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Letter to the Editor

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Letter to the Editor from Laidlaw et al: "Erythrocytosis in a Large Cohort of Transgender Men Using Testosterone: A Long-Term Follow-Up Study on Prevalence, Determinants, and Exposure Years"

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Although it is laudable to attempt to quantify the risk of erythrocytosis due to the administration of exogenous testosterone to transgender males, the methodology of the authors leads to a significant undercount of patients who may ultimately be at risk for cardiovascular events. Studies of transgender males taking testosterone have shown up to a nearly 5-fold increased risk of myocardial infarction relative to females not receiving testosterone (1).

The World Health Organization defines polycythemia in natal girls as a hematocrit greater than 48% (2). The Framingham study of the general population found the upper quintile of hematocrit levels in women to be greater than 45% (3). In the younger adult subset (aged 35-64 years) of this group was found a significantly increased risk of cardiovascular disease, coronary heart disease, and death due to both even after adjusting for age, systolic blood pressure, serum cholesterol, glucose intolerance, smoking, and left ventricular hypertrophy by electrocardiogram.

The authors' use of the erythrocytosis cutoff point for natal boys of 50% in their cohort misses a significant portion of transgender males who may be at increased risk of cardiovascular disease and death possibly associated with erythrocytosis secondary to exogenous testosterone.

Erythrocytosis in transgender males is highly likely to be directly related to an iatrogenic effect of high-dose androgens that results in serum testosterone levels for transgender males (300-1000 ng/dL) far exceeding the upper reference range of endogenous testosterone levels of natal girls (10-50 ng/dL) (4).

The root cause of this flaw in thinking about diagnostic ranges was exemplified in a response letter by Rosenthal et al claiming that gender identity determines the ideal physiologic range of cross-sex hormone levels (5).

Thus a psychological construct, the "gender identity," is imagined to affect physical reality and change a person's sex-specific laboratory reference ranges. This is clearly not the case, otherwise there would be no serious complications of high-dose androgen treatment in transgender males.

We believe that to help clinicians and patients to best assess erythrocytosis-related risks, diagnostic cutoff values for hemoglobin and hematocrit should be based on natal sex. The recent suggestion by Irwig "to provide both the male and female reference ranges for transgender patients" is a potential, though less optimal solution, as it will likely lead to confusion in assessing risk (6).

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It is well known that adolescents and young adults take more risks than any other age group in part because the adolescent brain is still developing (7). This suggests great caution in allowing adolescents to make their own decisions about cross-sex hormones. They and their parents should be afforded clear facts about potential complications such as erythrocytosis and related risks. Adolescents' limited ability to provide informed consent to treatment should be carefully considered so that optimal decisions may be made for their long-term health and wellness. This is particularly important as the numbers of adolescent females referred for gender incongruence and exposed to the iatrogenic risks of high-dose testosterone administration continues to rise (8).

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