23.5 Papulosquamous disease 5621 Christopher E.M.

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ESSENTIALS Papulosquamous diseases are characterized by well-demarcated areas of papules and scale, typically on an erythematous back- ground. The differential diagnosis includes psoriasis, lichen planus, mycosis fungoides, discoid lupus erythematosus, eczema/dermatitis, drug eruptions, tinea, pityriasis versicolor, secondary syphilis, and pityriasis rosea. The presence of significant pruritus is a useful marker to help with the differential diagnosis: lichen planus and discoid eczema are typically pruritic, whereas others, such as psoriasis, are less so. The distribution is also key to diagnosis, with psoriasis often showing characteristic symmetrical involvement of the extensor surfaces, scalp, and nails. Histology can be essential to reach a diagnosis and plan an appropriate approach to management. The most common form of psoriasis is chronic plaque psoriasis, which often first affects the scalp. The nails are affected in about 50% of cases. There is no cure. Topical corticosteroids and vitamin D3 analogues (e.g. calcipotriol) are the most commonly used treatment worldwide. Phototherapy and photochemotherapy can be effective. Systemic treatments, including biological therapies, are only required in the most refractory cases. Lichen planus is characterized by purple (violaceous) flat-topped polygonal papules that vary in size, most commonly on the flexor aspects of the wrists, the lower back, and the ankles. About 50% of patients have involvement of the mucous membranes. The skin dis- ease is usually self-limiting. Psoriasis Psoriasis is one of the most common and easily identifiable inflam- matory skin diseases. In Western Europe its prevalence is estimated at 2%, but is higher in parts of Scandinavia (e.g. the Faroe Islands, where it reaches 5%). Worldwide, the disease is rare in Inuit, Native American, Japanese, and Afro-Caribbean people, and has been estimated to affect just 0.3% of the general population in China. There is no evidence that the incidence of the disease is chan- ging, by contrast with the year-on-

year increase in atopic derma- titis. Overall, the sex incidence is equal, the mean age of onset is 20 years and in 75% of cases the disease begins before the age of 40 years. Psoriasis starts earlier in females than males, indicating hormonal influences. Late-onset disease (type II), first presenting after the age of 40 years, reaches a peak of onset between the ages of 55 and 65 years. There appears to be no association with either social class or diet. Early-onset, type I psoriasis is familial; one-third of patients have a first-degree relative with the disease. It is apparent that this form of psoriasis is genetically predetermined and polygenic. At least 47 psoriasis susceptibility loci have been identified worldwide. The most robust association is with the MHC class I allele HLA-C*06:02, which contributes up to 50% of the risk in patients with psoriasis. No gene or gene product has thus far been definitively associated with psoriasis. Type II psoriasis is not associated with HLA-C* 06:02, and may be a separate disease. Twin studies underscore the importance of an interaction be- tween environment and genotype for the expression of psoriasis, and concordance is 72% in monozygotes. Environmental triggers in gen- etically susceptible individuals include: β-haemolytic streptococcal tonsillitis/pharyngitis; physical and psychological stress; HIV infec- tion; drugs including β-blockers, nonsteroidal anti-inflammatories, lithium, antimalarials; and alcohol. Clinical features The most common form of psoriasis, chronic plaque psoriasis, or psoriasis vulgaris, accounts for 90% of cases. The characteristic fea- tures are well-circumscribed red plaques covered with silvery-white scales. These occur most commonly on the extensor aspects of the knees and elbows, the lower back, and scalp (Figs. 23.5.1 and 23.5.2), although any skin surface may be affected. Plaques are frequently strikingly symmetrical, varying in diameter from less than 1 cm to more than 10 cm. Individual plaques are dynamic, such that in ac- tive disease a plaque may clear from the centre to leave an annular or gyrate configuration that to the uninitiated could be misdiagnosed as tinea corporis. Various phenotypes of psoriasis exist: Guttate psoriasis Named from the Latin guttata, meaning a droplet. This form clas- sically occurs two to three weeks after streptococcal pharyngitis or tonsillitis, and is the most common presentation in childhood (Fig. 23.5.3). Onset is acute, with a predominantly centripetal 23.5 Papulosquamous disease Christopher E.M. Griffiths

