Review of the

Haemoglobin Colour Scale

Report of an informal consultation

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WHO headquarters, Geneva, Switzerland
Welcome address
Steffen Groth, WHO Department of Essential Health Technologies
Anaemia remains a major public health issue, although it can be tackled through effective interventions, particularly the timely measurement of haemoglobin in vulnerable populations. Essential health technologies can help to reach the United Nations Millennium Development Goal to reduce maternal and infant mortality. The place of the Haemoglobin Colour Scale within the various tools available needs to be determined.

Presentations

Introduction
Yvan Hutin, WHO Department of Essential Health Technologies
There is no "one fits all" intervention to control anaemia. WHO supported the Haemoglobin Colour Scale to fill the need for an inexpensive, simple device to measure haemoglobin levels in resource-poor settings. An initial evaluation shows that the introduction of the tool in developing countries has been suboptimal. This consultation has been convened to develop a consensus on the following issues:

1. the sensitivity and specificity of the HbCS;
2. the operational research agenda:
3. the role of the HbCS in an overall strategy to prevent and control anaemia;
4. the level of support that WHO should provide to assess further and/or promote the Scale.

The Department of Essential Health Technologies (EHT) invited all WHO programme areas that need to measure haemoglobin to discuss these issues.

Historical perspective
Kay Bond, WHO Department of Essential Health Technology
About 50% of pregnant women in developing countries are anaemic. The need for an appropriate device to detect anaemia in resource-poor setting was identified as far back as 1975.

The Tallqvist concept of comparing the colour of a drop of blood against pre-set values had both advantages (inexpensive, quick, simple and portable) and disadvantages (e.g. reliability of colours and blotting paper, problems interpreting the results). Thus, research was conducted during 1991-1995 to see if modern chromatography and spectrophotometry could solve these issues. The expected characteristics of the device were that it had to be reliable as a preliminary screening test, durable, require no external agents – e.g. electricity – and easy to use by staff with no formal training. Initial research results suggested a sensitivity of 95% and a specificity of 99.6% for the diagnosis of severe anaemia. Clients liked it, increasing the likelihood of compliance.

To start the production of the HbCS, an external tender was issued, to which only one manufacturer expressed interest, resulting in a four-year, renewable licence agreement with Copack GmbH that expires September 2004. In 2001, the HbCS became commercially avail-
able. Launch promotional activities were undertaken by WHO in collaboration with its partners, although this was hindered by restrictions on WHO promotion of a commercial product. Several options are available to procure the product. The basic kit containing the Scale, instructions and 200 test strips costs approx. €7.70. A version with 1000 tests is €19.80 and a refill box containing 2000 test strips is €29.76. It is also possible to procure the Scale with matching quantities of lancets in line with the bundling principle, to ensure the safety of all finger pricks. * This makes the cost per test very reasonable at approx. US$0.01. However, distribution and freight costs, as well as potential government levies, significantly increases this cost. Ways to reduce these have included placing the product on the UNICEF standard products list.

With diminishing sales in the absence of WHO marketing, difficulties for countries to find relevant information, and questions over the viability of the product, it is now timely to revisit the HbCS as a tool and determine the level of support that WHO should provide to this product, either in the area of evaluation or in the area of promotion.

Review of studies on the HbCS

*Imelda Bates, Liverpool School of Tropical Medicine*

**Background**

A systematic review was commissioned on studies carried out that compared the HbCS to a reference method.

**Methods for the review**

Studies were identified from the WHO bibliography, cited references, e-searches and personal contacts. Data was abstracted from papers describing original studies using a standardized data collection instrument that had been peer-reviewed. The quality of the studies identified was assessed against guidelines for assessing diagnostic tools. Studies kept in the analysis had to (1) specify inclusion and exclusion criteria, (2) explain withdrawals, (3) use a simultaneous analysis of samples, (4) be blinded and (5) include a reality check for real life use. It was not possible to combine estimates of sensitivity and specificity because (1) they were markedly variable, (2) the prevalence of anaemia differed substantially and (3) the cut-off values differed substantially. Results were presented in two tables. One includes the study characteristics and the second is about the results.

