Kirk D. Wuepper, M.D.

The world of dermatologic research lost one of its stalwarts when Dr. Kirk D. Wuepper died on December 1, 1994, from cardiac failure. Kirk will be remembered as an intelligent, insightful investigative strategist who contributed greatly to many basic and clinical aspects of skin research during the past three decades.

Kirk was born in Bay City, Michigan, in 1938, and felt great loyalty to his home state. He did both undergraduate and medical degree studies at the University of Michigan, receiving his M.D. in 1963. During undergraduate and medical school years, Kirk laid a foundation for his later, unwavering academic interests by doing research projects in pharmacology, zoology, and microbiology laboratories. He finished medical school with a characteristically well-formulated career plan in investigative pursuits.

After internship at Philadelphia General Hospital, he wavered between a dermatology residency at venerable Penn or moving to the program at an upstart new research-oriented department at University of California at San Francisco. He opted for the Western frontier (many young midwestern doctors were drawn to the west coast in those days) and in 1964 he joined Bill and John Epstein and Howard Maibach in the exciting, upwardly striving department headed by Rees B. Rees. It was an ideal union. Early into his training, Kirk wore three hats—dermatology resident, U.S.P.H.S. venereal disease fellow, and research fellow in Hugh Fudenberg's laboratory. He was quickly productive in all spheres with clinical publications on syphilis, contact dermatitis to parabens, and halogenated salicylanilide photo contact allergy (with John Epstein and Howard Maibach). He soon became expert in the new technique of immunofluorescence microscopy and published, with Denny Tuffanelli, *Journal of the American Medical Association* and *New England Journal of Medicine* articles on false-positive serologies and the fluorescent treponemal antibody test; later, with John Epstein, he described erythrocyte fluorescence testing for erythropoietic protoporphyria (*Journal of the American Medical Association* 1966 and 1970). He also began a long series of studies in the fledgling field of clinical immunology including autoimmune adrenal insufficiency (*Lancet* 1966) and immune complex glomerulonephritis.

After four years of residency and research training (and 18 first-rate publications), Kirk moved on to Scripps Clinic and Research Foundation and a highly productive series of investigations with Charles Cochrane on the plasma kinin system and associated complement pathways. He published an elegant long-running series of studies on kinin proenzyme components, isolation of prekallikrein, the relationship of the kinin-forming system with Hageman factors, and the interaction of these systems with immune complexes in microvascular injury. He utilized this background to publish later, elegant clinical investigations of patients with prekallikrein (Fletcher factor) deficiency, Flaujeac trait (plasma kininogen-deficiency), and the C3 nephritic factor association with partial lipodystrophy in subclinical glomerulonephritis.

He spent four years in LaJolla until 1972 when he came to Portland and turned his talents and expertise in protein characterization to the skin. With Melodie Buxman, Kirk described, in 1975, the role of epidermal transglutaminase in keratin cross-linking. They went on to purify, characterize, and localize this protein in the epidermis. In parallel with his studies of transglutaminase, Kirk became interested in the characteristics and function of the staphylococcal toxin causing the epidermal split in Lyell's syndrome. He and Bob Dimond devised an assay to detect epidermolysis in newborn mice and went on to purify the "epidermolytic toxin." These fascinating studies of staphylococcal toxins provided the base for a long, continuing interest in microbial toxins. He later purified the highly toxic streptococcal erythrogenic toxin at a time when the related toxins of toxic shock syndrome were being identified and functionally correlated. He and Tom Ray also developed a mouse model to delineate the mechanism of skin injury caused by the interaction of the complement-activating mannan derived from candida albicans. Throughout those productive years of basic protein characterizations, Kirk retained an interest in immune mechanisms of skin injury, investigating erythema multiforme, pemphigus vulgaris, and dermatitis herpetiformis.

In the midst of his most productive research years, Kirk shouldered the responsibility of Secretary/Treasurer of the Society for Investigative Dermatology from 1979 to 1984 and two years later served as President. He also served as associate editor of the *Journal of Investigative Dermatology* and, in 1980, took over the leadership of Montagna's Annual Symposia on Biology of Skin.

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During those years of administrative responsibilities, Kirk shifted his research focus from proteins to DNA, working to clone the staphylococcal exotoxin TSS-1. This introduction to molecular genetics stimulated Kirk to initiate early efforts at gene linkage in psoriasis. As usual, Kirk was thinking way ahead. His focus on psoriasis was personal and longstanding. It fueled his early interest in the keratinocyte stimulatory properties of streptococcal epidermolytic toxins and formed a thread that continued through the gene-linkage studies. Kirk's foresight greatly aided the planning efforts of the National Psoriasis Foundation and created the vision that eventuated in the National Psoriasis DNA Bank. His bank of DNA, obtained from a number of families in 1988, provided material for Bowcock's successful and highly promising gene mapping of psoriasis to chromosome 17q, reported in Science in 1994 with Kirk as a co-author.

Kirk Wuepper's insights to the dermatologic sciences and his always clear and questioning mind set a worthy example for all who worked with him. His short span of years burgeon with scientific accomplishments. He contributed greatly to our small Society for Investigative Dermatology and shared our pride in seeing its prolific growth in membership and quality of science during his career.

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