

Dermatology. Venereology

Part 2

*Textbook for 4-year dentistry
students (English medium)*

МІНІСТЕРСТВО ОХОРОНИ ЗДОРОВ'Я УКРАЇНИ
Харківський національний медичний університет

Dermatology. Venereology
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Дерматологія. Венерологія
Частина 2

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A textbook Dermatology. Venereology for stomatological faculty students of medical university. The issues of etiopathogenesis, clinic, diagnostic, treatment and prevention of allergodermatoses, lichenoid and bully dermatoses are shown in textbook.

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Dermatitis

Definition: Contact dermatitis is any skin disorder caused by contact with an exogenous substance that elicits an allergic or irritant and inflammatory skin reaction to low-molecular weight environmental chemicals (haptens). Contact dermatitis is divided into *irritant contact dermatitis* (ICD) and *allergic contact dermatitis* (ACD) according types of inflammation.

- ICD: danger signals delivered by chemical/innate immune response
- ACD: mediated by specific T cells (adaptive immune response)

Pathogenesis: In ICD, cytokines are directly released by stimulated or damaged keratinocytes. Damage to the corneum stratum or epidermal lipids is intrinsic part of ICD, but also makes sensitization more likely.

In the sensitization phase of ACD, allergens are taken up by Langerhans cells, processed and presented to T-cells in the regional lymph node following migration. On re-exposure, the sensitized T-cells are activated and trigger cutaneous inflammation at the site of exposure. The clinical reaction occurs 24–72 hours after antigen exposure.

Clinical features: *Acute* contact dermatitis is pruritic, erythematous, and often vesicular. *Subacute* lesions may be crusted but still inflamed, while *chronic* contact dermatitis is dominated by lichenification, hyperkeratosis and rhagades with little sign of inflammation. Except for the distribution patterns, the two variants are identical.

Histology: The microscopic pictures of ACD and ICD are identical. Acute disease will show spongiosis and a lymphocytic infiltrate perivascular infiltrate with dermal edema. More chronic lesions have signs of epidermal reaction including hyperkeratosis, parakeratosis, acanthosis and less infiltrate. ICD with toxic substances such as acids may show direct epidermal damage with necrotic keratinocytes, but this is the exception.

Irritant Contact Dermatitis

Synonyms: Toxic-irritant (contact) dermatitis.

Epidemiology: most common occupational disease in hairdressers, food handlers, health-care workers, cleaners, florists, farmers, foresters, painters, etc; wet work is most common irritant. Endogenous factors: young age (children), women, anatomic site, atopy, inherent basic (fillagrin gene mutation, TNF-gene polymorphism P308).

Etiological agents: soaps, detergents, abrasives, chemicals (hydrofluoric acid, cement, chromic acid, sodium hypochlorite, phenols etc.), industrial solvents (coal tar, petroleum, alcohol solvents, turpentine, acetone), plants (spurge, croton, buttercup, black mustard, nettles, capsaicin etc.), animal enzyme, secretions, desiccant powders, dust, fiberglass, soils, etc.

Pathogenesis: ICD occurs in everyone, depending on the penetrability and thickness of the stratum corneum. Wetting and drying causes decreased lipids in the epidermis with a resultant break in the epidermal barrier. Irritation depends on concentration, volume, duration of skin exposure. *Acute form* causes a direct cytotoxic damage of skin cells; *chronic* – slow damage to cell membranes.

Clinical features: ICD is confined to the area of exposure, sharply demarcated and never spreads. *Acute ICD:* erythema, vesiculation/blister formation, erosion, crusting, scaling, accompanied by burning, stinging, smarting. *Chronic ICD:* dryness, scaling, lichenification, accompanied by stinging, itching, pain.

Hands repeatedly exposed to water, cleansers or soaps show fissuring or a 'glazed' appearance.

Lip-licking habit – wetting and drying caused by saliva. Perioral area in babies – foods, saliva and rubbing the area.

Diaper area secondary to multiple factors such as wetting, maceration, urine, feces. It is manifested by hyperemia, epidermal maceration, oozing, a sensation of burning and pain (*intertrigo*).

Pressure and friction lead to development of sore skin (hyperemia, swelling, bullae) on the feet (if the footwear is tight and does not fit), on the palms (from instruments in heavy physical exertion). Under chronic exposure of small force the affected skin areas harden and undergo lichenification, thickening and hyperkeratosis (chronic ICD).

The effect on the skin of high temperature results burns (*combustion*) of four degrees: 1 – erythema and mild swelling; 2 – erythema, swelling and bullae; 3 – superficial dermal necrosis; 4 – all dermal necrosis.

Exposure to low external temperature leads to damage of the tissue is called frostbite (*congelatio*), four degrees of which are distinguished: 1 – congestive-bluish in color and swollen; 2 – bluish color, swelling, bullae; 3 – all dermal necrosis; 4 – deep necrosis of tissue to the bones. Latent period when affected area becomes cold, pale, insensible is preceded to the manifestation of frostbite. Chilblain (*perniones*) develops under long-term exposure to cold in combination with dampness with development of thickening or soft swelling cyanotic-reddish areas on the distal and middle phalanges on the fingers and toes, on the skin of joints or pale-red areas with a bluish hue on the cheeks.

Exposure of the skin to sun rays may lead to the development of *solar dermatitis*. *Acute solar dermatitis* manifested by redness and swelling of the skin, then vesicles and blisters, which appear a few hours after radiation. *Chronic solar dermatitis* is manifested by infiltration, pigmentation, dryness of skin is encountered in fishermen, seamen, open air workers.

Various types of ionizing radiation (X-ray, alfa-, beta-, gamma-rays, neutron radiation) may induce acute or chronic ICD. *Acute radiation ICD* may

be manifested by loss of hair, erythema, swelling, bullae, necrosis. The process terminates in atrophy of the skin, permanent alopecia, formation of teleangiectasia, disorders of pigmentation. Multiple soft radiation caused *chronic radiation ICD*. The process is characterized by poikiloderma (variegated skin): skin is dry, thinned out and lack elasticity, with multiple teleangiectasia, hyperpigmented and depigmented areas, onychodystrophy and itching, which conducive to the formation of papillomas, hyperkeratosis, warts and may undergo malignant degeneration. *Late radiation ICD* (late radiation trophic ulcer, radiation carcinoma) may develop at the site of persistent radiation dermatitis.

The chemical factors, which induce ICD, are strong acids and alkalis, salts of alkaline metals, mineral acids and many others. Dermatitis develops suddenly, is acute in character, and usually takes the course of necrosis with the formation of a scab leaving an ulcer when it drops off. Long-term exposure to weak concentration of these substances may induce chronic dermatitis manifested by desquamation and dryness of the skin by the formation of painful cracks.

The biological ICD (*phyto dermatitis*) may be caused by several plants, such as white dictamine, caw parsnip, primrose, crowfoot, cashew, redwood. The disease develops when walking through dew-covered grass, resting in meadows, during hay-making, among worker of the furniture manufacturing industry. Some ether oils and chlorophyll contained in plants are possessing a photosensitizing effect and developing photophyto dermatitis. Erythema, urticarial rash, vesicles, bullae form on the affected areas, which are leaving pigmentation.

Diagnostic approach: The diagnosis is made on the basis of history of appropriate exposure. If clinical questions exist or if the ICD is work-related, the patch testing should be carried out to exclude ACD, which can accompany ICD and is more easily avoided. Clinical findings. Histology: mild to moderate epidermal spongiosis; epidermal necrosis; usually does not contain eosinophils (as in allergic causes); perivascular lymphocytes and neutrophils.

Differential diagnosis: Allergic contact dermatitis, atopic dermatitis.

Therapy: Avoid offending agents and using topical corticosteroids. Blisters may benefit from therapeutic drainage by puncturing and should then be covered with antibiotic dressing or a dressing soaked in Burow solution. Occlusive pastes (zinc oxide paste) or emollients are widely used for noncavitary lesions.

Prognosis: Benign condition but usually reappears if same circumstances occur.

Prevention: protective clothing (goggles, shields, gloves), barrier creams or photo protective creams, if contact has occurred repeated washes with water or neutralizing solutions.

Allergic Contact Dermatitis

Definition: Dermatitis resulting from type IV reaction following exposure to topical substances in sensitized individuals.

Epidemiology: 2–5 % of population are affected; much higher in some occupational groups. Risk factors for developing ACD: ICD, atopic dermatitis, leg stasis.

Pathogenesis: Delayed-type hypersensitivity reaction (type IV). Three phases are operative from ACD. Sensitization phase (afferent/induction phase) lasts 5–25 days. First contact; allergen penetrates skin and acts as hapten, binding to skin proteins. Helper T-cells activated. Langerhans cells recognize antigen as nonself and present it to T-lymphocytes. Langerhans cells with hapten move from epidermis to lymph nodes. Native T-cells differentiate into clones of effector cells directed at foreign antigen. Results in committed sensitized T-cells reactive to specific antigen. Elicitation phase 24–48 hours. Re-exposure results in accumulation of effector cells which produce numerous cytotoxic molecules (e.g. IFN- γ , TNF, IL-17 etc.) and mediators which result in dermatitis in areas limited to skin contact. Resolution or regulation phase takes part after 9–10 days, when the regulatory and effector T-cells produce IL-10, which causes the resolution of allergic dermatitis.

Clinical features: The hallmark of ACD is initial confinement to the area of skin that came into contact with an allergen. This produces sharply localized, often irregular or unnatural patterns, which can suggest the correct diagnosis. If the allergen is absorbed or taken systemically, lesions may develop at sites that never came into contact with the trigger. The extreme version of this is *hematogenous contact dermatitis* when, for example, a patient sensitized to topical antihistamines takes the same medication systemically. Another variant of this is the *baboon syndrome*. The localization of ACD often gives clues as to the possible triggering agent. The eyelids are very sensitive and often react to products simply transferred there by the hands, rather than being applied intentionally. Hand dermatitis is covered separately. Some occupations have very high prevalence of ACD and often typical allergens. Occupational skin diseases are also reviewed elsewhere. An often overlooked cause of ACD is medication, especially over-the-counter products. Rhus dermatitis is the most common cause of ACD in North America. Exposure to poison ivy, poison oak or poison sumac typically causes a vesicular, often linear, pruritic eruption following outdoor exposure. Although the lesions look toxic, Rhus dermatitis is a true type IV allergy that develops only on repeated exposure to the plants. There are very unusual clinical forms of Rhus dermatitis including eyelid involvement and perianal disease (using the leaves as outdoor toilet paper). Patients with Rhus dermatitis may react to other plant products, such as some leather dyes, laundry marking ink in Asia, some varnishes, and the shell of cashew nuts (not the edible component).

