Dr. Joseph Eschbach

In Memory of Joseph Wetherill Eschbach

Kidney International (2008) **73**, 665–666. doi:10.1038/sj.ki.5002781

Joseph Eschbach, a leading United States nephrologist recognized worldwide for his ground-breaking work on the anemia of chronic renal failure, died in his home in Bellevue, Washington, on 7 September 2007. Although he had never smoked, the cause of his death was lung cancer. Joe was born in Detroit in January 1933. He attended Otterbein College in Ohio and obtained his medical degree from Jefferson Medical College in Philadelphia in 1959. In 1963, he joined Belding Scribner's Division of Nephrology at the University of Washington in Seattle as a research fellow. As was the custom, he sat down with Scrib to discuss possible research projects. He was told that only the topic of anemia of patients on chronic dialysis was left; all the other topics had been taken. This decision led him to begin working with John Adamson, then a research fellow in the Division of Hematology. They developed a partnership that lasted for more than thirty years.

At that time, the common belief was that the anemia in patients with chronic renal failure and dialysis patients was caused by bone marrow suppression from inhibitors in uremic plasma. Joe soon observed that, even though uremic red blood cell production in these patients was regulated by small amounts of erythropoietin that their kidneys still were producing, the results of the studies on possible inhibitors were contradictory and controversial. At that time, dialysis patients generally required transfusion of one to three units of red blood cells every month or so to relieve the symptoms of tissue hypoxia. However, transfusion was effective only temporarily; increased the risk of hepatitis, of other infections, and of effects of sensitization on possible transplantation; caused iron overload; suppressed endogenous erythropoietin production by the kidney; and resulted in transfusion dependence. Once repeated transfusion was halted, many dialysis patients could maintain hematocrits in the region of 25 without the need for transfusion except after blood loss or infection. Joe and John also carried out extensive studies on iron metabolism in chronic renal failure and showed that, contrary to previous views, intestinal iron absorption was normal in these patients.

Joe and John went on to develop an exquisite experimental model to study anemia in sheep made uremic by subtotal nephrectomy, some of which required dialysis. They used this model to examine the *in vivo* significance of uremic inhibitors by infusing increasing amounts of erythropoietin-rich plasma from normal sheep made anemic by venesection or administration of phenylhydrazine into the uremic sheep, and compared the results with the effects of infusing similar doses into the original anemic normal sheep. Erythropoiesis, quantified by reticulocyte response, plasma iron turnover, marrow transit time, and hemoglobin C synthesis, was similar in uremic sheep, whether dialyzed or not, and normal sheep. Red-cell production was increased, anemia was corrected, and the total dose of erythropoietin-rich plasma required depended on the degree of uremia. Dose–response curves were constructed; these and the identical response to the same amount of erythropoietin-rich plasma in uremic and anemic normal animals implied that no physiologically important erythropoietic inhibitors existed in uremic plasma. This finding led to the conclusion that if erythropoietin became available for clinical use, it would correct the anemia associated with chronic kidney disease and end-stage renal disease.

As a result of his work, Joe and patients at the Northwest Kidney Centers in Seattle, some of whom were from his private practice, were selected to carry out the first studies in humans with recombinant human erythropoietin when it first became available in December 1985. Transfusion requirements, hematocrit, ferrokinetics, and reticulocyte responses were monitored and showed dose-dependent increases in erythropoiesis. Hematocrits rose to 35 or more, and ferrokinetics measured as erythron transferrin uptake increased three or four times over basal levels. So began the saga of erythropoiesis-stimulating agents (ESAs).

Joe was very involved in ensuring approval of erythropoietin by the United States Food and Drug Administration. He and I went to Washington to tell Congressional staffers about the benefits of this exciting new drug and were taken aback that the first question asked was, 'How could this drug be

Christopher R Blagg
Professor Emeritus of Medicine, University of Washington, Seattle, Washington, USA; and Executive Director Emeritus, Northwest Kidney Centers, Seattle, Washington, USA
Correspondence: *Christopher R Blagg, Northwest Kidney Centers, 700 Broadway, Seattle, WA 98122.*
E-mail: blaggc@hotmail.com

abused?' This was something we had never considered. However, Congressional approval for its use in the Medicare End-Stage Renal Disease Program followed shortly, and the Centers for Medicare and Medicaid Services began to pay for erythropoietin for dialysis patients in 1989.