section 23 Disorders of the skin 5622 distribution of small (<1 cm diameter) papules. This form of psor- iasis is frequently self-limiting. Erythroderma Total skin involvement by psoriasis is known as erythroderma, al- though this term is also used for any inflammatory skin disease affecting more than 90% of the skin’s surface area. Other diseases producing erythroderma include atopic dermatitis, lichen planus, drug eruptions, and cutaneous T-cell lymphoma. Erythroderma, particularly in older people, can lead to fluid loss, hypocalcaemia, impaired thermoregulation (both hypo- and hyperthermia), and high-output cardiac failure. Generalized pustular psoriasis Generalized pustular psoriasis (GPP), also known as Von Zumbusch disease, is an acute onset of painful red plaques studded with small sterile pustules. This form of psoriasis is usually precipitated by in- fection or acute withdrawal of either systemic glucocorticosteroids or, on occasion, high-potency topical corticosteroids, leading to a re- bound pustular flare. The patient is systemically unwell, with pyrexia and influenza-like symptoms. Recent evidence indicates that gener- alized pustular psoriasis is more akin to the autoinflammatory dis- eases and should more accurately be termed generalized pustulosis, rather than as a variant of chronic plaque disease. It has been linked to a genetically determined deficiency in interleukin-36 receptor antagonist. Flexural psoriasis Flexural psoriasis (psoriasis inversa) pertains to a form that involves the groins, axillae, and inframammary regions. Psoriasis at these sites loses many of the characteristic clinical features, in that it is shiny, nonscaly, and bright red, but retains the characteristic clear

demarcation between involved and uninvolved skin. Sebopsoriasis This form of psoriasis occurs in the seborrhoeic sites of the nasolabial folds, eyebrows, scalp, post-auricular region, and Fig. 23.5.1 Plaques of psoriasis. Fig. 23.5.2 Widespread chronic plaque psoriasis. Fig. 23.5.3 Guttate psoriasis.

23.5 Papulosquamous disease 5623 presternum. At times it may be difficult to distinguish from seborrhoeic dermatitis. Scalp The scalp is often the first and sometimes the only site to be affected by psoriasis. Paradoxically, it may be the most difficult form of psoriasis to treat. The lesions vary from typical plaques to involve- ment of the entire scalp, with encroachment of scales along the hair shafts, a process known as tinea amiantacea (Fig. 23.5.4). Rarely do the lesions extend beyond the hairline. Alopecia may at times be a consequence. Koebner phenomenon The appearance of psoriasis at sites of recent trauma or pressure to the skin, such as under a tight waistband, is known as the iso- morphic or Koebner phenomenon. Although not unique to psor- iasis (it occurs also in lichen planus, viral warts, sarcoid, and vitiligo) it is a clinical marker of active, progressive disease. Nails Approximately 50% of patients with psoriasis have characteristic clinical involvement of any one or up to all the finger and toe nails. The involvement of the skin of the fingers by psoriasis, and the pres- ence of psoriatic arthritis, predispose to nail disease. The clinical fea- tures range from thimble-like pitting of the nail plate, to onycholysis (separation of the nail from the nail bed), oil spots (orange discol- ouration of the nail bed), and disabling nail dystrophy (Fig. 23.5.5). Patients are frequently concerned about nail disease, and may re- quest treatment for this aspect of psoriasis alone. Co-morbid diseases Chronic plaque psoriasis is associated with several co-morbid con- ditions, which include: Inflammatory bowel disease Ten per cent (10%) of patients with inflammatory bowel disease, particularly Crohn’s disease, have concomitant psoriasis. Palmoplantar pustulosis Now believed to be a condition separate from psoriasis, palmoplantar pustulosis has been reclassified as a co-morbid condition. Yellow sterile painful pustules occur on the palms and soles, fading to brown scaled lesions. Up to 25% of patients have coexistent chronic plaque psoriasis. This is a disease of middle-aged women (female:male ratio 9:1), and more than 95% are current or previous smokers. There is an association with thyroid disease. There is no association with HLA-C*06:02. Psoriatic arthritis This seronegative inflammatory arthritis occurs in more than 25% of patients with psoriasis. Most cases present either concomitantly with or after the first signs of skin disease, but on occasion (<10%) the arthritis predates psoriasis. Five clinical phenotypes of psoriatic arthritis exist: asymmetrical distal interphalangeal arthritis (most commonly and classically); oligoarthritis; polyarthritis; spondyl- itis; and arthritis mutilans (Fig. 23.5.6). A characteristic, perhaps pathognomonic, radiological feature is the presence of enthesitis— inflammation of a tendon sheath, particularly the Achilles. The immunogenetics of psoriatic arthritis are different from those of psoriasis, implying that the underlying pathogenic mechanisms are separate. Metabolic syndrome Emerging evidence suggests that patients with psoriasis have an increased incidence of the metabolic syndrome, particularly the components of diabetes mellitus, central obesity, hypertension, Fig. 23.5.4 Scalp involvement by psoriasis, showing tinea amiantacea. Fig. 23.5.5 Psoriatic nail dystrophy.

