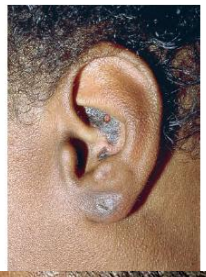

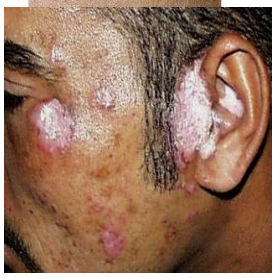

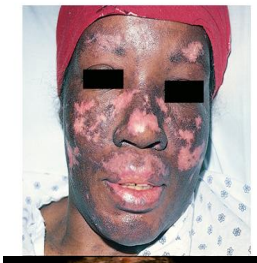

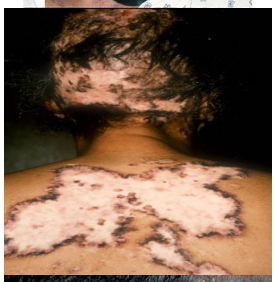

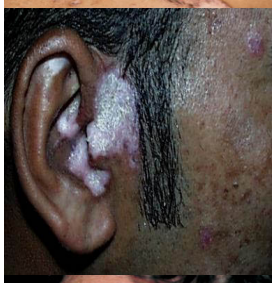

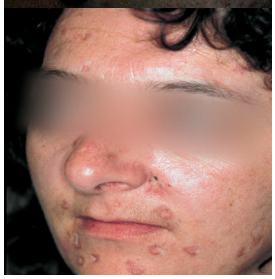

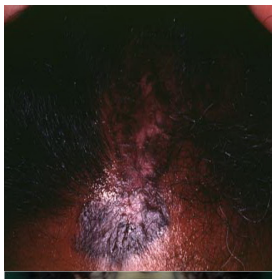

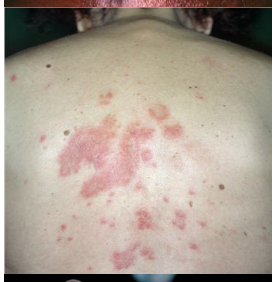

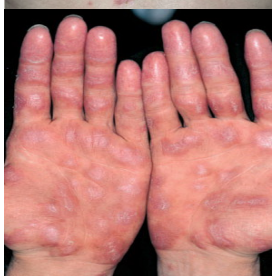

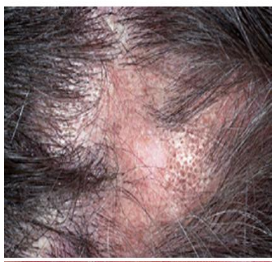

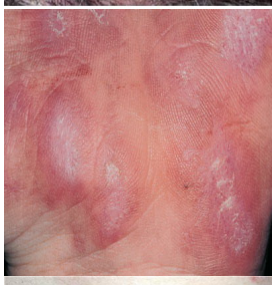

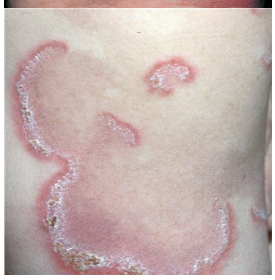

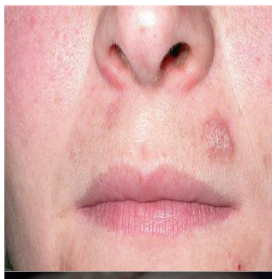

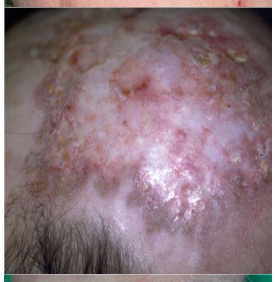

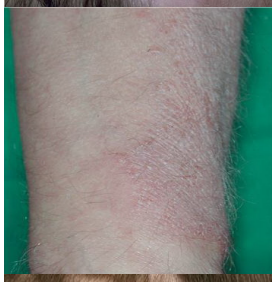

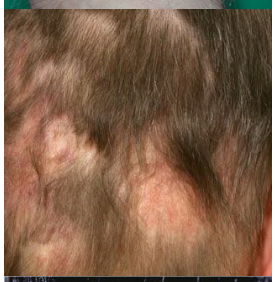

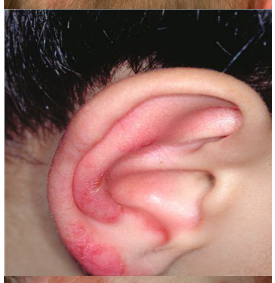

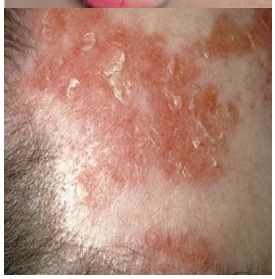

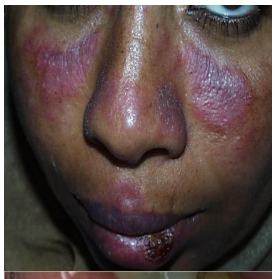
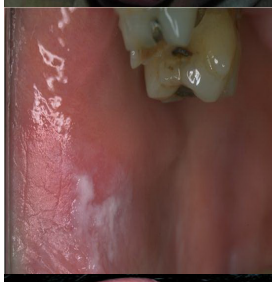
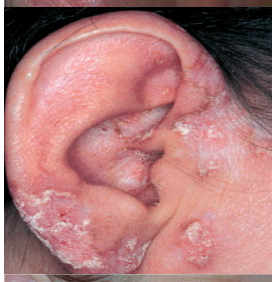
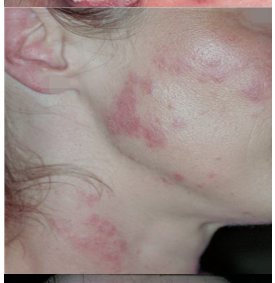
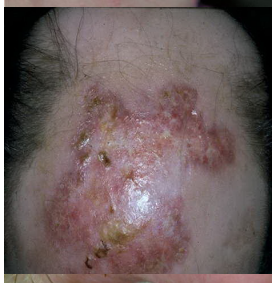
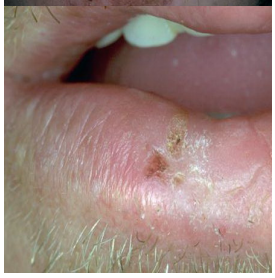

