

# Dubois' Lupus Erythematosus

S E V E N T H   E D I T I O N

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# DUBOIS' LUPUS ERYTHEMATOSUS

SEVENTH EDITION

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# Dedication



## Edmund Lawrence Dubois: 1923–1985

Edmund Lawrence Dubois (pronounced “Doo-Boyz”) was born on June 28, 1923, to a middle-class Jewish family in Newark, New Jersey. He was the only child of a general surgeon, and his mother worked in his father’s office. Ed, as he was known, graduated from high school in Newark in 1939. He then attended Johns Hopkins University, graduating with a bachelor’s degree in 1943. While serving in the Army, he stayed in Baltimore to attend Johns Hopkins Medical School, where he also did his internship under A. McGehee Harvey, the legendary Chief of Service who was a lupus pioneer in his own right. Ed’s tendency to know and train under the best and the brightest continued with a residency in medicine at the University of Utah under Max Wintrobe (author of the *Hematology* textbook) and at Parkland Hospital in Dallas under Tinsley Harrison (author of *Harrison’s Medicine* textbook). He also completed an autopsy pathology fellowship at Los Angeles County General Hospital in 1948.

Ed decided to stay in Southern California and went into private practice at his father’s office in July 1950. In 1951, he met—and, in 1952, married—Nancy Kully, the beautiful daughter of Barney Kully, a local ear, nose, and throat specialist. To keep professionally busy, he volunteered his time

at the Los Angeles County General Hospital. The “General,” as it was known, was the largest hospital in the United States at the time, with over 3,000 beds. Dr. Paul Starr, then Chairman of the Department of Medicine, asked him to start a clinic consisting of eight patients who had a newly diagnosed disorder that was characterized by a positive result on a recently described laboratory test known as the “LE cell prep.” Within 10 years, Ed had the largest lupus practice in the world, caring for 500 patients at the General Tuesday morning Lupus Clinic and another 500 patients in his private practice.

By the mid-1980s, more than one half of the rheumatologists in Southern California could say that Ed Dubois had taught them nearly everything they knew about lupus. His first publications on lupus appeared in the *Journal of the American Medical Association* (four of them!) and the *American Journal of Medicine* (two papers) in 1951 and 1952. They described autoimmune hemolytic anemia as a manifestation of systemic lupus erythematosus (SLE), showed that steroids ameliorate the disease, and described the general clinical and laboratory features of patients who had positive LE cell preps.

As the General became more closely affiliated with the University of Southern California, university resources allowed the establishment of lupus research laboratories. Ed Dubois’ keen clinical instincts and his demands for perfection among those who worked with him permitted him to publish seminal works that established him as the first, or among the first, to propose insights that we now take for granted. These include: use of nitrogen mustard for serious SLE (1954); use of Atabrine for cutaneous and mild systemic lupus (1954); high-dose steroid protocol for managing central nervous system disease (1956); analysis of why hydralazine induced LE cells (1957); the first description of avascular necrosis in lupus (1960); the first description of steroid-induced peptic ulcers (1960); the first description of gangrene from lupus vasculitis (1962); anticonvulsant drug-induced lupus (1963); establishment of one of the first NZB/NZW mouse research laboratories in the United States (1963), detailed analysis of an accrued, incredible series of 520 patients with lupus (1964); one of the first probes into familial SLE (1964); use of cyclophosphamide in SLE (1967); the first large series of procainamide-induced lupus (1968); absence of erosions in lupus synovitis (1970); phenothiazine-induced lupus (1972); the first report of lupus with myelofibrosis (1973); the first large analysis of causes of death, containing 212 patients (1974); HLA typing of patients with lupus (1974); ibuprofen for



SLE (1975); and the incidence of septic arthritis in lupus (1975).

In 1966, Ed wrote the first edition of his monograph, *Lupus Erythematosus: A Review of the Current Status of Discoid and Systemic Lupus Erythematosus and Their Variants*. Dedicated "to the patients from whom we have learned," this remarkable, largely single-authored textbook was enormously successful and now—with this volume—is in its seventh edition. More than any other publication, this book has shaped how rheumatologists approach and treat this disease. Although he authored 175 papers, abstracts, book chapters, and received numerous international honors while traveling, Ed was most proud of being the founding medical director of The American Lupus Society and President of the Southern California Rheumatism Society.

