Q & A Column, 8/14

Editor: Frederick L. Kiechle, MD, PhD

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Submit a Question

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Q. Is there a trough and crest occurrence with blood testosterone levels, or is it like thyroid testing, where one's result is the total of the previous several days?

A. Most hormones are influenced by many physiological factors, and testosterone is no exception. Perhaps the most significant effect described is lowered levels of testosterone observed in men in response to stress, both physical and psychological. But there is also a diurnal rhythm (in both men and women) linked to sleep patterns. Blood testosterone levels are highest upon waking (i.e. for most people, in the morning), decline during the day, and then lowest just before falling asleep. Although this would seem to indicate that a morning testosterone level would be the best specimen, most researchers believe using afternoon samples is the most reliable approach. It is also not uncommon to draw several specimens, sometimes pooling them and performing one testosterone determination, to reduce the variability that may be seen from day to day.

- Axelsson J, Ingre M, Akerstedt T, Holmbäck U. Effects of acutely displaced sleep on testosterone. *J Clin Endocrinol Metab.* 2005;90:4530–4535.

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Q. What is the relationship between the presence of moderate to many spherocytes and the MCHC parameter? We always thought cases that show spherocytes on the blood smear are usually associated with high MCHC. We had a case of autoimmune hemolytic anemia with moderate spherocytes, but the MCHC was normal.

A. Even though there are now flow cytometry methods for directly measuring RBC hemoglobin concentration, mean corpuscular hemoglobin concentration (MCHC) is most commonly calculated by dividing the hemoglobin level by the hematocrit and multiplying by 100. Resulting values are expressed as grams of hemoglobin per deciliter of red cell volume. High MCHC values result from a disproportionate elevation in hemoglobin

concentration relative to hematocrit. Because of the relative stability and narrow range of MCHC in normal and most abnormal circumstances (31–35 g/dL), laboratories use elevated MCHC values as a quality control indicator to trigger investigation into the presence of artifacts that result in underestimating RBC and hematocrit or overestimating hemoglobin level. Artifacts are most commonly due to RBC agglutination, lipemia, very high WBC, or excessive free plasma hemoglobin.

A high MCHC value in immune hemolytic anemia (IHA) is commonly due to effects of RBC agglutination from cold reactive antibodies, but may also be due to either hemolysis from the presence of complement-fixing antibodies on RBCs or to removal of immunoglobulin-coated RBC membrane by splenic macrophages (i.e. splenic "conditioning"). Other clinical disorders associated with elevated MCHC values include hereditary spherocytosis (HS), rare cases of congenital dyserythropoietic anemia type II, and rare cases of the dehydration form of stomatocytosis known as xerocytosis.

In HS, MCHC values overlap with the normal population and are not always elevated. In one study of non-splenectomized pediatric patients with HS, MCHC >35 g/dL was present in only 70 percent of the patients.[1] Unpublished data from my laboratory for 38 HS patients with positive osmotic fragility test results showed MCHC ranging from 32.4–38.1 g/dL. In a South American study, mean MCHC was 35.67 g/dL (± 1.33 g/dL) in HS patients and 33.48 g/dL (± 0.68 g/dL) in normal individuals.[2] Another study showed that MCHC values overlapped with 37 normal control samples and that both MCHC and RBC membrane loss are less in IHA than in HS.[3] Also, MCHC linearity may fall off with impedance-based measures when values exceed 35 g/dL,[4] indicating that instrument and methodologic variables are important considerations and may account for differences in MCHC between labs.

1. Michaels LA, Cohen AR, Zhao H, Raphael RI, Manno CS. Screening for hereditary spherocytosis by use of automated erythrocyte indexes. *J Pediatr*. 1997;130(6):957–960.
2. Eberle SE, Sciuccati G, Bonduel M, Diaz L, Staciuk R, Torres AF. [Erythrocyte indexes in hereditary spherocytosis]. *Medicina (B Aries)*. 2007; 67:698–700.
3. 3. Da Costa L, Mohandas N, Sorette M, Grange MJ, Tcher-nia G, Cynober T. Temporal differences in membrane loss lead to distinct reticulocyte features in hereditary spherocytosis and in immune hemolytic anemia. *Blood*. 2001;98(10):2894–2899.
4. Mohandas N, Kim YR, Tycko DH, Orlik J, Wyatt J, Groner W. Accurate and independent measurement of volume and hemoglobin concentration of individual red cells by laser light scattering. *Blood*. 1986;68(2):506–513.

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