Glucocorticoids

- **Potency (Groups I through VII).** The antiinflammatory properties of topical corticosteroids result in part from their ability to induce vasoconstriction of the small blood vessels in the upper dermis.
- These products are subsequently tabulated in seven groups, with group I the strongest and group VII the weakest.

- Patients who do not respond after 1 to 4 weeks of treatment should be reevaluated.
- Clobetasol propionate, halobetasol propionate, betamethasone dipropionate, and diflorasone diacetate are the most potent topical steroids available.
- In general, no more than 45 to 60 grams (gm) of cream or ointment should be used each week.

- Side effects are minimized and efficacy increased when

by 1 week of rest.

- Intermittent dosing (e.g., once or twice a week) can lead to a prolonged remission of psoriasis if used after initial clearing.
- clobetasol, halobetasol,and should not be used with occlusive dressings.

- Oral glucocorticoids are absorbed in the jejunum, with peak plasma levels occurring 30–90 minutes after intake. Administration of these with food may delay absorption but does not decrease the amount absorbed.
- Once glucocorticoids reach the plasma, the primary carrier protein is corticosteroid-binding globulin (CBG), also known as transcortin.
- Most endogenous cortisol is bound to CBG, and low doses of exogenous glucocorticoids.

- With higher glucocorticoid doses, some binding also occurs to albumin in a low-affinity fashion, but with a greater capacity because of the larger amount of albumin in plasma.
- Disorders that result in decreased binding proteins in the plasma, such as hepatic or renal disease, increase the free fraction of exogenous glucocorticoids and thereby augment the therapeutic effects and toxicities of these drugs.

- The hypothalamus produces corticotropin-releasing hormone, which is released in small pulses into the pituitary circulation. The anterior pituitary responds to corticotropinreleasing hormone with synthesis of ACTH and its subsequent pulsatile secretion into the peripheral circulation.
- ACTH is the hormone that stimulates the middle layer of the adrenal cortex to generate and release cortisol.

- Under basal conditions, the adrenals produce approximately 20–30 mg of cortisol (equivalent to 5–7.5 mg of prednisone) per day in an adult, but this may increase up to 10-fold under times of maximal stress.
- Therapy is considered short-term if it is administered for approximately 3 weeks or less.
- An oral agent with an intermediate duration of action, such as prednisone, is usually given in a single early-morning dose to achieve the least HPA axis suppression.

- The daily dose of prednisone varies depending on the severity of the dermatosis, but for most moderate conditions, a common initial dose is 40–60 mg/day in average-weight adults or approximately 1 mg/kg/day in children.
- Two important side effects of long-term glucocorticoid therapy that are not minimized by alternate-morning dosing are osteoporosis and cataracts.
- However, tapering to allow adrenal recovery is an important consideration when treatment is for longer than 3–4 weeks, especially at a dose ≥20 mg/day.

- Even in the absence of overt adrenal insufficiency, patients can develop a glucocorticoid withdrawal syndrome characterized by arthralgias, myalgias, mood changes, fatigue, headache, nausea,and anorexia.
- When this occurs, a return to the previous dose of glucocorticoid, followed by more gradual tapering, is recommended.

- The prednisone dose can usually be tapered in 20 mg increments at doses greater than 60 mg/day, 10 mg increments between 30 and 60 mg/day,and 5 mg increments between 30 mg and the physiologic dose range.
- Once the physiologic dose range of 5–7.5 mg/day of prednisone is reached, a more gradual reduction (e.g. in 1–2.5 mg increments) may be necessary to allow adrenal recovery.

Contraindications

- There are several contraindications to systemic or local glucocorticoid therapy.
- Herpes simplex keratitis is considered a contraindication to local glucocorticoid treatment of the eye, whereas active tuberculosis and systemic fungal infections are usually considered as contraindications to systemic glucocorticoid therapy.

- Relative contraindications to systemic glucocorticoid therapy include active peptic ulcer disease, severe depression or psychosis, and an extensive chronic dermatosis (e.g. psoriasis) likely to flare after rapid glucocorticoid taper.

Osteoporosis

- Osteoporosis is one of the most prevalent side effects in patients receiving long-term systemic glucocorticoid therapy. Without preventative measures, osteoporosis develops in 30–50% of all patients treated chronically with glucocorticoids.
- A rapid decline in bone mineraldensity occurs within the first 3 months of usage, and the rate of loss peaks at 6 months.
- Although routine radiographs can detect vertebral compression fractures, these plain X-ray studies are not sensitive enough to detect osteoporosis until 20–60% of bone mass is lost.

- Currently, the best measurement of osteoporosis is quantification of bone mineral density with dual-energy X-ray absorptiometry (DEXA), which is preferred because of its sensitivity, reproducibility, and low radiation exposure.
- Baseline DEXA examination of the hip and lumbar spine, with a repeat study performed every 1–3 years at the same sites.
- T score less than −2.5 defining osteoporosis..

