physiologic processes (hypertension, hemorrhage, infarction, and hypoxemia) seem to occur in all organs, the timing of the insult may ultimately determine its target and specificity.[2]

ZEEV N. KAIN, M.D.
TATIANA S. KAIN, M.D.
Yale–New Haven Hospital and Yale
New Haven, CT 06510 University School of Medicine

EMILE M. SCARPELLI, M.D., PH.D.
New York Hospital–
New York, NY 10021 Cornell University Medical Center

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To the Editor: In his review, Volpe concluded that vascular abnormalities are not a likely cause of the teratogenic effects of cocaine. We disagree, and to underscore this opinion we call attention to an important effect of maternal cocaine use during pregnancy that Volpe did not mention — limb-reduction defects.[1,2] These defects are the result of the interruption of blood flow to developing or previously developed structures.[3] Limb-reduction defects should also have been included in the review so that the question of the value of prenatal diagnosis of these defects as indicators of cocaine abuse during pregnancy[4] could be raised.

JOHN N. VAN DEN ANKER, M.D.
PIETER J.J. SAUER, M.D.
Rotterdam, University Hospital Rotterdam–
the Netherlands Sophia Children's Hospital

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Dr. Volpe replies:

To the Editor: Both letters describe important teratogenic and destructive lesions involving non-neural structures that are associated with fetal exposure to cocaine. These effects are important not only because of the morbidity and mortality associated with them, but also because they demonstrate further the deleterious consequences of intrauterine exposure to cocaine. I did not mention these effects because my review concerned only the neural effects of cocaine.

I agree with van den Anker and Sauer that the limb-reduction defects that occur in fetuses exposed to cocaine probably are caused by focal ischemia, but it is very unlikely that focal ischemia causes the teratogenic neurologic effects of cocaine. As I noted, however, focal ischemia clearly is involved in certain of the destructive neurologic effects of cocaine — notably, cerebral infarction.

JOSEPH J. VOLPE, M.D.
Boston, MA 02115 Children's Hospital

IMPAIRMENT OF RENAL FUNCTION WITH INCREASING BLOOD LEAD CONCENTRATIONS

To the Editor: The finding by Staessen et al. (July 16 issue)[1] that low blood lead and zinc protoporphyrin concentrations are associated with renal insufficiency in a large population confirms that lead is nephrotoxic. This report once again identifies lead as a dangerous and widespread environmental toxin. It also, however, adds to the confusion surrounding the diagnosis of lead poisoning in asymptomatic persons.

Reliance on blood lead and zinc protoporphyrin measurements may underestimate the number of persons with abnormal exposure to lead. Both blood lead and zinc protoporphyrin concentrations increase during exposure and fall soon after exposure ceases. Lead is stored mostly in the bone; only a small fraction of absorbed lead is excreted by the kidneys. Lead poisoning and associated morbidity, such as renal failure, hypertension, and gout, correlate better with the body burden of lead estimated by the EDTA lead-mobilization test, direct measurement of lead in bone-biopsy specimens, or x-ray fluorescence.[2-4] Although blood lead measurements may be helpful in identifying trends in large populations, they are not useful in studying selected populations, such as patients with gouty nephropathy or presumed hypertensive nephrosclerosis; only the EDTA lead-mobilization test reveals unsuspected lead poisoning among these patients.[2]

Staessen et al. state that renal insufficiency by itself might be responsible for the increased blood lead concentrations in the subjects they studied. This is unlikely, because the lead burdens in patients with renal failure of identifiable causes are not different from those in persons with normal renal function and no unusual exposure to lead.[2,4]

The identification of lead as a possible cause of kidney disease in asymptomatic persons with blood lead concentrations mostly in a range considered normal attests to the ubiquity of this environmental poison. The true extent of unsuspected environmental lead poisoning and its contribution to renal disease and hypertension, however, can be estimated only be determining the body burden of lead in large populations.

VECIHI BATUMAN, M.D.
Tulane University
New Orleans, LA 70112 School of Medicine

RICHARD P. WEDEEN, M.D.
East Orange, NJ 07019 New Jersey Medical School

1. Staessen JA, Lauwerys RR, Buchet J-P, et al. Impairment of renal function with increasing blood lead concentrations in the general population. N Engl J Med 1992;327:151-6.
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The authors reply:

To the Editor: We agree with the comment of Drs. Batuman and Wedeen that the total body burden of lead may be more reliably assessed by measuring the lead content of bone than by determining the lead concentration in blood, but we disagree with their assessment of the value of zinc protoporphyrin measurements. If, after exposure ceases, the amount of metabolically active lead remains elevated, zinc protoporphyrin concentrations often do not decline to nor-

mal, although blood lead concentrations do.[1] As compared with bone lead, most of which is biologically inactive, zinc protoporphyrin may be a better predictor of the lead burden of organs such as the kidney and the central nervous system.[2]

We believe that epidemiologic studies can convincingly demonstrate a relation between indexes of exposure and an effect, but they do not allow direct inferences about causality. As far as the problem of environmental exposure to lead is concerned, this is true for the presumed effects of lead on both renal function and blood pressure. Moreover, if an association is found in an epidemiologic study, not only its causality but also its biologic importance needs to be evaluated. The last point may be particularly relevant for the lead–hypertension issue, which is now being reassessed in 997 of our subjects in a longitudinal study. In this study we are not only measuring blood pressure, but also reassessing renal function, remeasuring blood lead and zinc protoporphyrin concentrations, and measuring the lead content of the tibia.[2] The results of these studies are likely to clarify further the important questions raised by Drs. Batuman and Wedeen.