Ed Dubois was a tireless workaholic. He would rise at 5 am and write for an hour or two before going to work. A humanist of the first order, one half of his time was spent giving free medical care. Ed was known to be exacting and did not suffer fools easily. Although he seemed to be a man of few words, his gentle kind-heartedness was always evident. Ed's probing intellect was apparent within moments of meeting him, and he was always relaxed, modest, and approachable. Ed could be a wonderful teacher when confronted with a student physician who had an inquiring mind and a capacity to work hard. Although he had well-known Hollywood luminaries as private patients, he was never snobbish or conceited, and he felt much more at home seeing indigent patients at the General's lupus clinic.

More than anything else, Ed Dubois was a private man

who was devoted to his family. He was happily married and had four children, all of whom now have successful careers. His first grandchild (of six) was born shortly before he died. He was an expert yachtsman who relaxed best on his boat. (When he was terminally ill, he bought a new boat that he named Dubious.) His other consuming passion was photography. Able to be privately tutored by the likes of Ansel Adams, his office was filled with creative and wonderful pictures showing his love of life.

While still a youthful 54 years of age in 1977, Ed complained of low back and knee pain, which turned out to be a compression fracture from multiple myeloma. He privately confided to me that excessive exposure to radiation during his training and in various research laboratories was responsible for this. A fighter to the end, Ed lived with myeloma for 8 years, which must be close to a record. He saw a full schedule of patients 2 weeks before he died, in February 1985, from pneumonia complicated by renal shut-down. I was fortunate to meet Ed Dubois as a medical student at the University of Southern California and as a resident at Cedars-Sinai Medical Center. Among the greatest honors in my life was when he asked me to help in his office part-time in 1977, while I was still a fellow in training, and to edit his book along with him in 1982. I will always value his friendship.

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*Neuroendocrine Immune Interactions: Principles and Relevance to Systemic Lupus Erythematosus.*

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*Issues in Drug Development in SLE: Clinical Trial Design, Outcome Measures, and Biomarkers.*

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*The Genetics of Murine Systemic Lupus Erythematosus.*

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*Ocular, Aural, and Oral Manifestations.*

### **Betty P. Tsao, PhD**

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*The Genetics of Human Lupus, Antibodies to DNA.*

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*B Cells in Systemic Lupus Erythematosus.*

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*The Definition and Classification of Systemic Lupus Erythematosus.*

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*Prognosis, Mortality, and Morbidity in Systemic Lupus Erythematosus.*

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*Fibromyalgia in SLE and the Use of Complementary and Alternative Medicine in SLE.*

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*The Importance of Sex Hormones in Systemic Lupus Erythematosus.*

### **Daniel J. Wallace, MD**

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*The Clinical Presentation of Systemic Lupus Erythematosus, The Musculoskeletal System, Clinical Aspects of Vasculitis and Selected Cutaneous Manifestations of Systemic Lupus Erythematosus, Manifestations Involving the Eye, Ear, and Larynx, Gastrointestinal and Hepatic Manifestations, Serum and Plasma Protein Abnormalities and Other Clinical Laboratory Determinations in Systemic Lupus Erythematosus, Differential Diagnosis and Disease Associations, Principles of Therapy and Local Measures, Antimalarial Therapies, Nonpharmacologic and Complementary Therapeutic Modalities, Additional Therapies Used in the Management of Lupus, Adjunctive Measures and Issues: Allergies, Antibiotics, Vaccines, and Disability, Biologics and Stem Cell Therapies for Lupus, A Patient's Guide to Lupus Erythematosus, Lupus Resources.*

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*Nonsteroidals and Salicylates for Systemic Lupus Erythematosus.*

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*Pathomechanisms of Cutaneous Lupus Erythematosus.*

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*The Nervous System.*

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*The Genetics of Human Lupus*

# Preface

Forty years have elapsed since Ed Dubois wrote the first edition of his monograph in 1966. He wrote 80% of the text himself, using notecards and a typewriter between 5 and 6 a.m. over a 2-year period. Ed would indeed be proud to see the explosion of information that has transformed what at the time was the arcane discipline of lupology. The 7th edition of *Dubois' Lupus Erythematosus* reflects the changes and developments in the field over the last 5 years. Lupus experts are now working together to form consortiums and registries which allow for clinical trials to be performed rapidly and efficiently; provide banks of shared sera, cells, and genetic materials; and permit new clinical indices and ascertainment methodologies to be developed and tested more rigorously. In keeping with the improved quality of studies and in order to focus on more evidence-based findings, we no longer cite every paper published on the subject of lupus but emphasize trends, treatment consensuses and practical clinical information along with succinct summaries of basic science insights. Ironically, the last time a drug was approved for lupus was also in 1966. Almost 20

biologics are now in various stages of clinical development for SLE, and this has created a palpable sense of excitement.

