Adjusting Hemoglobin Values in Program Surveys

Population-based studies show that the distribution of hemoglobin values is normal, with a standard deviation of 10 percent among apparently normal people and about 7 percent when those with iron deficiency anemia are excluded.[1] Hemoglobin values, however, vary with age, sex, and stage of pregnancy, and they are also affected by ethnicity, altitude, and smoking. For these reasons, it is important to adjust for these factors in population-based surveys when interpreting hemoglobin values.

This document describes when and how to adjust individual hemoglobin values in population-based surveys for the above factors.

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Children, Nonpregnant Women, and Men

For full-term infants, hemoglobin concentrations at birth are higher than at any other time in life, reflecting fetal adaptation to the oxygen-deficient environment of the uterus.[2] In the first 2 months of life, hemoglobin concentration falls, reaching its lowest point at the age of about 2 months. This is thought to be due to the sudden decrease in erythropoiesis, or red cell production, as a result of the increased delivery of oxygen to tissues.[3] Thereafter, hemoglobin concentration rises gradually to the age of about 6 months, after which it levels out. The concentration of hemoglobin in blood normally increases as children get older. During adolescence hemoglobin production increases even more as a result of accelerated growth. For these reasons, age-specific values must be used to define anemia in children. Also, men have higher hemoglobin concentrations than women because of testosterone, which results in both larger body size and larger erythrocyte mass.[4]

Table 1. Hemoglobin cutoffs to define anemia in people living at sea level

Age or sex group	Hemoglobin below (g/L)
Children	
6 months to 5 years	110
5 to 11 years	115
12 to 14 years	120
Nonpregnant females > 15 years	120
Men > 15 years	130

The World Health Organization defines anemia as a hemoglobin value below the age-specific 2.5th percentile value in a nonanemic distribution. The accepted cutoffs[5] to define anemia in people living at sea level are shown in Table 1.

Pregnant Women

Both plasma volume and red cell mass expand in pregnancy. Because the expansion in plasma volume is greater, the net result is that hemoglobin is diluted. In women with adequate iron nutrition, hemoglobin concentration starts to fall during the early part of the first trimester, reaches its lowest point near the end of the second trimester, and then gradually rises during the third trimester.[1] Trimester-specific adjustments[6] have been developed and are shown in Table 2 along with the generic value used when the trimester is unknown.[5]

Table 2. Hemoglobin adjustment for pregnancy in women living at sea level

Stage of pregnancy (trimester)	Hemoglobin (g/L)
First	−10
Second	−15
Third	−10
Trimester unknown	−10

Ethnicity

Data from the United States show that healthy people of African extraction of all age groups at all times, except during the perinatal period, have hemoglobin concentrations 5 to 10 g/L below those of whites and this difference is independent of iron deficiency and in some cases hemoglobinopathies and socio-economic factors.[7–11] Other US-based races including East Asians,[8] Hispanics,[12] Japanese,[13] and American Indians[14] have hemoglobin values similar to that for white Americans. The US Institute of Medicine[15] justifies adjusting the hemoglobin cutoff for children of African extraction below 6 years old downward by 0.3 g/L and that for adults of African extraction by 0.8 g/L on the basis that the hemoglobin values for Americans of African extraction are lower than those of other US-based populations of comparable iron status and also because doing so is consistent with the accepted definition of anemia as a hemoglobin concentration below the 2.5th percentile. The report goes on to say that using the lower cutoff value would result in fewer false-positive diagnoses of anemia, which would reduce the

Table 3. Hemoglobin adjustment for healthy people of African extraction living at sea level

	Hemoglobin (g/L)
Everyone	−10

likelihood of people being classified as failing to respond to treatment due to poor compliance or the anemia not being the result of iron deficiency. However, whether ethnic differences in hemoglobin concentrations exist in populations outside the USA, where the etiology of anemia is more complex, remains unknown. Based on the US data for healthy people of African extraction, and to achieve adequate sensitivity and specificity for screening purposes, WHO[5] indicates that hemoglobin concentrations be adjusted downward by 10 g/L in people of African extraction irrespective of age, as shown in Table 3.

Table 4. Hemoglobin adjustment for smokers

Amount smoked	Hemoglobin (g/L)
$^1/_2$–1 pack/day	+3
1–2 packs/day	+5
>2 packs/day	+7
All smokers	+3

Smoking

Hemoglobin concentration increases in smokers because the inhaled carbon monoxide results in increased carboxyhemoglobin, which has no oxygen-carrying capacity. To compensate, hemoglobin levels increase. To take into account the resulting elevated hemoglobin concentration, the U.S. Centers for Disease Control and Prevention developed a smoking-specific hemoglobin adjustment to define anemia in smokers.[6] Table 4 shows the values to add to normal hemoglobin cutoffs to define anemia in smokers. Alternatively, these values can be subtracted from observed hemoglobin values.

Table 5. Hemoglobin adjustments (g/L) for altitude

Altitude (m)	Hemoglobin (g/L)
<1000	0
1000	1
1500	4
2000	7
2500	12
3000	18
3500	26
4000	34
4500	44
5000	55
5500	67

Note: The numbers in red are extrapolated values.

