemia may become proportionately more important, but excepting sickle-cell anaemia in some populations of Africa, none are at levels requiring a public health response. Successful iron supplementation results in the disappearance of anaemia as a public health problem except where malaria is highly prevalent" (UNICEF/UNU/WHO/MI 1999).

This confusion has real implications for how we design intervention programs and evaluate their success. It also greatly influences how we estimate the prevalence and distribution of the public health problem, which leads us to our next historical topic.

WHERE HAVE WE COME FROM? NUMBERS

Since 1985, when DeMaeyer and Adiels-Tiegman first attempted to estimate the magnitude of the problem then called nutritional anemia, prevalence estimates have risen dramatically and at a rate exceeding global population growth (Fig. 2). It is important to consider the fact that all of the estimates that follow are derived from measurements of hemoglobin. Prevalence estimates for iron deficiency or iron-deficiency anemia have been derived from anemia data and are based on a variety of assumptions. Thus, the interpretation of hemoglobin values is fundamentally important. The thinking expressed in a 1972 WHO technical report has been greatly influential: "It is recognized that there is a homeostatic mechanism that sets the hemoglobin level in each individual. Whereas it is not known whether this is the optimum level for health, it is accepted as 'normal' for the individual. . . . This distribution of normal values is likely to be the same throughout the world when allowance is made for such factors as age, sex, pregnancy, and altitude" (Baker and DeMaeyer 1979). It is important to remember that the WHO definitions for anemia were explicitly not designed to indicate optimal human function nor to be

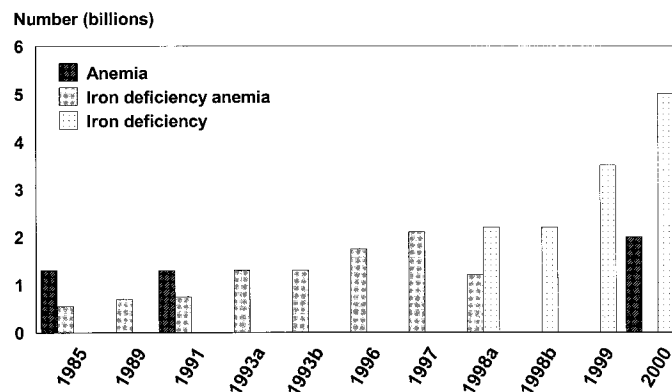


FIGURE 2 Estimates of the number of people in world with anemia, iron-deficiency anemia, or iron deficiency as stated by various expert groups since 1985. References (in chronological order) are the following: DeMaeyer and Adiels-Tegman 1985; DeMaeyer et al. 1989; Gillespie et al. 1991; Levin et al. 1993; WHO/UNICEF/UNU, unpublished, 1993; Murray and Lopez 1996; Draper 1997; Gillespie and Johnston 1998(a); Stoltzfus and Dreyfuss 1998(b); UNICEF/UNU/WHO/MI 1999; International Nutritional Anemia Consultative Group 2000.

sensitive or specific for iron deficiency as opposed to other causes. There is also growing opinion that the normative hemoglobin distribution is not the same throughout the world (UNICEF/UNU/WHO/MI 1999).

