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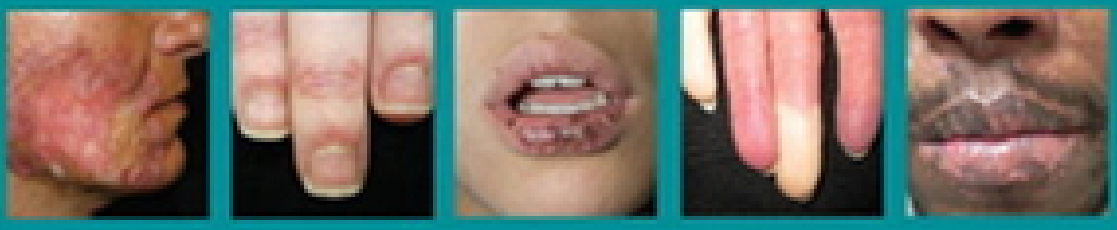
Dermatological Signs of SYSTEMIC DISEASE



Fifth Edition

ELSEVIER

DERMATOLOGICAL SIGNS OF SYSTEMIC DISEASE

FIFTH EDITION

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ELSEVIER

Edinburgh London New York Oxford Philadelphia St Louis Sydney Toronto 2017

ELSEVIER

First edition 1988
Second edition 1995
Third edition 2003
Fourth edition 2009

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ISBN: 978-0-323-35829-3
E-ISBN: 978-0-323-35831-6

Content Strategist: Russell Gabbedy
Content Development Specialist: Joanne Scott
Project Manager: Srividhya Vidhyashankar
Design: Miles Hitchen
Illustration Manager: Emily Costantino
Illustrator: Graphic World Inc.
Marketing Manager: Kristin Koehler

Printed in China

Last digit is the print number: 9 8 7 6 5 4 3 2 1

Dr. Callen dedicates this book to his wife Susan,
his children Amy Maidenberg and David Callen,
their Spouses Dan and Laura, and his grandchildren
Judah and Noa Callen, Aviva and Eden
Maidenberg and Liam Sondreal.

Dr. Jorizzo dedicates his contribution to this edition to
Irene Carros, John, Michael, Melina, to the late Joseph
and Margaret, and to Johanna and Paul.

Dr. Zone dedicates his contribution to his wife Judy,
and children Joe, Sara and Stephanie.
Stephanie has honored him by pursuing
a career in Academic Dermatology.

Dr. Piette dedicates this book to his wife Michelle,
son Evan, and daughter Lauren, and thanks them
for their patience and support.

Dr. Rosenbach dedicates this book to Anna, Lara, and
Jake, and thanks them for their patience and support.

Dr. Vleugels dedicates her contribution
to her husband Keith and to the rest of her family
for their many years of support.

PREFACE

This is the fifth edition of our book. We began this journey together in the mid-1980s having recognized a gap in the knowledge of practicing dermatologists and internists. We have somewhat altered our approach with each new edition and this one is no different. With this edition we said farewell to Jean Bolognia as an editor and welcome Misha Rosenbach and Ruth Ann Vleugels. Misha is one of the first people to train in a combined dermatology–medicine residency in the United States and has developed a focused interest in hospital medicine, with a specific research focus on granulomatous diseases. Ruth Ann began and runs one of the most successful rheumatology–dermatology clinics in the United States and has now successfully trained multiple others in a postresidency fellowship program. We have retained our collaboration with Warren Piette and John Zone.

In this revision of our book we added some additional chapters and have selected many new authors and coauthors to update and revise most of the chapters. We have continued our goal of providing the practicing physician, academic physician, or resident with a text that explores the relationship of the skin with internal diseases or conditions. Each chapter now has been reviewed by one of our associated editors as well as both of us. We continue our stance of providing suggested readings rather than an extensive reference list. These suggested readings have been updated so that the interested reader may delve into the most current literature. We have continued the use of color photographs throughout this edition of our text and in many cases have found new photographs for inclusion.

