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This Week's Citation Classic

McKusick V A. *Heritable disorders of connective tissue.*
St. Louis: C. V. Mosby Company, 1972 (4th cd.). 878 p.
[The Johns Hopkins Hospital, Baltimore, MD 21205]

The monograph presents a synthesis of information from the literature and the author's clinical experience, delineating mendelian disorders of collagens, elastins or mucopolysaccharides and presents a precis of normal biology of connective tissue and of clinical genetics as background. [The *SCI*® indicates that this book has been cited over 1085 times since 1961.]

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"The work on which this monograph was based began in 1950 when I saw a patient with the Marfan syndrome and severe aortic complications. I was then a resident. I became fascinated with the disorder, probably because it combined areas in which I had already worked: hereditary disorders (e.g., Peutz-Jeghers syndrome) and cardiology (e.g., electrokymography and constrictive pericarditis).

"When the book was published in June of 1956, the publisher produced, I am told, only 1,000 copies, on the advice that it would have limited interest, mainly to geneticists. What was not appreciated was that the wide distribution of connective tissue in the body is paralleled by a wide range of specialties that are concerned with these disorders. The first edition was sold out before the end of 1956 !

"Heritable disorders of connective tissue has been almost as successful a title as Garrod's *Inborn errors of metabolism.* I selected 'heritable' as the adjective because it indicates that the disorders are capable of being transmitted genetically, although in the individual case the disorder (those that are dominant, at least) may have arisen by new mutation.

"Rheumatologists are wont to refer to some of the conditions they treat as connective tissue diseases, eg, SLE. scleroderma, even rheumatoid arthritis. I like to chide them, saying that 'their' diseases are, yes, diseases *in* connective tissue, but not diseases *of* connective tissue, battle is fought in connective tissue and the connective tissue elements, as innocent bystanders, are in|ured, but 'mine' are the true diseases *of* connective tissue Consequently, imagine my satisfied amusement when, in the list of references of an article published in the 1960s, I saw my monograph referred to as *Veritable disorders of connective tissue.* A one-letter change, although resulting in an inaccuracy, conveyed a profound truth.

"The monograph (which had subsequent editions in 1960, 1966. and 1972, with a 5th edition presently in the mill, probably for 1979 publication) grew with the field —and the field grew with the book.

"My research, presented in the monograph, can be labelled genetic nosology, which I define as the delineation of genetic diseases. I have been lucky in my colleagues in many branches of clinical medicine, in genetics, and in biochemistry I was fortunate in working in a large general hospital that gave me access to patients in the pediatric, ophthalmologic, cardiologic, orthopedic, and other areas where patients with these protean diseases may first present Bentley Class, long Professor of Biology at Hopkins, encouraged and guided me in my self-education in general genetics.

"Collaborators with special expertise joined me in the study of these groups of patients: S. Harvey Mudd of the NIH (homocystinuria), David Kaplan of Downstate Medical Center (the specific mucopolysaccharidurias), Elizabeth F Neufeld of the NIH (the metabolic and enzymatic characteristics of cells from patients with mucopolysaccharidoses) and George R Martin of the NIH (biochemial abnormalities of collagen in the Ehlers-Danlos syndromes and osteogenesis imperfecta) Through the years I have also been helped in all this by a large group of the able junior associates. The nosology of these diseases illustrates the catalytic and mutually potentiating interaction between clinical, genetic, and biochemical study."