MANAGING ANEMIA IN DEVELOPING COUNTRIES

# ANEMIA AFFECTS ALMOST TWO BILLION PEOPLE IN THE WORLD: NOW IT IS TIME TO ACT!

## ANEMIA SUBSTANTIALLY IMPACTS LIFE IN THE DEVELOPING WORLD

Almost a quarter of the world's population is anemic with major consequences for individual health as well as for national economies. Women of reproductive age and children are the groups most at risk. On average, 38 % of pregnant women, 29 % of non-pregnant women and 43 % of pre-school children are anemic. The corresponding figure for men over the age of 15 is 13 %.[1] In the developing world, however, where anemia is most prevalent, these figures are substantially higher. The District Level Health Survey in India 2002-2004 reported an incidence of 98 % anemia in adolescent girls and 96 % in pregnant women.[2]

Left undetected and untreated, anemia in its most severe form can be fatal. But even less severe cases may have serious consequences for health and quality of life for large groups of people. Maternal anemia is associated with mortality and morbidity, both in mother and baby. Infants born to anemic mothers have a higher risk of anemia in the critical first six months of life which is a risk factor for impaired cognitive and physical development, impaired growth, and increased morbidity due to infections.[2,3]

In 2012 the World Health Assembly of the WHO adopted the six global nutrition targets to be reached by 2025.[4] The second target states that anemia in women of reproductive age should be reduced by 50%. Meeting this target will be an important step towards breaking the inter-generational cycle of anemia, and will result in benefits for individual health and quality of life, as well as economic growth for communities and countries.

In order to meet this global nutrition target – and the other five targets that are also linked to anemia – the WHO urges leaders and policymakers to make the necessary investments to fight anemia. These include: 1) improving identification, measurement and understanding of anemia, 2) scaling-up

THE GLOBAL NUTRITION TARGET[4]

1. **Stunting**
   TARGET: 40% reduction in the number of children under the age of five who are stunted.
2. **Anemia**
   TARGET: 50% reduction of anemia in women of reproductive age.
3. **Low birth weight**
   TARGET: 30% reduction in low birth weight.
4. **Childhood overweight**
   TARGET: No increase in childhood overweight.
5. **Breastfeeding**
   TARGET: Increase the rate of exclusive breastfeeding in the first six months up to at least 50%.
6. **Wasting**
   TARGET: Reduce and maintain childhood wasting to less than 5%.

of treatment actions, and 3) monitoring and evaluating the implementation of anemia control programs.[4]

**In order to reduce anemia in women of reproductive age by 50 % by 2025, identification, measurement and understanding of anemia need to be improved. Treatment actions, monitoring and evaluation of anemia control programs need to be scaled up.**

## A VARIETY OF METHODS TO MEASURE HEMOGLOBIN

The most reliable indicator of anemia at the population level, is estimating the concentration of hemoglobin, as opposed to clinical measures which are subjective and therefore often erroneous.[5] In a recent review, the authors searched the literature to investigate what methods for hemoglobin estimation are used. A total of 74 scientific papers were included in the review. The authors conclude that a variety of different methods are used worldwide. They all have advantages and disadvantages, and only few of them are suitable for field conditions.[2] The availability of quick, valid and reliable methods suitable for use where neither laboratory facilities nor power supply are available is vital.

The gold standard for measuring hemoglobin is the direct cyanmethemoglobin method. This method is cheap and has high sensitivity and specificity, but it is time consuming and requires lab facilities for dilution of samples and a spectrophotometer. For these reasons surveys in remote areas has limited use for this method. Moreover, the use of cyanide is a potential health risk as well as a risk for the environment. Another disadvantage with this method is that presence of turbidity in the blood sample gives inaccurate values since measurement is done at only one wavelength (540 nm). In India, this method is still used by approximately 70 % of laboratories. Another method sometimes used in India is Sahli's technique where a blood sample is first mixed with hydrochloric acid and then diluted in steps until it matches the color of hemoglobin standards in a color matching chamber.[2]