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Acknowledgments

Dr. Callen acknowledges and thanks the following physicians: Carol L. Kulp-Shorten, MD, Jyoti B. Burruss, MD, Kristin O. Donovan, MD, Shannon M. McAllister, MD, Alfred L. Knable, MD, Timothy S. Brown, MD, Janine Malone, MD, Anna Hayden, MD, Soon Bahrami, MD, Cindy E. Owen, MD, Courtney R. Schadt, MD, Sonya Burton, MD, and Michael W. McCall, Jr. for allowing him the time to write by providing care for his patients in his absence. In addition, he thanks all of the residents and staff at the University of Louisville for their academic stimulus and assistance with patients and their families.

Dr. Jorizzo acknowledges and thanks the faculty, residents, and staff at the Departments of Dermatology at both the Wake Forest University School of Medicine and the Weill Cornell Medical College for their ongoing support.

Dr. Zone acknowledges and thanks the faculty, residents and staff at the University of Utah Department of Dermatology for their support.

Dr. Piette thanks all of the dermatology residents and faculty at Cook County and at Rush Medical Center for their academic stimulus and assistance with patients and their families.

Dr. Rosenbach thanks his faculty, residents, staff, and mentors.

Dr. Vleugels acknowledges the continued support of the Department of Dermatology at Brigham and Women's Hospital and thanks her patients as well as her mentors, colleagues, staff, residents, and fellows.

CHAPTER 1

LUPUS ERYTHEMATOSUS

Christopher B. Hansen • Jeffrey P. Callen

KEY POINTS

- Lupus erythematosus is a multisystem disorder that frequently has cutaneous involvement
- Lupus-specific skin disease can be characterized as acute, subacute, or chronic based on clinical and laboratory features
- Other nonspecific cutaneous changes such as cutaneous vasculitis and Raynaud's phenomenon occur more commonly in lupus patients
- Prevention involves protection from ultraviolet radiation and smoking cessation
- Topical and intralesional corticosteroids and other topical immunomodulators may be effective for mild or localized disease
- Antimalarials are the first-line systemic treatment, with other systemic agents reserved for more severe or recalcitrant disease

Lupus erythematosus (LE) is a multisystem disorder that encompasses a spectrum from a relatively benign, self-limited cutaneous eruption to a severe, sometimes fatal, systemic disease. Prior to Hargraves' recognition of the LE cell, LE was diagnosed by a constellation of clinical findings. Ultimately, the American College of Rheumatology (ACR) developed a set of criteria that could be used for the classification of systemic lupus erythematosus (SLE). The criteria were revised in 1982 (Table 1-1). When a patient fulfills four or more of the ACR criteria, either concurrently or serially, during any period of observation, that patient can be classified as having SLE.

In the 1940s and 1950s, dermatologists first recognized that most of their patients with chronic, scarring discoid lupus erythematosus (DLE) lesions had few, if any, systemic findings, whereas those with malar erythema and/or photosensitivity frequently had systemic disease. They also recognized a middle group in whom the cutaneous lesions were more transient than in patients with DLE, but for whom the prognosis was not as poor as in those patients with SLE. These patients were later categorized as having subacute cutaneous LE (SCLE). The classification of cutaneous LE subsets was stressed by Gilliam and his coworkers. Gilliam proposed that cutaneous manifestations characterized by interface dermatitis (histopathologically- specific LE) be classified into one of three groups based on clinical features. An individual LE patient can present with more than one subtype of the disease. Gilliam also recognized that LE patients can have a skin disease that is not histopathologically specific (Table 1-2). Although each subset listed in Table 1-2 is generally predictive of outcome, it must be remembered that the full spectrum of LE-associated organ dysfunction is possible in any individual patient.

The prevalence of SLE is reported to be 17–48/100,000 people. The prevalence of cutaneous LE is not well established, but it appears to be at least as common as SLE. SLE has a strong female preponderance, with a 12:1 female-to-male ratio in the childbearing years. Cutaneous LE appears to be more common than SLE in males and older adults, but remains more common in women, with a 3:1 female-to-male ratio.