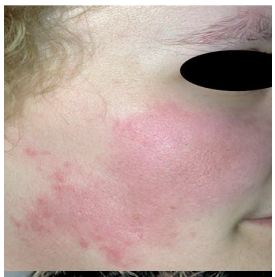
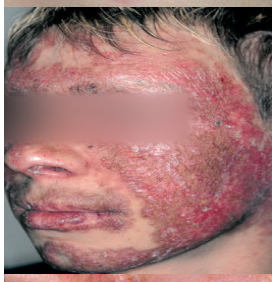
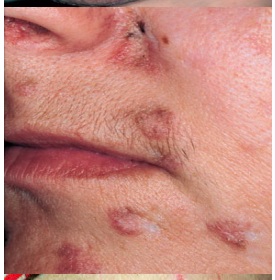
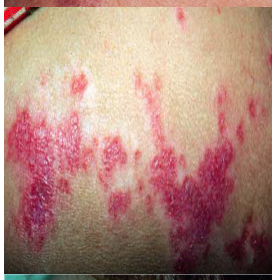
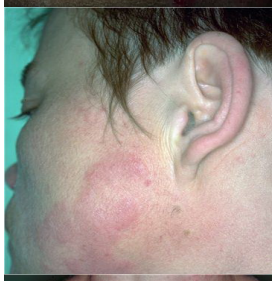
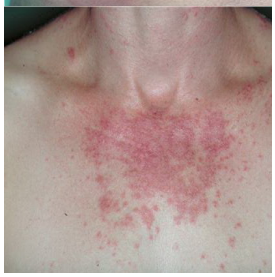

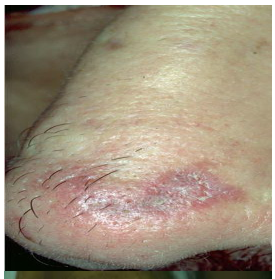
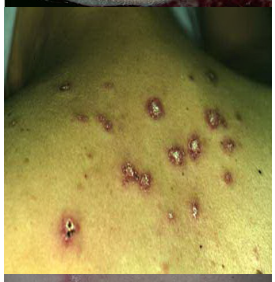
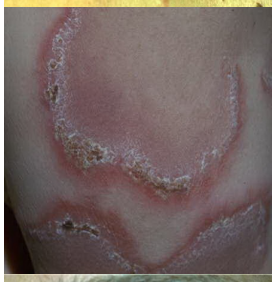
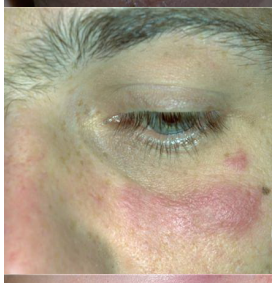
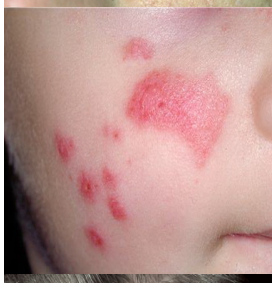
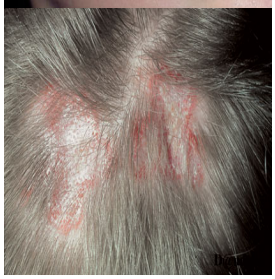

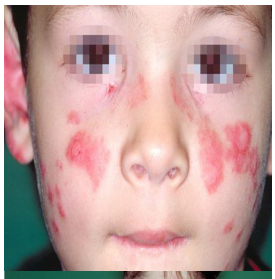
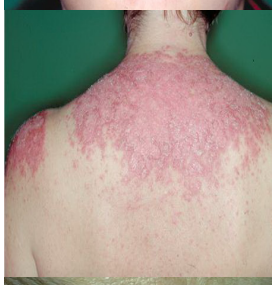
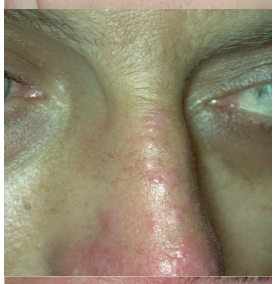
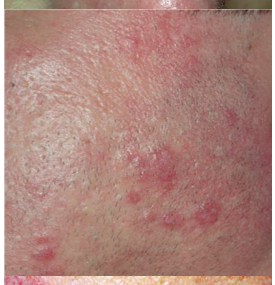
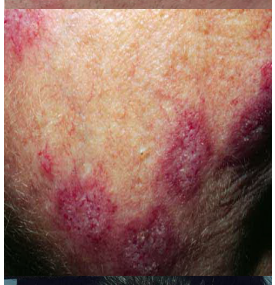
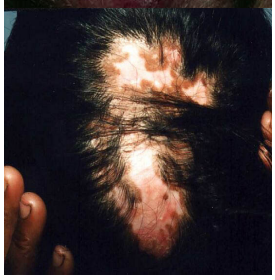