- In general, experts agree that patients with a history of low-impact fractures and adults with moderate to high fracture risk, especially postmenopausal women and men ≥50–65 years of age, should begin concomitant *bisphosphonate* therapy when started on long-term glucocorticoid treatment.
- Alendronate or risedronate are first-line oral agents given daily or weekly. They should be taken on an empty stomach, only with water,upon arising in the morning; patients should not lie flat for 1 hour after administration.

- Intravenous bisphosphonates such as pamidronate 30 mg IV every 3 months or zoledronate 4–5 mg IV once yearly are alternatives.
- Osteonecrosis of the jaw represents a potential complication of bisphosphonate therapy.
- In adults with a moderate to high fracture risk who are unable to take or have previously failed bisphosphonates, treatment with *teriparatide*, a fragmented portion of human parathyroid hormone (PTH),can be considered.

- *Denosumab*, a monoclonal antibody directed against RANKL (receptor activator of NF-κB ligand), has also been approved for the treatment of osteoporosis in postmenopausal women who are at high risk for osteoporotic fractures.

Osteonecrosis

- Osteonecrosis (also known as aseptic necrosis or avascular necrosis) has numerous causes, and it is an uncommon but serious complication of glucocorticoid treatment.
- The proximal femur is the most common site,although the distal femur or humeral head may be affected.

- Most patients who develop osteonecrosis while on glucocorticoids have been treated for at least 6–12 months, paralleling the time needed to induce changes in bone marrow fat deposition.

Cutaneous Effects

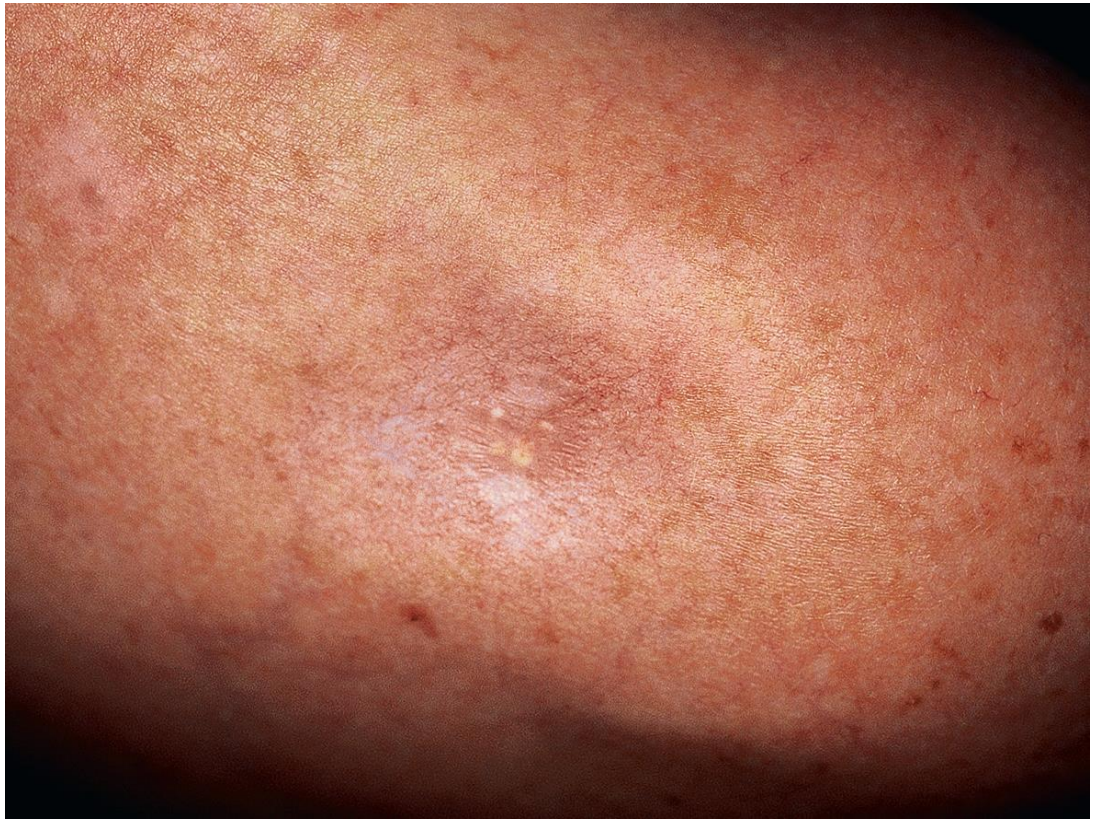
- Patients receiving systemic and topical glucocorticoids can develop a broad range of cutaneous effects, many of which are similar to those associated with endogenous Cushing syndrome.
- These include purpura, telangiectasias, atrophy, pseudoscars, acneiform or rosacea-like eruptions, and facial plethora.
- In one study, almost half of patients developed skin changes after 3 months of treatment with a mean prednisone dosage of 30 mg/day.