Major points: Characteristics

1. First exposure does not cause a reaction
2. Reaction begins 12–96 h after subsequent exposure if already allergic
3. Lesions can persist up to 3 weeks
4. Pruritus may vary from mild to severe

In ACD erythema, swelling and the papular and vesicular lesions are localized on areas, which had been exposed to the allergen, but in some patients the process tends to spread to the covered skin areas.

Diagnostic approach:

History: Ask the patient about work and hobbies, and about what materials are likely to reach or be applied to the involved area. Document the history carefully; some cases of contact dermatitis turn out to be work-related, and then documentation is crucial. Onset of problem, occupation, course of disease on weekends or in vacation. Previous therapy. Exposure to common contact allergens such as chemicals, detergents, medications, cleansing products, rubber or latex gloves. Previous skin diseases. Never forget the likelihood of contact dermatitis as a reaction to a medication. *Clinical features:*

The location and pattern usually suggest the diagnosis of ACD. Always check for disease other than at sites of suspected contact. *Patch testing:* The diagnosis is always confirmed with patch testing. The usual approach is to use an nationally accepted screening panel first, then specialized panels designed for a specific problem, such as for occupations (dentist), locations (hands) or special ingredients (fragrances or preservatives). *Testing with suspected product:* Patch testing with a suspected product is fraught with problems. False-positive reactions are common. Repeated open application test is better; product applied for 2 days to an antecubital fossa.

Histology: Multilocular intraepidermal spongiotic vesicles. Eosinophils in dermis and epidermis. Langerhans cells in the epidermis associated with lymphocytes. Immunohistochemical studies show primarily memory T-helper lymphocytes, although T-suppressor cells can be noted.

Differential diagnosis: ICD.

Tabl. 1.

Differential between ACD and ICD

	ACD	ICD
Skin lesion	Not limited to the contact site	Limited to the contact site
Symptoms	Itch	Burning
Epidemiology	Affects some subject handling the product	Affects the majority of subject handling the product
Histology	Spongiosis, exocytosis	Epidermal necrosis
Patch test	Positive	Negative
Skin immunology	Presence of activated T-cells	No activated T-cells
Blood immunology	Presence of specific T-cells	No specific T-cells

Tabl. 2.

Differential between ACD and ICD

ACD	ICD
only sensitized individuals	all subjects
first contact w/o symptoms	at first contact
approx. 48 hrs after re-exposure	within hours: first response
small amount of allergen	dose-dependent
risk of chronicity	fast remission
generalization	no generalization

Erysipelas: At first glance, can appear similar to well-defined erythematous area, but rapidly spreads, is not pruritic and patient is sick. Atopic dermatitis and nummular dermatitis can be similar. Clinical distinction is often difficult, so do patch testing when in doubt. *Tinea*: KOH examination. *Polymorphous light eruption*: Can be confusing when considering sunscreen allergy; otherwise, history clarifies.

Therapy: Avoidance of exposure to eliciting allergen. Acute dermatitis of any sort is best treated with moist compresses and high potency topical corticosteroid creams. In severe cases, a short burst of systemic corticosteroids, tapered over 7–10 days, is needed. More chronic cases can be treated with lower potency corticosteroids in an ointment base. Bath PUVA may be useful for severe hand and foot dermatitis. Oral cyclosporine (or azathioprine, or methotrexate) is a last gasp measure for therapy-resistant chronic disease. Retinoids (alitretinoin-9-cis-retinoic acid) is useful for hand ACD. Acute dermatitis with oozing and weeping, vesicles or bullae: compresses with Burrow’s solution for 15 min. Apply shaken lotion of calamine three times a day for drying effect. Avoid topical diphenhydramine or canes which are added to some products. Topical corticosteroids: medium to ultra-potent steroids (class 1–4) for about 5–7 days used two or three times a day then taper to lowest strength to keep erythema and itching under control. Oral antipruritics, diphenhydramine, hydroxyzine, cetirizine, fexofenadine. Systemic corticosteroids: oral prednisone 0.5–2 mg/kg per day tapered over 10–21 days for widespread or severe involvement. Barrier creams.

Prognosis: Most patients recover from acute hypersensitivity in 14–21 days. Hyposensitization injections not effective and may be unsafe. Oral hyposensitization used mainly for workers in forest industry who cannot avoid contact with toxicodendrons (of questionable value). Wash skin and clothes with water and soap immediately after contact. Most contact allergens bind to the epidermis and set up response within 0.5–2 h of contact. Chronic exposure to allergens such as rubber, perfumes, preservatives which are not obvious, would benefit from patch testing by a dermatologist skilled in this technique.

Toxicodermia (Drug eruptions)

Toxicodermia is acute inflammatory dermatosis characterized by widespread rash and appearing soon after enteral, parenteral or respiratory administration of the chemical substances into organism that have a general

effect on it. There are medications (antibiotics, sulfa drugs, vitamins, etc.) most commonly cause toxicoderma, almost any drug can cause toxicoderma.

Epidemiology: Many drug reactions start with skin findings. Increased prevalence of toxicoderma is registered from in-patients, women, elderly patients.

Risk factors for cutaneous drug reactions include:

- Patient factors: age, sex, atopic predisposition, immune status.
- Underlying diseases.
- Drug-related: dose, route of administration, number of drugs, drug interactions, drug metabolism.
- Genetic factors: pharmacogenetics is beyond our scope, but every individual has an almost unique array of enzymes that may influence how they react to medications.

The most common types of drug reactions are macular and maculopapular exanthems (40 %), along with urticaria and angioedema (37 %). Fixed drug eruption (6 %) and erythema multiforme / toxic epidermal necrolysis (5 %) are the only other frequently seen patterns; all others account for 0–3 %, but may be clinically distinctive.

Pathogenesis: In some instances, a drug reaction can be clearly assigned to an immunologic reaction type. Type I is immunoglobulin E (IgE): urticaria, angioedema and anaphylaxis. Type II is cytotoxic reactions: hemolysis and purpura. Type III is immune complex reactions: vasculitis, urticaria. Type IV is delayed-type reactions with cell-mediated hypersensitivity: contact dermatitis, bullous exanthema, maculopapular exanthema, pustular exanthema, fixed drug eruption and photoallergic reactions. Nonimmunologically mediated reactions are adverse effects, direct release of mast cell mediators, idiosyncratic reactions, intolerance, Jarisch-Herxheimer phenomenon, overdose or phototoxic dermatitis.

Clinical features: the clinical picture of drug toxicoderma is characterized by erythematous, papular, vesicular or papulovesicular eruptions. Diffuse papular or vesicular (bullous) eruption is often found on the skin and mucous membranes, diffuse erythematous foci or erythrodermia are rarer.

Iodine or bromide toxicoderma occurring in medication with iodine or bromine salts and alcohol iodine solutions, for instance, is characterized by the development of an acneiform eruption ('bromine' or 'iodine' acne) or tuberous bromoderma (iododerma), which is manifested by succulent soft plaques elevated above the skin surface and covered with purulent crust. On removal of the crusts, a vegetating surface of a pus secreting infiltrate is exposed.

Maculopapular exanthema. Most common reaction. Drugs commonly responsible: ampicillin, amoxicillin, aminoglycosides, allopurinol, barbiturates, benzodiazepines, carbamazepine, co-trimoxazole, gold salts, penicillin, phenytoin, piroxicam. Patients with allergic contact dermatitis to a topical agent such as an antihistamine may react to the systemic administration of the agent with a widespread erythematous or urticaria-like eruption, known as *hematogenous contact dermatitis*. The extreme variant of this reaction is perhaps the *baboon*

syndrome where patients have prominent flexural and genital erythema mimicking that of mandrels or baboons.

Urticaria. Drugs commonly responsible: penicillin and related antibiotics, aspirin, captopril, levamisole, NSAIDs, sulfonamides, insulin, radiography contrast media.

Fixed Drug Eruption. Cutaneous drug reaction that recurs at exactly the same site with repeated exposure to the agent. Drugs commonly responsible: ampicillin, aspirin, barbiturates, dapsone, metronidazole, NSAIDs, oral contraceptives, phenolphthalein, phenytoin, quinine, sulfonamides, tetracyclines. Typically red-brown patch or plaque which are demarcated and have rounded outlines; occasionally may be bullous. Most common sites are genitalia, palms, and soles, as well as mucosa. Lesions typically 5–10 cm in diameter but can be larger; often multiple. Start as edematous papule or plaque; later becomes darker. Frequently resolves with postinflammatory hyperpigmentation.

Diagnostic approach: The history is the most essential tool in diagnosing a drug reaction. Any exanthem in a hospitalized adult should be suspected of being a drug reaction. Obtain a complete list of all drugs; for in-patients, the chart offers complete documentation. For outpatients, even more effort is required. Ask about over-the-counter medications (laxatives, sleeping pills, herbal medications). Explore previous possible drug reactions and determine whether or not the current medications have been taken previously. Determine the correct time course. If a patient is exposed to a medication for the first time an allergic reaction cannot occur within the first 4–8 days. Reexposure, cross-reactions, or pseudoallergic reactions all occur more rapidly, sometimes almost instantaneously (anaphylaxis). Ask about associated signs and symptoms, such as fever, chills, diarrhea or arthralgias. Allergy testing: patch, prick, scratch, and intracutaneous tests can all be used. In addition, oral exposition may be helpful but must be used carefully.

Differential diagnosis: Main differential diagnostic consideration is viral exanthem or on occasion acute exanthem such as guttae psoriasis or pityriasis rosea.

Therapy: In most instances, discontinuation of the drug, topical antipruritic measures (polidocanol lotion) and mild topical steroids, systemic antihistamines suffice.

Severe Skin Reactions

Erythema Multiforme (EM) is an acute sometimes recurring polyetiological dermatosis, associated with viral and bacterial infections, medications and other triggers.

The classical clinical findings are iris or target lesions, in the infectious form most often on the distal limbs. Lesions caused by drugs are more often on the trunk and less like to have a target pattern. The mucous membranes of mouth and genitals are usually minimal or no involved. Erythematous spots, “exudative” papules, vesicles, bullae and urticarial lesions may be primary

manifestations. Plaques spread on the periphery and with a depression in the center. Their periphery is pinkish-red and the center violet-bluish. The bullae are filled with a serous or hemorrhagic fluid and are surrounded by an inflammatory ring. They rupture and grayish-yellow and hemorrhagic crusts form on the surface of the erosions. The papules often form garlands, arches and rings. Before the appearance of the eruptions and during the disease the patients complain of indisposition, prostration, and a chill, fever, pains in the joints.

Diagnostic approach: clinical picture, complete blood cell (leukocytosis with atypical lymphocytes and lymphopenia is possible), identification of HSV, histologically a lymphocytic infiltrate along the dermoepidermal junction associated with hydropic changes and dyskeratosis of basal keratinocytes.

