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Textbook of Dermatology

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Preface to First Edition

No comprehensive reference book on dermatology has been published in the English language for ten years and none in England for over a quarter of a century. The recent literature of dermatology is rich in shorter texts and in specialist monographs but the English-speaking dermatologist has long felt the need for a substantial text for regular reference and as a guide to the immense monographic and periodical literature. The editors have therefore planned the present volume primarily for the dermatologist in practice or in training, but have also considered the requirements of the specialist in other fields of medicine and of the many research workers interested in the skin in relation to toxicology or cosmetic science.

An attempt has been made throughout the book to integrate our growing knowledge of the biology of skin and of fundamental pathological processes with practical clinical problems. Often the gap is still very wide but the trends of basic research at least indicate how it may eventually be bridged. In a clinical textbook the space devoted to the basic sciences must necessarily be restricted but a special effort has been made to ensure that the short accounts which open many chapters are easily understood by the physician whose interests and experience are exclusively clinical.

For the benefit of the student we have encouraged our contributors to make each chapter readable as an independent entity, and have accepted that this must involve the repetition of some material.

The classification employed is conventional and pragmatic. Until our knowledge of the mechanisms of disease is more profound no truly scientific classification is possible. In so many clinical syndromes multiple aetiological factors are implicated. To emphasize one at the expense of others is often misleading. Most diseases are to some extent influenced by genetic factors and a large proportion of common skin reactions are modified by the emotional state of the patient. Our knowledge is in no way advanced by classifying hundreds of diseases as genodermatoses and dozens as psychosomatic.

The true prevalence of a disease may throw light on its aetiology but reported incidence figures are often unreliable and incorrectly interpreted. The scientific approach to the evaluation of racial and environmental factors has therefore been considered in some detail.

The effectiveness of any physician in practice must ultimately depend on his ability to make an accurate clinical diagnosis. Clinical descriptions are detailed and differential diagnosis is fully discussed. Histopathology is here considered mainly as an aid to diagnosis but references to fuller accounts are provided.

The approach to treatment is critical but practical. Many empirical measures are of proven value and should not be abandoned merely because their efficacy cannot yet be scientifically explained. However, many familiar remedies old and new have been omitted either because properly controlled clinical trials have shown them to be of no value or because they have been supplanted by more effective and safer preparations.

There are over nine hundred photographs but no attempt has been made to provide an illustration of every disease. To have done so would have increased the bulk and price of the book without increasing proportionately its practical value. The conditions selected for illustration are those in which a photograph significantly enhances the verbal description. There are a few conditions we wished to illustrate, but of which we could not obtain unpublished photographs of satisfactory quality.

The lists of references have been selected to provide a guide to the literature. Important articles now of largely historical interest have usually been omitted, except where a knowledge of the history of a disease simplifies the understanding of present concepts and terminology. Books and articles provided with substantial bibliography are marked with an asterisk.

Many of the chapters have been read and criticized by several members of the team and by other colleagues. Professor Wilson Jones, Dr. R.S. Wells

and Dr. W.E.Parish have given valuable assistance with histopathological, genetic and immunological problems respectively. Many advisers, whose services are acknowledged in the following pages, have helped us with individual chapters. Any errors which have not been eliminated are, however, the responsibility of the editors and authors.

The editors hope that this book will prove of value to all those who are interested in the skin either as physicians or as research workers. They will welcome readers' criticisms and suggestions which may help them to make the second edition the book they hope to produce.

Preface to Third Edition

The aim of the editors in this edition, as in its two predecessors, has been to provide a textbook which is soundly based in science, but which is nevertheless essentially a practical work of reference for the serious student of dermatology, whose main responsibility is the clinical care of patients. To incorporate the new knowledge of the skin and its diseases, published in the seven years since the second edition went to press has been a formidable task. Merely to add to the existing text the more important new facts, supported by the appropriate additions to the lists of references, would have greatly lengthened the book, without adding proportionately to its value. Much has therefore been rewritten or extensively revised. Of some 18,000 references cited, over a quarter are drawn from the literature of the past seven years.

We are happy to welcome new members to our team of contributors. Some have chosen entirely to rewrite the chapters they have taken over, others have made use of part of the text of the second edition. Dr. Kerdel-Vegas was prevented by other commitments from revising his contributions, but Dr. Roger Harman, who has undertaken their revision, found that only minor changes were required and we have therefore retained Dr. Kerdel-Vegas' name among the contributors.

We are still employing a practical and pragmatic classification of diseases. There have been few changes in the past seven years, but some disorders have been transferred to different chapters, either because advances in knowledge suggest that such a change is desirable, or because logic demands it, e.g. progeria is more appropriately considered with the other ageing syndromes than with the genodermatoses, and pyoderma gangrenosum is classified with vasculitis.