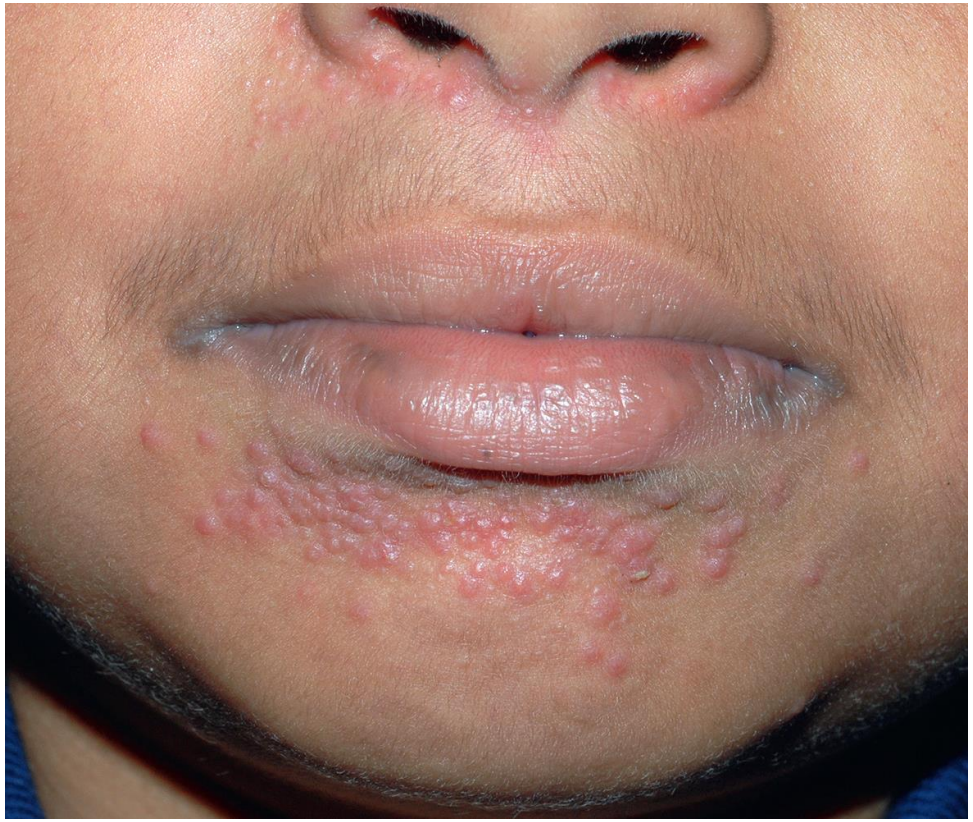
- Localized development of telangiectasias, atrophy, and hypopigmentation can result from chronic use of topical glucocorticoids, especially long-term daily application of
- potent agents or use under occlusion, and from intralesional glucocorticoid therapy.
- Intralesional administration occasionally leads to these findings in a linear pattern along pathways of lymphatic drainage.

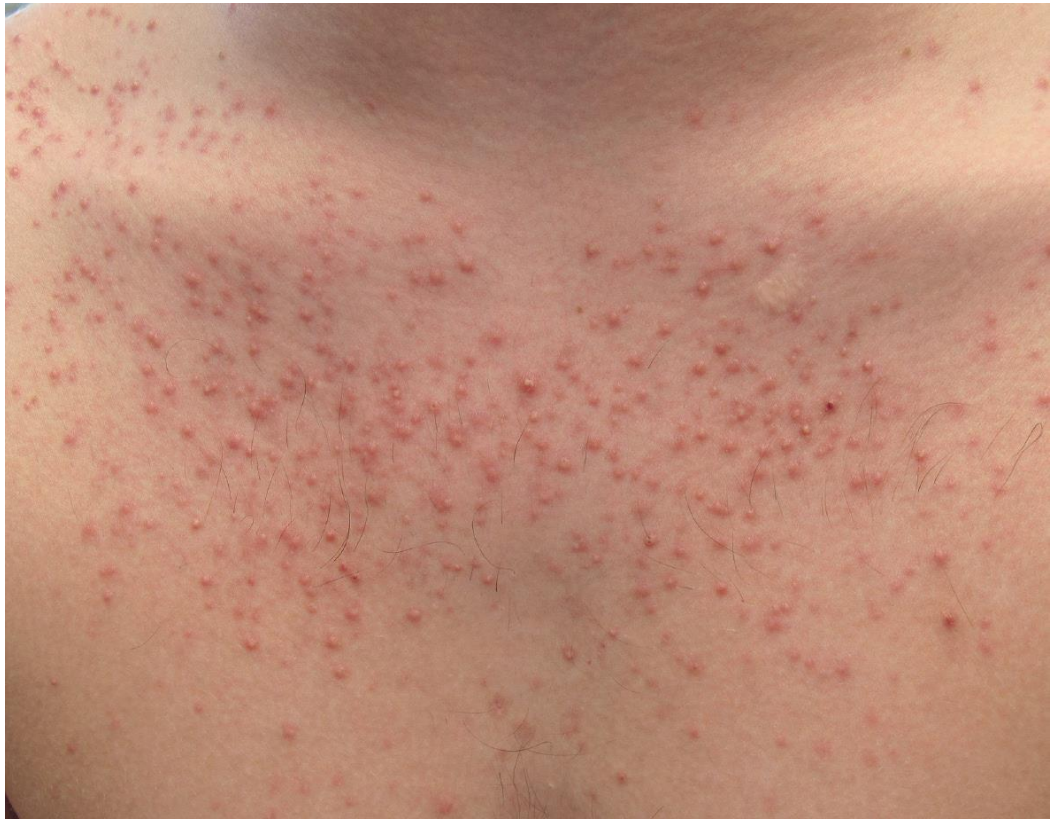
- Systemic glucocorticoid-induced acne or folliculitis characteristically presents with monomorphic papulopustules on the chest and back.
- Acne vulgaris itself is also frequently worsened by continuous
- glucocorticoid therapy, although inflammatory and cystic acne lesions may be temporarily improved by very short intermittent courses of systemic glucocorticoids, or by intralesional injections of cysts.

