# Reversible Acute Renal Failure Associated With Ibuprofen Ingestion and Binge Drinking

Gary N. Elsasser, PharmD, Lenora Lopez, MD, Ellen Evans, MD, and Eugene J. Barone, MD
*Omaha, Nebraska*

Nonsteroidal anti-inflammatory drugs (NSAIDs) are among the most commonly prescribed medications.[1] The side effects of these agents are well appreciated. Recent attention has focused on the effects these agents exert on renal hemodynamic mechanisms through inhibition of renal prostaglandin synthesis, renal vasoconstriction, and the development of acute renal failure.[2–6] Additional reports have attempted to identify those patients most at risk.[7,8] A case of reversible acute renal failure following ibuprofen ingestion and binge drinking of alcohol is described.

## CASE REPORT

A 19-year-old female college student presented to the emergency room on October 12, 1986, complaining of a wrist injury sustained during an argument. Ibuprofen, 400 mg, was prescribed for soft tissue injury, of which she took one tablet that evening and one the following morning. On October 13, 1986, she drank one half-fifth (375 mL) of rum followed by two 400 mg ibuprofen tablets. She again was seen in the emergency room on October 18, 1986 (evening prior to admission), for complaints of bilateral nonradiating lower to middle back pain that worsened despite 24 hours of self-treatment with heat, acetaminophen, and one 400-mg dose of ibuprofen. She denied vomiting, fever, chills, urinary frequency, urgency, hesitancy, dysuria, hematuria, or oliguria. She denied sexual activity or vaginal discharge. Her last menstrual period occurred two weeks prior and was normal. There was no history of trauma. She had no skin eruptions, recent infections, or joint pains. The patient was afebrile and actively mobile. She had some diffuse abdominal tenderness without rebound or guarding. Right-sided costovertebral angle tenderness was appreciated. The complete blood count (CBC) and differential was entirely normal. A clean catch of the urine revealed protein (3+) but no hematuria, bacteria, or other abnormalities. She was thought to have a musculoskeletal injury or viral syndrome and was discharged with instructions to return the next morning for a follow-up evaluation.

At 4:40 AM the patient returned to the emergency room stating that she was no better. Her temperature was elevated to 37.7°C, and she had had some bilious-like emesis. The physical examination was unchanged. A repeat CBC and differential was normal with the exception of a decrease in the hematocrit from 0.41 to 0.37 and the hemoglobin from 139 g/L (13.9 g/dL) to 128 g/L (12.8 g/dL). A clean-catch urinalysis revealed a specific gravity of 1.005, pH of 6.5, albuminurea (2+), occult blood (1+), 1 to 5 white blood cells per high power field, and no bacteria or casts. Orthostatic changes were noted with an increase in the heart rate from 84 beats per minute supine to 120 beats per minute standing.

At admission to the hospital, the patient denied any other drug use aside from that described. The physical examination revealed a healthy-appearing round-faced woman in no acute distress. Vital signs were temperature 37.4°C, pulse 96/min, respiratory rate 20/min, and blood pressure 104/84 mmHg. The abdominal examination was unchanged. There was bilateral costovertebral angle tenderness (right greater than left). Admission chemistries were remarkable for a blood urea nitrogen (BUN) of 9.6 mmol/L (27 mg/dL) and a serum creatinine of 460 μmol/L (5.2 mg/dL). Liver function studies were completely normal. An ultrasound of the abdomen revealed mild enlargement of both kidneys with increased but nonspecific echogenicity. A 24-hour urine protein and creatinine clearance was <0.24 g/d (240 mg/24 h) and 0.25 mL/s (15 mL/min), respectively. Additional laboratory data included a spot urine sodium of 84 mmol/d (84 mEq/h), urine osmolality of 24 mmol/kg (24 mOsm/kg), normal urine sediment, no urine eosinophils, and normal serum creatinine kinase and complement values. Antistreptolysin O titers and antinuclear antibody tests were negative.