Differential diagnosis: ACD, ICD, Stevens–Johnson Syndrome, Dermatologic Manifestations of Staphylococcal Scalded Skin Syndrome, other forms of toxicoderma, pemphigus.

Treatment and prevention: symptomatic (oral antihistamines, analgesics), topical steroids, Burrow solution for erosions. Antiherpes simplex virus drugs can prevent HSV-associated erythema multiforme, but if antiviral started after the eruption of EM has no effect on the course of the disease.

Stevens–Johnson Syndrome (SJS). It is severe variant of erythema multiforme with mucosal lesions as well as systemic signs and symptoms. Patients almost invariably have prodrome with fever, malaise, or arthralgias. Abrupt development of erythema multiforme. Mucosal involvement: Mouth (100 %): Erosions, hemorrhage and crusts on lips, and erosions in mouth covered by necrotic white pseudomembrane. Eyes (70–90 %): Erosive conjunctivitis, can lead to scarring. Genitalia (60–70 %): Painful erosions.

Diagnostic approach: Clinical appearance, search for drugs (most common are NSAIDs and antibiotics) and mycoplasma.

Differential diagnosis: EM, Lyell’s syndrome, severe manifestation of drug toxicoderma, ocular lesions can be confused with cicatricial pemphigoid.

Therapy: Short burst of systemic corticosteroids helpful in many cases. Exclude or treat underlying infection, which could be worsened by immunosuppression. Routine topical care: disinfectant mouth washes, antibiotic or corticosteroid eye drops (after ophthalmologic consultation).

Toxic Epidermal Necrolysis (TEN) Synonym: Lyell syndrome. Severe life-threatening disorder with generalized loss of epidermis and mucosa.

Pathogenesis: The trigger is always drugs; there is a cytotoxic T-cell reaction with apoptosis of keratinocytes mediated by Fas-Fas ligand. Responsible drugs include: Sulfamethoxazole/trimethoprim, sulfonamides, aminopenicillins, quinolones, cephalosporins, corticosteroids (surprisingly), carbamazepine, phenytoin, phenobarbital, valproic acid, lamotrigine, NSAIDs (especially oxamic types), allopurinol.

Classification: The German Center for Documenting Severe Skin Reactions uses the following grouping: erythema multiforme, SJS (10 % of body area involved), SJS–TEN overlap (10–30 % involvement) and TEN (30% involvement).

Clinical features: Prodrome depends on underlying disease and triggering drug. Sudden onset of either diffuse macula (erythema multiforme-like drug reaction) or diffuse erythema without maculae and flabby bullae form against their background. When the bullae rupture and the superficial epidermal layers are peeled off, extensive eroded oozing surface form. Skin lies in sheets and folds on the bedding. Extensive mucosal erosions. Possible loss of hair and nails, as well as extensive postinflammatory hypopigmentation. The patient's general condition is grave. Multiple systemic programs because of fluid and protein loss, difficulties in temperature regulation, fever, leukocytosis, and risk of secondary infections. Fatal in 10–30% of cases. Nikolsky's sign is positive.

Diagnostic approach: Clinical picture, skin biopsy from erythematous noneroded area. Granulocytopenia for more than 5 days is unfavorable sign.

Differential diagnosis: Depending on severity, SJS and overlap syndromes; staphylococcal scalded skin syndrome has different histology and usually affects children; severe burn (history). Histology: diffuse full-thickness epidermal necrosis with surprisingly little dermal change; stark contrast to staphylococcal scalded skin syndrome, which has only loss of stratum corneum.

Therapy: The mainstay is excellent burn care, ideally in a burn center, with careful attention to electrolyte balance, topical disinfection, and prompt treatment of secondary infections. Systemic corticosteroids, if employed, should be used early to attempt to abort the immunologic reaction. Later in the course, they probably increase risk of infection and slow healing. Dosages in the range of 80–120 mg prednisolone daily have been suggested. Intravenous immunoglobulins are promising and should be employed in severe cases. Ophthalmologic monitoring is essential, as risk of scarring and blindness is significant.

Urticaria

Definition: *Urticaria* (hives) is a group of inflammatory disorders characterized by wheal and flare type skin reactions (urtica, erythema) and pruritus resulting from the release of histamine and other mediators by activated skin mast cells. Similar reactions in the subcutaneous tissue or mucosa feature primarily swelling and are known as *angioedema*. *Urticaria* refers to a disease, *urtica* (wheal, hive) to its primary lesion.

Pathogenesis. Urticaria symptoms are mast cell-dependent and their induction requires mastcell activation (degranulation) by specific or nonspecific triggers. Mast cells are key effector cells in the immune response. Specific triggers of mast cell degranulation include stimulation of mast cell surface Ig E by selected allergens or drugs as well as physical stimuli (cold, friction, pressure) in physical urticaria disorders. Nonspecific triggers such as stress are relevant to all urticaria disorders. In addition, modulators of mast cell activation and/or degranulation (ambient temperature, alcoholic drinks, fever, emotions, hyperthyroidism, and other endocrine factors) can modify the induction of symptoms and the course of urticaria.

Clinical features. The basic lesion in urticaria is a hive or wheal. Wheals vary greatly in size and configuration but have three unifying features: Central swelling surrounded by reflex erythema. Marked pruritus. Transitory nature with individual lesions lasting 1–24 hours. The time course of urticaria is essential to describing and investigating the disease:

Acute urticaria lasts < 6 weeks; individual lesions are short-lived but the patient has urticaria daily for up to 6 weeks.

Chronic urticaria lasts > 6 weeks.

In general, patients with acute urticaria are evaluated with history alone and then treated; those with chronic urticaria are extensively investigated searching for a treatable underlying cause. The released mediators may cause associated signs and symptoms such as diarrhea, tachycardia, or respiratory problems, but they are not usually of major clinical significance.

Histology. The key features are dilated upper dermal vessels with marked tissue edema. Depending on the duration of the lesion, a mixed perivascular infiltrate can be seen, as well as eosinophils.

Classification. Urticaria is classified on the basis of both course and triggers. The categories are not mutually exclusive, as physical urticaria can be chronic.

Idiopathic urticaria: Acute urticaria (< 6 weeks), Chronic urticaria (> 6 weeks)

Physical urticaria: Dermographism (urticaria factitia), Cold contact urticaria, Solar urticaria, Delayed pressure urticaria, Heat contact urticaria, Vibratory urticaria/angioedema.

Other urticaria disorders: Cholinergic urticaria, Contact urticaria, Aquagenic urticaria, Exercise induced urticaria/anaphylaxis, Associated disorders.

Differential diagnosis. The main differential diagnostic consideration is deciding which form of urticaria is present. Urticarial drug reactions must also be excluded, as well as serum sickness, early lesions of bullous pemphigoid (especially when dealing with elderly patients), and arthropod assaults (often difficult to determine if lesions are multiple bites and stings, or a few bites and secondary urticaria). The lesions of bullous pemphigoid clinically resemble urticaria but are highly inflammatory with numerous eosinophils and sometimes histologically show early subepidermal blister formation. Some disorders that carry the name urticaria are not “urticaria disorders”. For example, “Urticaria pigmentosa” is a form of cutaneous mastocytosis and “urticarial vasculitis” is a vasculitis, as is “familial cold urticaria.”

Therapy: Nonsedating antihistamines are the mainstay of therapy; sedating agents can be used in the evening if desired. A short course of prednisolone (50 mg p. o. daily 3 days) may be helpful, but controlled studies are lacking. *Topical treatment* is not effective; if patient insists, a topical anesthetic (polidocanol) or distractor (menthol cream or lotion) may be tried. Ketotifen and doxepin are also occasionally effective. Immunosuppressive drugs such as cyclosporine A and corticosteroids should not be chosen for long-term use because of unavoidable severe side effects.

Angioneurotic edema. Quincke edema

Definition: Angioedema is the deep dermal and subcutaneous equivalent of urticaria, with increased vascular permeability and swelling.

Pathogenesis: Common angioedema is caused by the same spectrum of factors as urticaria. Two common triggers are Hymenoptera stings and angiotensin converting enzyme (ACE) inhibitors. A rare form related to abnormalities in complement metabolism is discussed below. In addition, hereditary vibratory angioedema has been described, as well as rare cases of acquired vibratory angioedema.

Clinical features: Angioedema can present in any site, but typically involves the face and neck. Many patients have massive facial swelling. Involvement of the tongue or of the neck can lead to airway obstruction. In addition, angioedema is far more likely to be accompanied by anaphylaxis than is urticaria. Thus angioedema is a potentially life-threatening situation. Many patients have accompanying urticaria, some do not. Pruritus is uncommon; some patients complain of burning.

Differential diagnosis: Infections (cellulitis), trauma, superior vena cava syndrome, subcutaneous emphysema, Melkersson–Rosenthal syndrome.

Therapy: Most patients are admitted because of the risk of airway obstruction and anaphylaxis. Treatment consists of antihistamines and usually i.v. corticosteroids with consideration for bronchodilators.

Atopic Dermatitis

Atopy: A familial predisposition to development of allergic asthma, conjunctivitis, rhinitis, and atopic dermatitis.

Atopic dermatitis: In the best tradition of a circular definition, atopic dermatitis is the dermatitis that develops in individuals with atopy. It usually appears in infancy, is chronic and intensely pruritic with varying clinical patterns at different stages of life.

Definition. Atopic dermatitis (AD) – is a chronic inflammation of the skin that occurs in persons of all ages but is more common in children. The condition is characterized by intense pruritus and a course marked by exacerbations and remissions.

Pathogenesis. Precise etiology is unknown, but current theories center on a disordered immune response, especially an imbalance of cytokines. The disease also appears to have a hereditary component; family history is positive for atopy (asthma, allergic rhinitis, atopic dermatitis) in two thirds of patients. AD typically manifests in infants aged 1–6 months. Approximately 60 % of patients experience their first outbreak by age 1 year and 90 % by age 5 years. Onset of AD in adolescence or later is uncommon and should prompt consideration of another diagnosis. Disease manifestations vary with age. AD has been reported to affect 10–15 % of children. Although the symptoms of AD resolve by adolescence in 50 % of affected children, the condition can persist into adulthood.

Predisposal factors: genetic background (atopy), immune dysfunction, impaired barrier function (dry skin), inflammation, microbial colonization, dysfunction of the peripheral nervous system, psychosomatic disorders, non-immune factors.

Epidemiology: Some 5–10 % of the population of western Europe develop atopic dermatitis. The disease is familial, with apparent polygenic inheritance. A number of suspected genoloci have been identified. A classic feature is that one family member may have allergic rhinitis and no skin findings, while another has only atopic dermatitis.