section 23 Disorders of the skin 5624 hyperlipidaemia, and coronary artery disease. It is currently un- known whether these signs are a consequence of psoriasis per se or of chronic inflammation, as is the case with arthritis. Indeed weight gain can be a precursor of the development of psoriasis and the pres- ence of psoriatic arthritis significantly increases the risk of cardio- vascular disease. Psychosocial aspects Psoriasis is associated with significant impairment of quality of life. Studies have shown that this is equivalent to or worse than other chronic diseases, including chronic

obstructive airways disease, dia- betes mellitus, and ischaemic heart disease. There is a significant association with clinical anxiety, depression, suicidal ideation, and stigmatization. Worry about the chronicity of psoriasis may produce resistance to therapy. Histology The classical histology of psoriasis comprises epidermal keratino- cyte hyperproliferation and thickening of the epidermis (acanthosis) accompanied by loss of markers of differentiation (e.g. keratins 1 and 10), loss of the granular cell layer, and parakeratosis of the stratum corneum. The epidermis also contains microabscesses (of Munro) and collections of neutrophils (micropustules of Kogoj (Fig. 23.5.7)). There is, at times, a significant inflammatory infiltrate com- prising predominantly T lymphocytes, with localization of CD8 + T cells in the epidermis and CD4 + T cells in the dermis. Dilated blood vessels are prominent in the dermis. Pathogenesis For many years it was believed that psoriasis was a disease primarily of keratinocytes, and that the inflammatory infiltrate was a sec- ondary phenomenon. Current understanding of psoriasis is that it is an immune-mediated inflammatory disease. Components of the innate and adaptive immune responses play important roles in pathogenesis. CD8 + T cells within plaques are clonal, and most T cells are positive for cutaneous lymphocyte- associated antigen. It is believed that in the case of streptococcal pharyngitis there is stimulation and subsequent expansion of T cells, which cross-react with components of keratin in the epi- dermis. The central importance of T cells to the psoriatic pro- cess has been confirmed by the efficacy of T-cell targeted drugs including ciclosporin, an interleukin 2 (IL-2) diphtheria fusion toxin that is cytolytic for activated T cells, and biological therapies. Natural killer and natural killer T cells also participate in the psori- atic process. Plaques of psoriasis contain a predominance of Th1 cytokines, including interferon-γ, IL-2, and IL-23. By contrast, atopic derma- titis is primarily a Th2-cytokine-driven disease. This is confirmed by observations that atopic dermatitis is relatively rare in patients with psoriasis. Cytokines and chemokines of the innate immune response, including tumour necrosis factor-α (TNFα), are also Fig. 23.5.6 Psoriasis with psoriatic arthritis. Fig. 23.5.7 Histological section of psoriasis showing epidermal acanthosis, elongation of rete ridges, and inflammation.