Chapters on cytokines and interferons, pathogenesis of atherosclerosis, immune tolerance, clinical indices, mixed connective tissue disease, reproductive immunology issues, fibromyalgia, women's issues, and biomarkers are included for the first time. We welcome 20 new authors and co-authors and thank our senior experts who graciously agreed to pass the baton on to young, promising investigators.

Dr. Wallace wishes to thank his family, Jody Stanley, and Nancy Winter for their hard work and support. Dr. Hahn thanks her mentors who started her off in lupus studies, Lawrence E. Shulman, MD, PhD and the late Mary Betty Stevens, MD; she also thanks her husband, Theodore John Hahn, MD, who further inspires her, and her daughters, Alysanne Yvonne Hahn and April Diane Hahn Lange, who make it all worthwhile.

Daniel J. Wallace  
Bevra Hannahs Hahn  
Los Angeles, CA





FIGURE 1.1

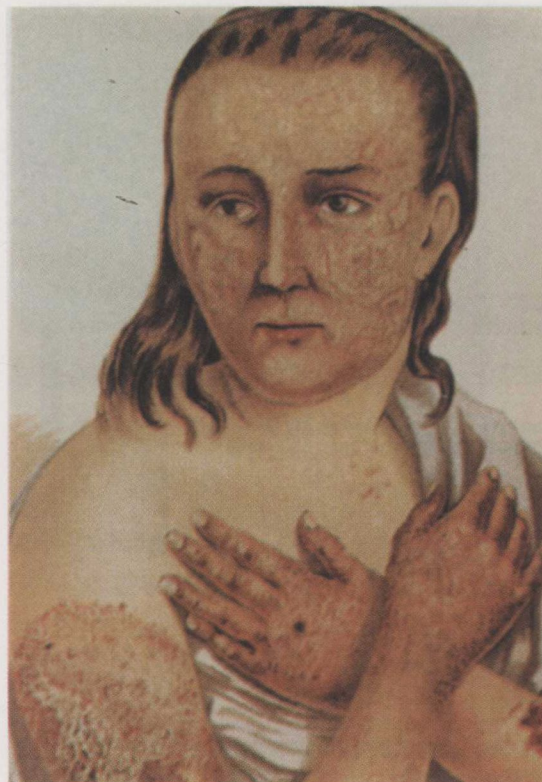


FIGURE 1.3



FIGURE 1.2

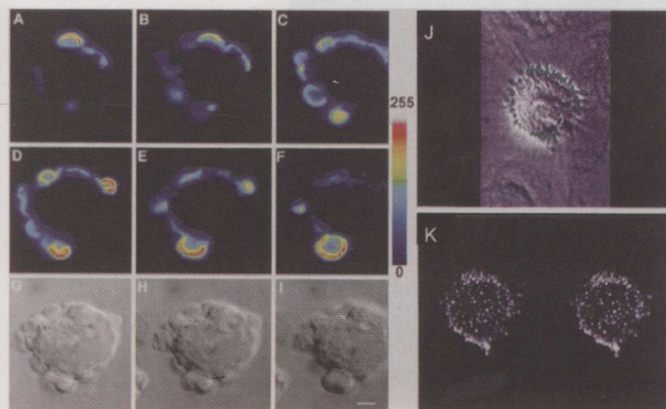


FIGURE 13.3

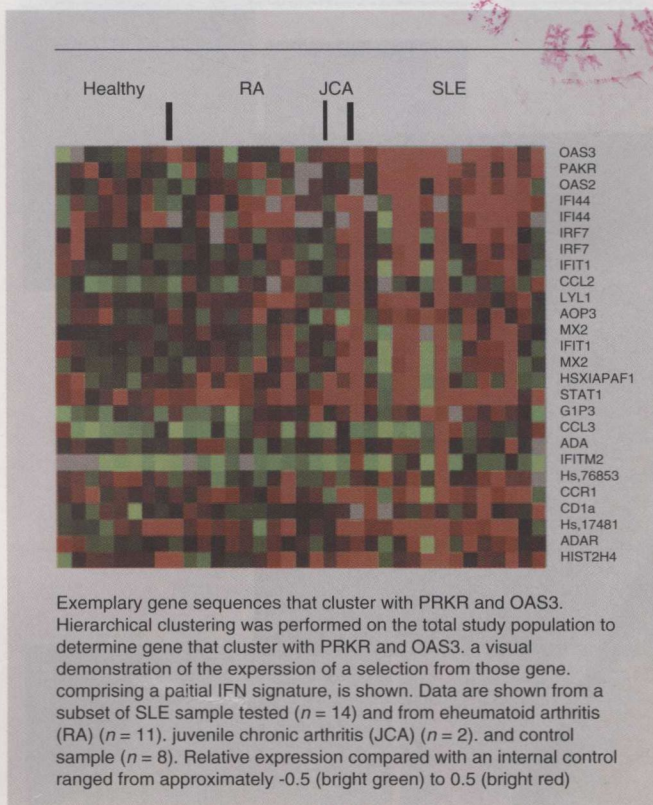


FIGURE 10.1



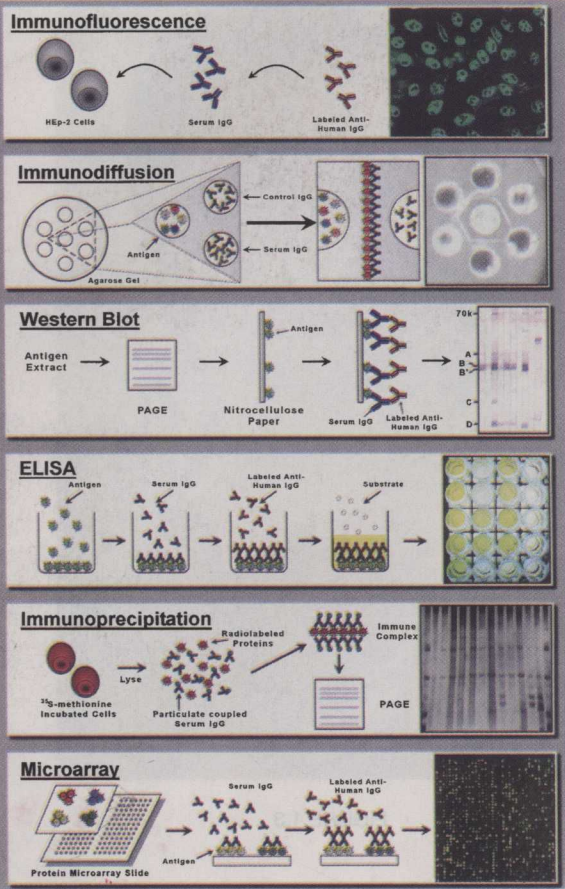


FIGURE 26.2



FIGURE 29.4

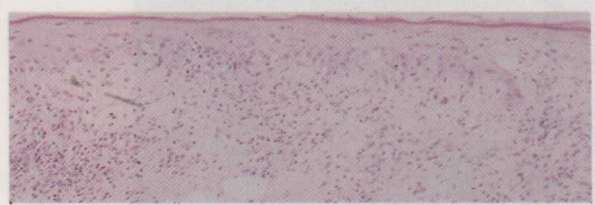


FIGURE 29.5

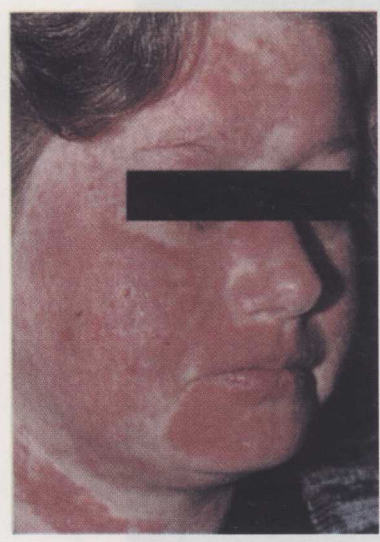


FIGURE 30.1