In the absence of a laboratory, anemia is often diagnosed based on clinical signs which invariably leads to inter- and intraobserver variation. There are a number of methods that do not require a hospital laboratory. Most of them are however, no longer very widely used because of various disadvantages or because they are inaccurate. These include the Haldane method, the Dare method, the Lovibond-Drabkin method, the Tallqvist method and the A.O. Spencer method. The Haldane method is one of the oldest, where the carbon carrying capacity of blood is estimated using a standard. In the Dare method, the blood sample is inserted into a small illuminated glass chamber, viewed thorough an eye piece and matched with a standard. The Lovibond-Drabkin method measures cyanmethemoglobin and the test result is interpolated by comparing the color of the blood sample with color standards on discs. In the Tallqvist method the blood sample is blotted on paper and the color is then matched to color standards on paper. The A.O. Spencer method requires an instrument where the blood sample, first agitated with a saponin coated stick, is analyzed with transmitted green light. The hemoglobin level is read by comparison with a standard.[2]

The copper sulphate method is mostly used to ensure blood donors have high enough hemoglobin levels before donation. It is only semi-quantitative as it categorizes blood as either below 80g/L, between 80 and 100g/L or above 100g/L, and therefore less suitable for detecting anemia.[2] There are however, also findings that even for blood donor screening it is not accurate enough and leads to false deferrals.[6] The method is based on the specific gravity of blood. A blood droplet from the sample is observed as it falls through copper sulphate solutions with specific gravities equivalent to those of blood with hemoglobin contents of 100g/L and 80g/L respectively.[2]

**The most reliable indicator of anemia is the concentration of hemoglobin. There are various methods, but few are accurate enough and suitable for field conditions.**

## THERE IS A NEED FOR A METHOD POSSIBLE TO USE UNDER FIELD CONDITIONS

In the 1970's the WHO emphasized the need for a simple, cheap and robust device for measuring hemoglobin concentration, useful for health workers outside the laboratory often in the absence of electricity, that would give reliable results. The WHO color scale was consequently developed, taking advantage of modern color printing technology and better test-strip paper than those available when previous color scale methods were developed. It consists of a reference paper strip with six color shades representing blood with different hemoglobin concentrations. A blood drop is placed on a test strip and is matched to the reference strip after 30 seconds. It is primarily intended to assist developing countries in the detection of anemia and not to compete with existing laboratory hemoglobinometry. It gives access to health technology for peripheral health services in resource-poor settings.[7] In a test for different purposes it was concluded that the method is reliable for detecting and assessing the severity of anemia. However, there were discrepancies between results obtained from the color scale and a standard laboratory method, mainly due to inconsistencies in applying the drop of blood on the test strips and incorrect handling of the scale.[8] The method has since then been assessed in several studies. Some conclude that it can be recommended in field settings, others that it's accuracy is not clinically acceptable.[2] The method is limited by the possibility to detect only significant levels of anemia, as well as not being sufficiently sensitive to small changes in hemoglobin.[9] It is also prone to inter-observer variablility.[2]

Another system for hemoglobin estimation is the HemoCue photometers to be used with disposable cuvettes. The HemoCue systems measure at two wavelengths which compensates for the possibility of turbidity. The HemoCue photometers has higher sensitivity and specificity for both capillary and venous blood compared to the direct cyanmethemoglobin method. Several studies have found the HemoCue systems to be reliable, accurate, rapid, cheap and to give reproducible results.[2] It is also easy to handle with no inter-observer variability as manual control is limited to turning on and off the battery-operated system.[2] There are however, studies that have found that the sensitivity and specificity varies depending on if venous or capillary blood is used.[2]

The authors of the aforementioned literature review on different hemoglobin methods conclude that HemoCue seems to be the method of choice for initial screening of anemia because it is reliable, portable, does not require power supply and is easy to use in poor resource settings without requiring extensive training of health workers.[2] The Technical Consultation on the assessment of iron status at the population level, held in Switzerland in 2004, concluded that in the absence of auto-analyzers and laboratory facilities, the use of instruments such as HemoCue that give highly reproducible results, should be in focus. They however, point out that there can be variability due to poor capillary sampling technique, which is therefore an important factor to consider with the HemoCue system.[10]