*Submitted, revised, January 6, 1988.*

*From the Department of Pharmacy Practice and the Department of Family Practice, Creighton University Medical Center, Omaha, Nebraska. Requests for reprints should be addressed to Dr. Gary N. Elsasser, Department of Family Practice, St. Joseph's Hospital, 601 North 30th St, Omaha, NE 68131.*

A period of high-output renal failure was followed by improvement, and the patient was discharged on the sixth hospital day. At discharge the BUN and serum creatinine had improved to 7.5 mmol/L (21 mg/dL) and 88.4 μmol/L (1 mg/dL), respectively. The costovertebral angle tenderness had resolved, and the roundness of the patient's face was no longer apparent. A 24-hour creatinine clearance at three-month follow-up was 1.68 mL/s (101 mL/min).

## DISCUSSION

Acute renal failure secondary to NSAID administration has mostly involved patients with preexisting renal disease or a decrease in effective circulatory volume, eg, congestive heart failure, hepatic cirrhosis with ascites, salt restriction, or diuretic-induced volume depletion.[9] Under these conditions, renal hemoperfusion is maintained by the vasodilatory effects of renally synthesized prostaglandins. In the absence of renal prostaglandin synthesis or when their effect is blocked by NSAID administration, circulating vasoconstricting substances may act unopposed. Renal ischemia appears responsible for the acute renal insufficiency, which may or may not be reversible.[7-10]

This case is the first reported of NSAID-induced renal failure associated with alcohol consumption. This patient had no history of renal disease. It was hypothesized that the alcohol ingestion was sufficient to render this otherwise healthy young adult's kidneys susceptible to the adverse renal effects of the NSAID. The patient's impressive orthostatic blood pressure drop supports this hypothesis.

The diuretic effects of ethanol can be significant. This diuresis is dependent on not only the individual patient but also the particular alcoholic beverage and the amount ingested.[11,12] Considered, but not currently supported by the literature,[11] is the possibility of alcohol as a renally toxic agent and an additive effect with regard to renal prostaglandin synthesis inhibition. Anggard et al[13] were unable to demonstrate a significant effect of alcohol on either renal prostaglandin tissue levels or urinary excretion in Sprague-Dawley rats.

Since the initial release of ibuprofen for over-the-counter use, ten ibuprofen-containing products have been released onto the market.[14] Hence, the potential for intentional as well as unintentional concomitant ingestion of ibuprofen and alcohol is great.

Whether this case report represents an isolated incident or a widespread yet undetected occurrence of NSAID-induced acute renal failure requires further study. Physicians and pharmacists need to be cognizant of the potential for NSAID-induced acute renal failure in healthy individuals ingesting these agents with alcohol. Concern for consumer product labeling of over-the-counter ibuprofen warning of potential adverse renal effects has been expressed.[15] Additional case reports of this nature may prompt just such a warning.