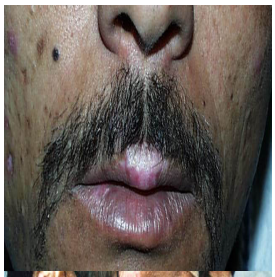
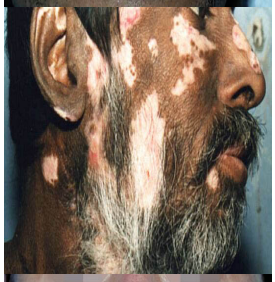
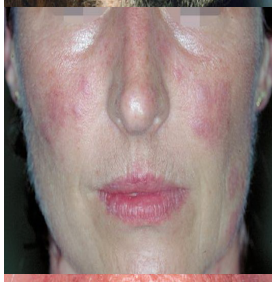
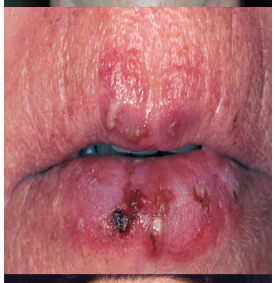
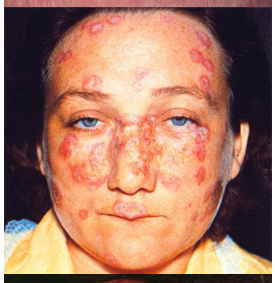
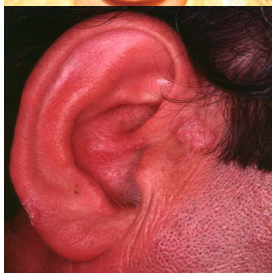

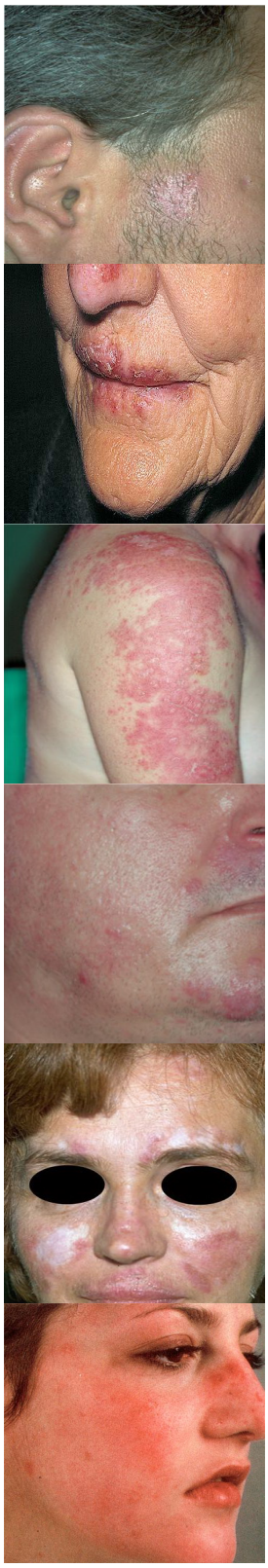

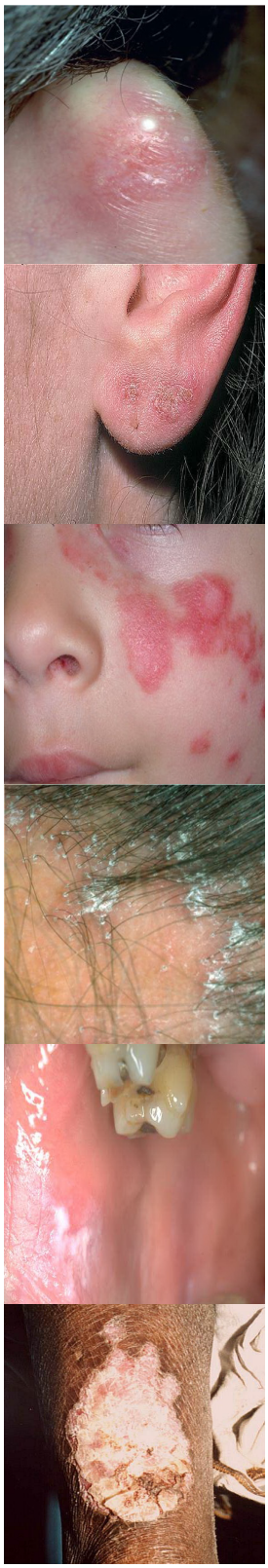

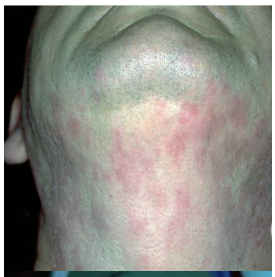
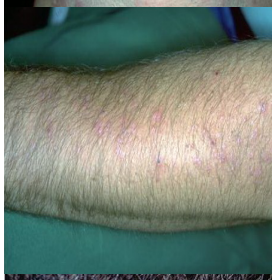
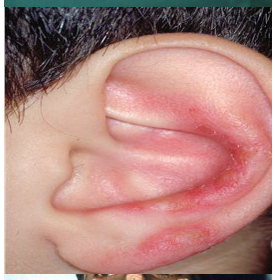
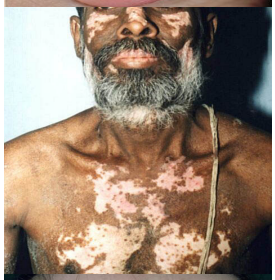
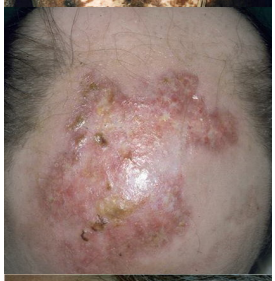
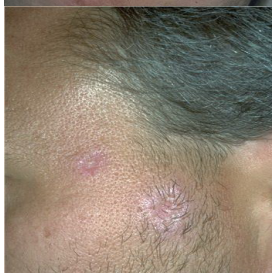