CHRONIC CUTANEOUS LUPUS ERYTHEMATOSUS

Chronic cutaneous LE can have several clinical manifestations. The most common subset is discoid lupus erythematosus (DLE). Patients with DLE may be classified as having either localized DLE, in which lesions are confined to the head and neck, or widespread DLE, in which lesions are found on other body surfaces in addition to the head and neck. DLE can also occur as a manifestation of SLE in approximately 20% of patients. Other less

TABLE 1-1 Revised ACR Criteria for the Diagnosis of Systemic Lupus Erythematosus

If four or more of the following criteria are present serially or simultaneously during any observation, the patient may be considered to have systemic lupus erythematosus:

1. Malar rash
2. Discoid lupus erythematosus lesions
3. Photosensitivity, by history or by observation
4. Oral ulcers, usually painless, observed by the physician
5. Arthritis, nonerosive, involving two or more joints
6. Serositis, pleuritic, or pericarditis
7. Renal disorder with proteinuria (>500 mg/day) or cellular casts
8. Central nervous system disorder with seizures or psychosis (absence of known cause)
9. Hematologic disorder, such as hemolytic anemia, leukopenia (<4000/mm^3), or thrombocytopenia (<100,000/mm^3)
10. Immunologic disorder, detected by positive lupus erythematosus preparation, abnormal titers of antinative DNA and anti-Sm, and false-positive Venereal Disease Research Laboratory or rapid plasma reagin results
11. Positive antinuclear antibody titers

From Tan EM, Cohen AS, Fries JF, et al. The 1982 revised criteria for the classification of systemic lupus erythematosus. Arthritis Rheum 1982;25:1271–7, with permission.

TABLE 1-2 A Classification of Mucocutaneous Lesions in Lupus Erythematosus

I. LE-specific histopathologic findings
  A. Chronic cutaneous LE
    1. DLE (localized versus generalized)
    2. Hypertrophic/verrucous LE
    3. Palmar/plantar LE
    4. Oral DLE
    5. LE panniculitis
    6. Tumid LE
  B. SCLE
    1. Polymorphous light eruption-type lesions
    2. Annular lesions (may be seen in Asian patients with SCLE [annular erythema of primary Sjögren's syndrome])
    3. Papulosquamous lesions
    4. Neonatal LE
    5. C2-deficient LE-like syndrome
    6. Drug-induced SCLE
  C. ACLE
    1. Malar erythema
    2. Photosensitivity dermatitis
    3. Generalized erythema
II. LE-nonspecific histopathologic findings
  A. Vasculopathy
    1. Urticaria
    2. Vasculitis
    3. Livedo reticularis/livedo racemosa/pyoderma gangrenosum-like leg ulcerations
  B. Mucosal lesions
  C. Nonscarring alopecia
  D. Bullous LE or epidermolysis bullosa acquisita
  E. Associated mucocutaneous problems
    1. Mucinous infiltrations
    2. Porphyrias
    3. Lichen planus
    4. Psoriasis
    5. Sjögren's syndrome
    6. Squamous cell carcinoma

LE, lupus erythematosus; DLE, discoid LE; SCLE, subacute cutaneous LE; ACLE, acute cutaneous LE.

common forms of chronic cutaneous LE include hypertrophic LE, tumid LE, lupus erythematosus panniculitis (LEP, or lupus profundus), oral DLE, as well as DLE lesions on the palms and/or soles.

Discoid Lupus Erythematosus

DLE lesions are characterized by erythema; telangiectasia; adherent scale, which varies from fine to thick; follicular plugging; dyspigmentation; and atrophy and scarring (Fig. 1-1). The lesions are usually sharply demarcated and can be round, thereby giving rise to the term discoid (or disc-like). The presence of scarring and/or atrophy is the characteristic that separates these lesions from those of SCLE. The differential diagnosis most often includes papulosquamous diseases such as psoriasis, lichen planus, secondary syphilis, superficial fungal infection, and sarcoidosis. A histopathologic examination is usually helpful in confirming the diagnosis, and only rarely is immunofluorescence microscopy necessary.