 present in plaques of psoriasis, and the demonstrated efficacy of biological agents targeted to TNFα, IL-17 A, and IL-23 has under- scored the key role of these cytokines in the pathogenesis of psoriasis. Indeed, psoriasis is now considered a prototypic IL-17 disease. Angiogenesis is an underinvestigated area in psoriasis, but there is compelling evidence for significant vascular proliferation and angio- genesis in the dermis, and this is associated with the overexpression of vascular endothelial growth factor produced by epidermal keratinocytes. Research on the pathogenesis of psoriasis is hindered by the ab- sence of an animal model for the disease: psoriasis occurs in no other animal but humans. The most reliable model for psoriasis is xenotransplantation, which involves transplantation of biopsies of uninvolved, clinically symptomless skin from patients with psoriasis onto the flanks of immunodeficient mice. Mice treated topically with imiquimod can develop an inflammatory dermatosis virtually indistinguishable from psoriasis. Management General principles The management of psoriasis, as with any other chronic skin dis- ease, involves a biopsychosocial approach and an understanding of the individual patient’s expectations of therapy. At present there is no cure. In the United Kingdom, 80% of patients with psoriasis can, with the use of topical agents, be treated adequately in pri- mary care. Patients should be educated about psoriasis (e.g. it is not caused by diet, and is neither contagious nor neoplastic). An understanding of how psoriasis interferes with a patient’s daily ac- tivities, and the psychosocial disability associated with anxiety and depression, are key aspects of the consultation. Indeed, cognitive behavioural therapy is often a useful adjunctive management

tool. Lifestyle management such as weight loss, smoking cessation, re- duction in alcohol intake, and exercise have all been shown to con- tribute to improved control of the disease. Environmental triggers of psoriasis should be ascertained, such as underlying infection, including streptococcal pharyngitis/tonsillitis, and drug triggers. Up to 20% of patients with psoriasis may enter spontaneous remis- sion for varying periods of time, but in most cases it is a persistent and lifelong disease. In all cases, the liberal use of emollients is important. Topical ther- apies are aimed at directly reducing the epidermal keratinocyte pro- liferation or the inflammatory mediators that drive the epidermal changes. Topical therapies Vitamin D3 analogues A major advance in the topical treatment of psoriasis in the past 30 years has been the introduction of vitamin D3 analogues. These include calcipotriol, calcitriol, and tacalcitol. All vitamin D3 ana- logues directly inhibit keratinocyte proliferation, but also switch intraplaque cytokines from a Th1 to a Th2 profile. Calcipotriol and calcitriol are applied twice daily, whereas tacalcitol is used once daily. Local side effects include the irritation of uninvolved skin, and if used over an extensive body surface area, a risk of hypercalcaemia. The combination of calcipotriol with betamethasone valerate in a once-daily preparation is the most commonly prescribed, active topical therapy in the United Kingdom. This enhances efficacy and reduces irritation. Topical corticosteroids Worldwide, topical corticosteroids are still the predominant therapy for localized chronic plaque psoriasis. If used appropriately, they can be a valuable component of the armamentarium. Medium- and high-potency topical corticosteroids in ointment formulation are the most effective, but should be used for no more than two weeks on a continuous basis, and not on the face or in the flexures. Higher potency steroids carry an increased risk of rebound flare on with- drawal. To minimize complications various innovative regimens are employed, such as weekends-only usage, combination with non- steroidal drugs such as calcipotriol, and tapering to less potent top- ical steroids. Calcineurin inhibitors The calcineurin inhibitor tacrolimus, although approved only for the treatment of atopic dermatitis, has an advantage over topical cor- ticosteroids in that it does not produce skin atrophy. It is effective for the treatment of facial and flexural psoriasis. Dithranol Dithranol (formerly anthralin) has been one of the main topical treatments for psoriasis for many years. The mechanism of action is via an inhibitory effect on mitochondria. Dithranol is applied once daily, usually in a short-contact (30–60 min) outpatient regimen. Significant skin irritation, and staining of involved and uninvolved skin, clothing, and furniture nowadays limits dithranol to inpatient and day-treatment centre usage. The Ingram regimen is the com- bination of dithranol with ultraviolet B (UVB) phototherapy. With the advent of vitamin D3 analogues the use of dithranol has declined significantly over the past 25 years. Coal tar Coal tar has been a standby of treatment for psoriasis for over 100 years; the classical psoriasis treatment, the Goeckerman regimen, involves a combination of crude coal tar with UVB photo- therapy. Dissatisfaction with the cosmetic aspects of crude coal tar, in addition to skin irritation and folliculitis, has considerably re- duced its use as a routine outpatient therapy, and it is mostly limited to day-treatment centre or inpatient management of psoriasis. Phototherapy Broadband and narrowband UVB Natural sunlight has been used for centuries for the treatment of psoriasis. The Dead Sea, because of its salinity and the abundant UV radiation, is a popular destination for psoriasis patients. The most effective wavelength of UV radiation for psoriasis is in the narrow- band (311–313 nm) range. Narrowband UVB phototherapy is an effective treatment for psoriasis, and is superior to traditional broadband UVB photo- therapy. UVB phototherapy is performed as an outpatient procedure following determination of the minimal erythema dose, based on an individual patient’s skin phototype. Twenty-five year follow-up studies have not demonstrated significant increases in either mel- anoma or nonmelanoma skin cancers in patients receiving narrow- band UVB phototherapy.