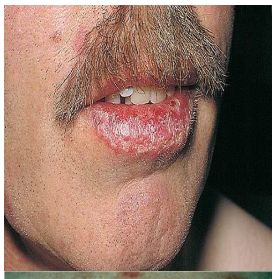

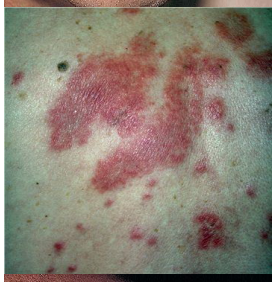

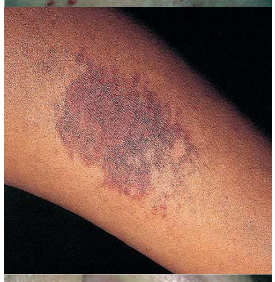

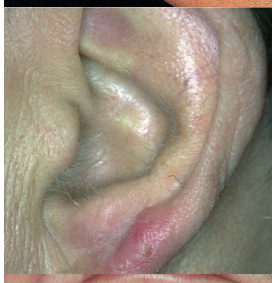

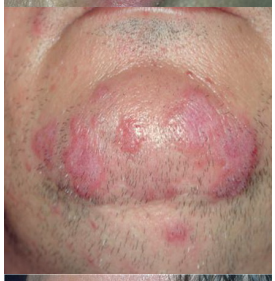

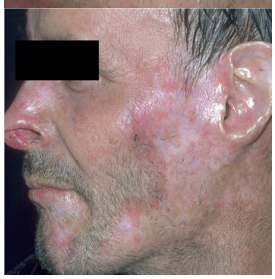

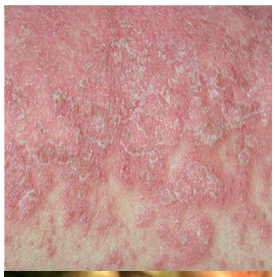
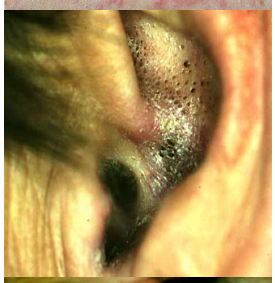
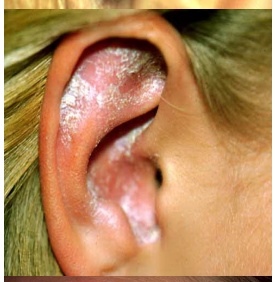
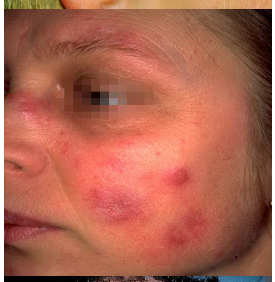
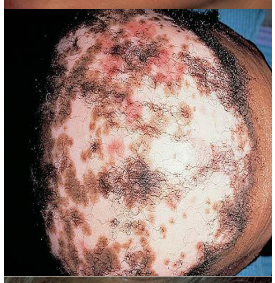
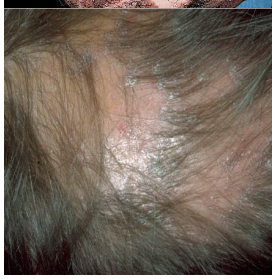

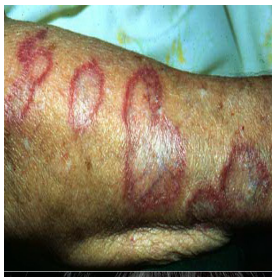
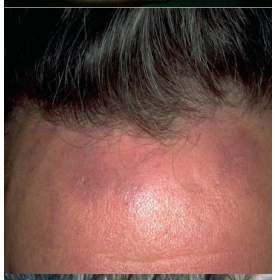
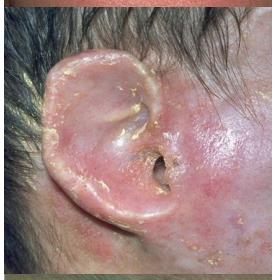
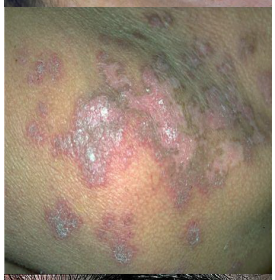
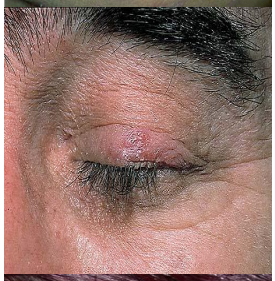
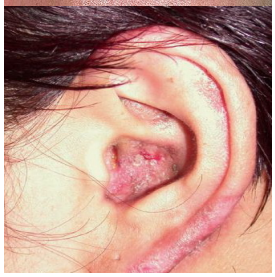

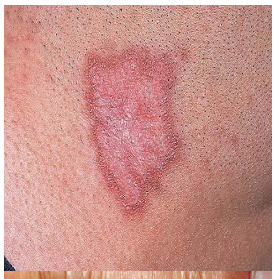
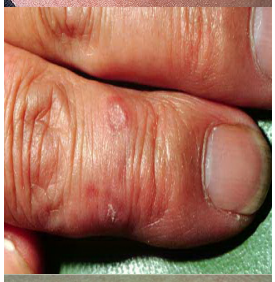
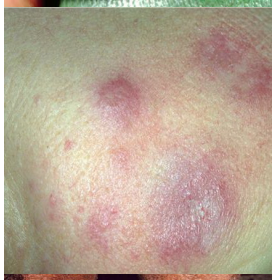
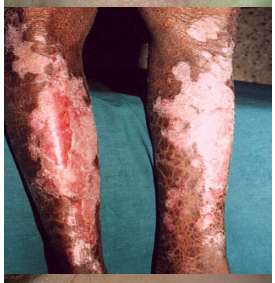
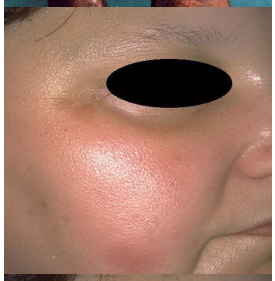
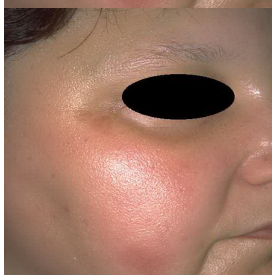

