To the Editor:

Recently, Beguin et al. described the variation of erythropoietin (Epo) production during pregnancy. Serum Epo concentrations were increased in pregnancy compared with nonpregnant controls; however, the concentrations of Epo found were considered to be relatively low for the degree of anemia. Similar conclusions were made earlier from data of a variety of clinical situations such as infectious syndromes and malignancy. In most of these conditions correlations between chronic inflammation and hypoferric anemia together with increased Epo were observed. Epo response by the kidney was usually considered to be inappropriate and insufficient for correcting anemia. We think that this conclusion requires some correction.

Erythroid progenitor cells are highly sensitive to Epo and, therefore, even a moderate increase of circulating Epo would initiate erythropoiesis in patients. For statistical reasons, anemia is very unlikely to develop in patients as long as Epo levels are higher than in controls. Anemia could only occur when responsiveness of erythroid progenitor cells to Epo is reduced. Indeed, it appears that erythropoiesis is inhibited in patients who have anemia despite increased Epo. Renal cells obviously respond to hypoxia. After examining data from patients with infections and malignancies, it turns out that activated T cells and increased amounts of endogenous cytokines such as interferon-γ are involved in the inhibition of erythropoiesis. A similar situation appears to exist in pregnancy; increased levels of the T-cell–derived cytokine interleukin-2 have been described, indicating activation of T cells.
pterin in pregnancy indicates the presence of endogenous interferon-γ. Thus, enhanced interferon-γ could be involved in the development of anemia in pregnancy.

In our view, a more appropriate conclusion from the data presented by Beguin et al. and, more generally, from studies showing decreased hematocrit or hemoglobin in the presence of increased Epo is that the kidney obviously responds to hypoxic conditions with Epo release. However, target cells seem to be less responsive to Epo in these studies than normally. It is no surprise then that in these situations exogenous administration of Epo to patients with infections or malignancy is able to induce erythropoiesis and to improve anemia.

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REFERENCES

Erythropoietin and decreased erythropoiesis in pregnancy [letter; comment]

D Fuchs, G Weiss, G Werner-Felmayer and H Wachter