This book is intended to provide the essential information needed by the dermatologist in training or in practice, while keeping its size within reasonable proportions. While retaining the essential histopathological details necessary to achieve this end, we have worked in close collaboration with the authors of a comprehensive histological volume which, we hope, will complement this work.

We have continued to abbreviate the references despite some criticisms. Bearing in mind the cost of the art paper which is so essential for the effective reproduction of illustrations, we feel that the consequent saving of space is justified.

The first two editions of this book stimulated some hundreds of readers in many countries to write to editors or contributors, drawing our attention to omissions or errors and suggesting improvements. We are very grateful for their advice. We have not been able to adopt every suggestion for the addition of rare diseases, but we have endeavoured to include every named disease entity founded on more than a few case reports. We shall continue to welcome further criticisms and suggestions.

A.J.R.
D.S.W.
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Acknowledgements

The revision of this textbook would have been impossible without the willing cooperation of a great many colleagues. Several chapters have been submitted to the criticism of various members of our team, and this mutual assistance has been greatly appreciated. Some contributors have sought the advice of other authorities on technical or specialized aspects of their chapters. We should like to express our gratitude to all those who have helped in this way.

Dr. Eric Waddington provided for our first edition an account of the clinical features of variola, based on his large personal experience; it has required little revision. Dr. Desmond Burrows and Dr. John Bridges gave advice on Letterer-Siwe disease and Dr. Helen Mawhinney on the Wiskott-Aldrich syndrome. Dr. Rodney Dawber gave advice on cryosurgical techniques, Dr. Margaret Spittle on radiotherapy and Dr. Graham Rook on immunological aspects of tuberculosis. Mrs S. Lomas, Staff Pharmacist, Wycombe General Hospital, has given invaluable help with the Formulary.

Dr. J.N.S. Mitchell, Dr. J.G. Reid and Dr. J.D. Wilkinson have given considerable help in many ways.

The source of almost every photograph or diagram is acknowledged in the legend which accompanies it. We are grateful to the publishers, editors and authors who have given us permission to reproduce those few illustrations which are not original.

A large proportion of the photographs are from the collections of Addenbrooke's Hospital, the hospitals of the Aylesbury and High Wycombe Group and St John's Hospital. We are very grateful to all those consultants who have allowed us to use photographs of their patients and apologize if we have inadvertently omitted any individual acknowledgment. The late Professor J.T. Ingram, Professor F.F. Hellier and Dr. S.T. Anning have kindly permitted photographs of their patients to be included in Chapters 35 and 36. The Addenbrooke's photographs are the work of our art editor, Mr. Leonard Beard, or of his predecessor, Mr. Vince. Mr. D.G. Standen provided most of the photographs from Stoke Mandeville Hospital, and Mr. Bernard Clark those from Wycombe General Hospital. The St John's photographs are the work of Mr. R.B. Phillips, Director of the Department of Medical Illustration and Lecturer in Medical Illustration at St John's Hospital, or of his predecessor, Mr. R.J. Lunnon. Mr. A.L. Pegg and Mr. W. Blackledge are responsible respectively for the clinical photographs and photomicrographs in Chapter 36. The Department of Medical Illustration of the Hallamshire Hospital, Sheffield, provided most of the photographs in Chapters 40 and 64. We are grateful to them all for their cooperation and technical skill. Messrs Glaxo have kindly covered the cost of Figure 24.4.

Our registrars have given us valuable assistance in many ways. We ask them to accept this collective acknowledgment of our appreciation.

Mr Freyhen, Librarian at St John's Hospital, has been most helpful. We are grateful, too, to our secretaries who have coped so efficiently with a heavy burden of additional work and to our colleagues who have shown so much understanding and tolerance of our absorption in and commitment to this book during the past two years.

In conclusion, on behalf of ourselves and the many contributors who are his former pupils we wish to place on record our indebtedness to the late Dr. G.B. Dowling and our gratitude for his teaching and example.

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CHAPTER 36

Lupus Erythematosus, Scleroderma and Dermatomyositis

THE 'COLLAGEN' OR 'CONNECTIVE-TISSUE' DISEASES

N.R. ROWELL

The continuation of the title of this chapter into the third edition is evidence of the failure of the author and editors to find any term which all could accept as accurate and appropriate for this important group of diseases. The term 'connective-tissue diseases' [5] has frequently been used in recent years, but whilst some authorities equate it with the older term, 'collagen diseases', others [4] apply it to all inherited or acquired disorders of the connective-tissue system. 'Collagen disease' is unacceptable since there is no evidence that collagen is primarily at fault. The increasing emphasis on immunological abnormalities in these conditions has brought the terms 'autoimmune diseases' [10] and 'immunological diseases' [14] some popularity but both are too comprehensive. To avoid the premature coining of a confusing new term we have preferred to continue to refer to connective-tissue disease, wherever the use of a collective term is unavoidable.

