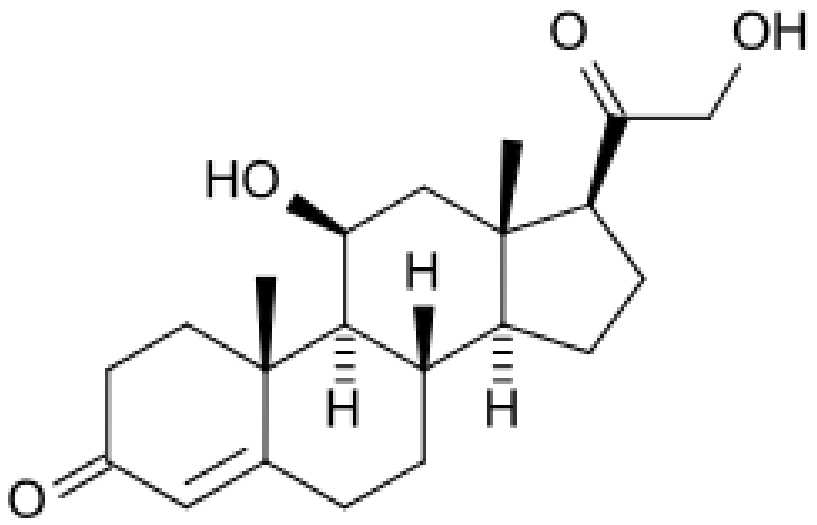
Corticosteroids



Abdulmoein Al-Agha, FRCPCH
Professor of Pediatric Endocrinology, King Abdulaziz University Hospital,
http://aagha.kau.edu.sa

History

1855 – Addison's disease

1856 – Adrenal glands essential for life

1930 – Cortex > medulla

1932 – Cushing’s syndrome

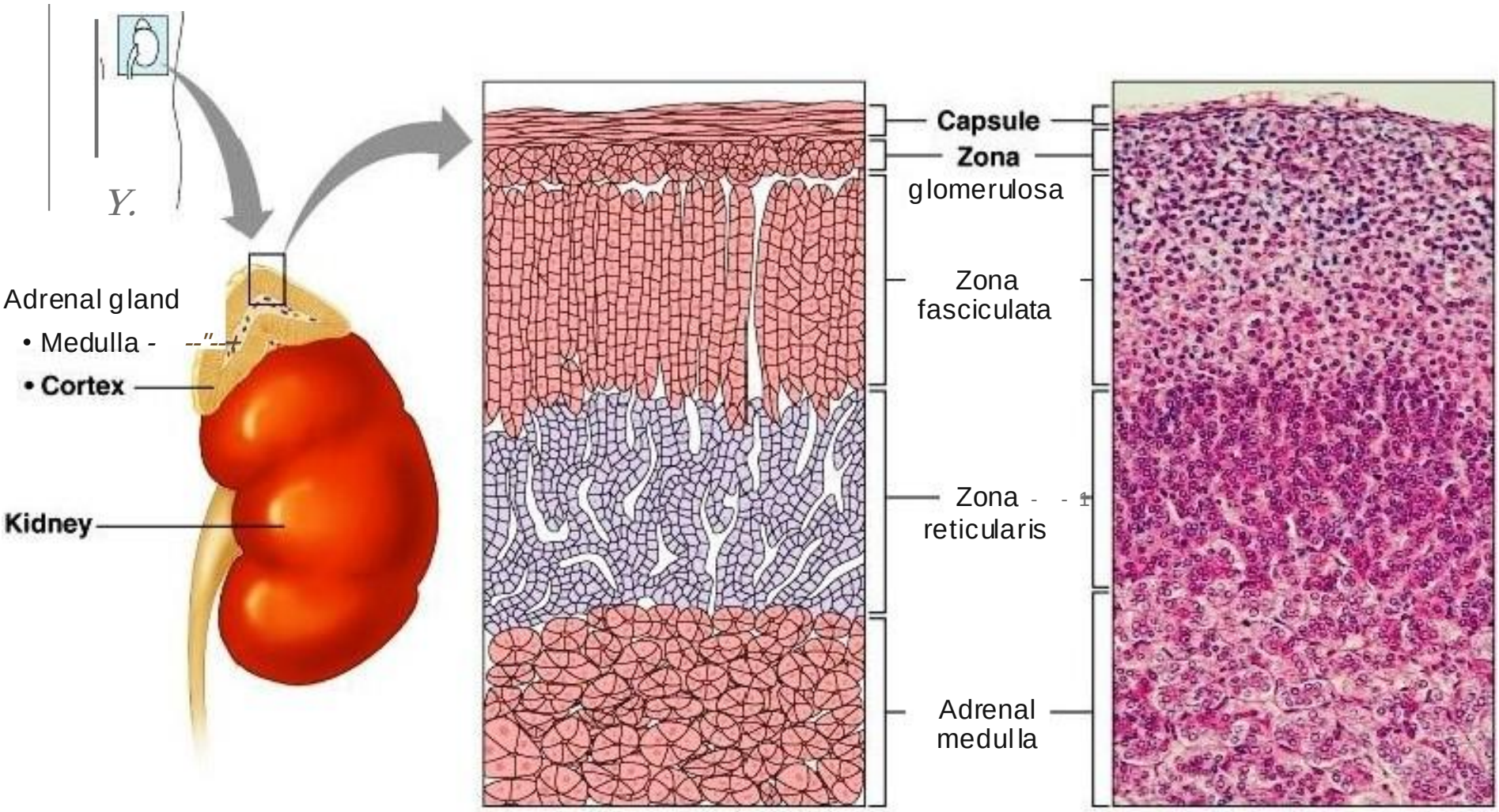
1949 – Hench et al (Steroids in rheumatoid arthritis)

