
بسم الله الرحمن الرحیم

Pharmacologic Use Of Glucocorticoids

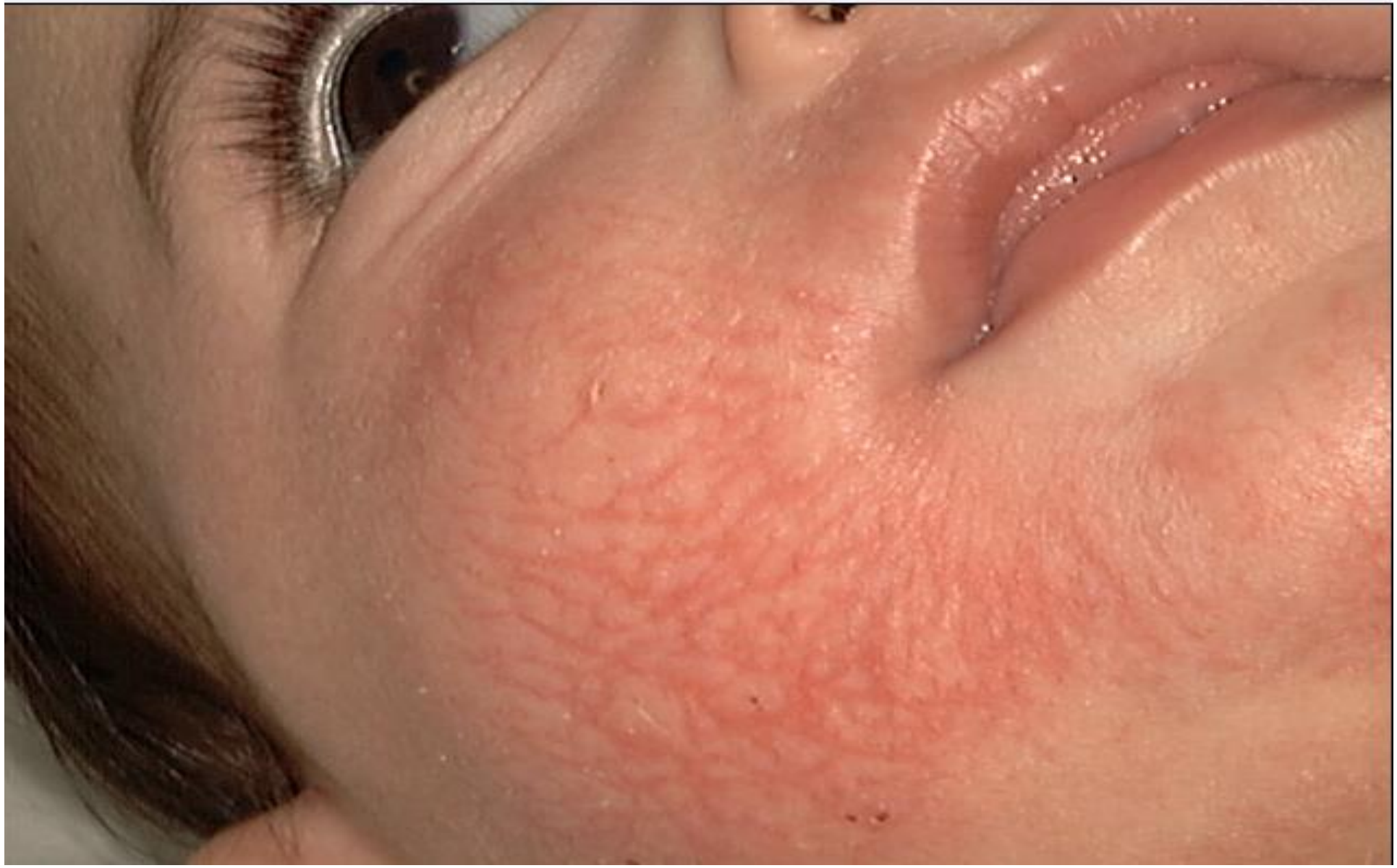
Dr Fahimeh Soheilipour

Professor of Pediatric Endocrinology

IUMS

- ✓A 9-month-old infant who referred due to Low Ht Growth Velocity & Short Stature!!

- ✓ She had a 5% Ht & 85% Wt according to WHO Growth Chart & a history of atopic dermatitis.



