RESEARCH LETTER

Parathyroidectomy and Improving Anemia

We have read with great interest the article written by Chow and coworkers[1] showing that anemia improved after total parathyroidectomy (PTX), especially in the patients who received therapy with human recombinant erythropoietin. As the mechanisms for the improvement were not considered in the article, we would like to share our results concerning increased erythropoiesis after PTX, even though they were obtained from an investigation of a small patient group.

Nine patients (5 men; mean [SD] age, 45.0 [15.4] years) who had been receiving regular hemodialysis for 76.8 [43.8] months were included in the study after subtotal PTX. All of them gave informed consent to participate in the study. Indication for PTX was based on clinical, biochemical, and radiological criteria.[2] Three patients (patients 6, 7, and 8 in the **Table**) were positive for hepatitis virus B or C. None of the patients had iron deficiency anemia or blood loss, and none of them were treated with human recombinant erythropoietin before or after PTX. Histological examination found hyperplasia in all extirpated glands. The following laboratory analyses were done before and 6 months after PTX in all patients: hemoglobin, serum calcium, phosphorus, alkaline phosphatase, intact parathormone (iPTH) (radioimmunoassay; Nichols Institute Diagnostics, San Juan Capistrano, California) (normal values, 10-55 pg/mL), erythropoietin (Epo) (enzyme-linked immunosorbent assay 500; Medac, Wedel, Germany) (normal values for healthy nonanemic adults, 4-25 mU/mL), bone marrow burst-forming units erythroid (BFU-E) (assayed by methyl cellulose culture technique in vitro[3]), and bone marrow cellularity.

Six months after PTX, serum iPTH levels were 10 to 69 times lower than the initial value in all but 1 patient (Table). In the first 8 patients presented in the Table, mean (SD) iPTH levels decreased significantly (1453.7 [634.2] vs 71.0 [75.8] pg/mL, $P=.02$) after successful PTX. This was accompanied by increases of mean (SD) hemoglobin level (88.5 [19.4] vs 99.2 [10.7] g/L, $P=.31$) and mean (SD) serum Epo level (23.54 [21.1] vs 31.1 [22.5] IU/mL, $P=.04$) and a decline in mean (SD) BFU-E number (40.1 [12.5] vs 26.2 [10.6], $P=.14$). Individual data showed that serum Epo concentration increased after successful PTX in 6 of 8 patients. In 2 patients who were positive for hepatitis virus, serum Epo levels were higher than the normal range even before PTX. The increase of serum Epo levels was accompanied by greater hemoglobin values and increased bone marrow cellularity from proliferation of erythroblasts, which lowered the myeloid to erythroid ratio in the bone marrow (4.4:1 before and 1.8:1 after PTX). Numbers of BFU-E were decreased in all the patients with successful PTX (including the patient with high initial Epo).

The results presented show erythropoiesis stimulation after successful PTX by an increase in serum Epo, which suggests a direct inhibitory effect of PTH on Epo synthesis. These data are in concert with those obtained by others[4] and confirm that even in patients with end-stage renal disease and without excretory kidney function, increase of erythropoietin synthesis could occur. Increased serum Epo before PTX found in 2 of our patients who were positive for hepatitis is in agreement with our previous results.[5] However, in all patients with successful PTX, including these 2, bone marrow cellularity improved and BFU-E numbers decreased. That indicated that more efficacious erythroid maturation after successful PTX resulted not only from the increase of Epo synthesis but also from a decrease of bone marrow suppression. The role of PTH as a uremic toxin and inhibitor of erythropoiesis was described 2 decades ago.[6]

Table. Individual Values of Hemoglobin, Erythropoietin, Bone Marrow Burst-Forming Units Erythroid, and Intact Parathormone Before and After Parathyroidectomy

Patient No.	Hemoglobin, g/L		Erythropoietin, U/mL		BFU-E/5 × 10^5 Cells		iPTH, pg/mL	
	Before	After	Before	After	Before	After	Before	After
1	53	98	3.36	18.3	48	22	1230	14
2	81	109	13.1	25.9	44.5	25	2100	158
3	105	107	19.4	52.2	37	20.5	1230	58
4	79	83	2.0	9.0	34	13.5	705	4
5	101	113	55.8	74.6	30	37.5	2300	215
6	76	86	9.1	11.5	34.5	29.5	1500	30
7	104	96	35.1	20.2	27	17	1469	66
8	109	102	50.5	37	66	45	1596	23
9	77	87	19.9	9.92	41	23.5	1521	2198

Abbreviations: BFU-E, bone marrow burst-forming units erythroid; iPTH, intact parathormone.