Clinical presentation. Clinical forms of AD include vesicular crusty, erythematous scaly, erythematous scaly with lichenification, lichenoid and prurigo-like. Minor features include affection of infraorbital folds, facial pallor, cheilitis, palmar hyperlinearity, xerosis, pityriasis alba, white dermographism, ichthyosis, keratosis pilaris, nonspecific dermatitis of the hands and feet, nipple eczema, positive type I hypersensitivity skin tests, propensity for cutaneous infections, elevated serum IgE level, food intolerance. Clinical picture depends on the age of the patient. In infants up to 1 year old predominant area of AD lesions is cheeks. At this age there is also dermatitis on the scalp. Excoriations are characteristic clinical feature in this age group. In addition to the head, there may be dermatitis on the extensor aspects of the extremities. Crawling of infants may cause hand eczema with large plaques of thickened skin on the wrists. Dermatitis around the mouth may be caused by saliva and various food. Infants with AD easily develop miliaria rubra. It is very pruritic rash with small papules due to the inflammation around the sweat glands.

By the 2–7 years the clinical picture of AD changes. In this age AD is typically seen in the elbow and knee flexures. Fissures in the dermatitis are colonised with *S.aureus* and it can lead to impetigo. Virus infection may cause multiple molluscum contagiosum or cause eczema herpeticum.

During 7–16 years flexural dermatitis continues to be the main characteristic manifestation of AD. Other characteristic features include mechanical irritation. On the soles of the feet dermatitis plantaris sicca (atopic winter feet in children) may be seen. A similar type of dermatitis develops on fingertips. Frequent, long showers, enjoyed by most teenagers, dry out the skin and damage the skin barrier, resulting in dehydration, pruritus and dermatitis. Ichthyosis is common especially in the shins of older children with AD. Keratosis pilaris with follicular keratotic papules may also be seen. Pityriasis alba is post-inflammatory hypopigmentation following nummular or annular AD lesions.

After 16 years involvement of face and upper trunk is seen alone with classical flexure involvement. Mechanical irritation can lead to treatment resistant dermatitis on the nipples from rubbing against clothing. Some adults with severe AD may develop generalized erythroderma with red, infiltrated, scaly skin.

The *clinical features* of atopic dermatitis can be divided into the basic features and the facultative or associated features. There are many diagnostic scoring schemes for atopic dermatitis; if a patient has three major features and three minor features, they are likely to have the disorder. The morphologic and histopathologic changes in all forms of dermatitis and eczema are similar. The earliest and mildest changes are erythema and edema. These early changes may progress to vesiculation and oozing and then to crusting and scaling. Finally, if the process becomes chronic, the skin will become lichenified (thickened, with prominent skin markings), excoriated, and either hypo- or hyperpigmented.

Major features: Pruritus. Typical dermatitis (face in children, flexures in adolescents, hands or nape in adults). Chronic or chronic, recurrent course. Positive personal or family history for atopy.

Minor features: Cradle cap as infant; yellow crusts on scalp. Dry skin with ichthyosis vulgaris, hyperlinear palms, keratosis pilaris. Thick, fine dry hair.

Elevated serum IgE; IgE-mediated skin reactions. Predisposition to skin infections (*Staphylococcus aureus*, herpes simplex virus, human papilloma virus, molluscum contagiosum) because of selective reduced cellular immunity. Dermatitis on palms and soles (juvenile plantar dermatosis). Nipple dermatitis. Pityriasis alba. White dermatographism. Increased pruritus with sweating. Diseases flares with emotional changes. Unable to tolerate wools or fat solvents. Food allergies. Recurrent conjunctivitis, keratoconus, anterior and/or posterior subcapsular cataracts. Absent or reduced corneal or gag reflex.

Atopic face: Cheilitis. Lateral thinning of the eyebrows (Hertoghe sign). Double fold of lower lid (Dennie-Morgan fold or line). Periorbital hyperpigmentation, obvious facial paleness or erythema.

Provocation factors: Irritants, type I allergens, pseudoallergens (citrus fruits; other foods or food additives), bacterial superantigens, hormones, increased sweating, dry air, emotional stress.

Histology. Acute: Parakeratosis, spongiosis, perivascular infiltrates. Chronic: Hyperkeratosis, acanthosis, sparse infiltrates.

Diagnostic approach: Typical skin changes varying with age of patient.

Diagnosis. Unfortunately, no specific laboratory findings or histologic features define AD. Although elevated IgE levels are found in 80 % of affected patients, IgE levels are also elevated in patients with other atopic diseases. The diagnosis requires the presence of at least three major features and at least three minor. Minor features include affection of infraorbital folds, facial pallor, cheilitis, palmar hyperlinearity, xerosis, pityriasis alba, white dermatographism, ichthyosis, keratosis pilaris, nonspecific dermatitis of the hands and feet, nipple eczema, positive type I hypersensitivity skin tests, propensity for cutaneous infections, elevated serum IgE level, food intolerance. Family and allergy history. Serum IgE level, CBC (looking for elevated eosinophil count). White dermatographism, reduced gag reflex. Eye examination. Prick testing with common food and

inhalant allergens. Allergen-specific IgE determinations. Atopy patch testing. Common aeroallergens are applied and interpreted as in routine patch test.

Differential diagnosis. The differential diagnostic considerations vary considerably over the lifetime of the patient and location of the findings. The classic pictures of facial, flexural, or nuchal dermatitis are extremely typical and can be diagnosed at a glance. In infants with scalp involvement, seborrheic dermatitis often is identical; often the diagnosis is made later in life as typical findings appear. Atopic dermatitis tends to appear after 6 months of age, where as seborrheic dermatitis may be present earlier. Allergic contact dermatitis should be excluded; even though patients with atopic dermatitis are hard to sensitize, they are exposed to so many creams and ointments that sensitization is not uncommon.

Adults may present with hand dermatitis, eyelid dermatitis, or nuchal dermatitis.

Therapy. Topical: Routine skin care with emollient creams or ointments; if tolerated, with urea ashumectant; bath oils. Using a moisturizing soap is recommended. *Topical anti-inflammatory agents:* Topical immunomodulators: Pimecrolimus (> 6 months); tacrolimus 0.03 % > 2 years, 0.1 % > 15 years. They have no side effects as corticosteroids and may be used continuously. Prevention is the mainstay of treatment for atopic dermatitis. Treat acute attacks with a low-to-moderate potency topical corticosteroid. Inform the patient about adverse effects of topical steroids (e.g. atrophy, hypopigmentation, striae, telangiectasia, thinning of the skin). Medium-to-high potency topical steroids should not be used on the face or neck area because of these potential adverse effects. Corticosteroids: Usually class I–II agents suffice; class III–IV reserved for flares, limited time period. In most instances once daily application is adequate; never more than b.i.d. Tars: Available as creams or mixed as ointments; perhaps for chronic lichenified lesions, such as hands; gels are designed for psoriasis and should not be used in atopic dermatitis. Tannic acid creams or ointments also useful on hands and feet. Topical antiseptics, used for baths and topical therapy; antiseptics (triclosan 1–3 % cream) are preferable to antibiotics because of less sensitization. *Systemic:* Antihistamines for severe pruritus; in general, the sedating (older) agents work better; some evidence that cetirizine is anti-inflammatory. In AD, because the pruritus is not histamine mediated, it does not respond well to histamine blockade. However, patients have a tendency to scratch in their sleep, and sedating them with an antihistamine at bedtime reduces scratching. Because scratching plays a major role in perpetuating rash, reducing it can improve the rash. Patients with severe flare-ups or weeping lesions may benefit from a 7-day course of oral prednisone (40–60 mg/d for adults, 1 mg/kg/d for children). As the lesions begin to dry, apply a topical steroid. Cyclosporine for severe refractory disease. Antibiotics for flares; cover for *Staphylococcus aureus*, which is usually involved. Phototherapy: Helpful in patients who report that they tolerate sunlight well. UVA1 is probably best for acute flares; selective UVB

phototherapy (SUP) and 311nm UVB best for chronic disease. Other measures: *Avoidance of triggers:* Wool clothes, fabric softeners often help, avoid work that requires frequent hand washing. If relevant type I allergens are identified, then avoidance: pollens, house dustmites. Elimination diet only if type I allergy is proven. Pseudoallergen-free diet if clinically suggested.

Eczema

Definition: Eczema – is the most common inflammatory skin disease. The term dermatitis is often used to refer to an eczematous rash and the word means skin inflammation and is not synonymous with eczematous processes. The components of eczematous inflammation are: erythema, vesicles and scale.

Etiology: inflammation could be caused by contact with specific allergens such as Rhus (poison ivy, oak, or sumac) and chemicals. Chronic eczematous inflammatory process may be caused by irritation of subacute inflammation, or it may appear as lichen simplex chronicus.

Classification: forms of eczema: acute, subacute, chronic, idiopathic, microbial, nummular, dyshidrotic, hyperkeratotic and hand eczema.

Clinical features: itching, burning, a bright red, swollen plaque, serum-filled vesicles, scaling. The eruption may not progress or it may evolve to develop blisters.

Therapy. Systemic: Antihistamines, antibiotics, immunosuppressive medications. *Topical:* Routine skin care with emollient creams or ointments; topical corticosteroids. Topical immunomodulators: pimecrolimus or tacrolimus.

Lichen simplex (local neurodermitis)

Lichen simplex, also called neurodermatitis, is a common skin problem. It generally affects adults, and may result in one, or many itchy patches. Lichen simplex is a type of dermatitis, and is usually the result of repeated rubbing or scratching. The stimulus to scratch may be unrecognized, perhaps a mosquito bite, stress, or simply a nervous habit.

The area most commonly affected by lichen simplex chronicus include outer lower portion of lower leg, wrists and ankles, back and side of neck (lichen simplex nuchae), forearm portion of elbow, scrotum, vulva, anal area, pubis, upper eyelids, opening of the ear, fold behind the ear.

Clinical features. The affected skin is thickened, often appearing as a group of small firm papules. The skin markings are more visible, and the hairs are often broken-off. The colour may be darker or sometimes paler than the surrounding skin. Lichen simplex tends to be very persistent, and readily recurs despite often initially effective treatment.

Therapy. Treatment of the itching is necessary to stop the scratching and resulting skin damage. Heat and fuzzy clothing worsen itching; cold and smooth clothing pacify it. If the itching is persistent, dressings may be applied to the affected areas. Among the topical medications that relieve itching are a

number of commercial preparations containing menthol, camphor, eucalyptus oil, and aloe. Topical corticosteroids are also used. In the places with the more thick skin we can apply potent corticosteroids. For broken skin, topical antibiotics help prevent infection. These should be used early to forestall further damage to the skin. Reducing the buildup of thick skin may require medicines that dissolve or melt keratin, the major chemical in skin's outer layer. These keratolytics include urea, lactic acid, and salicylic acid. Sedatives or tranquilizers may be prescribed to combat the nervous tension and anxiety that often accompanies the condition.

All these methods may be combined with the physiotherapy for better penetration - ultrasound, electrophoresis can be used for the damaged areas.