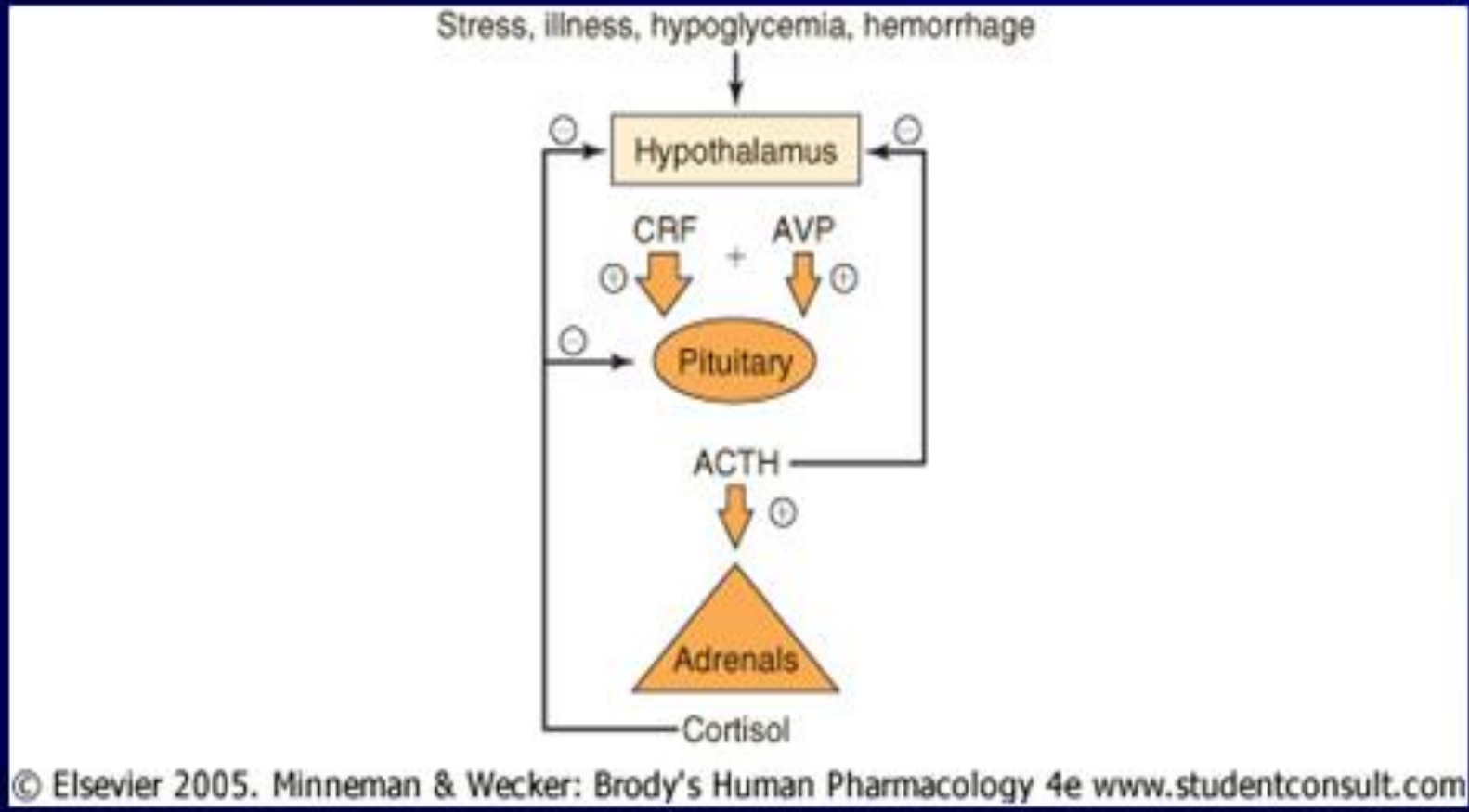
- She developed facial atrophy, telangiectasias, and erythema from 5 months application of a high potency topical steroid for treatment of infantile atopic dermatitis !!!

Glucocorticoids are important in the treatment of many disorders inclouding:

- ✓inflammatory,
- ✓ allergic,
- ✓ immunologic
- ✓ malignant &
- ✓Endocrine dis (Some times replacement therapy, So in Inter-current illness: Dose is doubled)

Mechanisms of action
Glucocorticoids

Regulatory feedback mechanisms in the HPA.