**Description of studies**

A total of 12 studies were included, six of which were conducted in sub-Saharan Africa. Three studies from the WHO bibliography were excluded. Cut-off values were different for non-anaemic or mild, moderate, severe and very severe anaemia. WHO does not have standardized cut-off values to define various levels of anaemia, largely because the needs are different according to the specific programme area. In addition, normal haemoglobin levels are age-dependent. The prevalence of anaemia varied between 5% and 85%. The higher the prevalence of anaemia, the more the health worker is looking to identify it. The amount of training required and the manner to handle intermediate results were generally not docu-

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* "Bundling" refers to the inclusion of the costs of auto-disable syringes and safety boxes in the costs of good quality vaccines provided by donors and lenders as described in the WHO/UNICEF/UNFPA/IFRC 1999 policy statement. "Bundling" has no physical connotation and does not imply that items must be "packaged" together.
Informal Consultation on the HbCS

Figure 1. Relationship between sensitivity, specificity and anaemia prevalence

0.00 0.20 0.40 0.60 0.80 1.00
Anaemia prevalence

Five studies compared the Colour Scale with a clinical diagnosis alone. In all studies, workers were blinded to the results of the anaemia test conducted using the other method. Some studies excluded poorly performing health care workers, which limits the capacity of these studies to determine the value of the test in the real world. Other deficiencies included a lack of information on the selection criteria use, the completeness of the sample and miscalculated statistics in one study.

Data analysis
The ability of the HbCS test to detect any anaemia was 23-97% with a specificity of 47-98%. For severe anaemia, sensitivity ranged from 50% to 94% with a specificity of 86-99%. The relationship between specificity and sensitivity according to the prevalence of anaemia is shown in Figure 1.

Five studies suggested that the Scale is a more sensitive method that a clinical assessment alone for the diagnosis of anaemia, particularly for mild to moderate anaemia and when the prevalence of anaemia is high, although the two methods do not differ in terms of specificity.

Cost considerations
A comparative study carried out in Malawi of seven methods to measure haemoglobin projected the total cost of using the HbCS for an annual workload of around 6000 tests, to be US$0.12 / test. The total cost of using the HemoCue for the same workload was US$0.75. In contrast to other methods for Hb measurement that have a cost / procedure that goes down with the number of procedures, the cost of HemoCue goes up because of the significant cost of the cuvettes.

Conclusions
Overall, the HbCS is more sensitive than a clinical diagnosis to screen for anaemia. However, specificity is problematic. Since most of the studies have been carried out under ideal conditions, more real life studies using a standardized protocol would collect concrete data on the tool in actual use. Such assessments would be invaluable since there is a clear need for such a tool from a clinical perspective. Finally, the Haemoglobin Colour Scale has the advantage of

† The HbCS measures levels of haemoglobin at 2g/dl levels; colours falling between these two values are recommended to be estimated at the intermediate value.
being popular among patients and health care providers. This may have a positive impact on health outcomes (e.g., reminding providers to screen for anaemia, increasing the likelihood of patients attending referral visits, introducing the idea of requested laboratory testing) that could be included in future evaluations.

**Need for measuring haemoglobin in various programme settings and usefulness of the HbCS**

**Blood Transfusion**  
*Neelam Dhingra, WHO Department of Essential Health Technologies*  
Haemoglobin levels are measured to (1) screen donors before donation and (2) screen patients before transfusion. According to the WHO Global Database on Blood Safety, the proportion of countries that perform pre-donation haemoglobin testing on all blood donors is 69%. The recommended cut-off point for anaemia in blood donors is 12.5 g/dl, which theoretically excludes the HbCS as a means to screen potential donors. A multicentre study has been designed to evaluate whether a cut-off value of 12 g/dl would affect the safety of blood donation, as it would increase significantly the quantity of available blood, particularly in developing countries. Funds are still lacking to carry out the study.

