Reply to: [Comment to: Hepcidin: from discovery to differential diagnosis. Haematologica 2008; 93:90-7]

Olsson and Norrby clearly pointed out that estimation of iron contents in various compartment of the body is a difficult exercise in which often older literature is the basis of discussion. We agree that putative knowledge still needs critical reading before it is presented in new overviews. Their remarks concern the estimation of iron contents in erythrocytes and the body stores.

Figure 1 illustrating the major storage sites in our review is based on the information reported by Andrews[1] and Hentze *et al*.[2] Indeed, the indicated iron contents of 1800 mg in the erythrocytes results in an anemic hemoglobin level of 10.6 g/dL (6.6 mmol/L). We agree that a corrected level of 2500 mg (hemoglobin 14.8 g/dL; 9.2 mmol/L) could be a better reference value.[3-6]

Estimation of the body iron store turns out to be more complicated. The statement of Olsson and Norrby that our figure represented a patient with elevated iron storage is possibly premature. In our opinion three factors must be kept in mind when it comes to interpretation of iron stores.

First, one has to be sure what is meant by the term *iron stores*. It is not only liver iron (about 1000 mg),[1-4,7] but rather the sum of liver iron, bone marrow, and reticuloendothelial macrophages (about 1900 mg) which almost doubles the amount.

Second, what model is used to calculate body iron store? A rule of thumb that is often used in clinical practice describes that 1 μg/L serum ferritin represents 10 mg body iron[4] and is likely based on phlebotomy studies published by Walters *et al*. in 1973.[8] As a result, currently accepted reference values for serum ferritin ranging from 20 to 250 μg/L[9] represent 200 to 2500 mg body iron which fits with the *iron stores* in our figure. Next, Cook *et al*.[10] reported a serum ferritin-based calculation on 2,800 samples extracted from the NHANES II survey which results in body iron values ranging from 88 to 527 mg which is much lower compared to the values we depicted.

Further improvement of this method by integration of serum transferrin receptor values[11] measured in a subset of samples extracted from the NHANES III survey resulted in averaged body iron stores of 776±313 mg (±1 SD) in men which is higher than in previous studies. A third factor is the use of different methods and lack of standardization in ferritin and serum transferrin receptor analysis, due to the lack of a common standard and the use of diverse antibodies.[12,13] These aforementioned three factors illustrate the complexity and limits when results from different studies are compared or even referred to, especially those performed in the early 70's where ferritin measurement made its entry in the clinical laboratory. They also show that basal knowledge lacks clear consensus which might lead to false interpretations.

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