ACTH, Adrenocorticotrophic hormone

Endocrine Disorders

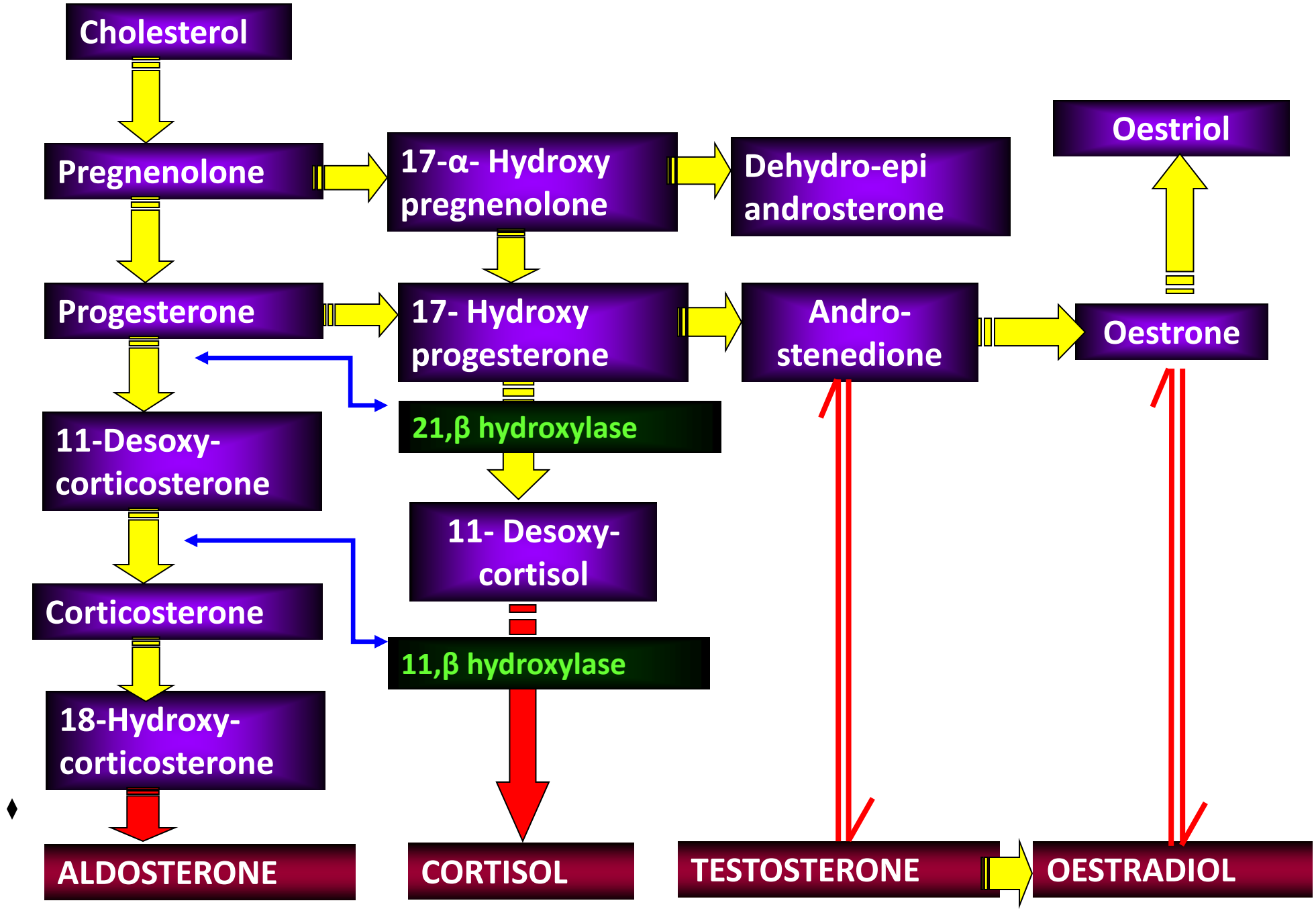
- **Acute adrenal insufficiency**
- **Primary adrenocortical insufficiency**
- **Ad. Insufficiency second. to Ant. Pituitary**
- **Congenital adrenal hyperplasia**

- **Isotonic saline**
- **Glucose**
- **Hydrocortisone inj. i.v.**
- **Gradullay substitue with i.m or oral**

Congenital adrenal hyperplasia

- Familial disorder
- Signs of cortisol deficiency
- Increased ACTH
- Excessive androgens

Deficiency of 21- β hydroxylase and 11 - β hydroxylase enzymes


Cholesterol
Pregnenolone
17-α- Hydroxy pregnenolone
Dehydro-epi androsterone
Oestriol
Progesterone
17- Hydroxy progesterone
Andro-stenedione
Oestrone
21,β hydroxylase
11-Desoxy-corticosterone
11- Desoxy-cortisol
Corticosterone
11,β hydroxylase
18-Hydroxy-corticosterone
ALDOSTERONE
CORTISOL
TESTOSTERONE
OESTRADIOL

Non-endocrine diseases

1. Arthritis

- **Not the drug of first choice**
- **Prednisolone 5 or 7.5 mg**
- **Intra-articular injection**

2. Rheumatic carditis

- **Not responding to salicylates**
- **Severely ill pts.**
- **Prednisolone 40mg in divided doses**
- **Salicylates given concurrently to prevent reactivation**

Non-endocrine diseases

3. Renal diseases (Nephrotic syndrome)

- **Prednisolone 60 mg in divided doses for 3 – 4 weeks**
- **If remission occurs continue for 1 year**
- **Do not modify the course of disease; Some may benefit**

4. Collagen diseases

- **DLE, pemphigus vulgaris, polyarteritis nodosa**
- **Defect in connective tissue proteins in joints, various organs and deeper layer of skin**
- **Prednisolone 1mg/Kg start; gradually reduce the dose**