There is now also a non-invasive hemoglobin instrument (NBM-200) where the sensor is placed on the thumb. A comparison of this method with HemoCue and an automated analyzer was done in blood donors. Both the sensitivity and specificity of the non-invasive method was found to be lower than for both the auto-analyzer and for the HemoCue. Therefore, the conclusion is that this instrument should be used with caution as a screening tool.[11]

**In the absence of autoanalyzers and laboratory facilities, instruments that give highly reproducible results such as the HemoCue systems, are recommended.**

## IRON DEFICIENCY ACCOUNTS FOR HALF OF THE WORLD'S ANEMIA BURDEN

Approximately half of the world's anemia burden is the result of iron deficiency.[12] In order to come to terms with the problem, a population approach is required. Several intervention programs show that

### CAUSES OF ANEMIA[4]

In an anemic person, the number of red blood cells is insufficient to meet the body's physiological needs. The most common cause of anemia is iron-deficiency resulting from inadequate dietary iron intake, increased needs such as during pregnancy or periods of strong growth, or excessive iron losses as a result of menstruation or helminth infestations. There are also other causes of anemia such as malaria, infections, other nutritional deficiencies or hereditary blood disorders. These additional factors may aggravate an already preexisting iron-deficiency anemia. For pregnant women for example, malaria is a substantial risk factor for developing severe anemia.

fighting anemia on a population scale is possible. Especially vulnerable to iron deficiency anemia are children and women of reproductive age because of menstruation, pregnancy and childbirth. Maternal iron status affects iron accumulation of the fetus, and if the pregnant woman is iron deficient, the child is at higher risk of iron deficiency anemia after birth.[13] After 6 months of age, when breast feeding is no longer enough to fulfil the nutritional needs of the infant, complementary foods must be part of the diet. Young infants, with a rapid expansion of red cell mass, have very high dietary iron requirements. There are estimations that a child aged 6 to 12 months needs even more dietary iron than an adult male.[14] In low-income settings, however, iron rich complementary foods are often inaccessible.

Even though the long-term solution to malnutrition and iron deficiency anemia involves genuine socioeconomic changes, and changes in food supply and the individual's access to it, a short-term solution includes supplementation with iron and possibly other micronutrients to those at risk. The WHO recommends weekly iron supplementation to children and menstruating women in areas where anemia prevalence exceeds 20 %.[12] Prophylactic supplementation can be given as fortification of foods that are consumed in sufficient amounts by at-risk-individuals, or as home-based fortification with micronutrient powders to be sprinkled over the food. Another alternative is intermittent iron supplementation in for example school based programmes. For pregnant women in these areas, daily supplementation is however, more appropriate.[13]

**Iron deficient mothers have a higher risk of giving birth to iron deficient and anemic babies. With accurate anemia monitoring in pregnant women, and adequate intervention when needed, these babies are given a better start in life and the inter-generational cycle of anemia can be broken.**

## ANEMIA CAN BE SUCCESSFULLY ALLEVIATED WITH HIGH QUALITY INTERVENTION PROGRAMMES

Implementation of anemia control programs requires careful baseline epidemiologic evaluation and selection of appropriate interventions. Since considerable effort, time and resources are often allocated to these types of programmes, there is a need also to demonstrate that they meet their objectives.

There are several examples of successful interventions to fight anemia – from smaller scale trials and interventions in emergency areas, to large-scale intervention programmes. In a review of 55 trials, it was shown that iron administration to children given parenterally, orally or in fortified food, resulted in a reduction of anemia prevalence by 37.9 % to 62.3 % in non-malaria-endemic settings.[15]

An example of an intervention in a disaster area is the intervention in Kang county of China after the devastating earthquake in 2008. The earthquake affected about 348 million people, whose lives were seriously disrupted. Food supply systems were