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Successful PTX in 8 of 9 patients was followed with a manifold decrease of serum iPTH levels, increase of serum Epo level, more efficient maturation of the erythroid line, and alleviation of anemia.

Tamara K. Jemcov, MD
Marijana Petakov, MD, PhD
Andrija Bogdanovic, MD
Ljubica Djukanovic, MD, PhD
Visnja D. Lezaic, MD, PhD

Correspondence: Dr Jemcov, Clinic of Nephrology, Clinical Center of Serbia, Pasterova 2, 11000 Belgrade, Serbia (tamara@jemcov.com).
Author Contributions: *Study concept and design:* Jemcov and Lezaic. *Analysis and interpretation of data:* Jemcov, Petakov, Bogdanovic, Djukanovic, and Lezaic. *Drafting of the manuscript:* Petakov and Bogdanovic. *Critical revision of the manuscript for important intellectual content:* Djukanovic and Lezaic. *Statistical analysis:* Jemcov and Lezaic. *Study supervision:* Petakov, Djukanovic, and Lezaic.
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COMMENTS AND OPINIONS

Pain as the Fifth Vital Sign

I read with interest the commentaries on pain as the fifth vital sign by Drs Kozol, Voytovich, and Livingston in the May issue of the *Archives*.[1,2] Although their subjective comments regarding the adverse consequences of pain as a fifth vital sign are bolstered by referenced studies, they fail to address one of the primary reasons for unfavorable outcomes in the arena of pain management: a lack of education among physicians regarding pain management principles and analgesic pharmacology. Dr Livingston makes the point best when he describes the litigation of an 85-year-old elderly gentleman with pulmonary compromise who suffered a respiratory arrest in the emergency department after receiving morphine (I wonder what dose of morphine he received and whether he was opioid naive) but was then admitted and variously prescribed a fentanyl citrate patch, meperidine, and acetaminophen/hydrocodone. Although the chronological use of these medications is not indicated, fentanyl patches are best used for nonacute pain (and it appears this gentleman was in acute pain), and meperidine is essentially contraindicated in someone 85 years of age, in part secondary to potential accumulation of the active metabolite normeperidine, which can precipitate anxiety, tremors, and seizures. The patient was then discharged, and because of apparent poor pain control, he visited another physician to seek pain relief and subsequently died of an alleged adverse response to morphine. The circumstances of this case are sad, and the outcome regrettable.

That said, I do concur with the authors when they criticize *sole* reliance on a numeric pain scale. I think the pain scale has revolutionized the treatment of pain, but it must also be used within the context of repeated clinical assessments, including assessment of all domains affected by pain. In other words, don't just look at the number: look at the patient.

In closing, my letter is not meant to denigrate concerns regarding pain as the fifth vital sign but rather to stress the need for physician education regarding the use of opioid analgesics as well as proper interpretation of the numeric pain scale. Like any drug, opioids are safe and efficacious when used in a cautious and appropriate manner, but such use requires thorough knowledge of their clinical indications and pharmacodynamics.

Paul Rousseau, MD

Correspondence: Dr Rousseau, VA Medical Center, 650 E Indian School Rd, Phoenix, AZ 85012 (palliativedoctor@aol.com).
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1. Kozol RA, Voytovich A. Misinterpretation of the fifth vital sign. *Arch Surg*. 2007;142(5):417-419.
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Pain Assessment Is Vital

I was appalled to read the recent article on "the fifth vital sign"[1] as well as the invited critique and found them to be scientifically unsound and socially irresponsible.

This article published in the May issue of *Archives* moves the advances in relief of pain back at least 20 years. The authors' dismissal of the subjective report of pain as a vital sign disregards critical national guidelines, evidence-based practice, and strong consensus by the Joint Commission, the National Consensus Project for Quality Palliative Care, the American Pain Society, the National Comprehensive Cancer Network, and dozens of other national scientific and professional organizations, all who strongly endorse using pain as the fifth vital sign.

Each of these organizations and guidelines also recognizes important issues as acknowledged by Drs Kozol and Voytovich that a decision regarding dosing of opioids must consider numerous other factors regarding the

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