Non-endocrine diseases

5. Allergic diseases

- **Anaphylactic shock, blood transfusion reaction, hay fever**
- **Prednisolone (short course)**

6. Bronchial asthma

- **Not routinely used except in Status asthmaticus**
- **Methyl prednisolone sodium i.v. given followed by oral prednisolone**
- **Inhaled steroids (Minimal HPA axis suppression)**

Non-endocrine diseases

7. Ocular diseases

Outer eye & anterior segment: local application

Posterior segment: systemic use

Caution: bacterial, viral & fungal conjunctivitis

8. Dermatological conditions

- Pempigus: Life saving therapy is steroids
- Eczema, dermatitis & psoriasis: respond well

Non-endocrine diseases

9. Diseases of intestinal Tract

- **Ulcerative colitis: cortisol retention enema**

10. Cerebral edema

- **Questionable value in cerebral edema following trauma, cerebrovascular edema**
- **Valuable in edema associated with neoplasm and parasites**

11. Malignancy

- **Part of multi drug regimens for acute lymphatic leukaemia (children), chronic lymphatic leukaemia (adult)**

Non-endocrine diseases

12. Liver diseases

- **Subacute hepatic necrosis & chronic active hepatitis**: **Improves survival rates**
- **Alcoholic hepatitis: reserved for pts. with severe illness**
- **Non-alcoholic cirrhosis: helpful if no ascites**

13. Shock

- **Often helpful but no convincing evidence**

14. Acute infectious diseases

- **Helpful due to its anti-stress & anti-toxic effects**
- **Used in gram –ve septicemia, endotoxic shock, TB meningitis, miliary T.B., encephalitis (post infectious)**
- **Appropriate anti-microbial agent is a MUST**

Non-endocrine diseases

- Miscellaneous

- Organ transplantation
- Bell’s palsy
- Thrombocytopenia
- Myasthenia gravis
- Spinal cord injury
- Sarcoidosis

Diagnostic Uses

- **Cushing's syndrome:**
  - ACTH dependent *(pituitary tumor, ectopic ACTH secreting tumors)*
  - Non-ACTH dependent *(tumor of adrenal cortex)*

(Dexamethsone suppression test is done)

- **To locate the source of androgen production in hirusitism**

(Dexamethasone suppress androgen secretion from ad.cortex)

- glucocorticoids toxicity is one of

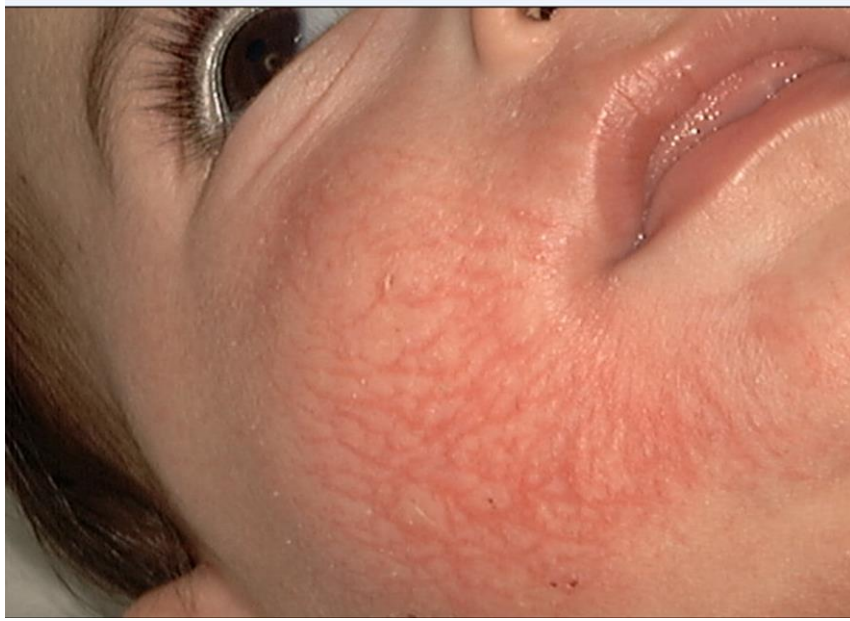
the commonest causes of iatrogenic illness

- Recognition of these toxicities, many of which are similar to the findings in endogenous Cushing's syndrome,

  is of value in their **prevention and management.**

- the ***toxicity*** of glucocorticoids is one of

the commonest causes of iatrogenic illness



- Recognition of these toxicities, many of which are similar to the findings in spontaneous (endogenous) Cushing's syndrome,

  is of value in their prevention and management.