section 23 Disorders of the skin 5626 Photochemotherapy Psoralen UVA (PUVA) photochemotherapy is a combination of an ingested psoralen photosensitizer (8-methoxypsoralen or 5- methoxypsoralen), followed by exposure to UVA. This is one of the most effective treatments available for psoriasis. Apart from imme- diate side effects, which include nausea, headache, sunburn, and photosensitivity, there is a significant risk of premature skin ageing (photodamage) and nonmelanoma skin cancer, particularly in those who have received a cumulative dose of 1000 mJ/m2 or 250 treat- ments. Side effects are reduced to some extent by bath PUVA, which involves immersion in a dilute aqueous solution of psoralen for 30 min before UVA exposure. PUVA patients should wear spectacles with plastic lenses, and avoid natural sun exposure on the day of treatment. Because of the complexities of treatment and significant skin cancer risk, the use of PUVA in psoriasis treatment has declined significantly in recent years. Systemic therapies Only a minority of psoriasis patients require therapy with systemic agents; most can be managed with topical therapies. However, some patients have disease that is too extensive, unstable, inflammatory, or recalcitrant for topical therapies, and thus phototherapy or sys- temic therapy is indicated. Methotrexate Methotrexate is a folic acid antagonist that inhibits DNA synthesis and thus cell replication; it also has T-cell suppressive activities. Methotrexate is the gold standard systemic therapy. Very few trials of the efficacy of methotrexate have been performed. Approximately 40% of patients achieve at least a 75% improvement in clinical se- verity as measured by the psoriasis area severity index (PASI). Methotrexate is prescribed orally, and increasingly subcutaneously, in a once-weekly dose following a 2.5 mg test dose. Doses range from 7.5 to 25 mg per week, dependent on clinical response. Folic acid 1–5 mg daily is added to prevent stomatitis and anaemia, and to reduce gastrointestinal side effects. Psoriasis patients receiving methotrexate require careful monitoring; they appear to have an increased risk of hepatotoxicity compared with rheumatoid arthritis patients pre- scribed the drug. Traditionally, hepatotoxicity from methotrexate was assessed by liver biopsy; however, serum assay of the amino propeptide of collagen III has been shown to be a reliable measure of hepatic fi- brosis, thereby obviating the need for liver biopsy in most patients. The use of pharmacogenetics may optimize the use of methotrexate by identifying individuals susceptible to hepatotoxicity and bone marrow suppression, and those likely to achieve a clinical response. Retinoids Oral retinoids (vitamin A derivatives) have been used in the treat- ment of psoriasis for over 30 years. The original third-generation retinoid used for psoriasis, etretinate, has been superseded by its natural metabolite acitretin. Monotherapy with acitretin is nor- mally commenced at a dose of 10–25 mg daily. Systemic retinoids are particularly effective for the treatment of the erythrodermic and pustular variants of psoriasis. As they are not immunosuppressive, retinoids have a role in the treatment of those psoriasis patients who are HIV-infected or have cancer, particularly nonmelanoma skin cancer following PUVA. Caution must be exercised when considering acitretin in women of childbearing potential, because of significant teratogenicity. Women should avoid pregnancy for up to two years (United Kingdom) or three years (United States of America) after completing acitretin treatment. Adverse psychiatric events, such as mood swings, de- pression, and suicidal ideation, have been reported as possible idio- syncratic reactions to the related retinoid isotretinoin. Retinoid toxicities are similar to those occurring with hypervitaminosis A, and can include mucocutaneous side effects including sticky skin, alopecia, and cheilitis. Osteoporosis, hyperlipidaemia, and pseudotumour cerebri may occur. Combining acitretin with PUVA (Re-PUVA) significantly enhances the response to PUVA but is nowadays rarely used. Ciclosporin Ciclosporin is a highly effective, short-term therapy for moderate to severe psoriasis. It inhibits the activation of T cells as a con- sequence of blockade of cytoplasmic calcineurin phosphatase. Ciclosporin therapy is used for psoriasis at doses between 2.5 and 5