Patients with localized DLE have lesions located solely on the head, neck, or both. These appear to represent the majority of cases of DLE. These patients differ from those with widespread discoid lesions of LE in a number of ways. They have fewer manifestations that suggest systemic disease, and they less frequently demonstrate a positive antinuclear antibody (ANA) or leukopenia. It appears that patients with DLE who progress to develop SLE are generally not in the subset with localized discoid lesions of LE. Those patients with disease localized to the head and neck will frequently (roughly 50%) have a remission, whereas the disease rarely becomes clinically inactive (less than 10%) in those with widespread involvement. Lastly, it also appears that those with widespread disease respond less well to antimalarial treatment. Thus, it seems that it is prognostically worthwhile to separate patients with localized DLE and those with generalized DLE into different subsets.

Hypertrophic Lupus Erythematosus

Hypertrophic or verrucous DLE (HLE) is a unique subset in which the thick, adherent scale is replaced by massive hyperkeratosis, and the resulting lesions resemble verruca or squamous cell carcinomas (Fig. 1-2). These lesions usually occur in the setting of other, more typical DLE lesions. Patients with HLE tend to have chronic disease, to have little in the way of systemic symptoms or abnormal laboratory findings, and to be extremely difficult to treat with conventional therapy. They may respond to oral retinoids.

Palmar/Plantar Discoid Lupus Erythematosus

The lesions of DLE can occur on the palms and/or soles (Fig. 1-3). The frequency of this subset is low, and there is no specific clinical or serologic correlation. Patients with DLE of the palms or soles can have chronic cutaneous disease, or the lesions can be present in patients with SLE. Palmar and/or plantar lesions are often difficult to treat.

Oral Discoid Lupus Erythematosus

Oral DLE lesions are histopathologically and clinically similar to cutaneous discoid lesions of LE (Fig. 1-4). Oral DLE lesions are distinct from the oral and nasal ulcerations that occur in SLE, which are associated with active systemic disease and are histopathologically nonspecific. Lesions that look like those of discoid lesions of LE in the oral mucosa have associations similar to those seen with localized or widespread discoid lesions of LE.

Tumid Lupus Erythematosus

Tumid lupus erythematosus (lupus tumidus) is characterized by erythematous to violaceous papules, plaques (Fig. 1-5), or nodules, that usually occur on sun-exposed surfaces. The lesions classically have no epidermal changes and tend to heal with no residual scarring or atrophy. Patients with tumid LE are photosensitive. Serologic abnormalities are distinctly uncommon in these patients, and patients with tumid LE rarely meet criteria for SLE. The pathology of tumid LE reveals an increase in mucin and a periappendiceal and perivascular dermal