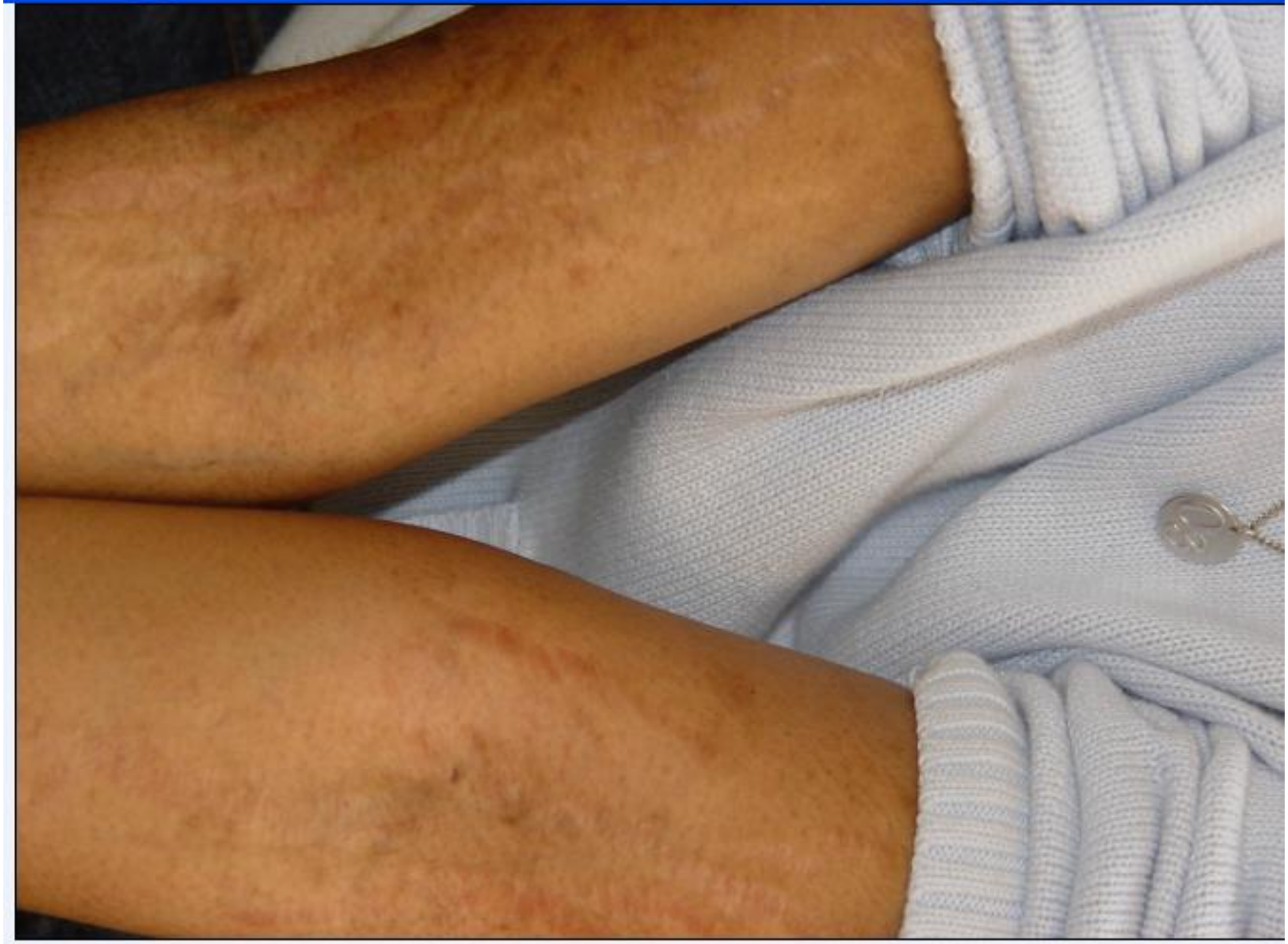
The following organ systems can be affected by systemic glucocorticoids to varying degrees

- Dermatologic effects and appearance
- Cardiovascular effects(Permanent AS)
- Gastrointestinal effects
- Bone and muscle effects(Permanent Osteoprosis)
- Neuropsychiatric effects
- Metabolic and endocrine effects
- Immune system effects
- Hematologic effects
- Ophtalmologic Effect(Permanent Cataract)