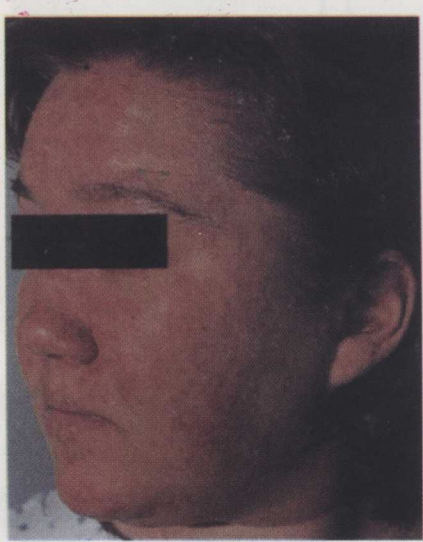


FIGURE 30.2



FIGURE 30.7





FIGURE 30.8



FIGURE 30.15

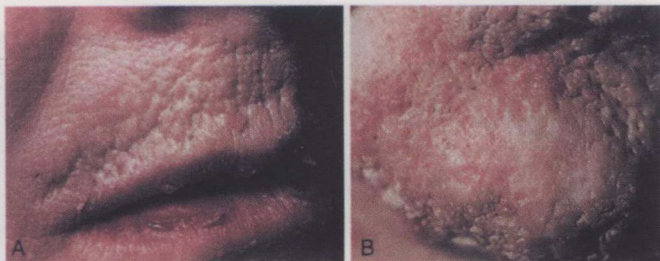


FIGURE 30.23



FIGURE 30.12



FIGURE 30.13



FIGURE 30.16



FIGURE 30.28



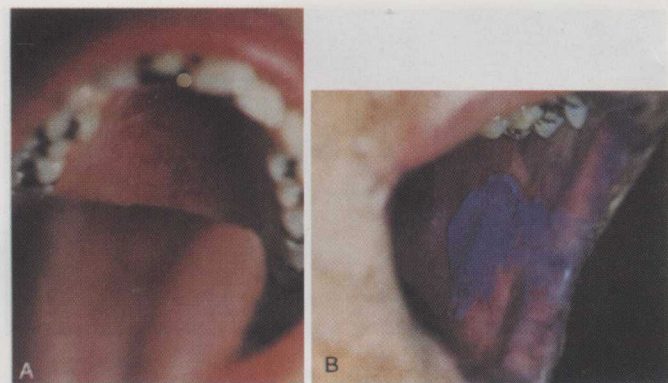


FIGURE 30.34



FIGURE 31.1



FIGURE 31.2



FIGURE 31.3



FIGURE 31.4



FIGURE 31.5



FIGURE 31.6

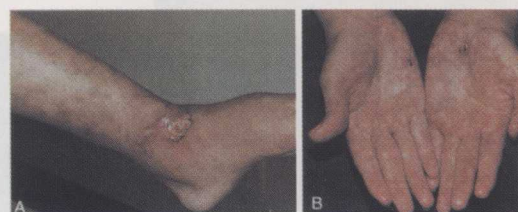


FIGURE 31.7



FIGURE 31.8



FIGURE 31.9





FIGURE 31.11



FIGURE 31.13



FIGURE 31.15

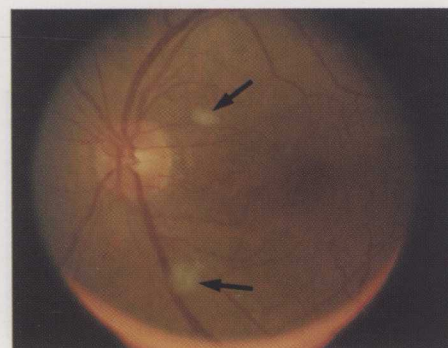


FIGURE 40.1



FIGURE 31.12



FIGURE 31.14

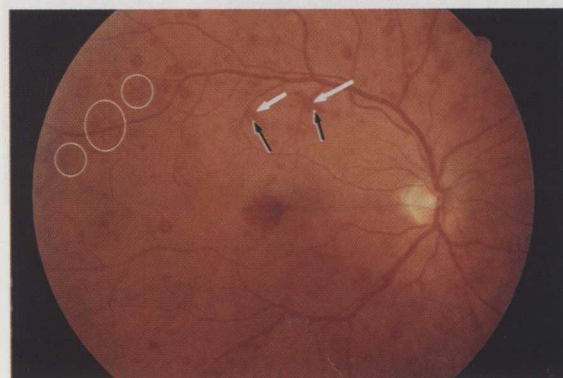


FIGURE 40.2