

Fauci A S, Haynes B F & Katz P. The spectrum of vasculitis: clinical, pathologic, immunologic, and therapeutic considerations. *Ann. Intern. Med.* 89:660-76, 1978.
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The vasculitic syndromes represent a spectrum ranging from limited disease, as in isolated cutaneous vasculitis, to severe systemic disease leading to irreversible organ system dysfunction and death. Certain vasculitic syndromes, such as Wegener's granulomatosis, respond dramatically to chronic, low-dose cytotoxic therapy, particularly cyclophosphamide, together with alternate-day prednisone. [The *SCI*[®] indicates that this paper has been cited in over 355 publications.]

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When I arrived at the National Institute of Allergy and Infectious Diseases of the National Institutes of Health (NIH) as a Fellow in immunology and infectious diseases in 1968, I became fascinated by a group of patients that Sheldon M. Wolff, my mentor, had been seeing over the previous eight years. He was studying prolonged (greater than one year) fever of unknown origin in relationship to his interest in the pathogenesis of fever. As it turned out, several patients who were referred to his study had vasculitis of one sort or another. It soon became clear to us that vasculitis was not a single entity. It represented a spectrum of disorders ranging from limited disease, such as isolated cutaneous vasculitis with very low mortality, to severe systemic vasculitis, such as Wegener's granulomatosis and polyarteritis nodosa with high morbidity and mortality. I requested of Wolff, and he agreed, to allow me to intensively

study these patients. His encouragement, support, and extraordinary base of knowledge were critical to the entire project.

Since it became clear that certain patients remitted with little or no therapy while others progressed in a fulminant manner to irreversible organ system dysfunction and death, we decided to initiate, at that time, a novel approach of aggressive therapy of Wegener's granulomatosis with chronic, low-dose cyclophosphamide together with alternate-day prednisone. We chose Wegener's granulomatosis as the first vasculitic syndrome in which to attempt this revolutionary approach since it was uniformly fatal and was quite a distinct disease, easy to distinguish from other vasculitic syndromes that might remit spontaneously.

The results were dramatic, with a 93 percent remission rate.^{1,2} This was unheard of at the time, and I became excited about categorizing as precisely as possible the broader range of vasculitic syndromes in order to attempt this aggressive approach in other diseases, such as polyarteritis nodosa. Wolff left NIH in 1977, and I continued the studies over the ensuing years. Quickly, we demonstrated the efficacy of this therapeutic approach in other diseases, such as severe systemic vasculitis of the polyarteritis nodosa group,³ Takayasu's arteritis,⁴ and lymphomatoid granulomatosis.⁵ I feel that the categorization of the broad scope of vasculitic syndromes, which allowed us to distinguish between those diseases that warranted aggressive therapy and those that did not, was critical to the success of this long-range protocol. This paper, written 10 years ago, was a comprehensive review of our experience at the halfway point between its inception in 1968 and today.

1. Fauci A S & Wolff S M. Wegener's granulomatosis: studies in eighteen patients and a review of the literature. *Medicine* 52:535-61, 1973. (Cited 335 times.)
2. Fauci A S, Haynes B F, Katz P & Wolff S M. Wegener's granulomatosis: prospective clinical and therapeutic experience with 85 patients over 21 years. *Ann. Intern. Med.* 98:76-85, 1983. (Cited 170 times.)
3. Fauci A S, Katz P, Haynes B F & Wolff S M. Cyclophosphamide therapy of severe systemic necrotizing vasculitis. *N. Engl. J. Med.* 301:235-8, 1979. (Cited 170 times.)
4. Shelhamer J H, Volkman D J, Parrillo J E, Lawley T J, Johnston M & Fauci A S. Takayasu's arteritis and its therapy in the United States. *Ann. Intern. Med.* 103:121-6, 1985. (Cited 20 times.)
5. Fauci A S, Haynes B F, Costa J, Katz P & Wolff S M. Lymphomatoid granulomatosis: prospective clinical and therapeutic experience over 10 years. *N. Engl. J. Med.* 306:68-74, 1982. (Cited 85 times.)