### WHO IS ANEMIC AND WHO IS NOT?[17]

| | Non-anemia* | Mild* | Moderate* | Severe* |
|---|---|---|---|---|
| Children 6-59 months of age | >110 | 100-109 | 70-99 | <70 |
| Children 5-11 years of age | >115 | 110-114 | 80-109 | <80 |
| Children 12-14 years of age | >120 | 110-119 | 80-109 | <80 |
| Non-pregnant women | >120 | 110-119 | 80-109 | <80 |
| Pregnant women | >110 | 100-109 | 70-99 | <70 |
| Men (>15 years of age) | >130 | 110-129 | 10-109 | <80 |

** Hemoglobin in grams per litre*

*Smoking and living at high altitude are known to increase hemoglobin concentrations. Therefore adjustments in the above cut-offs should be made for smokers and for people living at altitudes higher than 1000 meters above sea level.*

seriously damaged and food shortage became a primary post-earthquake feature. Previous experience had shown that especially infant and young children morbidity and mortality increases under such circumstances. In order to improve the nutritional status of infants and young children in the affected areas, all children aged 6 to 24 months were given complementary food supplements. The intervention started two years after the earthquake and went on until the children reached 24 months of age. A total of 250 to 300 children were randomly chosen for follow up to evaluate the effectiveness of the intervention at 6, 12 and 18 months. At baseline the prevalence of anemia was 74.3 %. Six months after the introduction of complementary food supplements the anemia prevalence had already decreased to 37.4 %. At the end of the intervention the corresponding figure had decreased by a further 7 % to nearly 30 %.[16]

"The Adolescent Girl's Anaemia Control Programme" in India, is an example of a well-organized large-scale program that has been successful in controlling anemia.[3] There are several reasons to specifically put adolescent girls in focus. Adolescents (age 10 -19 years), and especially girls, are at high risk of iron deficiency and anemia due to accelerated increase in requirements for iron, poor dietary intake of iron, malaria and worm infestation. Public health experts also attribute social and cultural factors such as early marriage, adolescent pregnancy, and repeated pregnancies, to vulnerability of girls to iron deficiency and anemia. There is global consensus that investing in particularly adolescent girls can accelerate the fight against deprivation, inequity and discrimination.[3]
"The Adolescent Girl's Anaemia Control Programme" started as a pilot study from 2000 to 2005, where adolescent girls in 13 states where supplemented with weekly iron and folic acid using schools and village centres of India's Integrated Child Development Services as delivery platforms. The Government of India and State Governments wanted to assess the cost and effectiveness of an innovative programme aimed at reducing the prevalence and severity of anemia in adolescent girls. The pilot study included at least two of the following interventions: weekly iron and folic acid supplementation, bi-annual deworming prophylaxis and information, counselling and support on for example how to improve the diet to prevent anemia. Both school-going and out of school girls were included in the study. At the end of the study almost nine million girls were included in the programme. Evaluation studies were carried out in six states. At baseline the prevalence of anemia ranged from 65 % to 88 %. After one year of intervention the average decrease in anemia prevalence was 24 percentage points. The proportion of girls who reported beneficial effects from the programme ranged from 31 % to 100 % in different states. Some of the benefits most frequently reported by the girls were feeling healthier, having more energy, not feeling sleepy,

having better concentration at school and having regular menstrual cycles. The adherence to the programme was very high, ranging from 88 % to 99 % in different states, with the exception of one state with intermittent supply stock-outs where adherence was 53 %. One area of improvement was found to be the information, education and communication component of the study. Even if the material was read by a majority of the girls many of them could not recall much of the content.

The encouraging results provided evidence for up-scaling the programme. In the second phase, from 2006 to 2010, particular attention was given to information strategies to reach the adolescent girls, their families and communities at large. By the end of 2010, the programme covered 14.5 million girls. The programme was then scaled up once again in 2011 when the flag ship programme "The Rjiv Gandhi Scheme for the Empowerment of Adolescent Girls" was implemented in about one third of India's districts. "The Adolescent Girl's Anaemia Control Programme" continued in 13 states and in total these two programmes reached 27.6 million adolescent girls. Once the initial training and monitoring capacity of the programme was in place, the additional cost ranged between 0.32 and 0.36 US dollar per girl per year.[3]

