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This Week's Citation Classic®

Doherty J E, Perkins W H & Flanigan W J. The distribution and concentration of tritiated digoxin in human tissues. *Ann. Intern. Med.* 66:116-24, 1967.
[Veterans Administration Hospital, and Department of Medicine, University of Arkansas School of Medicine, Little Rock, AR]

In postmortem tissue, concentrations of tritium-labeled digoxin were reported in 11 patients who died after receiving a dose of tritiated digoxin for treatment of congestive heart failure. [The *SCI*® indicates that this paper has been cited in over 200 publications since 1967.]

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This is the second *Citation Classic* that has resulted from 25 years of work with digoxin.[1] This particular paper collects data presented previously[2,3] and adds four additional patients on whom we were fortunate enough to obtain autopsies when they died during the course of our research study. At the time the paper was published, we had performed turnover studies (pharmacokinetics, serum levels, and serum half-time and excretion) on 108 patients, so mortality was not really unduly high in these patients with congestive heart failure, often with other complications.

Pat Flanigan had recently returned to Little Rock from Boston, and our studies in patients with renal disease were stimulated by him and led to several other publications regarding digoxin and renal disease.[4-8] We shared many evenings in our clinical research center collecting blood, scant urine, and *all* stools on these patients. Ours was the only study (at that time) interested in total stool collection, and this gave rise to a number of humorous remarks on the part of house staff and nurses.

I remember when we lost our first patient under study. What a disappointment it was after so much time and work had been invested in the patient. We were eager to have our data as complete as possible. Only after I obtained permission to perform the postmortem did it occur to me how important that information might become. We later initiated a tissue turnover study in dogs to determine the time-course of digoxin in the various tissues[9] because of its significance. High and consistent cardiac-muscle serum ratios were demonstrated, suggesting the potential value of a clinical test of digoxin in the serum.

As a result of this and associated work, I was given the Casimir Funk Award in 1975 by the Association of Military Surgeons.

1. **Doherty J E.** The clinical pharmacology of digitalis glycosides: a review. *Amer. J. Med. Sci.* 255:382-414, 1968. [See also: **Doherty J E.** Citation Classic. *Current Contents/Clinical Practice* 7(42):12, 15 October 1979.]
2. **Doherty J E, Perkins W H & Mitchell G K.** Tritiated digoxin studies in human subjects. *Arch. Intern. Med.* 108:531-9, 1961. (Cited 165 times.)
3. **Doherty J E, Perkins W H & Wilson M C.** Studies with tritiated digoxin in renal failure. *Amer. J. Med.* 37:536-44, 1964. (Cited 170 times.)
4. **Doherty J E, Flanigan W J & Perkins W H.** Studies with tritiated digoxin in anephric human subjects. *Circulation* 35:298-303, 1967. (Cited 85 times.)
5. **Ackerman G L, Doherty J E & Flanigan W J.** Peritoneal dialysis and hemodialysis of tritiated digoxin. *Ann. Intern. Med.* 67:718-23, 1967. (Cited 105 times.)
6. **Doherty J E, Flanigan W J & Perkins W H.** Tritiated digoxin excretion in human subjects following renal transplantation. *Circulation* 37:865-9, 1968.
7. **Doherty J E, Flanigan W J, Patterson R M & Dalrymple G V.** The excretion of tritiated digoxin in normal human volunteers before and after unilateral nephrectomy. *Circulation* 40:555-61, 1969.
8. **Doherty J E, Flanigan W J & Dalrymple G V.** Tritiated digoxin. XVII. Excretion and turnover times in normal donors before and after nephrectomy and in the paired recipient of the kidney after transplantation. *Amer. J. Cardiol.* 29:470-4, 1972.
9. **Doherty J E & Perkins W H.** Tissue concentration and turnover of tritiated digoxin in dogs. *Amer. J. Cardiol.* 17:47-52, 1966. (Cited 125 times.)