**Integrated Management of Child Illnesses (IMCI)**  
*Martin Weber, WHO Department of Child and Adolescent Health*  
The generic IMCI guidelines use the clinical assessment of palmar pallor as the sole means to screen for anaemia, since anaemia can be detected in this way with acceptable sensitivity and specificity. The evidence for performance of these clinical guidelines was derived from studies in inpatient and outpatient settings in the Gambia, Kenya, Bangladesh and Uganda, and are summarized in the IMCI adaptation guide. Furthermore, a study in Ethiopia showed that of 2,540 children age 2 months up to 5 years presenting to a rural health centre, the presence of a clinically detected pallor correlated with a haemoglobin of less than 8 g/dl with a sensitivity of 95% and a specificity of 68% while severe anaemia of haemoglobin less than 5 g/dl was detected clinically in 50% of cases with a specificity of 95% (Trop Med & Int Hlth 2000, 5(11) p637). Detection of mild and severe anaemia is more difficult using clinical signs alone and hence a study is being carried out to evaluate use of the HbCS within the current IMCI algorithm. Results should allow health workers to decide on whether to transfuse based on both clinical pallor and the HbCS. The IMCI clinical guideline addresses iron intakes through routine assessment and counselling on feeding of all children less than 2 years and older children with signs of malnutrition.

**Nutrition**  
*Ines Egli, WHO Department of Nutrition for Health and Development*  
The WHO department of nutrition is managing a global database on anaemia based on Hb levels (measured by various methods but not including HbCS). The anaemia prevalence in children is estimated to be between 40 and 50% and overall two billion people are estimated to be anaemic. A joint WHO/UNICEF statement has just been issued on the subject of the multifactorial aetiology of anaemia and the need for an integrated approach.

The Nutrition department is moving away from using anaemia as a proxy for the assessment of iron deficiency. A recently organized joint WHO/CDC technical consultation proposes to assess iron status by using haemoglobin levels in combination with transferrin receptor and serum ferritin. Exact measurement of haemoglobin is required and HbSC cannot replace any of the established methods for this purpose.
Malaria

Jane Crawley, WHO Department of Roll Back Malaria

Results obtained from malaria intervention studies provide compelling evidence that malaria contributes substantially to anaemia in endemic regions. For this reason, there is considerable current interest in using anaemia as an indicator to monitor the effectiveness of malaria control programmes. Accuracy of measurement is clearly important in these situations, and use will be made of data arising from nationally representative Demographic and Health Surveys (DHS), which use HemoCue as the haemoglobin measurement tool, in view of its well-validated, accurate results and user-friendliness.

For the clinical management of anemia, the choice of measurement tool varies at different levels of the health service. Since laboratory facilities are rarely available in peripheral health-care settings, the diagnosis of anaemia is generally made on the basis of clinical signs. In these settings, the HbCS may prove a valuable alternative. Laboratory facilities are likely to be available at the referral level facility, and here the method used to measure haemoglobin should have a high degree of accuracy, since clinical decisions made on the basis of inaccurate haemoglobin measurement may lead to inappropriate prescription of blood transfusion. In these settings HemoCue, or a tool of comparable accuracy, should be used.

Clinical Procedures

Meena Cherian, WHO Department of Essential Health Technologies

Measurement of Hb level is a regular procedure before surgery, as one-third to a half of surgical patients are anaemic due to their illness. Thus the HbCS could have a role in assessing patients for surgery in the outpatients department. The HbCS can detect a level of anaemia that would suggest that elective surgery be postponed while the patient is placed on treatment. In addition, post-operative anaemia may occur in up to 90% of patients. Therefore, after surgery and before discharge, the HbCS could be useful to screen patients for anaemia. However, the HbCS cannot be a reliable guide to decide for the use of blood transfusion.

HIV/AIDS

Matthew Chersich, WHO Department of HIV/AIDS Treatment, Care and Prevention

The WHO 3 by 5 Initiative target is to treat 3 million people with antiretroviral therapy by the end of 2005. Simplified and standardized guidelines have been developed. Clinical and laboratory monitoring of ARV therapy are designed for implementation at the community health centre and/or district hospital. The first-line treatment regimens for HIV infection include stavudine (which does not cause anaemia) or zidovudine (which does). Most commonly, because of the availability of fixed dose combinations, stavudine is more likely to be used than zidovudine. Thus, because zidovudine is not systematically used, WHO does not necessarily recommend Hb measurement before HIV treatment. Countries, for their part, may adapt WHO guidelines and require that Hb be measured before treatment. In terms of monitoring treatment schedules that include zidovudine, the measurement of Hb is indicated on a "symptom-directed" basis only. However, with Hb measurement only indicated in the case of symptoms, patients are not tested before they have severe anaemia causing symptoms (e.g., breathlessness). If Hb measurement is indicated in case of signs, then patients may benefit from the HbCS because clinician diagnosis of anaemia is known to be unreliable.