Major adverse effects associated with systemic glucocorticoid therapy*

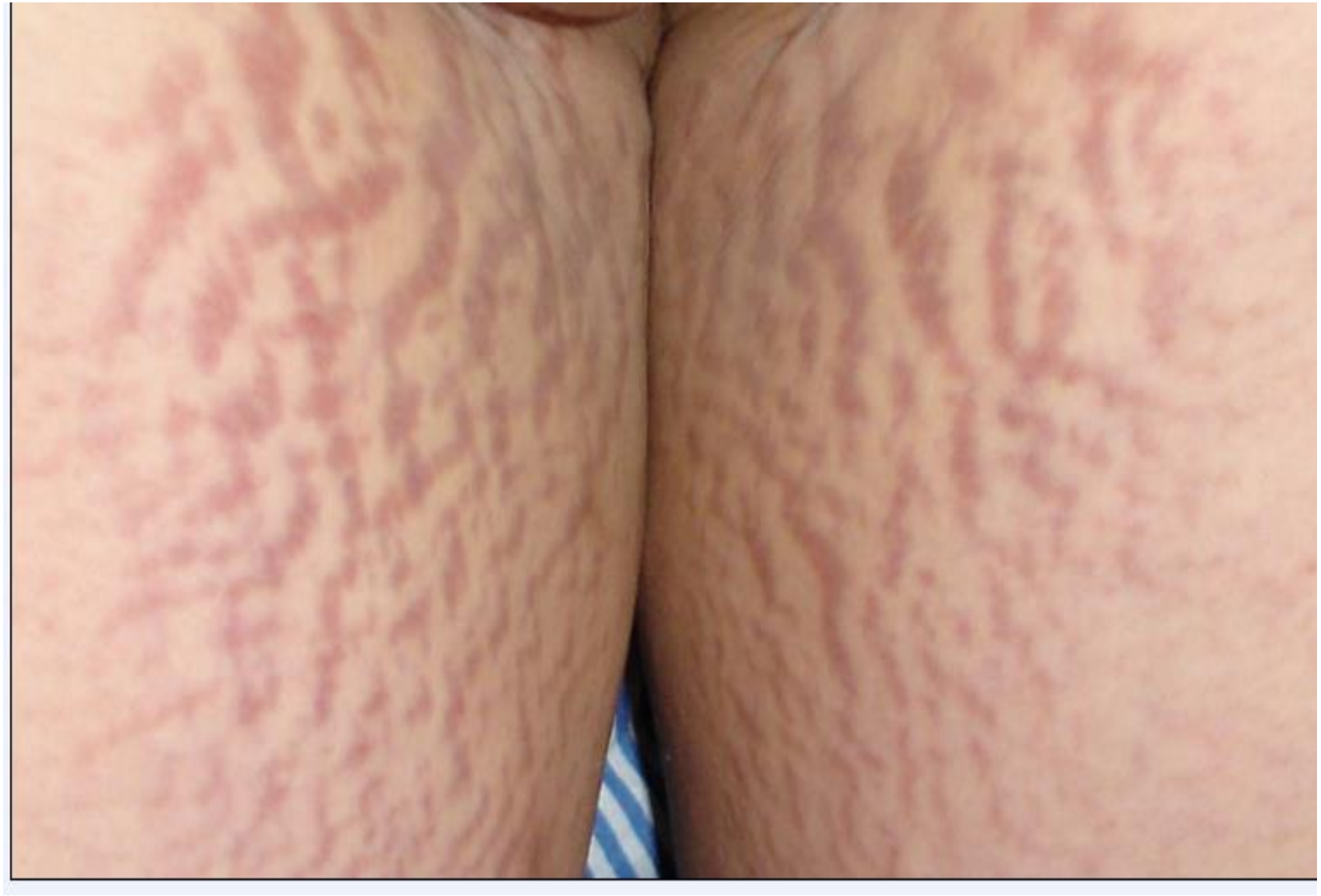
Dermatologic and appearance
Skin thinning, purpura, and/or ecchymoses
Weight gain
Cushingoid appearance
Acne
Hirsutism
Facial erythema
Striae
Ophthalmologic
Posterior subcapsular cataract
Elevated intraocular pressure/glaucoma
Exophthalmos
Cardiovascular
Fluid retention
Hypertension
Premature arteriosclerosis
Arrhythmias
Perturbations of serum lipoproteins
Gastrointestinal
Gastritis