Altitude

At elevations above 1000 m, hemoglobin concentrations increase as an adaptive response to the lower partial pressure of oxygen and reduced oxygen saturation of blood.[16] The compensatory increase in red cell production ensures that sufficient oxygen is supplied to tissues.

The CDC's Pediatric Nutrition Surveillance System used data from 2- to 5-year-old children with little or no iron deficiency from clinics at 1200 to 3000 m elevation to develop a curve that describes hemoglobin changes with altitude.[6] The progression is curvilinear, with the increase in hemoglobin concentration becoming steeper as altitude increases. The data in Table 5, which is based on the equation below, show the adjustment values in altitudes at 500-m intervals. (The altitude at which the blood sample is taken is rounded up or down to the nearest 500 m.)

$$\mathrm{Hb} = -0.32 \times (\text{altitude in meters} \times .0033) + 0.22 \times (\text{altitude in meters} \times .0033)^2$$

Data from iron-replete Ecuadorian children 6 to 59 months of age living at altitudes ranging from sea level to 3400 m were used to develop another hemoglobin adjustment curve.[17] The latter is based on a different equation (Hb = 6.83 × exp [0.000445 × altitude in meters] + 113.3), which gives values 2 to 3 g/L higher than the CDC values (see the Appendix Table). These higher values were ascribed to the smaller sample size in the Ecuador data set (R. Yip, personal communication, 1995). The investigators in the Ecuador study also assumed that the association between hemoglobin concentration and altitude is exponential from sea level, but there is no biological evidence that hemoglobin concentration varies at altitudes below 1000 m. Given the latter fact, and the fact that for practical purposes the small differences in hemoglobin concentration at the different altitudes are not critical, the CDC adjustment factors would appear to be more appropriate.

In adults, the hemoglobin concentration of Peruvian men was measured at a few high altitudes by Hurtado et al.[16] Their findings were similar to the predicted values obtained by the CDC (see the Appendix Table). In the absence of other data, the CDC values can be applied to adult men.

Cohen and Hass[18] used data from pregnant Bolivian women residing at altitudes between 1000 and 4800 m to determine adjustments for estimating the prevalence of anemia in pregnancy at high altitude. They derived a curve (Hb = 120 + 16.3 × [exp (0.00038 × (altitude in meters – 1000)]) that was theoretically grounded on the nonlinear shape of the oxygen disassociation curve. An important assumption in the Cohen and Hass model was that pregnancy plasma volume expansion at high altitude is similar to that at sea level, although, as the authors noted, it is not clear whether this is the case.[19,20] The Cohen and Hass values were similar to those of the CDC, although, unlike the Ecuador data set, they were 2 to 4 g/L lower depending on the altitude (see the Appendix Table). Again, because of the similarity between these values and the CDC values, it is recommended that the CDC values also be used for pregnant women.

How to Adjust Hemoglobin Concentrations for Different Populations at Different Altitudes

The adjustment values in Table 5 can be used in one of two ways:

- to add the correction value to the sea-level cutoff values shown in Table 1, or
- to subtract the adjustment from the measured hemoglobin concentration at the relevant altitude—to the nearest 500 m—to get the sea-level value.

The above is important because the WHO hemoglobin cutoffs for anemia refer to sea-level values.

Along with the pregnancy and race adjustments, smoking and altitude adjustments are additive[6] to the values given in Table 1. For example, the cutoff hemoglobin value for a 2-year-old child of African extraction at 700 m would be:

110 (2-year-old) – 10 (ethnicity) + 0 (altitude) = 100 g/L,

whereas that for a pregnant Asian woman living at 4200 m and smoking half a pack of cigarettes a day would be

120 (nonpregnant) – 0 (ethnicity) + 34 (altitude) + 3 (smoking) = 157 g/L.

Individual observed values are adjusted by subtracting the appropriate values for smoking and altitude. For example, a 3-year-old living at 1800 m whose hemoglobin measurement is 114 g/L would be

$$114 \text{ (observed hemoglobin)} - 7 \text{ (altitude)} = 107 \text{ g/L at sea level.}$$

Similarly a pregnant woman who smokes and whose hemoglobin measurement is 105 g/L at 3100 m would be

$$105 \text{ (observed hemoglobin)} - 3 \text{ (smokes)} - 18 \text{ (altitude)} = 84 \text{ g/L at sea level.}$$

Appendix Table. Hemoglobin adjustments (g/L) for altitude according to different studies

	Children		Men	Pregnant women
Altitude (m)	CDC[6]	Dirren et al.[17]	(Hurtado et al.[16])	(Cohen and Hass[18])
0	0	0		
1000	1	4		0
1500	4	6	6	3
2000	7	10		7
2500	12	14		11
3000	18	19		16
3500	26	26	26	23
4000	34	34		31
4500	44	44	44	40
5000	55	56	56	51
5500	67	72		65

Note: The numbers in red are extrapolated values.

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About INACG

The International Nutritional Anemia Consultative Group (INACG) is dedicated to reducing the prevalence of iron deficiency anemia and other nutritionally preventable anemias worldwide. It sponsors international meetings and scientific reviews and convenes task forces to analyze issues related to etiology, treatment, and prevention of nutritional anemias. Examination of these issues is important to the establishment of public policy and action programs.

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