mg/kg per day, usually for no more than 12 weeks. Intermittent short-course therapies are recommended because of the association of long-term continuous ciclosporin therapy with nephrotoxicity and hypertension. Unlike methotrexate or acitretin, ciclosporin is not teratogenic, thus it is the only systemic therapy that can be used in pregnancy. In those patients who have received significant PUVA, there is an increased risk of nonmelanoma skin cancer. Patients may have other side effects, including hypertrichosis, gum hyperplasia, and paraes- thesia. Long-term continuous therapy with ciclosporin is used on occasion at a daily dosage of 3–4 mg/kg, but regular monitoring of glomerular filtration rate is required. Ciclosporin has been used in combination with acitretin, low-dose methotrexate, and the newer biological agents. Fumaric acid esters
A commercially available mixture of four fumaric acid esters (fu- marates) has been used to treat psoriasis in Europe for at least 50 years. They are hindered by several subjective side effects, mainly gastrointestinal in nature, including abdominal cramps, diarrhoea, nausea, and flushing. Lymphopenia (disconnected from efficacy) has recently become a concern because of the risk of progressive multifocal leucoencephalopathy. Other systemic therapies Less frequently used second-tier systemic agents include hydroxycarbamide, mycophenolate mofetil, sulphasalazine, and leflunomide. Few randomized controlled trials are available to con- firm their effectiveness. Biological agents A major advance in the management of patients with moderate to severe psoriasis has been the introduction of biological agents. These are defined as recombinant molecules designed from the genetic sequence of existing living organisms, and are often similar or iden- tical to proteins produced by humans. They include fusion proteins, recombinant proteins, and monoclonal antibodies, and have been in common use for diseases such as rheumatoid arthritis and Crohn’s

23.5 Papulosquamous disease 5627 disease. There are several biological agents licensed currently for the management of moderate-severe psoriasis; these block cytokines TNFα, IL-12/IL-23, and IL-17 A. Cytokine-blocking agents Etanercept Etanercept is a human recombinant p75 TNF receptor/Fc fusion protein that binds TNF and is self-administered subcutaneously at doses from 25 to 50 mg twice weekly. At the lower dose, 34% of pa- tients achieve PASI 75 at 12 weeks, and at the higher dose 49% of pa- tients achieve this level of improvement. In addition to its beneficial effects on psoriasis, etanercept, in common with other TNF antag- onists, is an effective treatment for psoriatic arthritis. Infliximab Infliximab, a chimeric monoclonal antibody, binds to and neutral- izes the activity of TNFα. It is given as a 5 mg/kg intravenous in- fusion, with three loading infusions at 0, 2, and 6 weeks, and then subsequently at 8-week intervals. Infliximab is a highly effective, rapid-acting biological therapy in that more than 80% of patients achieve PASI 75 by 10 weeks. It can be used long term, and at 1 year 61% of patients maintain PASI 75 with a regular 8-week infusion. Infliximab is also effective for psoriatic arthritis. Adalimumab Adalimumab, a fully human anti-TNFα monoclonal antibody, is self-administered subcutaneously with an initial loading dose of 80 mg followed by 40 mg at week 1 and subsequently on alternate weeks. Twenty-four weeks of treatment with adalimumab signifi- cantly improves psoriasis, 54% of patients achieving PASI 75; psori- atic arthritis is improved also. TNFa antagonist monitoring Because of the role of TNFα in granuloma formation, infections such as tuberculosis, histoplasmosis, and deep fungal infections require careful monitoring with appropriate tuberculosis screening before starting therapy. Other reported serious adverse effects with TNF antagonists include demyelination, exacerbation of pre-existing cardiac failure, development of lupus, enhanced risk of soft-tissue infections, and the potential development of nonmelanoma skin cancer in patients who have received significant PUVA. Prospective pharmacovigilance under the auspices of national registries is of importance for