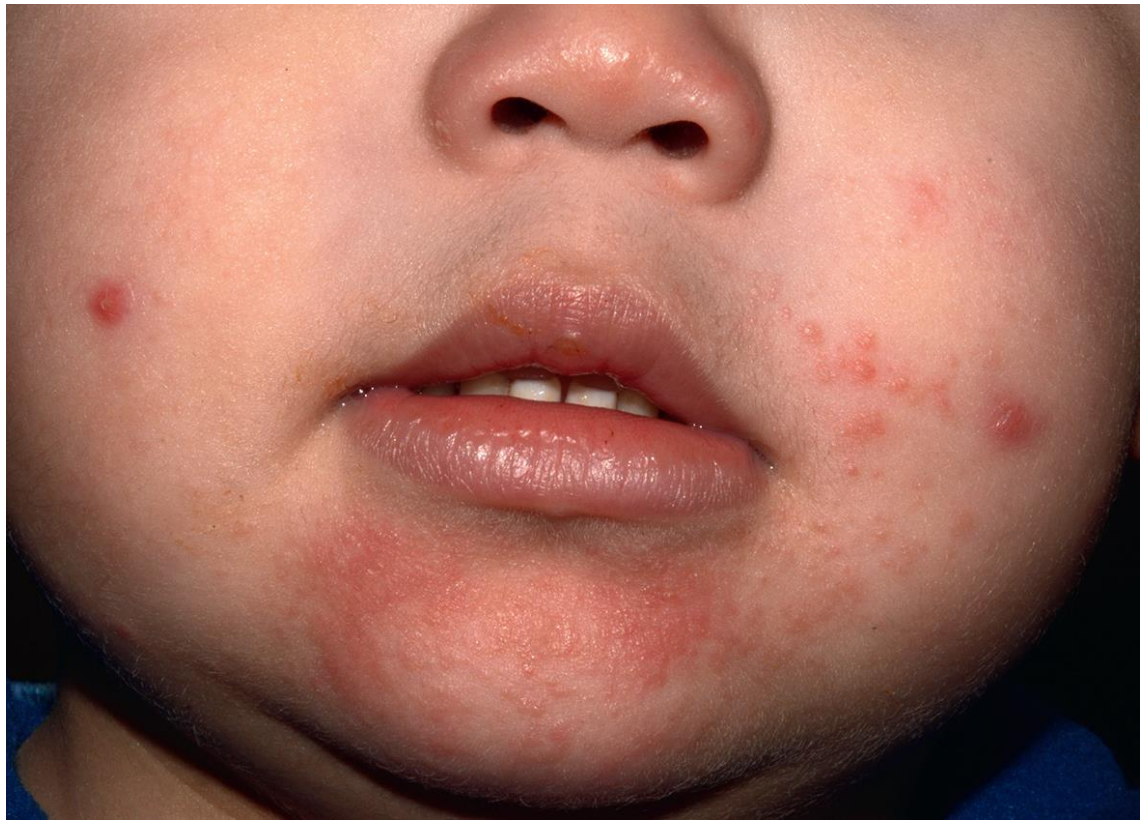
- An acneiform or rosacea-like perioral, perinasal, or periorbital eruption can also occur secondary to use of inhaled glucocorticoids or application of topical glucocorticoids (especially more potent agents) to the face.
- In addition, long-term inappropriate use of potent topical glucocorticoids on the face or in the groin can lead to erythema, edema, papulopustules, and a burning sensation upon their discontinuation, referred to as “topical steroid addiction” in social media.