It may be necessary to change the antiretroviral regimen that a person is receiving because of either toxicity or treatment failure. When toxicity is related to an identifiable drug in the regimen, the offending drug can be replaced with another drug that does not have the same side-effects, e.g. substitution of stavudine for zidovudine (for anaemia). A Hb test with a low specificity (leading to a high proportion of false positive diagnoses of anaemia), could result
in unnecessary drug substitution. Changes in antiretroviral drugs regimen, though often necessary, can result in several potential adverse consequences including compromising future treatment options. WHO does not recommend a specific test for the measurement of Hb before or during HIV treatment, which can be problematic at the district level.

Making Pregnancy Safer

*Rita Kabra, WHO Department of Reproductive Health and Research*

Anaemia is a major cause of maternal and perinatal mortality and morbidity. The WHO Making Pregnancy Safer programme issued a guideline on essential care at primary health care level. This recommends routine, universal screening for anaemia of pregnant women as well as women postpartum where iron deficiency anaemia is prevalent. The diagnostic method could be clinical or – preferably – using a test (the guideline does not mention which one). Based upon the level of Hb or, in its absence, signs and symptoms, women are classified into three categories that require specific management: severe anaemia which is managed according to the stage of pregnancy/postpartum and may require emergency management and admission as an in-patient; moderate anaemia treated by a double dose of iron/folate; and routine supplementation with iron and folic acid in the absence of anaemia.

This guideline is supplemented by an Adaptation Guide that includes technical and financial details on the various diagnostic tests available (including the HbCS) that should assist in the choice of a specific screening method. From the MPR perspective, the HbCS has been found a useful preliminary method to screen for anaemia to supplement a clinical and biological diagnosis, and not a test to confirm a clinical diagnosis of anaemia. A second MPR guideline – Managing Complications for Pregnancy and Childbirth – is available on the clinical management of severe anaemia in women, once diagnosed.

Use of the HbCS in developing counties: Mongolia as a case study

*Dr Ya. Buyanjargal, Department of Quality Assurance, Ministry of Health, Mongolia*

Mongolia is a landlocked country with a very young population of 2.4 million. The antenatal care coverage is high (over 95%), but difficult geographic conditions make it necessary to identify high risk women so that they may be referred early to a maternity waiting home to wait for delivery under safe circumstances.

Figure 2: Maternal mortality trend in Mongolia, 1992-2003

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1 Pregnancy, Childbirth, Postpartum and newborn Care
The major causes of maternal mortality are given as general complications during pregnancy or during labour and delivery (see Figures 2 and 3 for maternal and infant mortality ratios over time).

**Use of the HbCS in Mongolia**

In 2002, 600 Scales were sent to Mongolia using funds made available by the WHO Office of the Western Pacific region. A ministerial order was distributed to all provinces, recommending the inclusion of the HbCS in the list of supplies of health care facilities. The principal usefulness of the HbCS was seen as screening for anaemia in material health clinics, particularly in remote areas. Most provinces organized group training of district hospital health workers (soum doctors) using the instructions that had been translated into Mongolia.

![Figure 3: Infant mortality ratio in Mongolia, 1999-2003](image)

**Achievements and challenges**

The device has had widespread use for the screening of anaemia and the identification of patients requiring treatment. Today, 90% of the supplies have been used and a new order will be placed, although funds to support this have not yet been identified. Overall, the Mongolian experience has been very positive for the early detection of anaemia in pregnant women, leading to better treatment and management of anaemia, particularly at the primary health care level. It is also useful because it can be distributed at low cost and requires no major investment. Interestingly, the prevalence of anaemia in Mongolia decreased from 40% in 1995 to 22% in 2003 among pregnant women. Challenges include the need for more practice, the training of midwives and application of the Scale in other conditions. Since the use of the HbCS has been extensive in Mongolia, it could be a good setting for an evaluation.
**Recommendations**

**Policy**

The HbCS deserves continued attention from public health specialists because:

- a. there are no other inexpensive methods to diagnose anaemia at the primary health care level in resource-limited settings;
- b. some studies suggest that the HbCS may perform better than a clinical diagnosis of anaemia in certain circumstances.