ascertaining the true risk of biological therapies. Ustekinumab Ustekinumab, a fully human monoclonal antibody directed to the shared p40 subunit of IL-12 and IL-23 is self-administered subcuta- neously at 0 and 4 weeks and 12 weekly thereafter at a dose of 45 mg or 90 mg. Twelve weeks of treatment significantly improves psor- iasis, 70% of patients achieving PAS1 75, response is maintained with continuous therapy to five years. Secukinumab Secukinumab is a fully human anti-IL17A self-administered sub- cutaneously at a dose of 300 mg weekly for the initial four weeks followed by four-weekly administration thereafter. Results to date with this biological therapy and the newly licensed ixekizumab anti-IL17A are impressive with up to 70% of subjects achieving PASI 90 and close to 40% of patients achieving complete clearance (PASI 100). Biosimilars As the patents on the original ant-TNF biologic therapies expire, a new generation of biosimilar drugs has started to enter the market. These are the biosimilars, so-called because they are similar to pre- viously authorized biotherapeutics in quality, efficacy, and safety. Furthermore, they are cheaper to produce. Oral small-molecules These target intracellular signalling pathways. Currently only one such agent is approved for use in the United Kingdom, namely apremilast, a phosphodiesterase E4 inhibitor which achieves a PASI 75 in approximately 40% of patients with psoriasis. It is dosed at 30 mg twice daily with minimal monitoring required. Apremilast is also effective for psoriatic arthritis. Lichen planus Lichen planus is a relatively common benign skin disease, estimated to account for 1.2% of new patients presenting to dermatology de- partments. It is slightly more common in women and, although occurring at all ages, most commonly presents between the ages of 40 and 50 years. The familial incidence has been quoted as 11%, implying genetic susceptibility. The underlying aetiology is un- known; however, several drugs (gold, methyldopa) can produce a lichenoid reaction that is at times almost indistinguishable from li- chen planus. In parts of Europe, including Italy and Spain, hepatitis C infection is associated with lichen planus, but this has not been noted in patients from northern Europe, the United Kingdom, and the United States of America. There is no consistent MHC associ- ation, although HLA A3 and HLA A5 have been linked. The clinical features are highly characteristic in that lichen planus is characterized by purple (violaceous) flat-topped polygonal pap- ules that vary in size (Fig. 23.5.8). The surface of the papules has a fine tracery of white lines known as Wickham’s striae. Lichen planus can occur at sites of excoriation or scars: the Koebner phe- nomenon (Fig. 23.5.9). Annular lesions are seen, particularly on the penis. Although lichen planus can affect any skin surface, it most Fig. 23.5.8 Typical flat-topped polygonal papules of lichen planus.

 commonly occurs on the flexor aspects of the wrists, the lower back, and the ankles. Hypertrophic lesions occur most commonly on the anterior shins, and involvement of the hair follicles of the scalp (li- chen planopilaris) can produce significant scarring alopecia. Resolution of lesions can lead to significant post-inflammatory hyperpigmentation, particularly in black and Asian skin. Approximately 50% of patients have involvement of mucous membranes, most commonly the buccal mucosa, where the ap- pearance is of a lacework of white streaks. Oral involvement can be significant, with painful erosions. In the absence of cutaneous manifestations, oral lichen planus may present solely to dentists. The skin lesions are classically highly pruritic, but can be variable in pattern and morphology, including hypertrophic, atrophic, fol- licular, annular, and linear forms. Involvement of the nails occurs in approximately 10% of cases, and when present can be pathogno- monic. The most common changes are longitudinal ridges caused by thinning of the nail plate, but adhesion between the dorsal nailfold, causing destruction of the lateral aspect of the nail (pterygium), is characteristic (Fig. 23.5.10). Chronic oral ulceration as a conse- quence of lichen planus can lead to the development of squamous cell carcinoma.