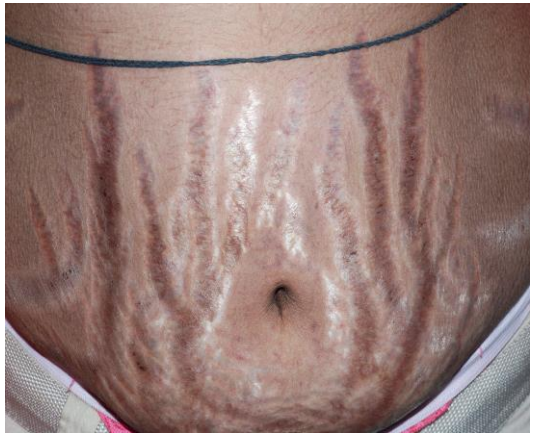
- Other cutaneous effects from systemic glucocorticoids include acanthosis nigricans and telogen effluvium of scalp hair. Hirsutism and hypertrichosis can develop on other areas of the body.
- Topical and systemic glucocorticoid therapy may impair wound healing by inhibiting fibroblast function and collagen production.
- Angiogenesis, production of the extrafibrillar matrix (“ground substance”),and re-epithelialization of wounds are also inhibited.

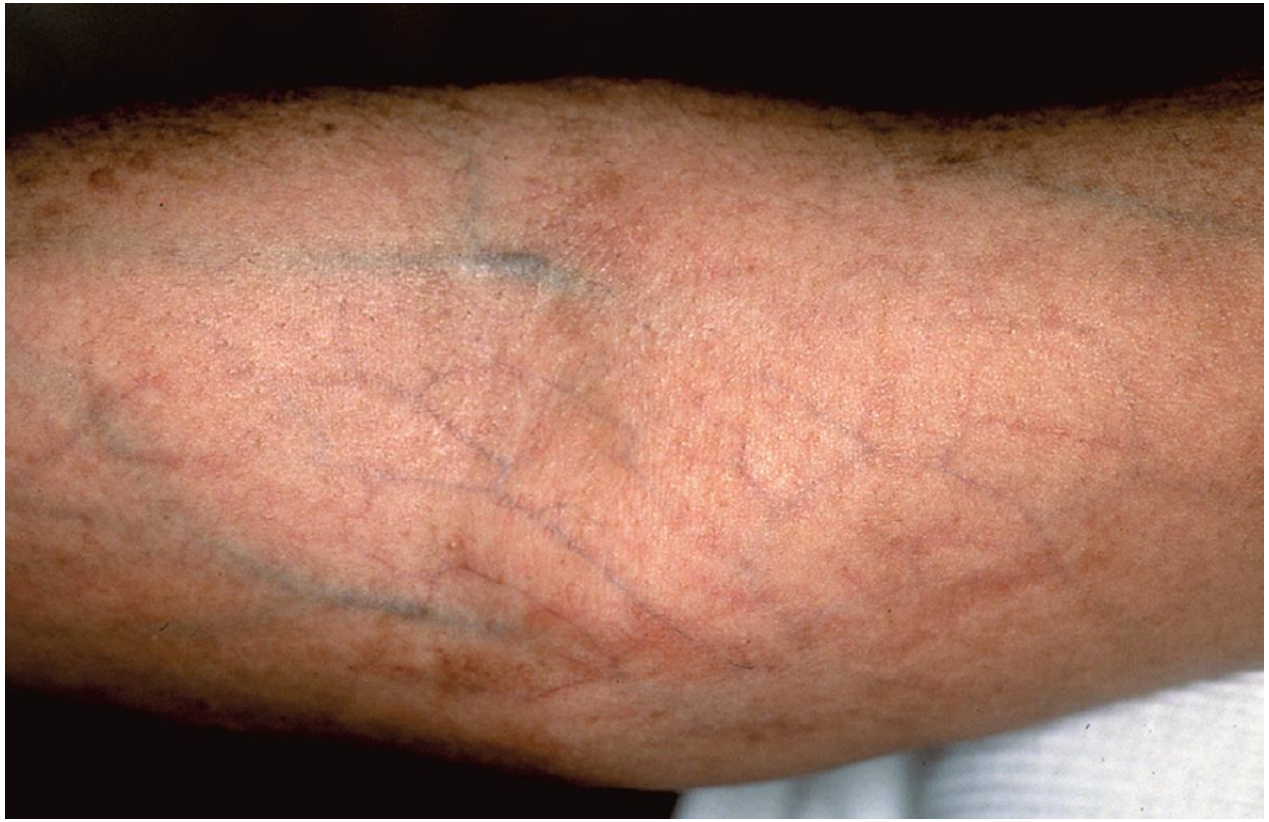


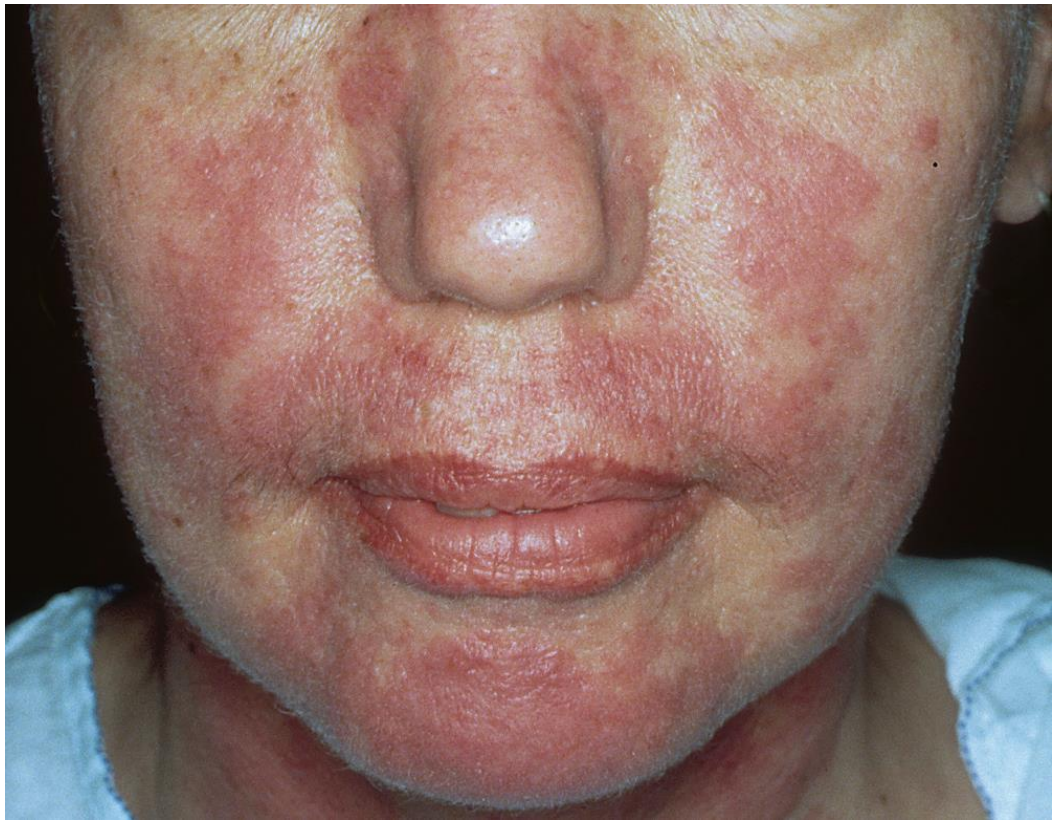


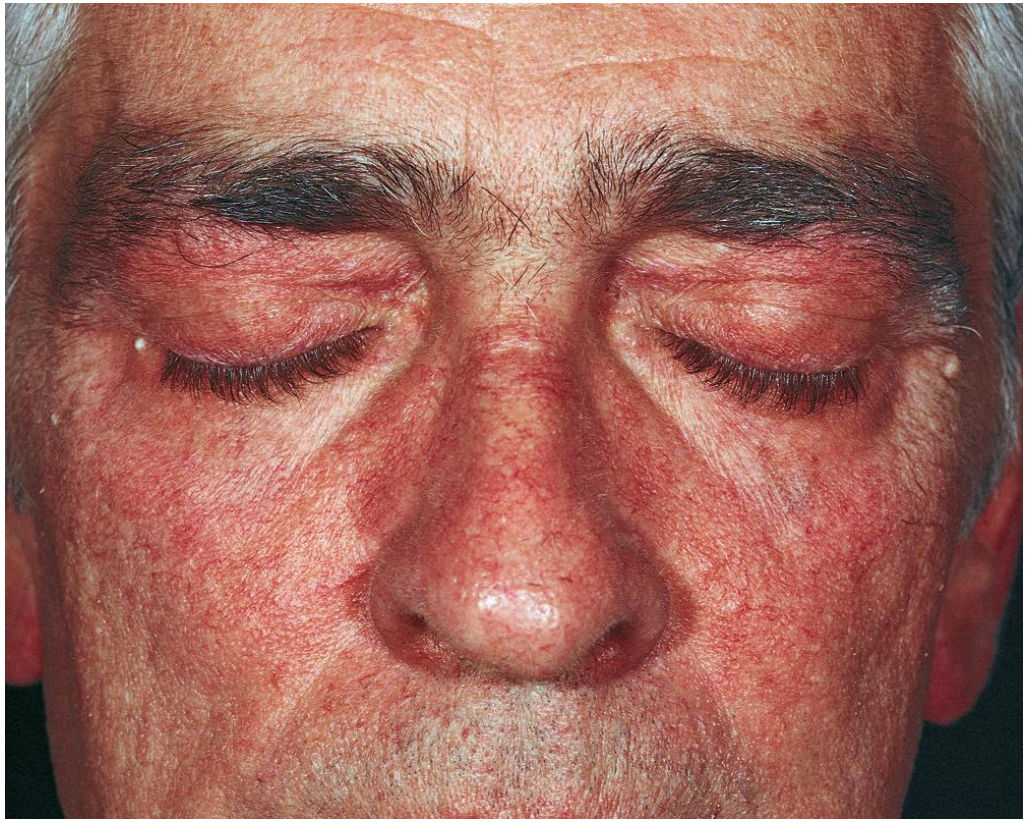