WHO should continue defining the role of the HbCS in public health, through assisting operational research, increasing its availability in developing countries, and conducting information, education and communication (IEC) activities to ensure its safe, appropriate and cost effective use.

**Operational research**

WHO's Essential Health Technologies department will develop terms of reference ("check-list") for studies comparing the performance of the HbCS to that of clinical diagnosis of anaemia and studies evaluating the impact of the HbCS on outcome indicators (e.g., number of pregnant women referred for treatment, baby weights).

The WHO Anaemia Advisory Group will consolidate the various programme-specific criteria for mild, moderate, severe and very severe anaemia into a WHO document listing the various cut-off values used to define levels of anaemia based according to various clinical settings. This document should reflect the lack of evidence in some areas and the fact that this is work in progress.

WHO will use settings where the HbCS has been or will be widely introduced (e.g., Mongolia) to conduct field evaluation / experience recovery in real size.

**Access**

WHO's Essential Health Technologies department will identify public health partners (e.g., UNICEF) who could increase the availability of the HbCS for ministries of health who express a need for it.

**Promoting cost effective and appropriate use**

WHO's Making Pregnancy Safer programme will examine options to determine whether the arrangements (including training) made to introduce the HbCS in Mongolia were sufficient to ensure its appropriate use.

Efforts should be made to prevent cross infection by ensuring that lancets are available to be used with the HbCS.

WHO will re-convene a follow up meeting when new information is available to review progress on this agenda.
List of participants

Dr BATES Imelda, Liverpool School of Tropical Medicine, Pembroke Place, Liverpool L3 5QA, UK. Tel: +44 151 705 3115. E-mail: ibates@liverpool.ac.uk

Dr BUYANJARGAL, Ya, Quality Assurance Department, Directorate of Medical Services, Government Implementing Agency, Ministry of Health, Ulaanbaatar, Mongolia. Tel: 976-99190750. E-mail: buyanaa@yahoo.com

Dr LEWIS Mitchell, Department of Haematology, Hammersmith Hospital, London W12 0NN, UK. Tel: +44 208 946 2727. E-mail: smlenl@blueyonder.co.uk

Dr STOTT Gordon, Passagay, 74500 Saint Paul en Chablais, France. Tel: +33 4 50 75 3636

WHO Secretariat

Dr GROTH Steffen, Director, Department of Essential Health Technologies. Tel: +41 22 791 4387. E-mail: groths@who.int

Dr de BERNIS Luc, Medical Officer, Making Pregnancy Safer, Department of Reproductive Health and Research. Tel: +41 22 791 2187. E-mail: debernisl@who.int

Ms BOND Kay, Technical Officer, Devices and Clinical Technology, Department of Essential Health Technologies. Tel: +41 22 791 2262. E-mail: bondk@who.int

Dr CHERIAN Meena, Medical Officer, Clinical Procedures, Department of Essential Health Technologies. Tel: +41 22 791 4011. E-mail: cherianm@who.ch

Dr CHERSICH Matthew, Technical Officer, Prevention, Department of HIV/AIDS. Tel: +41 22 791 4217. E-mail: chersichm@who.int

Dr CRAWLEY Jane, Medical Officer, Roll Back Malaria. Tel: +41 22 791 3214. E-mail: crawleyj@who.int

Dr EGLI Ines, Technical Officer, Department of Nutrition for Health and Development. Tel: +41 22 791 3554. E-mail: eglii@who.int

Dr HUTIN Yvan, Acting Coordinator, Devices and Clinical Technology, Department of Essential Health Technologies. Tel: +41 22 791 3431. E-mail: hutiny@who.int

Dr KABRA Rita, Technical Officer, Making Pregnancy Safer, Department of Reproductive Health and Research. Tel: +41 22 791 3396. E-mail: kabrar@who.int

Ms MAS Françoise, Procurement Officer, Contracting and Procurement Services, Department of Infrastructure and Logistics Services. Tel: +41 22 791 1254. E-mail: masf@who.int

Dr WEBER Martin, Medical Officer, Department of Child and Adolescent Health and Development. Tel: +41 22 791 2603. E-mail: weberm@who.int