Psoriasis

Definition: Psoriasis (Ps) is a chronic, inflammatory autoimmune, genetic disease manifesting in the skin or joints or both. The immune pathways that become activated in psoriasis represent amplifications of background immune circuits that exist as constitutive or inducible pathways in normal human skin.1 Keratinocytes are key participants in innate immunity recruiting T-cells to the skin, and T-cells are important in sustaining disease activity. Inflammatory myeloid dendritic cells (DCs) release interleukin (IL)-23 and IL-12 to activate IL-17-producing T-cells, T-helper (Th) 1 cells, and Th22-cells to produce abundant psoriatic cytokines IL-17, interferon (IFN)- γ , tumor necrosis factor (TNF)- α , and IL-22.1,2 These cytokines mediate effects on keratinocytes to amplify psoriatic inflammation.

Etiology. The cause of psoriasis is not fully understood. Abnormal keratin formation, epidermal proliferation, activation of the immune system and hereditary factors appear to play roles in the pathogenesis of the disease. Psoriasis occurs more frequently in some families. The risk of a child developing psoriasis is 41 % if both parents are affected with psoriasis, 14 % if one parent is affected and 6% if one sibling is affected. Both external and systemic factors can trigger psoriasis in genetically predisposed individuals. In about a quarter of people with psoriasis, lesions are provoked by injury to the skin. Psoriatic lesions can also be induced by sunburn and skin diseases. Psychogenic stress also can trigger psoriasis with initial presentations of the disease as well as exacerbations being seen a few weeks to months after a stressful event. In up to 45 % of cases, bacterial infections may induce or aggravate psoriasis. Pharyngitis is the most common trigger but dental abscesses and skin infections may also be triggers. HIV infection may aggravate psoriasis; in HIV-positive patients psoriasis is more often resistant to treatment and more frequently associated with arthritis.

Psoriasis affects health-related quality of life to an extent similar to other noncommunicable diseases. Depending on the severity and location of skin lesions, individuals may experience significant physical discomfort and disability. Itching and pain can interfere with basic functions, such as self-care

and sleep. Skin lesions in the hands can prevent individuals from working at certain occupations, engaging in sports and caring for family members at home.

The clinical picture in typical cases is very distinctive. The disease occurs suddenly, without prodromal phenomena. The rash can either be limited to the election localization (the area of the elbow and knee joints), or common across the skin surface). When irrational therapy, as well as under the influence of other factors rash may merge, capturing almost the entire skin – psoriatic erythroderma.

The primary element rash, psoriasis is a papule rounded, pink covered with white-silvery scales. Expanding peripheral papules assume the nature of plaques. For psoriatic rash characterized by three symptom, or phenomenon (the so-called psoriatic triad). 1. The phenomenon of a stearin stain. By scratching elements rash scales are crushed and fall as fine silver pollen, as if scratching stearic spots. 2. The phenomenon of terminal film. This film is visible after scraping from the surface of psoriatic element of all scales. 3. The phenomenon of blood dew, or the point of bleeding. After scraping a terminal film on the surface of psoriatic papules or plaques appear smallest drops of blood.

Kubner phenomenon: Minor skin damage or injury can lead to the development of psoriasis in the lesion (isomorphic response). Systemic factors must play a role as the Kubner phenomenon can occur anywhere on skin, but is far more likely to develop during a time when psoriasis is on the upsurge than when it is stable or resolving. Kubner phenomenon is not restricted psoriasis; it may occur with lichen planus, vitiligo, and many other diseases.

Classification:

Psoriasis vulgaris: Chronic stable, plaque-type psoriasis. Guttate psoriasis. *Inverse psoriasis*.

Psoriatic erythroderma.

Pustular psoriasis: Palmoplantar pustular psoriasis (Barber–Kunigsbeck). Acrodermatitis continua suppurativa (Hallopeau). Generalized pustular psoriasis (von Zumbusch). Annular pustular psoriasis. Impetigo herpetiformis (pustular psoriasis in pregnancy).

Drug-induced psoriasis and psoriasiform drug reactions.

Psoriatic nail disease.

Psoriatic arthritis.

Lesion morphology: Sharply bordered erythematous patches and plaques with silvery scale.

Psoriasis vulgaris: Chronic plaque-type psoriasis: Small papules evolve through confluence into large irregular, well-circumscribed plaques, 3–20cm. Silvery scale is extremely typical. Sites of predilection include knees, elbows, sacrum, scalp, retroauricular area. Untreated, the plaques can remain stable for months or years. May be less distinct in dark skin.

Guttate psoriasis: Appears as exanthem over 2–3 weeks; starting with small macules and papules that evolve into 1–2 cm plaques with silvery scale. Favor the trunk, less often extremities or face. Most patients are children or young

adults, usually after a streptococcal pharyngitis; sometimes following treatment or tonsillectomy, the psoriasis resolves completely and never returns. Differential diagnosis includes pityriasis lichenoides et varioliformis acuta, pityriasis rosea.

Intertriginous psoriasis: Involves axillae and groin; often misdiagnosed. Differential diagnosis includes candidiasis and other forms of intertrigo. Macerated and fissured; thick plaques and silvery scale usually missing. Requires less aggressive therapy.

Inverse psoriasis: Overlaps with intertriginous; describes form where involvement is flexural and classical sites such as knees and elbows are spared.

Psoriatic erythroderma: Involves the entire integument: can develop suddenly out of a guttate psoriasis, or from a long-standing psoriasis following too aggressive therapy or abrupt discontinuation of medications. When confronted with possible psoriatic erythroderma, always think about pityriasis rubra pilaris. In erythrodermic form, very hard to separate.

Pustular psoriasis: Palmoplantar pustular psoriasis (Barber–Kunigsbeck): Numerous pustules on palms and soles. Always check for psoriasis elsewhere and in history. Generalized pustular psoriasis (von Zumbusch): Patients with widespread psoriasis and on the verge of erythroderma develop diffuse pustules and are critically ill with fever, chills, and malaise. Annular pustular psoriasis: 5–30 cm dusky erythematous lesions with peripheral rim of pustules and a collarette scale pointing toward the center. Often associated with psoriasis vulgaris; in other instances, an intermediate stop on the way to erythroderma. Differential diagnosis includes the figurate erythemas.

Three main types of psoriatic arthritis: Mono- or oligoarthritis with muscular or tendon attachment pain (enthesitis) similar to reactive arthritis (30–50%). Symmetric polyarthritis resembling rheumatoid arthritis (30–50%). Axial disease resembling ankylosing spondylitis (<10%). Clinical examination should search for all three types of disease, looking for swollen or painful joints. Definite identification of joint fluid is a crucial diagnostic skill. It is unusual to have psoriatic arthritis in a digit with an entirely normal nail.

Histology: Many distinctive features: acanthosis with parakeratosis, lack of stratum granulosum, elongation of rete ridges, dilated tortuous vessels in papillary dermis, dermal lymphocytic infiltrate, exocytosis of neutrophils into epidermis producing spongiform pustules and subcorneal microabscesses (Munro).

Psoriatic nail disease: Valuable diagnostic clues: Dorsal nail matrix: Pitting of nail plate. Ventral nail matrix: Onycholysis, oil spots (greasy dark stain; preonycholysis), distal subungual debris, red spots on lunula.

Diagnostic approach: The diagnosis of psoriasis can usually be made clinically with ease; the problem is therapy. If you suspect the diagnosis of psoriasis, always check the gluteal cleft, scalp, and nails for typical changes.

There are three stages of psoriasis: 1) acute stage, characterized by the appearance of new lesions, their intensive peripheral growth, a positive phenomenon, Cabrera (skin rash appears on the site of application scratches); 2) stationary

phase, when the progression of the process was stopped symptoms regression skin rash; 3) the stage of remission – all lesions are reverse, leaving depigmented spots. In the elbow and knee joints often remain so-called duty of psoriatic plaques.

The disease long, often throughout the life of the patient. Flare-UPS occur more frequently in autumn and winter. The most severe course differs inverse form of psoriasis and psoriatic erythroderma, often leading the patient to disability.

Diagnosis of psoriasis is usually simple. Differential diagnosis should be carried out with the parapsoriasis, secondary syphilis. The location of psoriatic items on the scalp conduct differential diagnosis seborrheic eczema.

Considerations include tinea, contact dermatitis, nummular dermatitis. Secondary syphilis can be psoriasiform clinically; it is always so under the microscope. Acute cases resemble pityriasis lichenoides et varioliformis acuta and pityriasis rosea. The distinction between psoriasis and seborrheic dermatitis can be extremely difficult. In HIV/AIDS, the two appear to overlap with Reiter syndrome. Pityriasis rubra pilaris is another diagnostic challenge; if palms and soles are prominently involved, if there are areas of sparing, or if things just don't fit with psoriasis, always think of pityriasis rubra pilaris. Always take a drug history; many drug reactions are psoriasiform, and in some instances lead to true psoriasis in susceptible hosts. The choice of which medication to use must always be based on the age, sex, social setting, and ability of the patient to apply topical medications or travel for light therapy, as well as on contradictions.

Topical therapy: 2–5 % salicylic acid is a useful keratolytic to remove scales. It facilitates all other topical measures. Concentrations up to 20 % may be used on the palms and soles. Anthralin-is a keystone for most topical regimens. It requires a well-trained, compliant patient and is easier to use in in-patients than outpatients. It can easily be combined with phototherapy (Ingram regimen). Vitamin D analogues – most widely available are calcipotriol and tacalcitol; they are most useful for small areas of moderate psoriasis. Retinoids: Tazarotene is effective in moderate psoriasis, with few irritating effects. Corticosteroids: useful for small areas, on scalp and in inverse psoriasis; simple for patient to use; available in many forms (creams, ointments, lotions); can be combined with occlusion. UVB 311 narrow band light (TL01): Relatively long wavelength UVB has good penetration and has both anti-inflammatory (induces apoptosis of immune cells) and antiproliferative effects. The more carcinogenic shorter wavelength UVB is avoided. Suitable for all forms of psoriasis except pustular psoriasis. Balneophototherapy: combination of selective ultraviolet phototherapy (SUP) (305–325 nm) with prior bath in 5–10 % table salt or solution simulating ocean water. Based on climatotherapy regimens at Dead Sea and other health spas. Because the Dead Sea is 400 meters below sea level, UVB is increasingly absorbed, so the radiant light is dominated by UVA.

PUVA (psoralens and UVA): is well-established for severe forms of psoriasis. In young patients, be aware of increased lifetime risk for skin cancers and increased photodamage.