That disease can involve the whole of the connective-tissue system is a relatively recent concept. In 1933 Klinge [9] was the first to propose that rheumatic fever and rheumatoid arthritis were disorders of the entire connective tissue. The changes in the intercellular components of the connective tissue, the presence of fibrinoid necrosis in collagenous tissue and the myxomatous swelling of ground substance were similar to those seen in experimental animals made hypersensitive to foreign protein, and for these reasons he concluded that the rheumatic diseases were due to hypersensitivity. He included other conditions in which fibrinoid necrosis was a feature, such as polyarteritis nodosa, dermatomyositis and malignant hypertension. The presence of widespread fibrinoid change in the vessels led to the inclusion of systemic sclerosis by Masugi and Yä-Shu [11] and also of systemic lupus erythematosus. However, Klemperer and his colleagues [8], with whose work the term 'collagen disease' is associated, struck a note of caution by pointing out that fibrinoid necrosis could be seen in the absence of hypersensitivity mechanisms, for example, in the base of peptic ulcers. It has been stated [1] that the presence of fibrinoid degeneration does not warrant the grouping of the conditions showing this change, nor does it imply an allergic mechanism. It is now recognized that there are various types of fibrinoid with somewhat similar staining properties. They have a multiple origin from the degeneration of collagen, from the ground substance, muscle, and fibrin and other plasma proteins.

In 1950 Klemperer [7] stated: 'the term diffuse collagen disease was originally applied to acute and chronic maladies which are characterized anatomically by generalized alterations of the connective tissue, particularly by abnormalities of its extracellular components. In this case the term can include rheumatic fever, rheumatoid arthritis, polyarteritis nodosa, acute lupus erythematosus, generalized scleroderma and dermatomyositis'. Klemperer emphasized his dissension from the widespread indiscriminate use of the term 'collagen disease' for disorders with unusual clinical or pathological features. He confirmed that his sole intention was to put forward the concept that 'in

certain diseases anatomical investigations reveal conspicuous alterations in the intermediary substances of the connective tissue in a systemic manner'. It is now realized that the connective tissue is not the only tissue involved in these disorders.

It has been customary to consider that systemic and discoid lupus erythematosus, systemic sclerosis, localized and generalized morphoea, polyarteritis nodosa, Wegener's granulomatosis, giant-cell arteritis, dermatomyositis, rheumatoid arthritis and Sjögren's syndrome, should be grouped together, and this has been supported by evidence of clinical, pathological and immunological overlap. But this grouping may not be justified and may even hamper our understanding of these diseases. On the other hand, certain patients with evidence of clinical overlap can be distinguished by characteristic immunological abnormalities. The importance of so-called 'mixed connective tissue disease' (see p. 1228) is that the prognosis may be better than for patients who have only one disease. Other conditions may have to be added to the group. These include the recently described eosinophilic fasciitis [15] (see p. 1208).

There is an urgent need for precise and universally acceptable criteria for diagnosis. When adequate criteria and modern investigational techniques are used it is apparent that each disorder can be distinguished as a separate entity. For example, evidence has been produced that discoid lupus erythematosus is a separate disorder and not a benign variant of systemic lupus erythematosus [2,3,12]. Moreover, certain diseases which appear clinically homogeneous may be genetically heterogeneous. For example, there appear to be at least three separate genotypes in discoid lupus erythematosus related to age of onset [3,12] and the severity of disease in systemic sclerosis is related to the presence of HLA-B8 [6]. Immunological subgroupings are also found. It appears that the connective-tissue disorders can be divided into two groups on the basis of the antinuclear factor test [13]: those such as lupus erythematosus and systemic sclerosis in which antinuclear antibodies are frequently found in high titre, and those like polyarteritis nodosa, various types of cutaneous vasculitis and dermatomyositis in which antinuclear antibodies are usually absent.

It must be admitted that diagnosis of these disorders is sometimes far from easy and extensive investigation may be required. Although recently developed techniques, such as estimation of DNA binding and immunohistology, have proved very helpful, results have to be interpreted in association with the clinical features and other laboratory data. A diagnosis of 'collagen vascular disease' or 'collagenosis' in a patient suffering from an illness with obscure symptoms and signs, possibly associated with an elevated erythrocyte sedimentation rate, which responds to corticosteroids, is the resort of the intellectually destitute and must be avoided. It is usually possible to make a precise diagnosis and this is very important for modern epidemiological and statistical techniques. However, it is more than an academic exercise as, in the future, specific therapy may well depend on the precision of diagnosis.