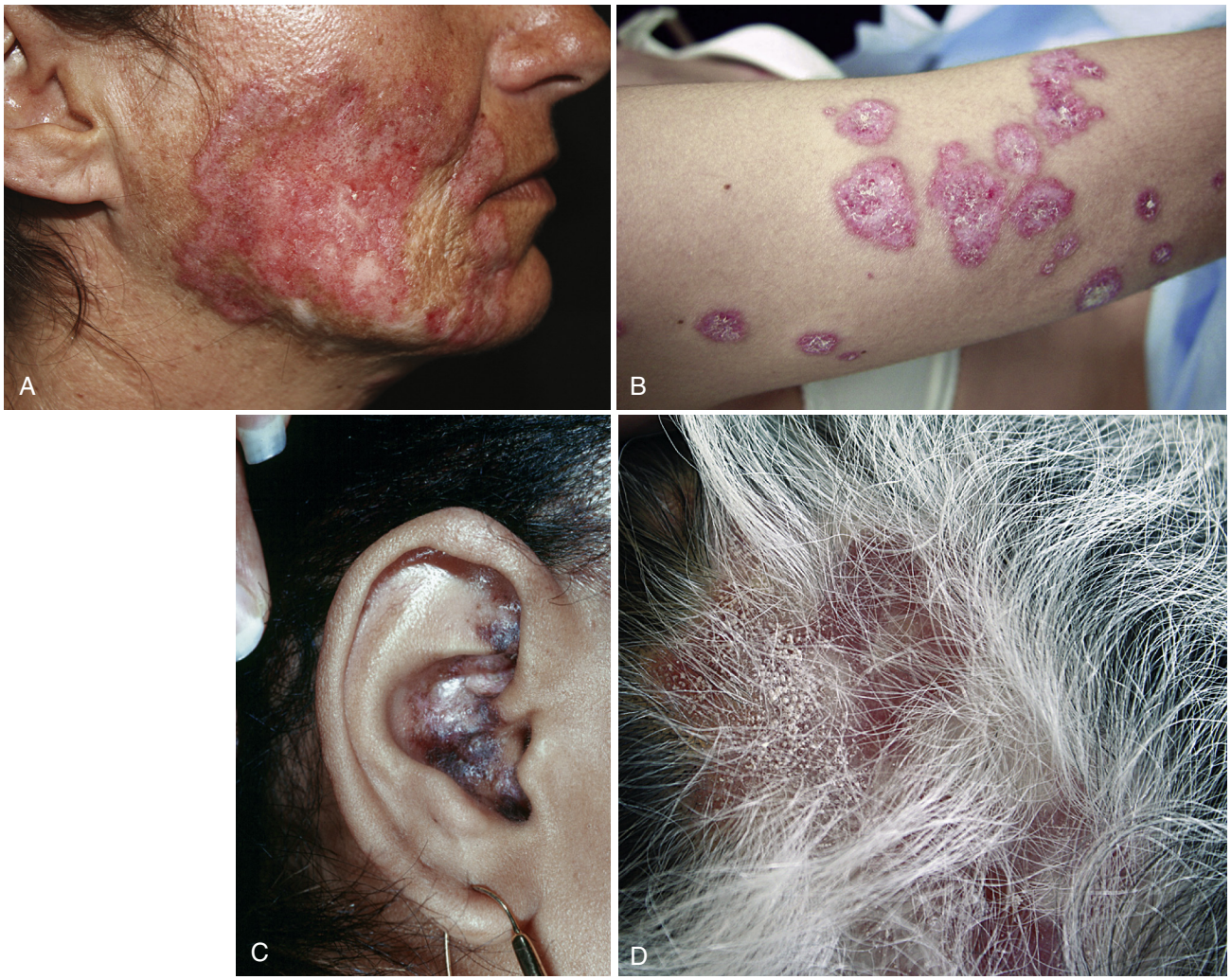

FIGURE 1-1 ■ Discoid lesions of lupus erythematosus. Erythematous to violaceous lesions with adherent scale, slight atrophy, and early scar formation. **A,** Facial lesion; **B,** lesions on the extensor surface of the arms; **C,** patulous follicles in the conchal bowl; **D,** scarring scalp lesion.

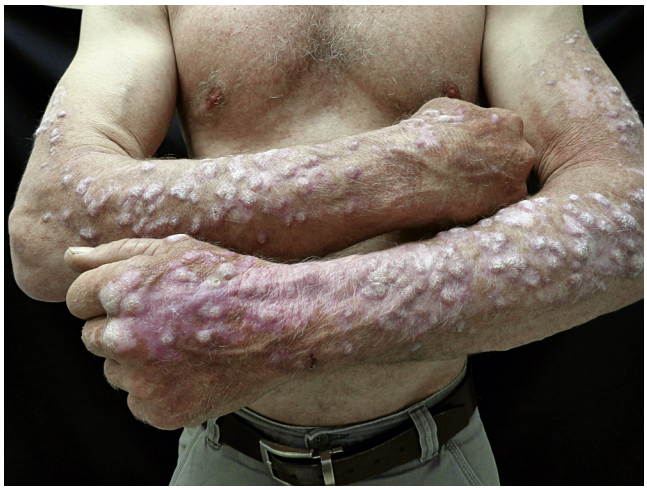

FIGURE 1-2 ■ Hypertrophic (verrucous) lupus erythematosus. These lesions simulate verruca, keratoacanthoma, or squamous cell carcinoma.