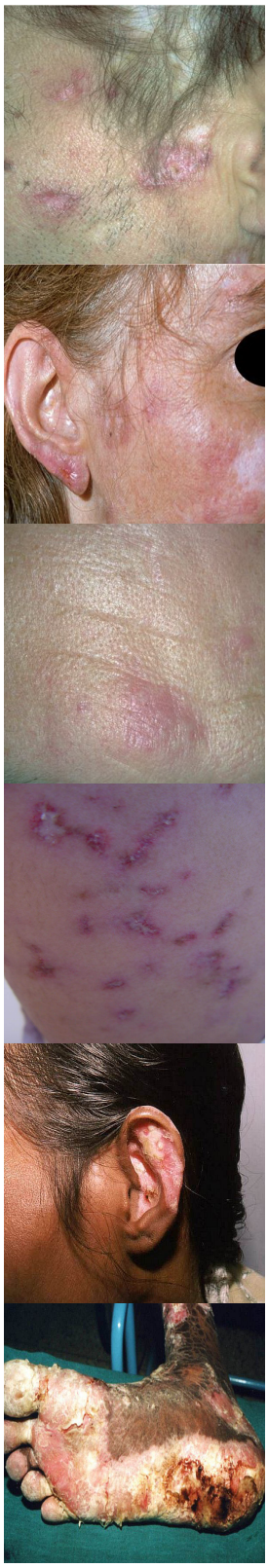

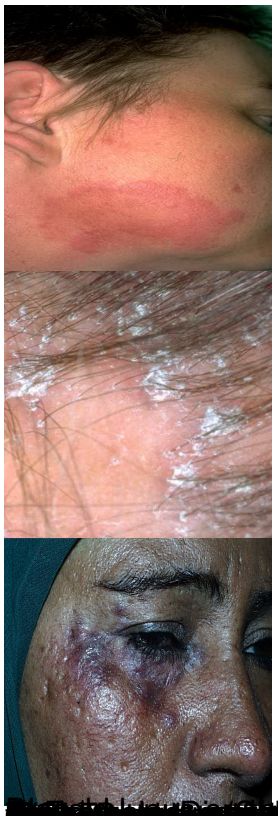

Physical

Discoid lupus erythematosus lesions (DLE) frequently are characteristic. The primary lesion is an erythematous papule or plaque with slight-to-moderate scaling (see images below). As the lesion progresses, the scale may thicken and become adherent, and pigmentary changes may develop, with hypopigmentation in the central or inactive area and hyperpigmentation at the active border.

Lesions spread centrifugally and may merge. As lesions age, dilation of follicular openings occurs with a keratinous plug, termed follicular plugging or patulous follicles (see image below). Resolution of the active lesion results in atrophy and scarring

At any time, individual lesions may have any or all of these features. Early lesions may be difficult to distinguish from SCLE. Discoid lupus erythematosus lesions often are photodistributed, but relatively unexposed skin also may be affected. The scalp is a common area of involvement, and permanent alopecia may result

Patients with discoid lupus erythematosus often are divided into 2 subsets: localized and widespread. Localized discoid lupus erythematosus occurs when the head and neck only are affected, while widespread discoid lupus erythematosus occurs when other areas are affected, regardless of whether disease of the head and neck is seen (see image below). Patients with widespread involvement often have hematologic and serologic abnormalities, are more likely to develop SLE, and are more difficult to treat

Several unusual variants of chronic CLE, other than discoid lupus erythematosus, have been reported. Mucosal surfaces may be affected by lesions that appear identical to discoid lupus erythematosus of the skin or by lesions that may simulate lichen planus. Palms and soles may be affected, but this occurs in less than 2% of patients

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Discoid lupus erythematosus lesions may become hypertrophic or verrucous (see image below). This subset is manifested by wartlike lesions, most often on the extensor arms. Hypertrophic lesions of LE must be differentiated from warts, keratoacanthomas, or squamous cell carcinoma. These lesions are more difficult to treat

Lupus panniculitis is a form of chronic CLE that may be accompanied by typical DLE lesions or may occur in patients with SLE.[6]

Causes

Patients with discoid lupus erythematosus probably have genetic predisposition; however, the precise genetic factors that increase the risk of this disease are unknown. The disease usually manifests following UV light exposure, but other triggers or inciting factors also must contribute. Toll-like receptors are possibly involved in the pathogenesis

Laboratory Studies

Serologic testing is as follows:

- Some patients with discoid lupus erythematosus (DLE) (approximately 20%) manifest a positive antinuclear antibody (ANA) when tested with human substrates. HEp-2 cells currently are the most common substrate used in commercial laboratories.
- Anti-Ro (SS-A) autoantibodies are present in approximately 1-3% of patients.
- Antinative DNA (double-stranded or nDNA) or anti-Sm antibodies usually reflect SLE, and they may occur in some patients (<5%).

Other laboratory findings are as follows:

- Cytopenias may be present.
- Elevated sedimentation rate may occur in some patients.
- Rheumatoid factor may be positive.
- Complement levels may be depressed.
- Urinalysis may reflect the presence of renal involvement with proteinuria.

Other Tests

Immunopathology findings are as follows:

- Deposition of immunoglobulin and/or complement at the dermal-epidermal junction is a characteristic feature of LE referred to in most texts and articles. Tissue may be examined from skin lesions (lesional) or normal skin (nonlesional). Nonlesional biopsies may be from exposed or nonexposed surfaces. Testing of nonlesional, nonexposed skin is termed the lupus band test (LBT).
- The use and interpretation of these tests varies according to the biopsy site. Approximately 90% of patients with discoid lupus erythematosus manifest a positive direct immunofluorescence (DIF) test on lesional skin; however, the presence of immunoreactants in the basement membrane zone of lesional skin is not specific for lupus and can be seen in a variety of inflammatory skin diseases. Older lesions or very early lesions may be more likely to be negative on immunofluorescence microscopy. Only patients with SLE have a positive LBT, defined as the presence of multiple immunoreactants in the basement membrane zone. LBTs are neither sensitive nor specific and mostly have been replaced by advances in serologic testing.