1952 – Aldosterone

Introduction

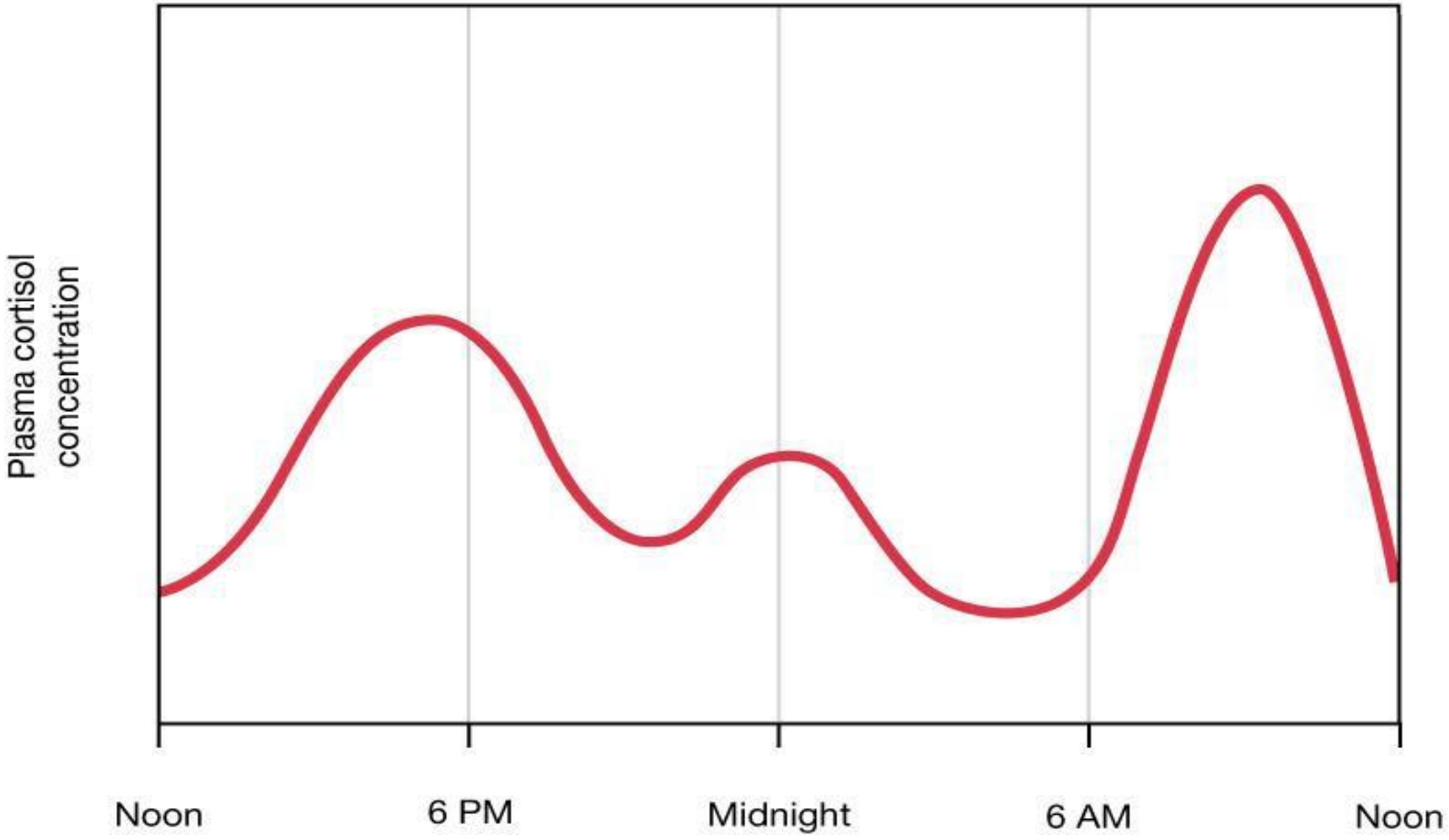
- Synthetic corticosteroids have been used to treat inflammatory diseases since 1949
- Dermatologists are among the most frequent and experienced users of the synthetic corticosteroids
- The systemic use of steroids can require real clinical skill in achieving a maximum of benefit and a minimum of side effects
- It is wise to review the real and potential consequences of corticosteroid usage and to examine the methods of administration that are most likely to minimize side effects