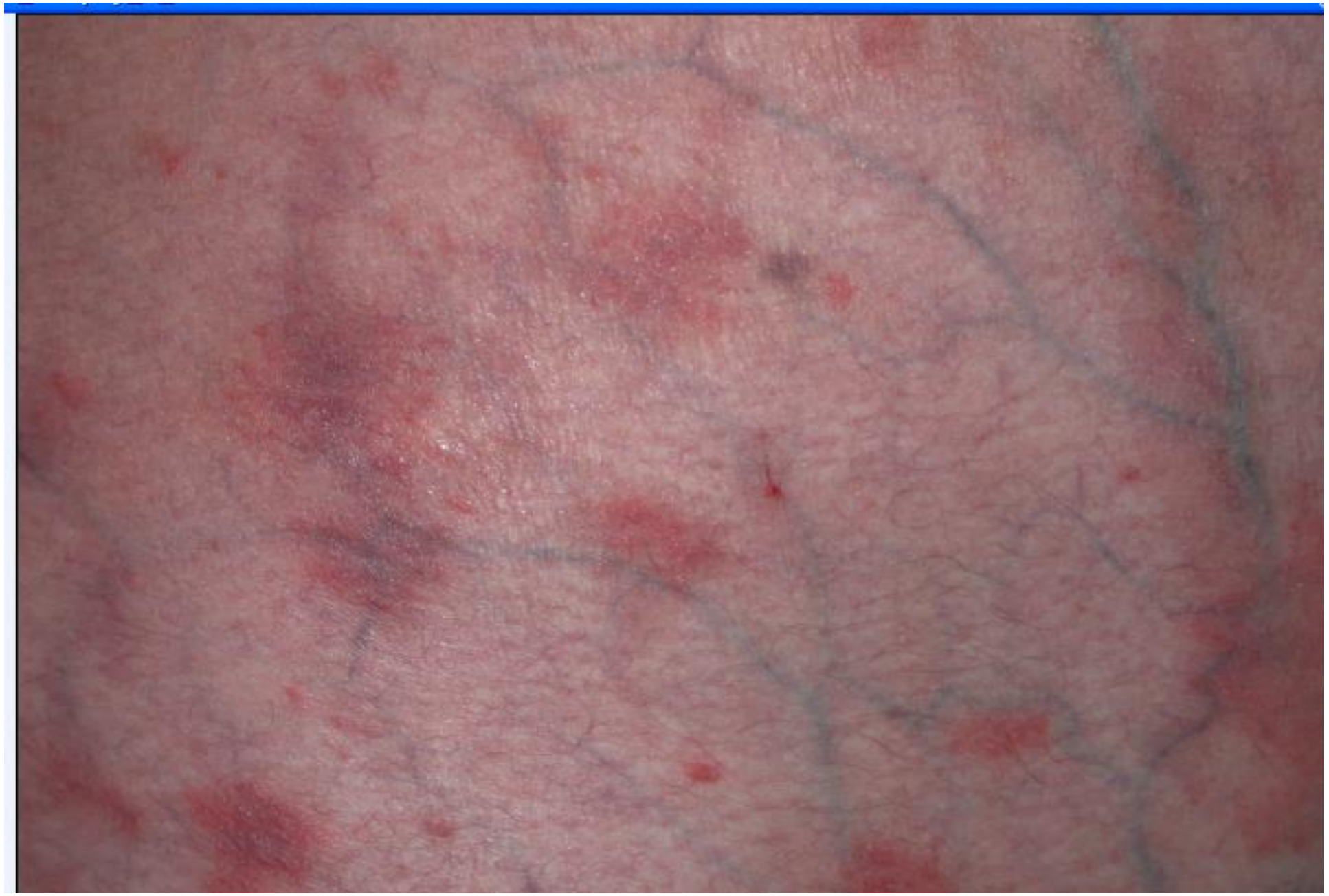
Bone and muscle
Osteoporosis
Avascular necrosis
Myopathy
Neuropsychiatric
Euphoria
Dysphoria/depression
Insomnia
Akathisia
Mania/psychosis
Pseudotumor cerebri
Metabolic and endocrine
Hyperglycemia
Hypothalamic-pituitary-adrenal insufficiency
Immune system
Increased risk of infections¶
Hematologic
Leukocytosis



- linear atrophic hypopigmented plaques

Comments:This adolescent girl developed striae on the arm creases following a year of application of a high potency topical steroid for atopic dermatitis. She was tapered off the topical steroids and treated with a non-steroidal medication





Factors that influence both the therapeutic and adverse effects of glucocorticoids include:

- ❑ biologic potency,
- ❑ pharmacokinetic properties of the glucocorticoid,
- ❑ daily dose,
- ❑ timing of doses during the day,
- ❑ individual differences in steroid metabolism,
- ❑ duration of treatment
- ❑ Concomitant disease & Medications

Pharmacokinetics

- **Absorption:** **all are rapidly & completely absorbed**

  (Except DOCA)

- **Transport:**
  - **Transcortin 75%**
  - **Albumin 5%**
  - **Free form 20%**
- **Metabolism:**
  - **by liver enzymes, conjugation & excretion by urine**
  - **partly excreted as 17-ketosteroids.**
  - **$t_{1/2}$ of cortisol 1.5 hours**

Preparations

- **Glucocorticoids**
  - **Short acting**
  - **Intermediate acting**
  - **Long acting**
- **Mineralocorticoids**
- **Inhalant steroids**
- **Topical steroids**

Short Acting Preparations (t1/2 < 12 h)			
Drug	**Anti-inflam.**	**Salt retaining**	**Preapartions & dose**
Cortisol	1	1.0	• 10 mg tablet • 100 mg/vial (i.m., i.v) • Topical; enema
Cortisone	0.8	0.8	• 10 mg tablet • 25 mg/vial (i.m)
Intermediate Acting Preparations ($t_{1/2}$ = 12 -36 h)			
Prednisone	4	0.8	-
Prednisolone	5	0.3	• 5, 10 mg tablet • 20 mg/vial (i.m, intrarti)
Methyl prednisolone	5	0	• 0.5, 1.0 gm inj. for i.m. or slow i.v.
Triamcinolone	5	0	• 4 mg Tab., • 10, 40 mg/ml for i.m. & intrarticular inj.