Histologic Findings

The characteristic histopathologic alterations observed in discoid lupus erythematosus include vacuolar alteration of the basal cell layer, thickening of the basement membrane, follicular plugging, hyperkeratosis, atrophy of the epidermis, incontinence of pigment, and inflammatory cell infiltrate (usually lymphocytic) in a perivascular, periappendiceal, and subepidermal location. Often, an abundance of mucin is seen within the dermis. The histopathologic features differ depending upon the type and age of the lesion.

Medical Care

The goals of discoid lupus erythematosus (DLE) management are to improve the patient's appearance, to control existing lesions and limit scarring, and to prevent the development of further lesions. Advise patients that the risk of serious systemic disease is possible, although rare. Regular repeat clinical evaluation accompanied by simple laboratory studies usually is sufficient to evaluate the possible progression from the primary cutaneous disorder to the disorder accompanied by systemic involvement.

Therapy begins with sun-protective measures, including sunscreens, protective clothing, and behavior alteration. Cosmetic measures, such as cover-up makeup or wigs, may be suggested for appropriately selected patients. Makeup used for camouflage includes Covermark and Dermablend.[7]

Smoking appears to decrease the efficacy of antimalarial agents, and efforts regarding smoking cessation are advisable in patients who smoke or are exposed to secondary smoke.[8,9,10]

Standard medical therapy includes corticosteroids (topical or intralesional) and antimalarials. Antimalarials appear less effective in patients who smoke; however, discoid lupus erythematosus possibly is worse in these patients. In addition, antimalarial therapy seems to lessen the progression to SLE and to lower the risk of thrombovascular disease.[11,12] Alternative therapies include auranofin, thalidomide,
[13,14,15,16]

oral or topical retinoids, and immunosuppressive agents.
[17,18]

Thalidomide is regularly used in antimalarial-resistant patients. In most patients, the antimalarial should be continued during thalidomide therapy, unless a complication due to the antimalarial occurs. In addition, lenalidomide may be useful in some patients.
[19]

Topical corticosteroids are selected for the type of lesion under treatment and for the site of involvement. For example, lotions or foams are preferred for the scalp, weaker agents are used on the face, and superpotent agents are used for hypertrophic lesions.

Topical calcineurin inhibitors have also been used in patients with cutaneous lesions of LE. In addition, topical retinoids have been reported to be helpful. Lastly, topical imiquimod has been reported to be effective in one patient.

Intralesional injection of corticosteroids (typically, this author uses triamcinolone acetonide 3 mg/mL) is useful as adjunctive therapy for individual lesions. Potential for atrophy relates to the amount of corticosteroid injected in any one area; therefore, dilute concentrations are preferred. In addition, the treating physician must take care to limit the total dose of the injections at any given office/clinic visit to avoid systemic toxicity from the steroids eg, if a patient is given 10 mL of triamcinolone 3 mg/mL, this means that the patient has received a total of 30 mg, and toxicity is the same as if it had been delivered orally or by intramuscular injection.

Among immunosuppressives, methotrexate (MTX) may be considered.[20] In this author's experience, azathioprine and, recently, mycophenolate mofetil, have been more successful than MTX, while systemic corticosteroids are rarely effective.

Surgical Care

Excision of burned-out scarred lesions is possible; however, reactivation of inactive lesions has been reported in some patients.

Laser therapy may be useful for lesions with prominent telangiectases. Reactivation also is a consideration with this form of therapy. An open trial in a small group of patients has demonstrated efficacy of pulsed dye laser therapy for discoid lupus erythematosus lesions. However, before using this therapy in additional patients, at a minimum, a test area should be treated to make certain that the discoid lupus erythematosus does not flare.[22]

21

Medication

The goals of pharmacotherapy are to reduce morbidity and to prevent complications. Hydroxychloroquine and chloroquine phosphate have shown beneficial effects in treating DLE. Alternative therapies, anecdotal reports, and small open-label trials (as reported by Callen[23]) suggest that the following agents may be useful in some patients: dapsone, auranofin, quinacrine, thalidomide, isotretinoin,
[24]
acitretin, azathioprine, mycophenolate mofetil, phenytoin, interferon, and chimeric monoclonal antibody.
[25]

Antimalarial agents

May have immunomodulatory properties. Hydroxychloroquine is DOC when a systemic agent is needed for DLE. Chloroquine is second-line therapy.

Hydroxychloroquine (Plaquenil)

For treatment of DLE and SLE. Inhibits chemotaxis of eosinophils, locomotion of neutrophils, and impairs complement-dependent antigen-antibody reactions.
Hydroxychloroquine sulfate 200 mg is equivalent to 155 mg hydroxychloroquine base and 250 mg chloroquine phosphate.

Adult

200-400 mg/d PO; not to exceed 6.5 mg/kg/d; 310 mg PO qd or bid for several wk depending on response; 155-310 mg/d for prolonged maintenance therapy

Pediatric

6.5 mg/kg/d PO; 3-5 mg base/kg/d PO qd or divided bid; not to exceed 7 mg/kg/d

Penicillamine levels may increase; serum levels increase with cimetidine; magnesium trisilicate may decrease absorption

Documented hypersensitivity; psoriasis; retinal and visual field changes attributable to 4-aminoquinolones

Pregnancy

C - Fetal risk revealed in studies in animals but not established or not studied in humans; may use if benefits outweigh risk to fetus

Precautions

Crosses placenta and may cause ocular, CNS, or ototoxicity in the fetus; do not use if breast-feeding; limit pediatric use to established safe doses to avoid potential fatality; ocular toxicity is possible for hydroxychloroquine and chloroquine but not quinacrine; perform regular ophthalmologic examinations during therapy

Chloroquine (Aralen)

Inhibits chemotaxis of eosinophils, locomotion of neutrophils, and impairs complement-dependent antigen-antibody reactions.