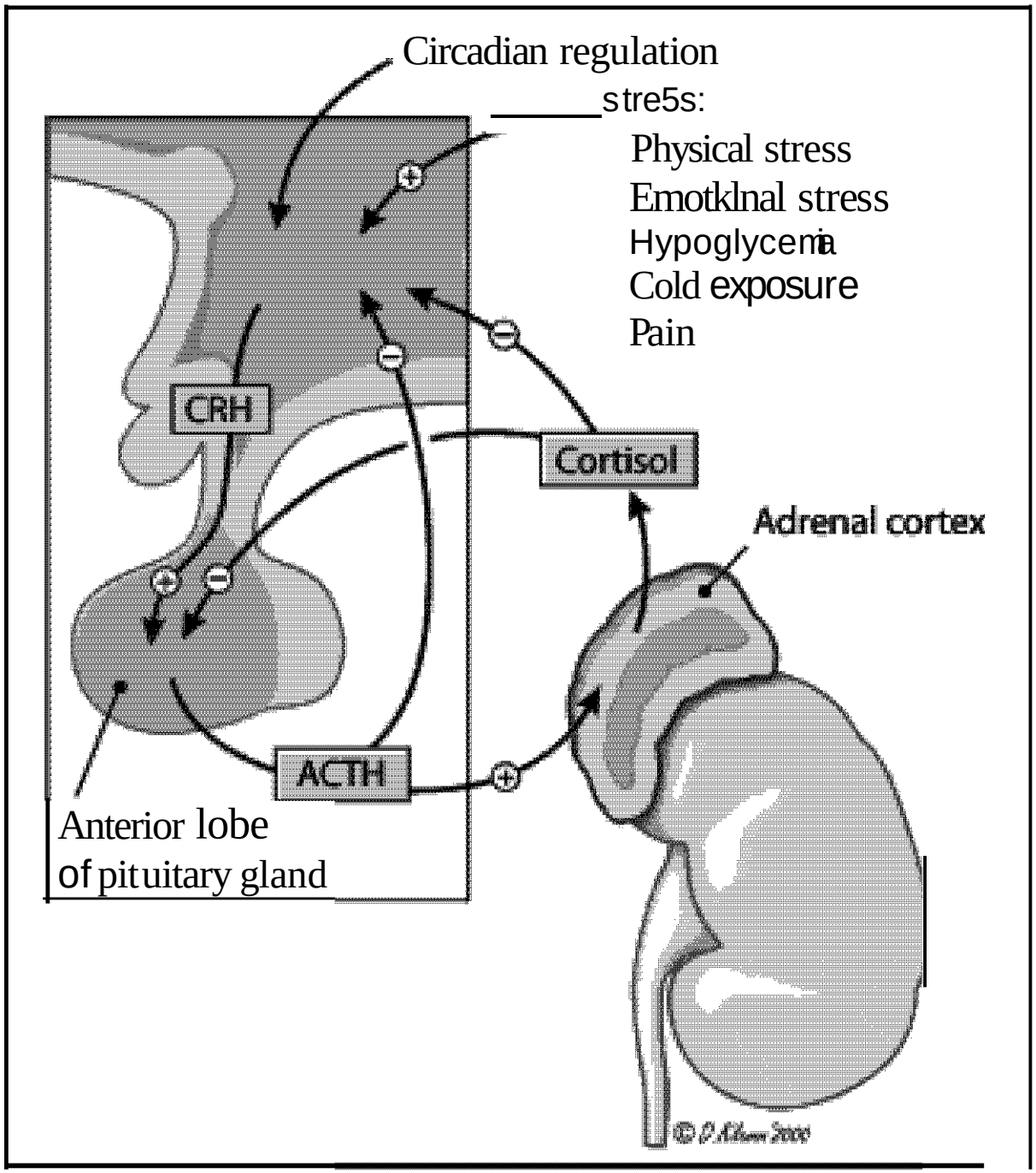
Physiology


Y.
Adrenal gland
• Medulla
• Cortex
Kidney
Capsule
Zona
glomerulosa
Zona
fasciculata
Zona
reticularis
Adrenal
medulla

- Anatomically, the adrenal gland is divided into 3 zones:
  - Zona glomerulosa, which produces predominately mineralocorticoid
  - Zona fasciculata, which produces predominately Glucocorticoids
  - Zona reticularis, which produces predominately androgens