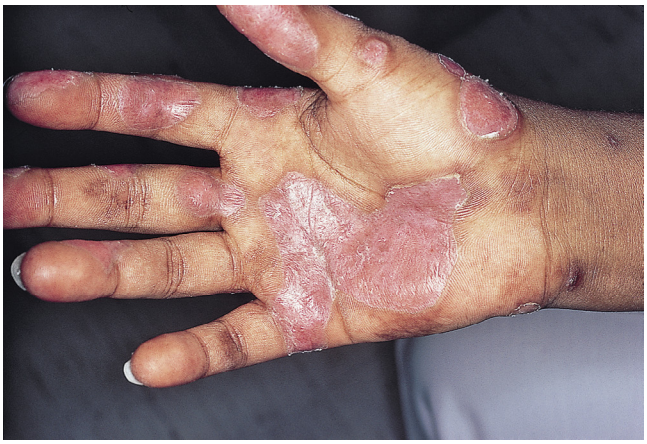

FIGURE 1-3 ■ Erosive lesions of discoid lupus erythematosus involving the palms. Typical lesions of discoid lupus erythematosus are present elsewhere.

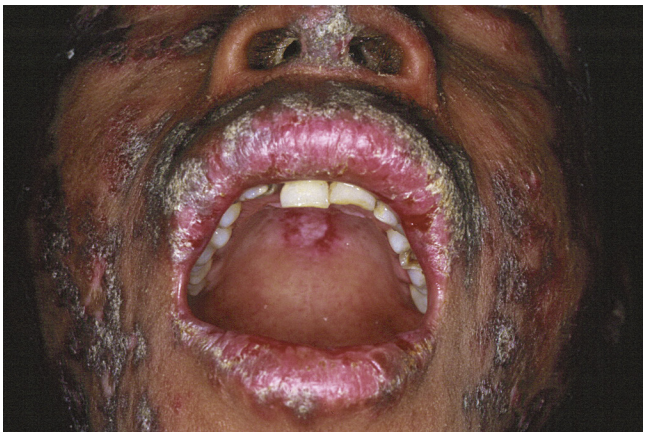

FIGURE 1-4 ■ Oral lesions in a patient with chronic cutaneous lupus erythematosus. Note the discoid lupus erythematosus lesion on the palate.

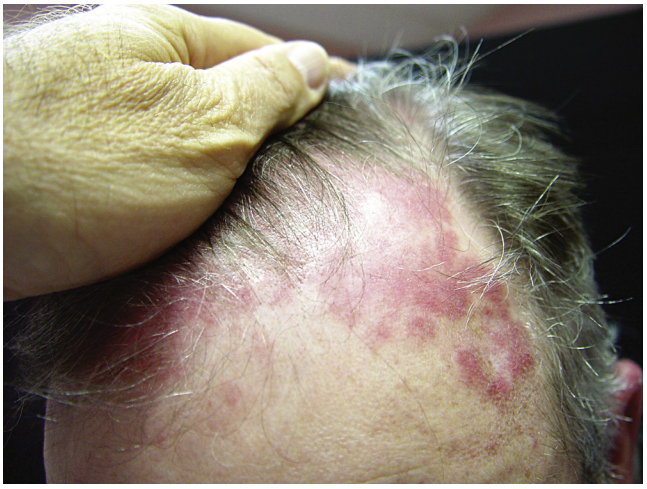

FIGURE 1-5 ■ Lupus tumidus. This patient has erythematous plaques on the forehead without surface change. Biopsy of these lesions revealed a perivascular and periadnexal lymphocytic infiltrate without an interface dermatitis. Extensive mucin deposition was also noted.

infiltrate composed of lymphocytes, but there is little if any change at the dermal–epidermal interface. It is possible that there is overlap, both clinically and histologically, between reticulated erythematous mucinosis and tumid LE.