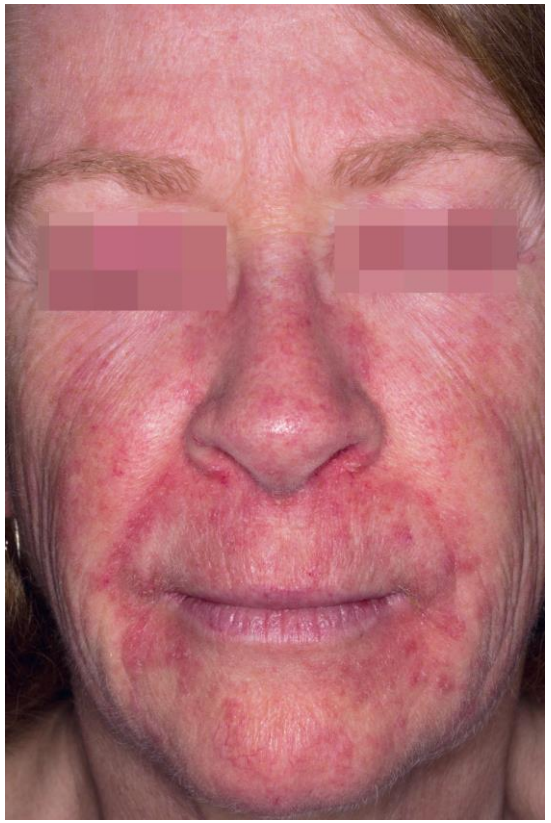


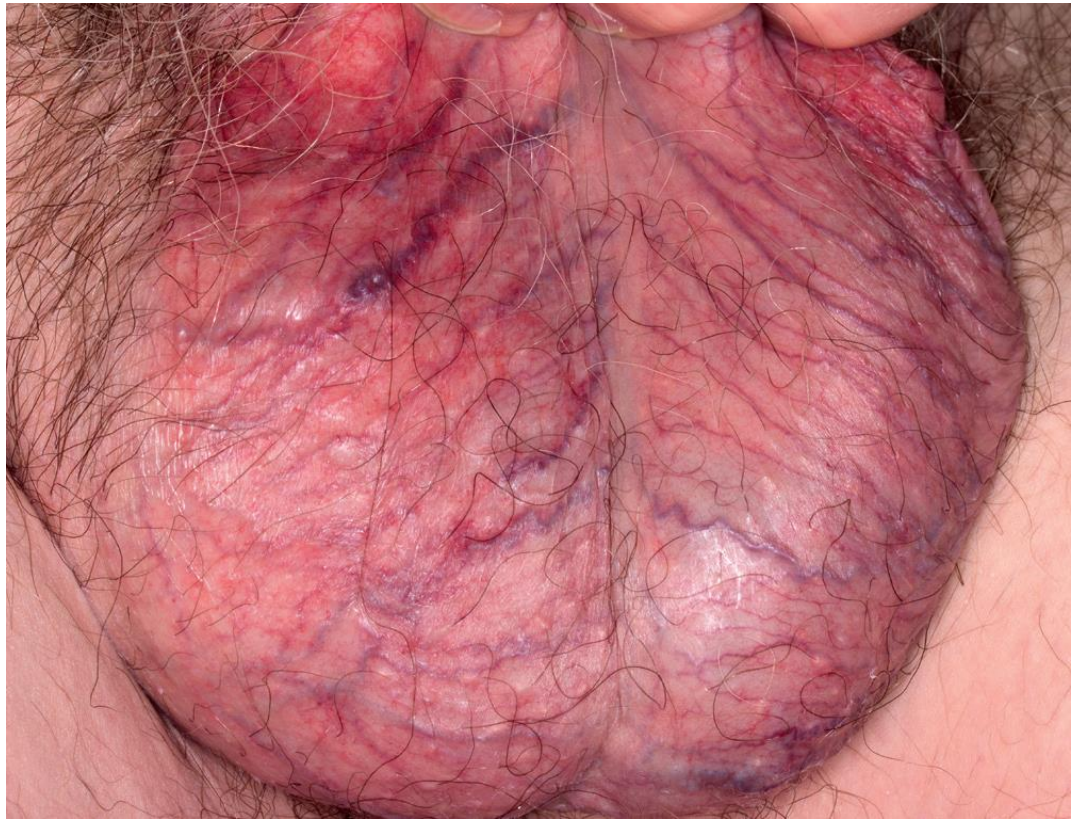


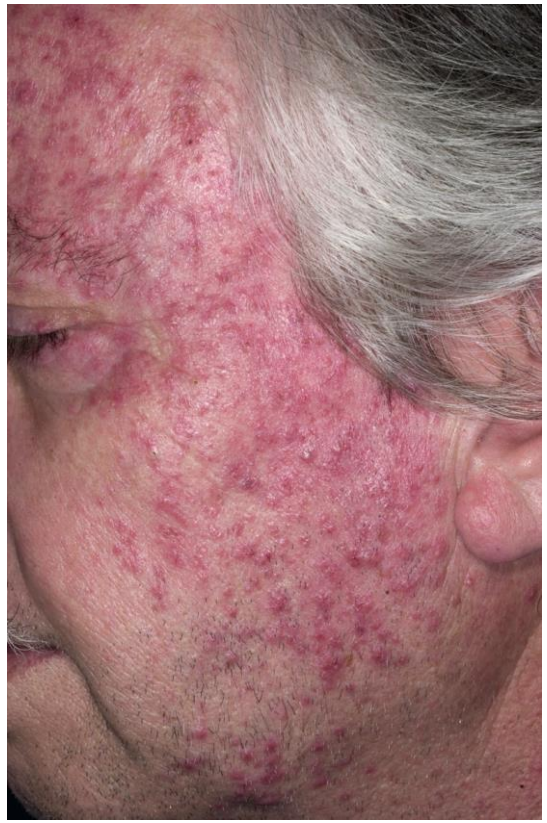


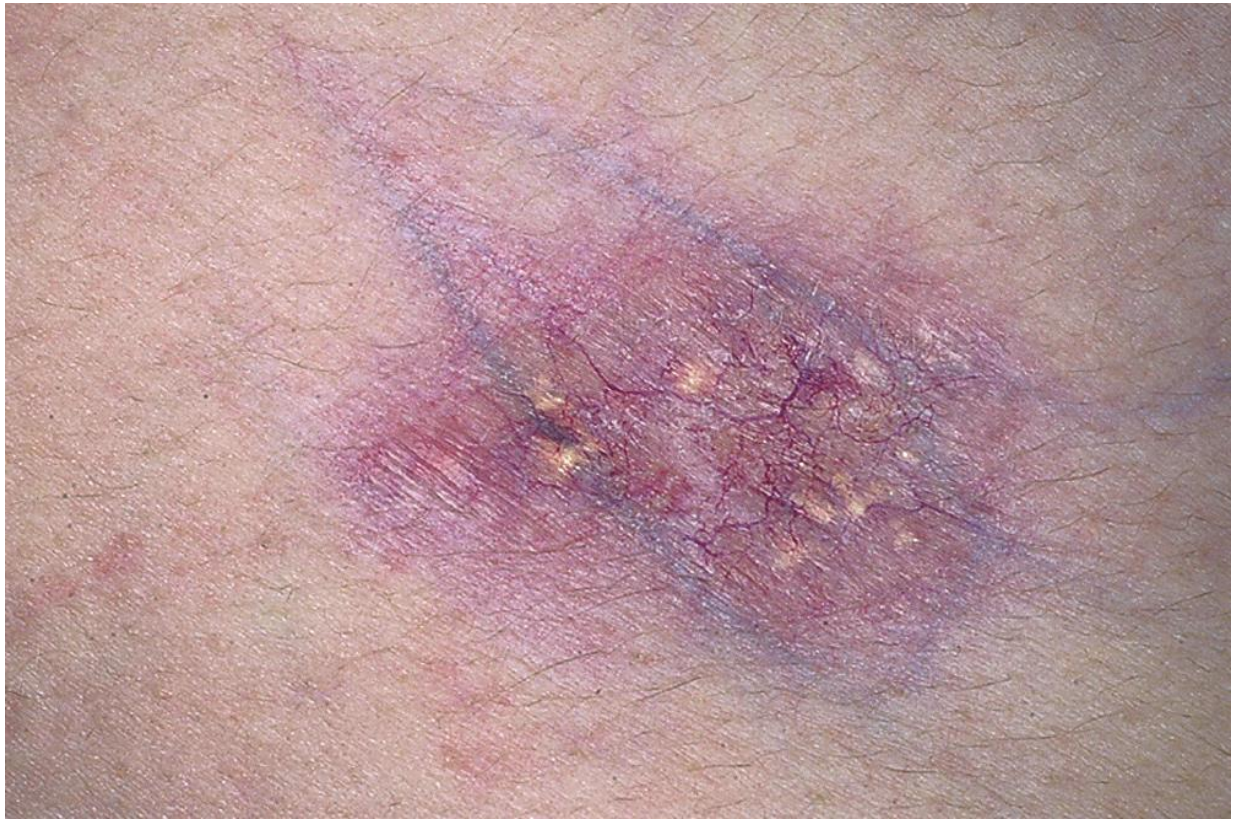












Acute contact allergy to a preservative