Joe had other clinical interests. In 1965, he was appointed director of the home-hemodialysis center at the University of Washington, a prototype for such centers. Because dialysis was not yet widely available, over the next several years more than 50 patients from elsewhere in the United States, Australia, the Philippines, Chile, and the Sudan came to Seattle with a family member and their doctor to be trained to do home hemodialysis. This practice showed that home hemodialysis remote from a dialysis center and managed by an internist was safe and effective. Joe also developed what he called an orientation unit at the Northwest Kidney Centers to provide concentrated patient education for all new patients during the first two months after starting dialysis.

Joe continued his interest in and research into renal anemia, erythropoietin, and iron metabolism until shortly before his death. In 2003, he was appointed senior research advisor at the Northwest Kidney Centers.

He was in great demand to talk about renal anemia, erythropoietin, and his research all over the United States and in some 26 other countries around the world. He published in the range of 150 articles, including 12 chapters in textbooks, and was coeditor of two books. When the National Kidney Foundation Dialysis Outcomes Quality Initiative was established in 1995, he was the first chairman of the Anemia Work Group, and he continued in this role until 2001. Many honors came to him as a result of his work, including the David M Hume Award from the National Kidney Foundation in 1995, election to the Institute of Medicine of the National Academy of Sciences in 1990, the Haviland Award of Excellence of the Northwest Kidney Centers in 1991, and the American Kidney Fund Torchbearer Award in 2003, and culminating in the International Society of Nephrology Amgen International Prize for Therapeutic Advancement in Nephrology in 2005. He shared this award with Dr. Eugene Goldwasser, who had done most of the original laboratory research on the identification and physiology of erythropoietin. Shortly before Joe's death, the Northwest Kidney Centers and Kirin-Amgen Inc. established the Joseph W Eschbach Endowed Chair in Kidney Research at the University of Washington.

Joe was appointed clinical professor of medicine at the University of Washington in 1975 and emeritus professor in 1994. He was director of the home-hemodialysis training center at the University of Washington from 1965 to 1972, president of the King County Medical Society in 1987, a member of the Northwest Kidney Centers Board of Trustees for many years and its president from 1985 to 1987, president of the Washington Association for Biomedical Research from 1991 to 2001, and senior research advisor at the Northwest Kidney Centers from 2003 until his death.

Remarkably, almost all of Joe's research was carried out after he went into part-time private practice in nephrology and internal medicine in Seattle in 1965. This gave him a unique perspective, as he was personally responsible for a large number of dialysis patients over the years. Even more remarkable, while many practicing physicians in Seattle knew Joe was a great doctor, they knew him as a humble person, and few of them realized that he was so well known throughout the world for his research.

He was described by his colleagues and patients as gentle, caring, considerate, and ethical, and his patients said he took the extra time to truly listen to them and understand their concerns. As one of his colleagues said, "Joe was the kind of doctor that a doctor would want as his doctor."

In addition, Joe had many other interests. Music was important in his life from an early age; he was an accomplished singer and, on one occasion, sang in the chorus of the Seattle Opera's Ring Cycle. He was an ardent skier who had a retirement wish to ski every slope in the western United States. Other interests included woodworking, sculpture, squash, golf, theology, and reading. He was also very much a family man, married to Mary Ann for fifty years and with three children and five grandchildren.

To describe someone as a Renaissance man has become something of a hackneyed expression. However, it certainly fits as a description of Joseph Eschbach and his life.

SELECTED BIBLIOGRAPHY

Eschbach JW Jr., Funk D, Adamson J *et al.* Erythropoiesis in patients with chronic renal failure undergoing chronic dialysis. *N Engl J Med* 1967; **276**: 653–658.

Eschbach JW, Cook JD, Scribner BH, Finch CA. Iron balance in hemodialysis patients. *Ann Intern Med* 1977; **87**: 710–713.

Eschbach JW, Mladenovic J, Garcia JF *et al.* The anemia of chronic renal failure in sheep. Response to erythropoietin-rich plasma in vivo. *J Clin Invest* 1984; **74**: 434–441.

Eschbach JW, Egrie JC, Downing MR *et al.* Correction of the anemia of end-stage renal disease with recombinant human erythropoietin. Results of a combined phase I and II clinical trial. *N Engl J Med* 1987; **316**: 73–78.

Eschbach JW. Anemia management in chronic renal disease: role of factors affecting erythropoietin responsiveness. *J Am Soc Nephrol* 2002; **13**: 1412–1414.