Adult

250-500 mg PO qd

Pediatric

10 mg/kg PO d 1, then 5 mg/kg 6 h later, followed by 5 mg/kg d 2 and 3

Cimetidine may increase serum levels of chloroquine (possibly other 4-aminoquinolones);

magnesium trisilicate may decrease absorption of 4-aminoquinolones

Documented hypersensitivity; psoriasis, retinal and visual field changes attributable to 4-aminoquinolones

Pregnancy

C - Fetal risk revealed in studies in animals but not established or not studied in humans; may use if benefits outweigh risk to fetus

Precautions

Caution in hepatic disease, G-6-PD deficiency, psoriasis, porphyria; not recommended for long-term use in children; perform periodic ophthalmologic examinations; test for muscle weakness

Leprostatic agents

May modulate the immune system.

Dapsone (Avlosulfon)

Mechanism of action is similar to sulfonamides where competitive antagonists of PABA prevent formation of folic acid, inhibiting bacterial growth. The anti-inflammatory action may relate to suppression of neutrophil function by inhibition of the halide-myeloperoxidase system.

Adult

100-200 mg PO qd

Pediatric

Not established

May inhibit anti-inflammatory effects of clofazimine; hematologic reactions may increase with folic acid antagonists, eg, pyrimethamine (monitor for agranulocytosis during second and third mo of therapy); probenecid increases dapsone toxicity; trimethoprim with dapsone may increase toxicity of both; because of increased renal clearance, dapsone levels may significantly decrease when administered concurrently with rifampin

Documented hypersensitivity; G-6-PD deficiency

Pregnancy

C - Fetal risk revealed in studies in animals but not established or not studied in humans; may use if benefits outweigh risk to fetus

Precautions

Perform weekly or biweekly blood counts (first mo), then perform WBC counts monthly (6 mo), then semiannually; discontinue if significant reduction in platelets, leukocytes, or hematopoiesis is seen; caution in methemoglobin reductase deficiency, G-6-PD deficiency, or hemoglobin M because of high risk for hemolysis and Heinz body formation; caution in patients exposed to other agents or conditions (eg, infection, diabetic ketosis) capable of producing hemolysis; peripheral neuropathy can occur (rare); phototoxicity may occur when exposed to UV light

Gold compounds

Have proven effective in the treatment of inflammation with autoimmune etiology.

Auranofin (Ridaura)

Gold is taken up by macrophages, which, in turn, inhibit phagocytosis and lysosomal membrane stabilization. Alters immunoglobulins, decreasing prostaglandin synthesis and lysosomal enzyme activity.

Adult

6 mg/d PO qd or divided bid; after 3 mo, may increase to 9 mg/d divided tid; then, if no response, discontinue drug

Pediatric

Initial dose: 0.1 mg/kg/d PO divided bid
Maintenance dose: 0.15 mg/kg/d PO qd or divided bid

Penicillamine, hydroxychloroquine, and antimalarials may increase toxicity

- Documented hypersensitivity; renal impairment; history of blood dyscrasias, exfoliative dermatitis, congestive heart failure, necrotizing enterocolitis

Pregnancy

B - Fetal risk not confirmed in studies in humans but has been shown in some studies in animals

Precautions

Discontinue therapy if platelet counts fall <100,000/µL, WBC count <4,000/µL, granulocyte count <1,500/µL

Immunomodulators

Affect factors that regulate the immune system.

Methotrexate (Rheumatrex, Trexall)

Reversibly inhibits dihydrofolate reductase; limits the availability of 1-carbon fragments necessary for synthesis of purines and the conversion of deoxyuridylate to thymidylate in the synthesis of DNA and cell reproduction. Extensively used for cancer treatment, rheumatoid arthritis, psoriasis, and as a steroid-sparing agent in various autoimmune conditions.

Adult

In autoimmune conditions: 7.5-25 mg/wk as a single dose PO/SC
Folic acid supplementation is usually given concomitantly

Pediatric

5-15 mg/m^2/wk as a single dose PO/SC

Oral aminoglycosides may decrease absorption and blood levels of concurrent oral MTX; charcoal lowers levels; coadministration with etretinate may increase hepatotoxicity; folic acid or its derivatives contained in some vitamins may decrease response to MTX
Probenecid, NSAIDs, salicylates, procarbazine, and sulfonamides (including TMP-SMZ) can increase MTX plasma levels; may decrease phenytoin plasma levels; may increase plasma levels of thiopurines

Documented hypersensitivity; alcoholism; hepatic insufficiency; documented immunodeficiency syndromes; preexisting blood dyscrasias (eg, bone marrow hypoplasia, leukopenia, thrombocytopenia, significant anemia); renal insufficiency

Pregnancy

X - Contraindicated; benefit does not outweigh risk

Precautions

Monitor CBC counts monthly, and liver and renal function q1-3mo during therapy (monitor more frequently during initial dosing, dose adjustments, or when risk of elevated MTX levels, eg, dehydration); has toxic effects on hematologic, renal, GI, pulmonary, and neurologic systems; discontinue if significant drop in blood counts occurs; fatal reactions reported when administered concurrently with NSAIDs

Thalidomide (Thalomid)

Immunomodulatory agent that may suppress excessive production of TNF-alpha and may down-regulate selected cell-surface adhesion molecules involved in leukocyte migration.
If <50 kg (110 lb), start at low end of dose regimen.