This summary of numbers begins in 1985 (DeMaeyer and Adiels-Tegman 1985). The 1985 anemia estimate and the 50% attribution of anemia to iron deficiency were cited in two subsequent documents by WHO (DeMaeyer et al. 1989) and the United Nations Subcommittee on Nutrition (Gillespie et al. 1991). However in 1993, two documents (Levin et al. 1993, WHO/UNICEF/UNU, unpublished) used De Maeyer and Adiels-Tegman's 1985 anemia number but named it iron-deficiency anemia. In 1996, the Global Burden of Disease project adjusted these numbers upward on the basis of a new global population figure but continued to call this the prevalence of iron-deficiency anemia. In 1997–1998, three expert documents used a higher prevalence number of 2.1 billion people affected; Draper (1997) used this as the figure for iron-deficiency anemia, whereas the other documents (Gillespie and Johnson 1998, Stoltzfus and Dreyfuss 1998) stated this to be the number with iron deficiency. The UNICEF/UNU/WHO/MI (1999) Technical Workshop stated that 3.5 billion people suffer from "iron deficiency and its anemia." Finally, in 1999, a WHO report at an INACG meeting (INACG 2000) estimated that 2 billion people were anemic (applying the 30% prevalence figure of DeMaeyer and Adiels-Tegman to a new global population of >6 billion) and tentatively estimated that the number of iron-deficient people could be as high as 5 billion, or 80% of the world's population. The latter figure was obtained by multiplying the number of anemic people by 2.5. This factor, discussed in the WHO/UNICEF/UNU consultation (unpublished 1993), is based on U.S. national data for women and children, in which the ratio of iron-deficient people to iron-deficient anemic people was 2.5 (Yip 1994). Applying that figure to global data assumes that this relationship found in the United States is generalizable to the world—a troubling assumption that was clearly acknowledged at the INACG meeting. In addition, the factor should rightly be applied only to the number of iron-deficient anemic people, not to all anemic people.

Thus, in the 15 years since 1985, as our conceptualization of the problem has evolved from iron-deficiency anemia to become iron deficiency with or without anemia, the number of people supposedly affected has grown from 0.6 million to 3.5–5 million. When global population growth is controlled for, prevalence estimates have risen from 15 to 60–80% of the world's population. I suggest to you that these estimates have become incredible.

WHERE DO WE GO FROM HERE?

The purpose of this meeting is to begin to redefine the public health problem of iron deficiency on the basis of empirical evidence linking the potential risk factors (e.g., iron deficiency or iron-deficiency anemia) to important health consequences. Our goal is to define the problem in terms that are important, measurable and addressable. The point is not to generate the largest prevalence estimates that we can. Incredibly large prevalence estimates have not brought about public health success in this area in the past decade. The point is to create a basis for prevalence estimates that we can measure and that represent real and important health risks.

Public health scientists and practitioners working on the problem of iron-deficiency anemia have lamented two challenges, i.e., it is difficult to rally political support for the problem and it is difficult to demonstrate success in controlling it. Our reaction to the first problem has been to hold more meetings and advocate more vociferously. Our reaction to the

second problem has been to question our interventions and their efficacy. It is possible that a clearer and more compelling definition of the problem could contribute greatly to meeting both of these challenges. If we define the problem in terms of functional consequences rather than normative indicator distributions, our advocacy to the international health community may be more effective. If we set goals and evaluate programs on the basis of concepts and biological processes that are clear and measurable, we might find that our interventions are more successful than we have documented in the past.

I suggest that at least four steps are key to this process. The first step is to identify the causal factor. What is it that causes functional deficits (i.e., disease, disability or death) in humans? Is it iron deficiency per se? Iron-deficiency anemia? Severe anemia from any cause? The second step is to estimate the magnitude of its effect on important public health outcomes. How large are the relative risks or other measures of effect size? The third step is to estimate the prevalence of the causal factor, and the fourth step is to demonstrate effective ways to reduce the causal factor or to interrupt its link to adverse health consequences. The papers that follow address the first two steps in this process.

John Beard and Lindsay Allen present background papers that describe what we know about the possible causal factors and how they affect human physiology in the relevant outcome domains. Bernard Brabin, Kathleen Rasmussen, Stephen Oppenheimer, Sally Grantham-McGregor and Jere Haas present critical reviews of the causal evidence that links iron deficiency, anemia or both to the six outcome areas. Additional commentaries by Sue Horton and Carol Levin on work productivity and Ernesto Pollitt on child development are included with the respective evidence reviews. The supplement concludes with a summary of how the meeting participants synthesized the evidence.

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