Lichen planus and lichenoid drug eruptions are characterized histologically by thickening of the epidermis (acanthosis) and hypokeratosis, in which the basal layer of the epidermis is dam- aged, producing colloid bodies that may be clumped. Rete ridges of the epidermis are irregular and flattened, giving a saw-tooth appearance, and a band-like infiltrate of lymphocytes hugging the dermal–epidermal junction is a characteristic feature. Hyperpigmentation is due to pigmentary incontinence. At times, complete separation of the epidermis from the dermis may result in blister formation. Treatment The cutaneous disease is usually self-limiting, with 85% of cases clearing spontaneously within two years. Oral lichen planus and scarring alopecia are difficult to treat, but local skin lesions can be treated with high-potency topical corticosteroids (e.g. clobetasol propionate 0.5%). Sometimes systemic corticoster- oids or other immunosuppressant agents, such as ciclosporin, are required. Phototherapy, either PUVA or narrowband UVB, and a variety of immunosuppressant therapies including methotrexate, azathioprine, and thalidomide, have also been used. Oral mucous membrane disease can be treated with topical corticosteroids such as triamcinolone in a carmellose and gelatine paste that adheres to mucous surfaces, clobetasol propionate ointment, or fluticasone propionate asthma inhaler spray directed to the lesions. Ciclosporin oral rinse has also been used effectively for the treatment of oral li- chen planus. Other papulosquamous diseases Numerous other disorders can present with a papulosquamous phenotype, including mycosis fungoides (see Chapter 23.14), dis- coid lupus erythematosus (see Chapter 23.7), eczema/derma- titis (see Chapter 23.6), drug eruptions (see Chapter 23.16), tinea (Chapter 23.10), pityriasis versicolor (Chapter 23.10), secondary syph- ilis (Chapter 8.6.37), and pityriasis rosea. Pityriasis rosea Most cases of pityriasis rosea occur between the ages 10 and 35 years, and onset is often seasonal. In many cases it is likely to be viral in aetiology, and various herpes viruses have been impli- cated. In addition, a prolonged pityriasis rosea-like rash can occur in association with various drugs (e.g. angiotensin-converting en- zyme inhibitors and hydroxychloroquine). Histology may show epidermal hyperplasia, spongiosis, and focal parakeratosis, with a superficial dermal infiltrate of lymphocytes, histiocytes, and occa- sional eosinophils. Most patients with pityriasis rosea present initially with one plaque (herald patch), and then after several days many smaller plaques appear on the trunk, neck, and extremities, and sometimes other sites. In Africans, the lesions tend to be more papular. The plaques themselves are pink, with a fine peripheral scale and a well- defined and sometimes elevated margin. The scaling usually forms a ring (collarette) at the outer edge of the lesion, with its free edge inwards. Lesions are arranged with the long axes running in parallel Fig. 23.5.9 Lichen planus with linear Koebner response. Fig. 23.5.10 Nail dystrophy from lichen planus, with pterygium.

 to the ribs, resulting in a characteristic ‘Christmas tree’ distribution pattern. Lesions typically evolve over a few weeks, with subsequent spontaneous resolution. As secondary syphilis can mimic pityriasis rosea so closely, testing for syphilis is advised. The classical disease is self-limiting, and no treatment is usually required. FURTHER READING Burden AD, Kirby B (2016). Psoriasis and related disorders. In: Griffiths CEM, et al. (eds) Rook’s textbook of dermatology, 9th edition, Ch. 35. Wiley-Blackwell, Oxford. Eisen D (2003). The clinical manifestations and treatment of oral li- chen planus. Dermatol Clin, 21, 79–89. Gelfand JM, et al. (2006). Risk of myocardial infarction in patients with psoriasis. JAMA, 296, 1735–41. Griffiths CEM, Barker JNWN (2007). Pathogenesis and clinical fea- tures of psoriasis. Lancet, 370, 263–71. Helliwell PS, Taylor WJ (2005). Classification and diagnostic criteria for psoriatic arthritis. Ann Rheum Dis, 64 Suppl 2, ii3–8. Krueger JG, Bowcock A (2005). Psoriasis pathophysiology: current concepts of pathogenesis. Ann Rheum Dis, 64 Suppl 2, ii30–6. Menter A, Griffiths CEM (2007). Current and future management of psoriasis. Lancet, 370, 272–84. Piguet V, et al. (2016). Lichen

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