-

Adult

100-300 mg PO hs aq, and >1 h pc

Pediatric

Not established

May increase sedation effects of alcohol, barbiturates, chlorpromazine, and reserpine; because of teratogenic effects, women must use 2 additional methods of contraception or abstain from intercourse

Documented hypersensitivity

Pregnancy

X - Contraindicated; benefit does not outweigh risk

Precautions

Perform pregnancy test within 24 h prior to initiating therapy (weekly during first mo, followed by monthly tests in women with regular menstrual cycles or q2wk with irregular menstrual cycles); bradycardia may occur; use protective measures (eg, sunscreens, protective clothing) against exposure to sunlight or UV light (eg, tanning beds)

Azathioprine (Imuran)

Antagonizes purine metabolism and inhibits synthesis of DNA, RNA, and proteins. May decrease proliferation of immune cells, which results in lower autoimmune activity.

Adult

1 mg/kg/d PO for 6-8 wk; increase by 0.5 mg/kg q4wk until response is seen or dose reaches 2.5 mg/kg/d

Pediatric

Initial dose: 2-5 mg/kg/d PO/IV
Maintenance dose: 1-2 mg/kg/d PO/IV

Toxicity increases with allopurinol; concurrent use with ACE inhibitors may induce severe leukopenia; may increase levels of MTX metabolites and decrease effects of anticoagulants, neuromuscular blockers, and cyclosporine

Documented hypersensitivity

Pregnancy

D - Fetal risk shown in humans; use only if benefits outweigh risk to fetus

Precautions

Increases risk of neoplasia; caution with liver disease and renal impairment; hematologic toxicities may occur

Interferon alfa-2a and alfa-2b (Roferon and Intron A)

Protein product manufactured by recombinant DNA technology. Mechanism of antitumor activity is not clearly understood; however, direct antiproliferative effects against malignant cells and modulation of host immune response may be important factors. Has antiviral, antitumor, and immunomodulatory actions.

-

Adult

2 million U/m^2 SC 3 times/wk for 30 d

Pediatric

Not established

-

Theophylline may increase toxicity; cimetidine may increase antitumor effects; zidovudine and vinblastine may increase toxicity

-

Documented hypersensitivity

Pregnancy

C - Fetal risk revealed in studies in animals but not established or not studied in humans; may use if benefits outweigh risk to fetus

Precautions

Caution in brain metastases, severe hepatic or renal insufficiencies, seizure disorders, multiple sclerosis, or compromised CNS

Mycophenolate (CellCept)

Inhibits inosine monophosphate dehydrogenase and suppresses de novo purine synthesis by lymphocytes, thereby inhibiting their proliferation. Inhibits antibody production.

Adult

1 g PO bid

Pediatric

Not established; 15-23 mg/kg PO bid suggested

-

May elevate levels of acyclovir and ganciclovir; antacids and cholestyramine decrease absorption, reducing levels (do not administer together); probenecid may increase levels of mycophenolate; salicylates may increase toxicity of mycophenolate

-

Documented hypersensitivity

Pregnancy

D - Fetal risk shown in humans; use only if benefits outweigh risk to fetus

Precautions

Increases risk for infection; increases toxicity in patients with renal impairment; caution in active peptic ulcer disease

Corticosteroids

Anti-inflammatory agents that suppress the immune system at several levels including inhibition of inflammatory cells and the production of antibodies.

Triamcinolone (Aristocort)

Can be administered intralesionally in a concentration of 3-5 mg/mL. Amounts injected should be recorded. Systemic adverse effects are uncommon with low doses. Atrophy is possible and is dose dependent.

Adult

3-5 mg/mL; not to exceed 2 mL at any single setting

Pediatric

Not established

Rare for intralesional, but if administered IM or in sufficient dosage, potential adverse effects may occur with coadministration with barbiturates, phenytoin, and rifampin, which decrease effects of triamcinolone

Documented hypersensitivity; fungal, viral, and bacterial skin infections

Pregnancy

C - Fetal risk revealed in studies in animals but not established or not studied in humans; may use if benefits outweigh risk to fetus

Precautions

Adverse effects of intralesional corticosteroids include atrophy and hypopigmentation; significant systemic exposure to corticosteroids may result in multiple complications (eg, severe infections, hyperglycemia, edema, osteonecrosis, myopathy, peptic ulcer disease, hypokalemia, osteoporosis, euphoria, psychosis, myasthenia gravis, and growth suppression); abrupt discontinuation of glucocorticoids may cause adrenal crisis

Retinoids

Have the ability to regulate cell proliferation and regulate immune system.

Acitretin (Soriatane)

Retinoic acid analog, similar to etretinate and isotretinoin. Etretinate is main metabolite and acitretin has demonstrated clinical effects close to those seen with etretinate. Mechanism of action is unknown.

Adult

Initial dose: 25 or 50 mg/d PO single dose with main meal
Maintenance dose: 25-50 mg/d PO after initial response; terminate therapy when lesions have resolved sufficiently

Pediatric

Not established

-

Increases toxicity of MTX (avoid concomitant use); interferes with effects of microdosed progestin minipill; coadministration with alcohol may enhance synthesis of etretinate, which has much longer half-life than acitretin (>120 d)

- Documented hypersensitivity

-

Pregnancy

X - Contraindicated; benefit does not outweigh risk

Precautions

Do not use in severe obesity; women of childbearing age must be able to comply with effective contraceptive measures, abstain from alcohol intake, and continue contraceptive measures for a minimum of 3 y following cessation of therapy; perform AST, ALT, and LDH tests prior to initiation of acitretin therapy at 1- to 2-wk intervals until stable and thereafter, at intervals as indicated clinically

Isotretinoin (Accutane)

Synthetic 13-*cis* isomer of naturally occurring tretinoin (*trans* -retinoic acid). Both agents are structurally related to vitamin A.
Decreases sebaceous gland size and sebum production. May inhibit sebaceous gland differentiation and abnormal keratinization.
A US Food and Drug Administration–mandated registry is now in place for all individuals prescribing, dispensing, or taking isotretinoin. For more information on this registry, see iPLEDGE. This registry aims to further decrease the risk of pregnancy and other unwanted and potentially dangerous adverse effects during a course of isotretinoin therapy.

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Adult

40-60 mg/d PO for 4 mo

Pediatric

Not established