JAN A. STAESSEN, M.D., PH.D.
ANTOON AMERY, M.D., PH.D.
B-3000 Leuven, Belgium Katholieke Universiteit Leuven

B-1200 Brussels, Belgium ROBERT R. LAUWERYS, M.D., PH.D.
Université Catholique de Louvain

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CLINICAL PROBLEM-SOLVING: FAILURE TO RESOLVE A DIAGNOSTIC INCONSISTENCY

To the Editor: In the recent Clinical Problem-Solving article, "Failure to Resolve a Diagnostic Inconsistency" (July 2 issue),[1] we are presented with a 56-year-old obese woman who arrives at the emergency room with arterial embolus, hypoxemia, and chest pain with clear lung fields.

Both the author and the discussant correctly rule out most of the possibilities in their overview. However, we believe that the possibility of right ventricular infarction should have been investigated further. Mild ST-segment elevation in electrocardiographic Leads II, III and aVF, accompanied by reduced right ventricular function, support the diagnosis of right ventricular infarction.

Several simple and safe diagnostic studies would have been helpful. Right-sided electrocardiographic leads (V_{3R} and V_{4R}) should have been examined for ST-segment elevation, which would have supported a diagnosis of right ventricular infarction. In addition, evidence of pulmonary hypertension on Doppler echocardiography would have supported the diagnosis of pulmonary emboli. On the other hand, the absence of pulmonary hypertension, in the face of severely reduced right ventricular function, would have strongly supported the diagnosis of right ventricular infarction.

The author states, "No pathophysiologic mechanism exists by which . . . right ventricular infarction can cause severe hypoxemia in the absence of pulmonary edema." In fact, hypoxemia can be explained by right ventricular infarction when it is complicated by right-to-left intracardiac shunting as a result of a patent foramen ovale.[2] This right-to-left shunting occurs as a result of decreased right ventricular compliance and increased right-sided pressures.

JOSHUA KERSTEIN, M.D.
GERALD HOLLANDER, M.D.
Brooklyn, NY 11219 Maimonides Medical Center

1. Thibault GE. Failure to resolve a diagnostic inconsistency. N Engl J Med 1992;327:36-9.
2. Manno BV, Bemis CE, Carver J, Mintz GS. Right ventricular infarction complicated by right to left shunt. J Am Coll Cardiol 1983;1:554-7.

To the Editor: As I was reading the first half of the very interesting clinical problem presented by Dr. Thibault, the idea that this patient had had a right ventricular infarct, pulmonary embolism, and embolism to the subclavian artery through an open foramen ovale came immediately to my mind. It is, however, one thing to read a Clinical Problem-Solving article, and another to sit at the bedside of a patient who is rapidly deteriorating. Frankly, in the atmosphere in which the physician in the United States nowadays has to practice, with malpractice lawyers virtually accompanying him or her on rounds, I wonder whether I would have had the guts to use even thrombolytic therapy — much less surgical intervention — in such a case. I have to give credit to the internist treating this patient.

ALEXANDER B. WHITE, M.D.
Olympia Fields, IL 60461 2605 Lincoln Hwy.

Dr. Thibault replies:

To the Editor: Drs. Kerstein and Hollander are quite correct that acute right ventricular infarction with a patent foramen ovale resulting in a right-to-left shunt should have been part of the differential diagnosis in this case. All the reported cases of this entity also involved acute inferior or posterior left ventricular infarction. The absence of clear evidence of acute left ventricular infarction in this patient would therefore have been an argument against this unifying diagnosis. Nonetheless, it should have been mentioned as a possible cause of severe hypoxemia in a patient with suspected myocardial infarction and clear lungs.

I have recently seen a patient with right ventricular infarction and right-to-left shunting and have reviewed the nine cases in the English literature. This entity is real, but rare. It is still true that the pathophysiologic mechanism of hypoxemia in myocardial infarction is pulmonary edema in almost every instance.

I agree with Dr. White that the physicians caring for this patient should be complimented (as they were) for acting on their diagnostic reasoning and initiating thrombolytic therapy for massive life-threatening pulmonary embolism. In spite of this treatment, the outcome of the patient was bad. This is a clear example of how a single bad outcome is not necessarily indicative of faulty clinical reasoning or practice.

GEORGE E. THIBAULT, M.D.
West Roxbury Veterans Affairs
West Roxbury, MA 02132 Medical Center

CAT-SCRATCH SALPINGITIS

To the Editor: We wish to report a case of *Pasteurella multocida* salpingitis.

A 37-year-old woman, gravida 2, para 1, with one spontaneous abortion, presented with a two-day history of crampy, intermittent right-lower-quadrant pain radiating to the back and epigastrium. Her most recent menstrual period had