Systemic Therapy: Fumaric acid esters are helpful in all forms of psoriasis and have been successfully used for moderate to severe disease. They can be tried for therapy-resistant forms, such as severe scalp psoriasis, pustular psoriasis, inverse psoriasis and even psoriatic arthritis. Methotrexate is the most widely used disease-modifying agent for both psoriasis and psoriatic arthritis. Retinoids: the most effective retinoid for psoriasis is acitretin. Retinoids suppress epidermal proliferation, leading to a reduction in thickness of psoriatic lesions and therefore increasing the effectiveness of other measures, especially phototherapy. Cyclosporine is highly effective for psoriasis and capable of perhaps inducing the most rapid response of any of the systemic agents. The dramatic effectiveness of cyclosporine was the first hard clue pointing to the central role of T-cells in psoriasis and triggering the many investigative efforts that made possible the host of biological agents that are now available. Biologicals: These are therapeutic molecules that are specifically targeted in order to imitate or inhibit naturally occurring proteins. The main categories currently used are antibodies and fusion proteins, which either antagonize mediators with a central pro-inflammatory role or interfere with the interactions between T-cells and endothelial cells or antigen-presenting cells (APC). They are Alefacept, Efalizumab, Etanercept, Infliximab. Shows quartier – hydrosulphuric baths, sea, river swimming, sunbathing.

Psoriasis patients should be under medical supervision, to get re-treatment courses. Prevention of psoriatic erythroderma should not apply strongly irritating ointment in acute exudative form of psoriasis.

Lichen ruber planus

Definition: Lichen ruber planus (LP) is a common inflammatory disease featuring pruritus, distinctive violaceous flat-topped papules and often oral erosions.

Epidemiology: Appears at all ages, but most common between 30–60 years of age.

Pathogenesis: Infiltrate of Th1-cells and cytotoxic cells on keratinocytes basal cell layer damage reactive hyperkeratosis (model of T-cell-mediated epidermal damage). In some countries, especially Italy, association between lichen planus and hepatitis viruses (usually hepatitis C). IFN therapy for hepatitis can trigger LP. Eruptions resembling lichen planus are frequently induced by medications (a long list, including pain medications, antibiotics, antiepileptics, chloroquine, quinidine, ACE inhibitors, antituberculosis agents, and hypoglycemic agents and chemicals) and chemicals (most often color film processing materials).

Clinical features: Classic skin findings: Classic lesions are glistening violaceous flat-topped papules, usually 2–10 mm in diameter. Fine lacy white markings on top of papules known as Wickham striae. Scratching and trauma induce new lesions: Kubner phenomenon. In exanthematous form, sudden development of widespread disease. Pruritus usually present and sometimes intense. Sites of predilection include inner aspects of wrists, ankles, anterior

shins, buttocks. There are many cutaneous variants: hypertrophic lichen planus, verrucous persistent plaques, especially shins and ankles; painful when on soles.

Lichen planopilaris: Hyperkeratotic follicular papules, usually on scalp (Graham–Little syndrome); infiltrate confined to follicular epithelium; can lead to scarring alopecia and one of precursors of pseudopelade.

Linear lichen planus: Linear grouping of lichen planus papules that cannot be explained by Kubner phenomenon; usually on legs of children.

Erosive lichen planus: Most common on oral mucosa, less often genital mucosa or soles; painful, often chronic erythematous erosions.

Bullous lichen planus: Sometimes ordinary lesions become bullous because of intensity of dermoepidermal junction damage.

Lichen planus pemphigoides: Combination of lichen planus and bullous pemphigoid; separation from bullous lichen planus has been controversial, but now better established. Also triggered by drugs such as captopril, PUVA, and cinnarizine.

Atrophic lichen planus: Atrophic, often hyperpigmented areas, sometimes with violaceous rim.

Mucosal findings: Large lacy white network on buccal mucosa, less often on tongue, lips or labial mucosa. Painful erosions also present, often on hard palate.

Similar reticulate pattern with erosions can be seen on genital mucosa 80–90 % clear within 2 years; isolated mucosal disease more likely to be chronic.

Histology: Acanthotic epidermis with prominent stratum granulosum and saw tooth pattern of rete ridges; band-like dermal lymphocytic infiltrate that damages basal layer. In drug-induced lichen planus, histologic changes often less pronounced.

Diagnostic approach: Clinical features, histology, drug history; depending on local pattern, hepatitis screening.

Differential diagnosis: Classic lesions: Lichenoid drug eruptions, lichen nitidus, secondary syphilis, pityriasis lichenoides et varioliformis acuta, early pityriasis rubra pilaris. Hyperkeratotic lesions: Lichen simplex chronicus, prurigo nodularis, warts. Linear lesions: Lichen striatus, linear epidermal nevus, linear psoriasis. Lichen planopilaris: Early lesions – keratosis pilaris, other follicular keratoses, Darier disease, early pityriasis rubra pilaris. Advanced lesions – lupus erythematosus; other forms of scarring alopecia. Erosive lichen planus: Oral lesions-lupus erythematosus, autoimmune bullous diseases. Soles-secondary syphilis.

Therapy: In most instances, high-potency topical corticosteroids, perhaps under occlusion are most effective. For erosive lichen planus, either corticosteroid solutions or intralesional injections; hypertrophic lesions may also do better with intralesional corticosteroids. Systemic corticosteroids is needed for widespread or rapidly spreading disease. Other choices include acitretin, antimalarials, and even cyclosporine as a last resort. Bath and cream PUVA are promising alternatives; effective and with much less risk of triggering flare than ordinary PUVA.

Cutaneous lupus erythematoses

Lupus erythematosus (LE) is a chronic inflammatory autoimmune connective-tissue disease of unknown etiology, that affects the skin and inner organs. LE appears from the interplay of genetical, hormonal and environmental factors, which ultimately leads to B-cells activation with production of antibodies and T-cell dysfunction. Cutaneous lupus erythematosus (CLE) can be divided into three main subtypes: acute, subacute, and chronic, all of which demonstrate photosensitivity.

Acute cutaneous lupus erythematosus (ACLE) is the most common form of cutaneous lesions of lupus associated with systemic lupus erythematosus (SLE).

Epidemiology: ACLE may develop spontaneously or in exacerbation of chronic erythematosus after triggers exposure (infections, sun exposure). The disease prevails among females at the age 20–40 years. Significant morbidity and potential mortality are associated with ACLE.

Clinical picture. ACLE can be classified on 3 categories: localized ACLE, generalized ACLE and Toxic epidermal necrolysis (TEN)–like ACLE. Facial form usually a typical malar eruption in a butterfly pattern localized to the central portion of the face. Erythema can be scaly or ulcerated, often itchy, sometimes painful, often spares the nasolabial folds. Generalized form is a maculopapular eruption representing a photosensitive dermatitis, erythematous rash and scaly eruption on the dorsal hands, often between joints. Vesicles, bullae on the erythematous skin and less frequently pustules and urticaria, caused by severe inflammatory infiltrate, are typical for TEN–like ACLE. The involvement of oral mucosal with superficial ulcers is very common. Various internal organs and systems are involved in ACLE: cardiovascular system (endocarditis, myocarditis, pericarditis, phlebitis, vasculitis, Raynaud’s syndrome, hypotension, periarteritis nodosa), the respiratory system (interstitial pneumonia, interlobular pleurisy), lupus nephritis, polyserositis (arthritis, arthralgia), interstitial or parenchymatous hepatitis, episcleritis, corneal ulcer, conjunctivitis.

Differential diagnosis: ACD, dermatomyositis, toxicodermia, rosacea, seborrheic dermatitis, erysipelas, phototoxic reaction.

Diagnostic approach: CBC - lymphopenia, leucopenia, thrombopenia, shift of the differential count left, hypergammaglobulinemia, increased ESR up to 60–70. Discovery of LE cells. Anti–double-stranded deoxyribonucleic acid (DNA) antibody (anti-dsDNA) assay, depressed complement level, Anti-Sm antibody assay are specific for ACLE. Histopathology: fibrinoid degeneration of collagen, vacuolar degeneration and atrophy of the cells of stratum basale, prevalence of leucocytic infiltration of the papillary and subpapillary layers in the dermis.

Treatment: systemic corticosteroids, immunosuppressive agents (methotrexate, azathioprine, cyclophosphamide, thalidomide), antimalarial drugs (hydroxyl-chloroquine), intravenous IgG and rituximab. Topical: steroid cream, calcium vit D3, sun protection.

Subacute cutaneous lupus erythematosus (SCLE) may develop from the chronic discoid form, systemic form, may be drug-induced or may occur spontaneously. It is non-scarring, non-atrophy-producing, photosensitive process.

Clinical picture: persistent erythema on the face, annular, polycyclic, scaly red-brown erythematous or papulosquamous lesions on the limbs, chest, scalp. Disease develops slowly and for a lengthy period of time is manifested only by erythematous-papular lesions and astheno-vegetative syndrome, after which chronic hepatitis, pleurisy and other symptoms of systemic affection of the body appear, though they are less pronounced than in the acute form.

Diagnostic approaches: CBC: anemia, leucopenia, thrombocytopenia. Positive serologic tests: ANA, Anti-Ro (SS-A), Anti-La (SS-B) autoantibodies. Histopathology: vacuolar degeneration of the stratum basale and oedema of the dermis, perivascular and periappendiceal lymphocytic cell infiltration,

Differential diagnosis: ACLE, DLE, erythema multiforme, vasculitis, psoriasis, tinea corporis, lichen planus, nummular eczema, dermatomyositis, seborrheic dermatitis.

Treatment and prevention: 1) sun-protective measures: sunscreens, protective clothing, and behavior alteration; 2) topical and/or intralesional corticosteroids and antimalarials such as hydroxychloroquine or chloroquine; 3) additional therapies: thalidomide, methotrexate, mycophenolate mofetil, azathioprine, retinoids, dapsone, intravenous immunoglobulin, cyclosporine, auranofin, clofazimine, interferon, cyclophosphamide, rituximab and belimumab.

Chronic cutaneous lupus erythematosus. The following three clinical varieties of CCLE are distinguished: discoid, tumid and lupus panniculitis.

Clinical picture. The chronic discoid form is most common; it may be manifest on anybody areas, including the face, mouth, lips, hands, feet, chest, back and scalp. The lesions are circumscribed disk shape pink-red scaly spots, which grow on the periphery, that heal with scarring and accompanied plugged hair follicles, telangiectasia. The infundibul of the follicular orifices are exposed when the scales are removed (follicular hyperkeratosis) and tiny projections are often found on the undersurface of the scales (the “ladies heel” sign). Scraping of the scales is usually painful (Besnier-Meshersky’s sign). Three zones may be discerned in the foci of affection: a zone of cicatricial atrophy in the center, a zone of hyperkeratosis next to it and a zone of redness on the periphery. Telangiectasia, hyperpigmentation and depigmentation, whiteheads and blackheads and follicular orifices are found in the region on the foci. The cicatricial atrophic process on the scalp causes scarring alopecia. Leukoplakia, ulcers, erosions may form on the oral mucosa, and localized edema with timorous thickening and cracks on the lips. The tumid lupus is only dermal process without surface changes. The tumid lupus is presented by pinkish-violaceous papules and plaques that lack scale and heal without scarring.