Drug	Anti-inflam.	Salt retaining	Preapartions & dose
Long Acting Preparations ($t_{1/2}$ > 36 h)			
Dexamethasone	25	0	0.5 mg tab. 4mg/ml inj (i.m., i.v.)
Betamethasone	25	0	0.5, 1 mg tab. 4mg/ml inj (i.m., i.v.)
Paramethasone	10	0	2- 20 mg/day (oral)

Mineralocorticoids - Preparations			
Drug	Anti-inflammatory	Salt retaining	Preapartions & dose
Fludrocortisone	10	150	100 mcg tab.
DOCA	0	100	2.5 mg sublingual
Aldosterone	0.3	3000	Not used clinically

Inhalant Steroids: Bronchial Asthma	
Beclomethasone dipropionate	**50,100,200 mcg/md inhaler** **100, 200, 400 mcg Rotacaps**
Fluticasone propionate	**25, 50 mcg/md inhaler** **25,50,125/md MDI** **50, 100, 250 mcg Rotacaps**
Budesonide	**100,200 mcg/md inhaler** **0.25, 0.5 mg/ml respules**

Topical steroids

Drug	Topical preparation	Potency
Beclomethasone dipropionate	0.025 % cream	Potent
Betamethasone benzoate & B. valerate	0.025 % cream, ointment 0.12 % cream, ointment	Potent
* Clobetasol propionate	0.05 % cream	Potent
Halcinonide	0.1 cream	Potent
Triamcinolone actonide	0.1 % ointment	Potent
Fluocinolone actonide	0.025% ointment	Moderate
Mometasone	0.1 % cream, ointment	Moderate
Fluticasone	0.05 % cream	Moderate
Hydrocortisone acetate	2.5 % ointment	Moderate
Hydrocortisone acetate	0.1 – 1.0% ointment	Mild

Guidelines for topical steroids

- **Penetration differs at different sites:**
  - **High:** axilla, groin, face, scalp, scrotum
  - **Medium:** limbs, trunk
  - **Low:** palm, sole, elbow, knee
- **Occlusive dressing enhance absorption (10 fold)**
- **Absorption is greater in infants & Children**
- **Absorption depends on nature of lesion:**
  - **High:** atopic & exfoliative dermatitis
  - **Low:** hyperkeratinized & plaque forming lesions
- **More than 3 applications a day is not needed**
- **Choice of vehicle is important**
  - **Lotions & creams:** for exudative lesions
  - **Sprays & gels:** for hairy regions
  - **Ointments:** for chronic scaly lesions

- Treatment efficacy should be monitored with quantitative measurements rather than subjective well-being.

- The smallest effective dose for the least amount of time is the goal.

- When possible, non systemic glucocorticoid therapy should be used to minimize adverse effects of systemic exposure.

- All non systemic steroids have some systemic absorption.

- One Complication of glucocorticoid therapy is :

❑suppression of hypothalamic-pituitary-adrenal (HPA) function &

❑iatrogenic Cushing's syndrome.

- The time required to develop these complications depends upon the dose and duration of therapy and varies among patients.

- Suppression is unlikely in patients receiving nonparenteral steroids for less than 3 weeks or alternate-day glucocorticoids at physiologic doses.

- Suppression can be assumed in patients :
- receiving more than 20 mg of prednisone a day for more than 3 weeks and
- any patient who has clinical Cushing's syndrome.

Take Home Massage 1

- glucocorticoids toxicity is one of

the commonest causes of iatrogenic illness

- Adverse effects range from:

✓ those that are not necessarily serious but are displeasing to patients (eg, Cushingoid appearance) to

✓those that are life-threatening (eg, serious infections).

- Some adverse effects, such as accelerated reductions in bone mineral density or early cataracts, may be largely asymptomatic until later manifestations develop that require medical attention

Take Home Massage 2

Topical steroid absorption depends on

- ✓the area of the body on which it is applied,
- ✓the type of the vehicle,
- ✓ use of an occlusive dressing,
- ✓ skin integrity, and
- ✓ the patient's age.

Take Home Massage 3

<u>for limiting adverse effects of glucocorticoids take the following steps</u>

- Use of the lowest dose of glucocorticoids for the shortest period of time needed to achieve the treatment goals

- Management of preexisting comorbid conditions that may increase risk when glucocorticoids are required

- Monitoring of patients under treatment for adverse effects who may benefit from additional intervention

Take Home Massage 4

Certain measures may ameliorate undesirable side effects:

- ✓exercise programs to reduce the risk of myopathy and osteoporosis;
- ✓ calcium,
- ✓ vitamin D,
- ✓ bisphosphonates &
- ✓ in postmenopausal women, estrogen therapy to minimize lumbar vertebral bone mineral loss.