In 2012 the Government of India launched the National Weekly Iron and Folic Acid Supplementation Programme to expand the benefits of the previous programmes to all adolescent girls in India.[3]

**With a knowledge-based approach, interventions to fight anemia can be successful in improving health and the quality of life for large groups of people living in at-risk areas.**

References:

1. WHO. The global prevalence of anaemia in 2011. Geneva: World Health Organization; 2015.
2. Srivastava T, Negandhi H, Neogi SB, Sharma J, Saxena R. Methods for Hemoglobin Estimation: A Review of "What Works". J Hematol Transfus 2014;2(3): 1028.
3. Aguayo VM, Paintal K and Singh G. The Adolescent Girl's Anemia Control Programme: a decade of programming experience to break the inter-generational cycle of malnutrition in India. Publ Health Nutr 2013 Sep;16(9):1667-76.
4. WHA. Global nutrition targets 2025: anaemia policy brief (WHO/NMH/NHD/14.4). Geneva: World Health Organization; 2014.
5. Worldwide prevalence of anaemia 1993–2005: WHO global database on anaemia / Edited by Bruno de Benoist, Erin McLean, Ines Egli and Mary Cogswell.
6. Sawant RB, Bharucha ZS, Rajadhyaksha SB. Evaluation of hemoglobin of blood donors deferred by the copper sulphate method for hemoglobin estimation. Transfus Apher Sci. 2007;36(2):143-8.
7. Dobson. M. World Health Organization Haemoglobin Colour Scale. A practical answer to a vital need. Bulletin of the World Health Organization, 1995;73:369-73.
8. Lewis SM, Stott G J, Wynn KJ. An inexpensive and reliable new haemoglobin colour scale for assessing anaemia. J Clin Pathol 1998;51: 21-24.
9. Bates I, McKew S, Sarkinfada F. Anaemia: A Useful Indicator of Neglected Disease Burden and Control. Plos Med 2007;4(8):1285-1290.
10. Assessing the iron status of populations. Second edition. Including literature reviews. Report of a Joint World Health Organization/Centers for Disease Control and Prevention Technical Consultation on the Assessment of Iron Status at the Population Level, Geneva, Switzerland, 6–8 April 2004.
11. Kim MJ, Park Q, Kim MH, Shin JW, Kim HO. Comparison of the accuracy of the noninvasive hemoglobin sensor (NBM-200) and portable hemoglobinometer (HemoCue) with an automated hematology analyzer (LH500) in blood donor screening. Ann Lab Med 2013; 33(4): 261–267.
12. WHO/UNICEF/UNU. Iron deficiency anemia: assessment, prevention and control. A guide for programme managers. Geneva, Switzerland: World Health Organization; 2001.
13. Pasricha S-R, drakesmith, H, Black J, Hipgrave D, Biggs B-A. Control of iron deficiency anemia in low and middle-income countries. Blood. 2013;21(14): 2607-2617.
14. Part III. Vitamins and minerals. In Otten JJ, Hellvwig JP, Meyers LD eds. Dietary reference intakes: The essential guide to nutrient requirements. Washington DC: The National Academic Press; 2006.
15. Gera T, Sachdev HP, Nestel P, Sachdev SS. Effect of iron supplementation on haemoglobin response in children: systematic review of randomised controlled trials. J Pediatr Gastroenterol Nutr 2007;44(4):468-86.
16. Dong C, Ge P, Ren X, Wang J, Fan H, Yan X, Yin S-A. Prospective study on the effectiveness of complementary food supplements on improving status on elder infants and young children in the areas affected by Wenchuan earthquake. PLoS One 2013;8(9): e72711.
17. WHO. Haemoglobin concentrations for the diagnosis of anemia and assessment of severity. Vitamin and mineral nutrition information system. Geneva. World Health Organization, 2011 (WHO/NMH/NHD/MNM/11.1).

GPM432INT 170210

HemoCue AB | Box 1204 | SE-262 23 Ängelholm | Sverige
Tel: 077 570 02 10 | Fax: 077 570 02 12 | info@hemocue.se | hemocue.com