There are several controversies regarding tumid LE: (1) some authorities believe that tumid LE is not a variant of lupus erythematosus; and (2) as there is no residual scarring or atrophy, it differs from other types of chronic cutaneous lupus. Some have argued that it would fit better as a variant of subacute cutaneous lupus or in a separate classification. Patients with tumid LE are usually responsive to photoprotection and antimalarials.

Lupus Panniculitis

Lupus erythematosus panniculitis (LEP, lupus panniculitis) is a lobular panniculitis that occurs rarely in patients with DLE or SLE (Fig. 1-6). Whether LEP is histopathologically distinct is controversial; thus, in the authors' opinion, the patient should have documented SLE or DLE to be classified as having LEP. The term lupus profundus is sometimes used as a synonym for LEP, while others reserve this term for LEP with overlying discoid lesions. LEP is often chronic, and it can lead to cutaneous and subcutaneous atrophy, calcification, and occasional ulceration. Lesions preferentially involve the face as well as areas with prominent subcutaneous tissue, such as the upper arms, thighs, and buttocks. Twice as many patients with LEP do not have systemic disease as have systemic disease. It has been postulated that in the patient with LEP, renal disease is rarely present, and when present, it is among the more benign forms.

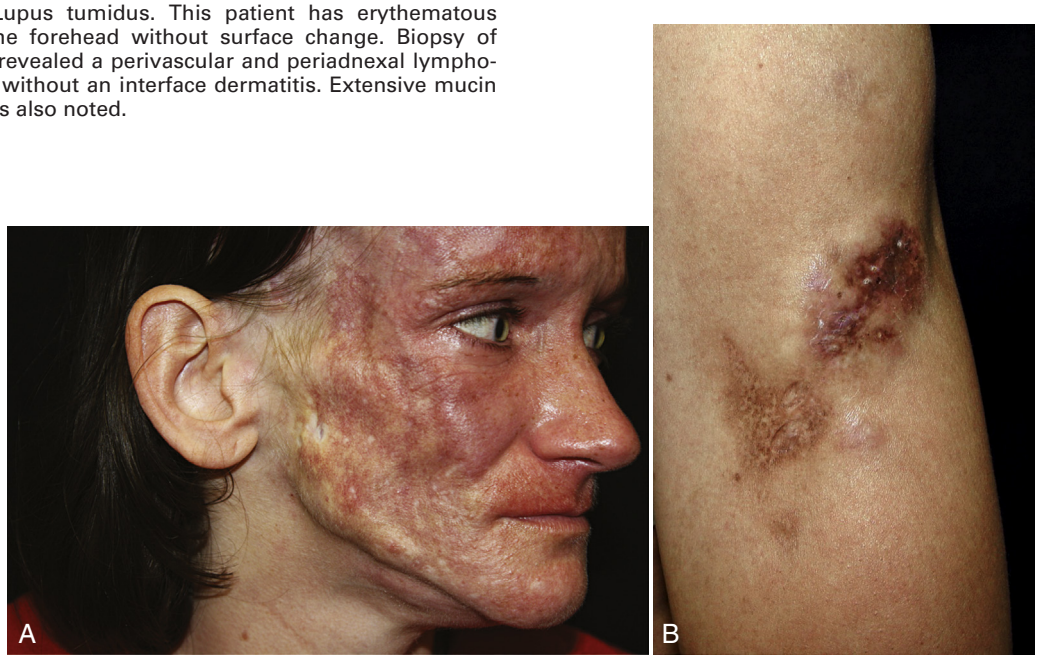

FIGURE 1-6 ■ Lupus panniculitis. **A,** This woman has inflammatory, subcutaneous nodules that have resulted in severe subcutaneous atrophy on the face. Typical lesions of discoid lupus erythematosus were present on other body sites. **B,** Calcified subcutaneous nodules and atrophy on the lateral arm.