The lupus panniculitis is characterized by an infiltrate penetrating the subcutaneous fat in the region of the erythematous spots or without superficial changes. Such deep-seated foci of affection are usually localized on proximal extremities, face and upper trunk. Sometimes they undergo ulceration with drain yellow oily fluid (liquefied fat).

Diagnostic approaches: only 20 % of ANA and Anti-Ro (SS-A) autoantibodies of blood are positive; DIF of lesional skin – deposition of immunoglobulin and/or complement at the dermoepidermal junction). Histological finding: vacuolar alteration of the basal cell layer, thickening of the basal membrane, follicular plugging, hyperkeratosis, atrophy of the epidermis, incontinence of pigment, inflammatory cell infiltrate (usually lymphocytic) in a perivascular, periappendageal, and subepidermal location.

Differential diagnosis: lichen planus, psoriasis, rosacea, SCLE, syphilis, verruca.

Treatment: sun-protective measures (sunscreens, protective clothing, wide-brimmed hats, behavior alteration), intralesional or topical steroids, antimalarials (plaquenil, chloroquine, quinacrine), oral steroids, dapsone (for lupus panniculitis), low dose of thalidomide, mycophenolate, cyclophosphamide, IVIG, rituximab.

Scleroderma

Autoimmune connective tissue diseases of unknown etiology that affects the skin, blood vessels and internal organs, characterized by excessive deposition of collagen and other connective tissue macromolecules in skin, multiple internal organs, blood vessels walls and numerous humoral and cellular immunologic abnormalities. Scleroderma is characterized by focal or diffuse induration (hardening) of tissue as the result of fibrosis.

Systemic sclerosis (SSc) has two major subtypes. *Limited SSc:* fibrotic skin changes limited to the hands and face. This form includes CREST syndrome (calcinosis, raynaud's phenomenon, esophageal dysmotility, sclerodactyly, telangiectasia). *Diffuse SSc:* generalized fibrotic skin changes, starts in the fingers and hands, but spreads to involve the forearms, arms, trunk, face and lower extremities.

Cutaneous features. Edematous phase: edema of digits prior to onset of fibrosis.

- Indurated phase: fibrosis of skin with taut, shiny appearance.
- Atrophic phase: thinning of skin, possible contractures, ulceration, beaked nose, microstomia.

Other cutaneous features: dyspigmentation (hyperpigmentation in sun exposed areas, "salt and pepper sign" depigmentation that spare hair follicles),

telangiectasia, nail fold changes (capillary loss and dilated loops), Raynaud's and digital ulceration, dystrophic calcinosis of cutis.

Diagnostic approaches: Antinuclear antibodies, Scl-70 (Topoisomerase I antibodies) more typical for diffuse disease, anticentromere antibodies more typical for limited disease. Skin biopsies: edema, hypertrophy, homogenization, fibrinoid degeneration, intensified synthesis of collagenous fibres; round cell, predominantly lymphocytic, infiltrates around the vessels and between the homogenous collagenous bundles, fibrous thickening of the vascular walls; homogenization and atrophy of the muscle fibres, thinning of the fatty tissue.

Differential diagnosis: generalized morphea, graft versus host disease, radiation dermatitis.

Treatment: Raynaud's phenomenon – calcium channel blockers (nifedipine, almodipine), alpha-1-blockers (prazosin), phosphodiesterase inhibitors (sildenafil), pentoxifylline, stanozol, ganglionectomy, endothelin receptor antagonists (bosental), aspirin. Skin: UVA, methotrexate, systemic steroids, mycophenolate mofetil, D-penicillamine, rituximab.

Localized scleroderma (morphea). Idiopathic, inflammatory disorder that cause sclerotic changes in the skin. Morphea is classified into circumscribed scleroderma, generalized scleroderma, linear scleroderma and deep scleroderma (morphea profunda).

Pathogenesis: immune dysfunction (activated T-lymphocytes in demal infiltrate, Th2 cytokine and TGF-beta stimulate fibroblasts to produce collagen), vascular dysfunction (reduced numbers of dermal capillaries, abnormalities in basal lamina of blood vessels, endothelial cell damage), genetics (familial case reports).

Etiology: unknown. An autoimmune mechanism is suggested by an increased autoantibody formation and personal and familial autoimmune disease in affected patients.

Epidemiology: uncommon disease occurs in persons of all races, more common in whites, women are affected approximately three times as often as men. Linear morphea commonly manifests in children and adolescents.

Clinical presentation. Three stages typically encountered in course of the disease. Rounded bluish-red patches appear first. The affected skin is edematous and of a pasty consistency. Hardening of the skin develops in a few weeks: it sits tightly on the underlying tissues, does not gather in folds, turns wax-yellow, and its pattern is smoothed out; no hairs grow in the focus (the stage of collagenous hypertrophy). The skin becomes thin ultimately. It acquires a parchment-like appearance and the lilac ring (the ring of peripheral growth) disappears (stage of atrophy).

Circumscribed (Plaque morphea): single or multiple, well- defined, oval to round plaques.

Generalized: ≥ 4 morphea form plaques at least two different anatomic sites.

Linear: plaques arranged in a linear distribution. *En coup de sabre*: form of linear disease that affects the head and neck.

Deep (morphea profunda): primarily involves the deep dermis, subcutaneous tissue; linear areas of depression (“groove sign”) at sites with underlying tendons and ligaments.

Other variants. *Guttate morphea*: small (< 10 mm in diameter) and superficial lesions, with less induration and a sharply demarcated border. *Keloidal (nodular) morphea*: nodules resembling keloids in the presence of typical plaque-type morphea. *Atrophoderma of Pasini and Pierini*: “burnt-out” plaque-type lesions on the trunk, which are characterized by hyperpigmented, slightly depressed areas with well-defined “cliff-drop” borders and no obvious induration. *Bullous morphea*: rare variant in which tense subepidermal bullae develop overlying plaque-type, linear, or deep morphea lesions.

Diagnostic approaches: Peripheral eosinophilia and increased ESR are possible in early active morphea, RF is positive in 50 %; ANA (anti–single-stranded DNA antibodies, antihistone antibodies) are present in 85 %; antiphospholipid antibodies are present in 45 %; antitopoisomerase II-alpha antibodies are present in 75 %; anti-Cu/Zn-superoxide dismutase antibodies are present in 90 % of morphea patients. Histological findings are similar with systemic sclerosis.

Differential diagnosis: LE panniculitis, radiation fibrosis, fixed drug eruption, keloid and hypertrophic scar.

Treatment: topical or intralesional corticosteroids, tacrolimus 0.1 % ointment, topical calcipotriene, combination of topical calcipotriol with betamethasone dipropionate, Imiquimod 5 % cream, systemic corticosteroids, methotrexate, broadband UVA (320–400 nm, low-dose), long-wavelength UVA (UVA1; 340–400 nm, low- or medium-dose), and psoralen plus UVA (oral or bath) photochemotherapy, narrowband UVB.

Cutaneous dermatomyositis

Dermatomyositis (DM) – idiopathic inflammatory autoimmune systemic disease of unclear etiology marked by muscle weakness and a distinctive skin rash. Skin disease often precedes muscle disease. Amyopathic DM-skin disease without muscle disease more than 2 years. Hypomyopathic DM – evidence of muscles involvement by labs or imaging but no clinical symptoms.

Pathogenesis: DM is a result of a humoral attack against the endothelium of the endomysial blood vessels.

Epidemiology: DM is associated with interstitial lung disease and malignancy, that is why all patients with skin lesions of DM need evaluation for muscle and lung disease, as well as cancer screen. Bimodal onset of DM: juvenile 10–15 y.o. and adult 45–65 y.o.

Clinical presentation. Cutaneous DM can manifest as follow: localization on photo-exposed surfaces, pruritus of skin lesions, mid-face erythema, eruption along the eyelid margins, with or without periorbital edema, eruption on the dorsal hands, particularly over the knuckles, changes in the nailfolds of the fingers, eruption of the upper outer thighs, scaly scalp or diffuse hair loss. *Heliotrope rash* on periorbital skin is violaceous to erythematous with or without edema. *Gottron papules* are flat-topped, erythematous to violaceous papules and plaques found over metacarpophalangeal joints, the proximal interphalangeal joints, and/or the distal interphalangeal joints of hands. Heliotrop rash and Gottron papules are pathognomonic features of cutaneous DM. Characteristic rash but not pathognomonic are malar erythema, poikiloderma in a photosensitive distribution (erythema, hypopigmentation, hyperpigmentation, and telangiectasia on extensor surfaces of the arm and lateral thighs, upper chest and back, in a "V-neck" configuration), periungual and cuticular changes (dilated capillary loops at the base of the fingernail), mechanic's hands (rough and cracked palmar and lateral surfaces of the fingers). Calcinosis of skin is a complication of juvenile dermatomyositis.

Diagnostic approaches: elevated level of creatine kinase, aldolase, aspartate aminotransferase, lactic dehydrogenase, except in patients with amyopathic dermatomyositis. Anti-Mi-2 antibodies are highly specific for dermatomyositis. Anti-Jo-1 (antihistidyl transfer RNA [t-RNA] synthetase) antibodies are associated with pulmonary involvement (interstitial lung disease) in DM. Positive anti-p155/140 antibodies are associated with malignancy in dermatomyositis. Histologic findings: hypertrophy, sclerosis, homogenization of collagenous fibres, severe degeneration, splitting, and atrophy of the muscular bundles, inflammatory perivascular and diffuse lymphocytic infiltrate are found.

Differential diagnosis: DLE, lichen planus, psoriasis, photodermatitis, allergic dermatitis, rosacea, tinea corporis.

Treatment: strict photoprotection, topical corticosteroids or calcineurin inhibitors, systemic antimalarial, methotrexate, azathioprine, mycophenolate mophetil, IVIG.

Calcinosis cutis: channel blocker diltiazem, oral bisphosphonate, surgical excision.

Pemphigus Vulgaris (PV)

Definition: Severe, potentially fatal disease with intraepidermal blister formation on skin and mucosa caused by autoantibodies against desmogleins.

Epidemiology: Incidence 0.1–0.5/100 000 yearly, but higher in some ethnic groups. Most patients middle-aged.

Pathogenesis: Genetic predisposition: HLA-DRQ402, DQ0505. Patients develop antibodies against desmoglein 3 (Dsg3) and later desmoglein 1 (Dsg1).