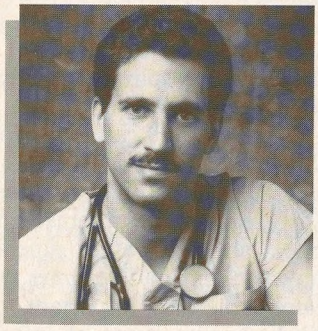
### References


1. The top 200 prescription drugs of 1986. Am Druggist 1987; 195: 19–32
2. Justiniani FR: Over-the-counter ibuprofen and nephrotic syndrome. Ann Intern Med 1986; 105:303
3. Moss AH, Riley R, Murgo A, Skaff LA: Over-the-counter ibuprofen and acute renal failure. Ann Intern Med 1986; 105:303
4. Adams DH, Michael J, Bacon PA, et al: Non-steroidal anti-inflammatory drugs and renal failure. Lancet 1986; 1:57–59
5. Reeves WB, Foley RJ, Weinman EJ: Nephrotoxicity from nonsteroidal anti-inflammatory drugs. South Med J 1985; 78:318-322
6. Poirier TI: Reversible renal failure associated with ibuprofen: Case report and review of the literature. Drug Intell Clin Pharm 1984; 18:27–32
7. Garella S, Matarese RA: Renal effects of prostaglandins and clinical adverse effects of nonsteroidal anti-inflammatory agents. Medicine 1984; 63:165–181
8. Lamy PP: Renal effects of nonsteroidal antiinflammatory drugs, heightened risk to the elderly? J Am Geriatr Soc 1986; 34:361-367
9. Blackshear JL, Napier JS, Davidman M, Stillman MT: Renal complications of nonsteroidal antiinflammatory drugs: Identification and monitoring of those at risk. Semin Arthritis Rheum 1985; 14: 3:163–175
10. Walshe JJ, Venuto RC: Acute oliguric renal failure induced by indomethacin: Possible mechanism. Ann Intern Med 1979; 90: 783
11. Beard JD, Sargent WO: Water and electrolyte metabolism following ethanol intake and during acute withdrawal from ethanol. In Biochemistry and Pharmacology of Ethanol, vol 2. New York, Plenum Press, 1979, pp 3–16
12. Haggard HW, Greenberg LA, Carroll RP: Studies in the absorption, distribution and elimination of alcohol. J Pharmacol Exp Ther 1941; 71:349–357
13. Anggard E, Jones AW, Neri A: Effect of acute and chronic ethanol treatment on renal prostaglandin in the rat. Alcohol 1985; 2:647-650
14. Physicians Desk Reference for Nonprescription Drugs, ed 9. Oradell, NJ, Medical Economics, 1988
15. Henrich WL, Bennett WM, Brater DC, et al: Statement on the release of ibuprofen as an over-the-counter medicine. Am J Kidney Dis 1985; 5:4–6

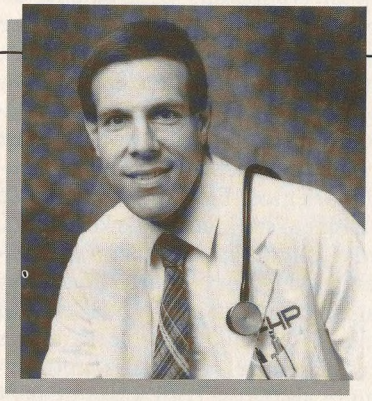
# Quality medicine isn't just possible here — it's required.

FHP® has been bringing quality to prepaid managed healthcare for 28 years. Much of our success is due to the high standards among our medical staff.

- ☐ Well respected physicians in every field—only one applicant in ten is accepted.



- ☐ Professional latitude to practice good medicine, and a strong voice in assuring overall quality healthcare.
- ☐ State-of-the-art equipment.
- ☐ CME encouraged, with time off, tuition subsidies and in-service programs.



**Kim G. Linares, MD,** came to FHP from the faculty of USC Medical School in Los Angeles, where he completed his fellowship in pulmonary diseases. He is currently Director of Respiratory Care at FHP Hospital, and Chairman of the Pulmonology Department.

**Diana L. Patton, MD,** joined FHP after finishing residency at Akron General Medical Center, where she served as a clinical instructor at the Northeastern Ohio University College of Medicine.

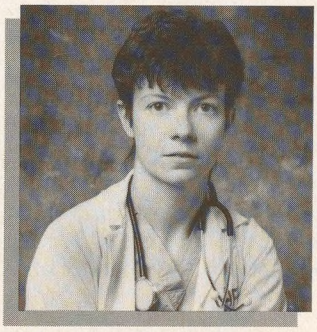
**Robert P. Realmuto, MD,** is a graduate of the Albert Einstein College of Medicine. He currently serves as Chief of Emergency Medicine Services at FHP, and as Assistant Clinical Professor at University of California, Irvine Medical Center.

The Reason You're In Medicine

FHP®

Equal Opportunity Employer

- ☐ Diverse specialties on-staff.
- ☐ A financially stable organization.
- ☐ Opportunities in Southern California, Utah, Arizona, New Mexico and Guam.



If you're a physician who insists on practicing quality medicine, get the full FHP story. Call FHP at (800) 446-2255 (U.S.) or (800) 336-2255 (within California), or send your CV to FHP, Professional Staffing, Dept. 50, 9900 Talbert Avenue, Fountain Valley, CA 92708.

**Emergency Procedures and Techniques (2nd Edition).** *Robert R. Simon, Barry E. Brenner. Williams & Wilkins, Baltimore, 1987, 432 pp., $29.95.*

This outstanding paperback textbook is in its second edition because of its relevance of content to family practice. It is particularly helpful to the family physician working in the emergency room or as a primary responder to any medical or surgical emergency.