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LUPUS ERYTHEMATOSUS

Lupus erythematosus is usually divided into two main types—discoid and systemic. Some authors [10,14] subdivide discoid lupus erythematosus into a localized form in which lesions are confined to the face above the chin, the scalp and the ears, and a disseminated form in which lesions also occur elsewhere on the body. Although haematological and serological abnormalities occur slightly more frequently in the disseminated form, the natural history of the two subgroups is similar and in my view they are the same disorder.

The more controversial point is whether discoid and systemic lupus erythematosus are variants of

the same disease. The evidence in favour of this thesis may be summarized as follows:

(i) The cutaneous lesions of systemic and discoid lupus erythematosus may be clinically and histologically indistinguishable.
(ii) Certain clinical features are found in both conditions (see Table 36.1).
(iii) Similar haematological, biochemical and immunological abnormalities can be demonstrated in both conditions (see Table 36.1), although the incidence of abnormalities is lower in discoid lupus erythematosus.
(iv) Patients with discoid lupus erythematosus occasionally develop evidence of overt systemic lupus erythematosus.
(v) Patients with systemic lupus erythematosus may develop typical lesions of discoid lupus erythematosus when the active phase subsides [11].

This seems to be formidable evidence but the following observations require explanation.

1. The risk of a patient with discoid lupus erythematosus developing overt systemic lupus erythematosus is small. It varies from 1·3% [9] to about 5% [19]. My own observations suggest that despite the fact that 55% of patients with discoid lupus erythematosus show some haematological or serological abnormality the risk of such conversion is about 5% [1,18]. In some series [12,15,20] such conversion was not encountered despite follow up for nearly 30 years. A retrospective study [17] of 127 patients with systemic lupus erythematosus showed that eight patients had had discoid lesions from 2 to 29 years.

2. The presence of laboratory abnormalities in discoid lupus erythematosus does not appear to predispose to the development of systemic lupus erythematosus [18]. Haematological abnormalities were still present in 50% of 77 patients with discoid lupus erythematosus, 5 years after initial assessment, yet none had developed systemic lupus erythematosus in the same period [15]. The same prognosis was found in a subgroup intermediate between discoid and systemic lupus erythematosus as in patients with uncomplicated lupus erythematosus [20].

3. Immunoglobulins and complement are present in uninvolved skin of patients with systemic lupus erythematosus and absent in patients with discoid lupus erythematosus [21].

4. Most patients with discoid lupus erythematosus exposed to ultraviolet light, stress, trauma, etc. do not develop the systemic disease.

5. The age and sex distribution of systemic lupus erythematosus [4,13] is strikingly different from that of discoid lupus erythematosus [3,17].

It has been proposed [3,4,5,6] that both systemic and discoid lupus erythematosus are initiated by the occurrence of somatic mutations in lymphocytic stem cells of predisposed individuals (see diagram 36.1 p. 1173), and that they are genetically distinct. The significantly different incidence of HLA-B8 between discoid and systemic lupus erythematosus provides evidence for this view [16]. There are at least three genotypes related to age of onset in discoid lupus erythematosus [6] and there is some confirmation of this from histocompatibility typing [16]. It has long been recognized that the sex ratio is markedly different in the two diseases. The female:male ratio of carriers at birth in systemic lupus erythematosus is about 4·5:1 [4], although it may vary between countries [6], and it has been proposed that the genotype in systemic lupus erythematosus involves three dominant X-linked alleles. By contrast the sex ratio (female:male) of carriers at birth in discoid lupus erythematosus is

TABLE 36.1. Comparison of data on a personal series of patients with discoid and systemic lupus erythematosus

	Discoid lupus erythematosus	Systemic lupus erythematosus
Number of cases	120	40
Rash	100%	80%
Joint pains	23%	70%
Fever	0%	40%
Raynaud's phenomenon	14%	35%
Chilblains	22%	22%
Poor peripheral circulation	26%	32%
ESR > 20 mm in first hour	20%	85%
Serum globulin > 3G%	29%	76%
L.E. cells	1·7%	83%
Antinuclear factor(s)	35%	87%
Homogeneous	24%	74%
Speckled	11%	26%
Nucleolar	0%	5·4%
Precipitating auto-antibody(ies)	4%	42%
Wasserman reaction positive	5%	22%
Rheumatoid factor test positive	15%	37%
Direct Coombs' test positive	2·5%	15%
Leucopenia	12·5%	37%
Thrombocytopenia	5%	21%