The bound antibodies activate proteases that damage the desmosome, leading to acantholysis. Serum antibody titer usually correlates with severity of disease and course. Occasionally drugs cause pemphigus vulgaris and pemphigus foliaceus. Agents containing sulfhydryl groups (penicillamine, captopril, piroxicam) are more likely to cause pemphigus foliaceus; those without sulfhydryl groups tend to cause pemphigus vulgaris. The latter group includes β -blockers, cephalosporins, penicillin, and rifampicin.

Clinical features: Sites of predilection include oral mucosa, scalp, face, mechanically stressed areas, nail fold, intertriginous areas (can present as intertrigo). The blisters are not stable, as the epidermis falls apart; therefore, erosions and crusts common. Usually has three stages: Oral involvement: In 70 % of patients, PV starts in the mouth with painful erosions. Other mucosal surfaces can also be involved. Additional localized disease, often on scalp. Painful, poorly healing crusted erosions and ulcers; blisters hard to find. Pruritus uncommon.

Histology: When a fresh lesion is biopsied (small excision, not punch biopsy), acantholysis is seen (free-floating, rounded keratinocytes) with retention of basal layer keratinocytes (tombstone effect) and mild dermal perivascular infiltrates.

Diagnostic approach: Clinical evaluation; check sites of predilection. Nikolsky sign: True Nikolsky sign: Gentle rubbing allows one to separate upper layer of epidermis from lower, producing blister or erosion – fairly specific for pemphigus. Pseudo-Nikolsky sign (Asboe–Hansen sign): Pressure at edge of blister makes it spread – less specific, seen with many blisters. Histology: Can be helpful, but often just erosions or nonspecific changes. Direct immunofluorescence: Perilesional skin shows deposition of IgG (100 %), C3 (80 %) or IgA (> 20 %), as well C1q in early lesions. Antibodies surround the individual keratinocytes. Indirect immunofluorescence: Using monkey esophagus, 90 % of sera show positive reaction; titer can be used to monitor disease course. ELISA: Can be used to identify anti-Dsg3 with mucosal disease or anti-Dsg1 or anti-Dsg3 with widespread disease. Check for associated diseases, especially thymoma and myasthenia gravis.

Differential diagnosis: When the skin is involved, the question is usually which autoimmune bullous disease. On rare occasions, bullous impetigo, dyskeratotic acantholytic disorders (Darier disease, Hailey–Hailey disease, Grover disease) can cause problems. When only the oral mucosa is involved, the following should be considered: Denture intolerance reactions. Erosive candidiasis: Not all oral candidiasis features white plaques (thrush); sometimes atrophy and erosions.

Chronic recurrent aphthae: Usually smaller lesions with erythematous border but sometimes large, persistent ulcers. Erythema multiforme: erosions on lips and mucosa associated with target lesions on skin. Herpetic gingivostomatitis: Usually in children. Erosive lichen planus: Look for signs of lichen planus elsewhere; if only in mouth, biopsy and direct immunofluorescence often needed.

Therapy: Systemic corticosteroids are necessary for long periods of time. The main cause of morbidity and mortality today in patients with pemphigus vulgaris is corticosteroid side-effects. For this reason, corticosteroids are always combined with steroid-sparing agents. Patients should be screened for osteoporosis and latent tuberculosis before embarking on long-term corticosteroid therapy. Osteoporosis prophylaxis may be warranted. Combination pulse therapy: Treatment of choice. prednisolone plus cyclophosphamide. Prednisolone-azathioprine therapy. Alternative immunosuppressive agents: Chlorambucil; cyclosporine; mycophenolate mofetil. Topical measures: Local anesthetic gels in the mouth before meals may relieve pain and making eating less traumatic; antiseptics and anticandidal measures may also be useful.

Pemphigus Vegetans

Definition: Unusual variant of PV with hyperkeratotic verruciform reaction (vegetans).

Clinical features: Two forms: Pemphigus vegetans Neumann type: Originally typical PV, then development of white macerated plaques in involved areas.

Pemphigus vegetans Hallopeau type: Also known as pyodermite v'g'tante, limited to intertriginous areas, starts as pustules that evolve into vegetating lesions.

Histology: Can be tricky; pseudoepitheliomatous hyperplasia and numerous eosinophils; acantholysis can be hard to find.

Diagnostic approach: As for PV.

Differential diagnosis: If mild and localized, can be confused with Hailey–Hailey disease.

Therapy: See PV.

Pemphigus Foliaceus

Definition: Form of pemphigus with superficial blisters caused by autoantibodies against Dsg1.

Epidemiology: All age groups affected; not infrequently children.

Pathogenesis: Autoantibodies against Dsg1, the main desmoglein in the upper epidermis; rarely antibody shift so that they later are formed against Dsg3 and patient develops PV. More often drug-induced than PV. Usual agents have sulfhydryl groups such as captopril, penicillamine, and piroxicam. May be caused by sunburn or as paraneoplastic sign.

Clinical features: Sites of predilection include scalp, face, chest, and back (seborrheic areas) with diffuse scale and erosions. Can progress to involve large areas (exfoliative erythroderma). Facial rash sometimes butterfly pattern. Oral mucosa usually spared (Dsg1 is scarcely expressed in oral epithelia). Individual lesions are slowly developing slack blisters that rupture easily, forming erosions and red-brown crusts.

Histology: Blister forms in stratum corneum or stratum granulosum; acantholysis rarely seen; usually just a denuded epithelium and sparse dermal perivascular inflammation.

Diagnostic approach: Clinical appearance. Skin biopsy often not helpful. Direct and indirect immunofluorescence show superficial deposition of IgG. ELISA reveals IgG antibodies against Dgs1. Medication history: See PV. Agents with sulfhydryl groups most likely to cause pemphigus foliaceus; main actors are captopril, penicillamine, and piroxicam.

Differential diagnosis: Frequently misdiagnosed, as blisters are so uncommon. Depending on clinical variant, possibilities include drug reaction, photodermatosis, seborrheic dermatitis, lupus erythematosus.

Therapy: Same approach as PV but usually more responsive to therapy. Dapsone may be helpful.

Fogo Selvagem

Synonyms: Brazilian pemphigus, South American pemphigus, wildfire pemphigus (fogo selvagem is Portuguese for wildfire).

Definition: Endemic form of pemphigus foliaceus.

Epidemiology: Found in areas where development is pushing back the jungle in Brazil; transfer of some infectious trigger suspected; common in families; patients usually 30 years of age; women affected more often.

Clinical features: Same as pemphigus foliaceus; burning is a typical feature, perhaps because of less adequate topical care; classic lesion is denuded burning erosion with roll of pushed-back upper epidermis at periphery. Can evolve into erythroderma. No oral involvement. Without therapy, 40 % die within 2 years; others develop chronic disease persisting for decades.

Diagnostic approach: Same as for pemphigus foliaceus.

Therapy: Usually corticosteroids and steroid-sparing agent (azathioprine) suffice; otherwise, regimens as under PV.

Pemphigus Erythematosus

Synonym: Senear–Usher syndrome.

Definition: Uncommon variant of pemphigus foliaceus with additional features of lupus erythematosus.

Pathogenesis: More likely to be triggered by sunlight or medications than other forms of pemphigus foliaceus.

Clinical features: Older patients with erythema and crusting in butterfly distribution and seborrheic areas; often eroded.

Histology: Superficial acantholysis and blister formation, sometimes vacuolar change in basal layer.

Diagnostic approach: Direct immunofluorescence: Intercellular IgG, sometimes with C3; deposits of IgG, IgM, and C3 at BMZ in 50–70 %. IgG and IgM can be found in normal skin. ANA positive in 80%; usually homogenous pattern; no specific autoantibodies for lupus erythematosus. Check drug history

Therapy: Usually responds to prednisolone 1–2 mg/kg tapered to low maintenance dose; can be combined with antimalarials. Meticulous sun avoidance and sunscreens. Dapsone also sometimes effective. If still not responsive, whole spectrum of agents discussed under PV can be used.

Dermatitis Herpetiformis

Definition: Pruritic vesicular disease caused by IgA autoantibodies directed against epidermal transglutaminase and presenting with granular pattern in papillary dermis.

Epidemiology: Men are affected twice as often women. Disease of young adults.

Pathogenesis: Dermatitis herpetiformis and gluten-sensitive enteropathy are closely related. They are the result of an abnormal immune response to gluten antigens. Gluten is the main adhesive substance of many grains. The most important sensitizing protein is gliadin, which is the substrate for tissue transglutaminase. Autoantibodies against tissue transglutaminase also cross-react with the similar epidermal transglutaminase, producing dermatitis herpetiformis. The antibodies in dermatitis herpetiformis patients have more affinity for epidermal transglutaminase than do those in patients with gluten-sensitive enteropathy. There is a strong HLA association. Other genetic factors are involved. Rare patients with enteropathy have skin involvement; few patients with skin findings have symptomatic bowel disease, but most have an abnormal bowel biopsy.

Clinical features: Sites of predilection include the knees and elbows (Cottini type when limited to these areas), as well as buttocks and upper trunk. Facial involvement rare. Hallmark is intensely pruritic or burning tiny vesicles, which are usually scratched away by the time the patient presents. In undisturbed lesions, there may be a rim of peripheral vesicles arranged in herpetiform fashion. Less often there are larger blisters. Occasional signs and symptoms of enteropathy with malabsorption, voluminous loose stools, and weight loss. Occasional association with other autoimmune diseases such as diabetes mellitus, pernicious anemia, thyroid disease, and vitiligo. Patients often are not able to tolerate iodine and flare with exposures, such as when eating seafood. Iodine challenge or iodine patch test are old diagnostic measures. Spontaneous remissions may occur, but disease often lifelong.

Histology: Neutrophilic microabscesses in the papillary dermis are the hallmark. Often admixed with eosinophils. Edema leads to subepidermal blister formation.

Diagnostic approach: Skin biopsy; often hard to obtain fresh lesion. Direct immunofluorescence: Granular deposits of IgA in dermal papillae; sometimes granular-linear along BMZ. Present in > 95 % of patients, also in normal skin (buttocks); persist long after therapy is started. Indirect immunofluorescence: IgA antibodies against smooth muscle endomysium (source of tissue transglutaminase) present in 80%. ELISA identifies IgA antibodies against tissue transglutaminase in at least 80%;antigliadin antibodies also present, but less specific. Jejunal biopsy: flattening of villi (85 %) with intraepithelial lymphocytes in 100 %.

Differential diagnosis: Dermatitis herpetiformis is probably incorrectly invoked as a differential diagnostic consideration more than any other skin disease as it is suspected in anyone with pruritus where there is no obvious cause. Scabies, BP before the development of blisters, and the prurigo group are the main issues.

Therapy: The mainstay of therapy is a gluten-free diet, which also protects against gastrointestinal lymphoma. The diet is hard to follow and only takes effect after months, but is essential. Dapsone is amazingly effective; hours to days after the first dose, the pruritus disappears. Usually a low dose of 25–50 mg suffices; for details on usage.

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