It is extremely readable and well organized. Interspaced between outstanding illustrations are highlighted cautions and axioms that are important clinical points for the family physician who is performing these procedures. The indications, contraindications, and techniques necessary for performing the procedures are clearly delineated. The authors very nicely mix this format with a multitude of diagrams and illustrations.

Certainly this book was published for not only the emergency room physician, but also for the family physician dealing with trauma in a small community. Its paperback form places it in an inexpensive category, and it would be well suited for the family physician practicing in a rural setting.

*David Driggers, MD*
*Family Practice Residency Program*
*Casper, Wyoming*

**Textbook of Diagnostic Medicine.** *A. H. Samiy (ed), R. Gordon Douglas, Jr., Jeremiah A. Barondess (eds). Lea & Febiger, Philadelphia, 1987, 900 pp., $69.50. ISBN 0-8121-1006-4.*

In a world of proliferating medical imaging and laboratory technologies, it is a breath of fresh air to have a book that reexamines the place of patient historical and physical examination data in the clinical problem-solving process. This encyclopedic, well-organized, and highly readable text succeeds in this important task.

The editors have done a masterful job in pulling together the contributions of 35 academically based medical subspecialists. Two excellent introductory chapters provide an overview of (1) the principles of clinical diagnosis, and (2) the selection and interpretation of laboratory tests and diagnostic procedures. In the following 20 chapters, more than 500 patient complaints or problems affecting different organ systems are discussed in terms of their definition, pathophysiology, clinical presentation, differential diagnosis, and diagnostic evaluation and workup. The writing is clear, succinct, and practically oriented. Frequent use is made of tables to summarize the key points, and a helpful appendix includes reference values for common laboratory tests in both conventional and SI units. I was quickly able to access needed clinical diagnostic information by using the book's comprehensive index.

As might be expected in any multiauthored text that tries to cover the waterfront, there are a number of limitations. The coverage of topics is at times uneven (eg, 202 pages are dedicated to endocrine and metabolic problems and only 17 pages to constitutional and nonspecific problems). Significant overlapping of content occurs in a number of chapters. More liberal use of illustrations and other visual graphics would have greatly assisted the reader in understanding discussions of anatomy and pathophysiology.

Finally, this reviewer would have liked to see more discussion about (1) the epidemiology of different medical problems, especially by patient age and clinical setting; (2) psychosocial and family contributions to patients' presenting problems; (3) the relative sensitivity, specificity, and predictive values of symptoms, signs, and tests for particular diseases; (4) estimated costs of various laboratory tests and diagnostic workups; and (5) available computer software for medical diagnosis.

Despite these deficiencies, I believe that this text would be a valuable addition to the reference library of busy practicing family physicians and should be carefully studied by family practice residents and medical students interested in improving their differential diagnostic abilities. By taking a patient- rather than disease-oriented approach to diagnosis, the authors have come closer to capturing the reality of everyday clinical practice than have many other standard textbooks of medicine.

*Robert C. Like, MD, MS*
*University of Medicine and Dentistry of New Jersey—Robert Wood Johnson Medical School*
*New Brunswick*

**Procedures in Ambulatory Care.** *Robert D. Gillette. McGraw-Hill Book Company, New York, 1987, 245 pp., $16.95 (paper). ISBN 0-07-023265-2.*

*Procedures in Ambulatory Care* is an interesting book that reviews a variety of procedures and activities included in family medicine. It is divided into a somewhat confusing mixture of specific procedures based on anatomic location and is then subdivided by categories of procedures such as spirometry, electrocardiography, and others.

The content is certainly relevant to family practice and includes things that all of us do on a daily basis. It is fairly readable and a somewhat useful book, although rather superficial in its treatment and at times not containing the most important and least likely known items of information necessary to performing the procedure. The illustrations are well done, although not so many as would be expected for a procedural book.

The audience best served would be medical students and allied health professionals. Most residents and practicing family physicians and academic faculty are likely to be already well versed in the contents. The book could be appropriate for a medical school library as well as a library within a residency training program.

*Sam Cullison, MD*
*Monroe Family Practice*
*Monroe, Washington*