Cortisol Effects: Circadian secretion to match our daily activities




Circadian regulation
stre5s:
Physical stress
Emotklnal stress
Hypoglycemia
Cold exposure
Pain
CRH
Cortisol
Adrenal cortex
ACTH
Anterior lobe
of pituitary gland

Pharmacological Actions

1. Carbohydrate
2. Protein
3. Lipid
4. Electrolyte and H_2O
5. CVS
6. Skeletal Muscle
7. CNS
8. Stomach
9. Blood
10. Anti-inflammatory
11. Immunosuppressant
12. Respiratory system
13. Growth and Cell Division
14. Calcium metabolism

Pharmacological Preparations

Types of Steroids

- Replacement Therapy
  - glucocorticoid (hydrocortisone)
  - mineralocorticoids (fludrocortisone)
- Anti-inflammatory Therapy
  - Short acting: hydrocortisone
  - Intermediate acting: prednisolone; Methylprednisolone; Triamcinolone
  - Long acting: Dexamethasone

Pharmacological Actions

- For most clinical purposes, synthetic glucocorticoids are used because they have a higher affinity for the receptor & have little or no salt-retaining properties
  - Hydrocortisone used for: orally for replacement therapy, iv for shock and asthma, topically for eczema (ointment) and enemas (ulcerative colitis)
- Prednisolone the most widely used drug given orally in inflammation and allergic diseases

Pharmacological Actions

- Betamethasone and dexamethasone: very potent, w/o salt-retaining properties; thus, very useful for high-dose therapies (*e.g.*, cerebral edemas).
- Beclometasone, diproprionate, budesonide: pass membranes poorly; more active when applied topically (severe eczema for local anti-inflammatory effects) than orally; used in asthma, (aerosol)
- Triamcinolone: used for severe asthma and for local joint inflammation (intra-articular inj).

Preparations

Drug	Anti-inflam.	Salt retaining	Topical
Cortisol	1	1.0	1
Cortisone	0.8	0.8	0
Prednisone	4	0.8	0
Prednisolone	5	0.3	4
Methylpredni-solone	5	0	5
Intermediate acting			
Triamcinolone	5	0	5
Paramethasone	10	0	-
Fluprednisolone	15	0	7

Preparations			
Drug	**Anti-inflam.**	**Salt retaining**	**Topical**
Long acting			
Betamethasone	25-40	0	10
Dexamethasone	30	0	10
Mineralocorticoids			
Fludrocortisone	10	250	10
DOCA	0	20	0

Corticosteroids Uses

- Reduce inflammation (asthma, arthritis) and swelling (cerebral oedema)
- Suppress the immune response (systemic lupus erythematosis)
- Reduce nausea and vomiting (as in cancer chemotherapy)
- Reduce terminal pain (associated with cancer)
- Replacement therapy (in Adrenal insufficiency disease)

Common therapeutic uses of glucocorticoids

THE MOST COMMON INDICATION FOR STEROID USE IS AS AN ANTI-INFLAMMATORY DRUG

- Respiratory disease
  - Bronchial asthma, COPD
- Rheumatological disease
  - SLE, polymyalgia rheumatica, vasculitides,rheumatoid arthritis
- Cardiac disease e.g. Post-myocardial infarction syndrome
- Neurological disease
  - Cerebral edema
- Renal
  - Some nephrotic syndromes, Lupus glomerulonephritides
- Skin disease
  - Pemphigus,eczema
- Tumors
  - Hodgkin's lymphoma, other lymphomas
- GI disease
  - Ulcerative colitis, Crohn's disease
  - Autoimmune hepatitis
- Transplantation & Immunosuppression

How corticosteroids work

- Cellular (nuclear) level:
- *anti-inflammatory and immunosuppressive actions:*
  - ↓ number and activity of leucocytes, proliferation of blood vessels, activity of mononuclear cells, activity of cytokine secreting cells, production of cytokines, generation of eicosanoids and PAF, complement components in blood, histamine release

How corticosteroids work

- Gross (metabolic) actions
  - Glucose: diabetogenic
    - (↓glucose uptake and utilisation; ↑gluconeogenesis)
  - Fat: Cushing's syndrome
    - (redistribution, lipolysis)
  - Protein: muscle wasting
    - (↑catabolism, ↓anabolism)
  - Minerals: hypertension (mineralocorticoids effect)

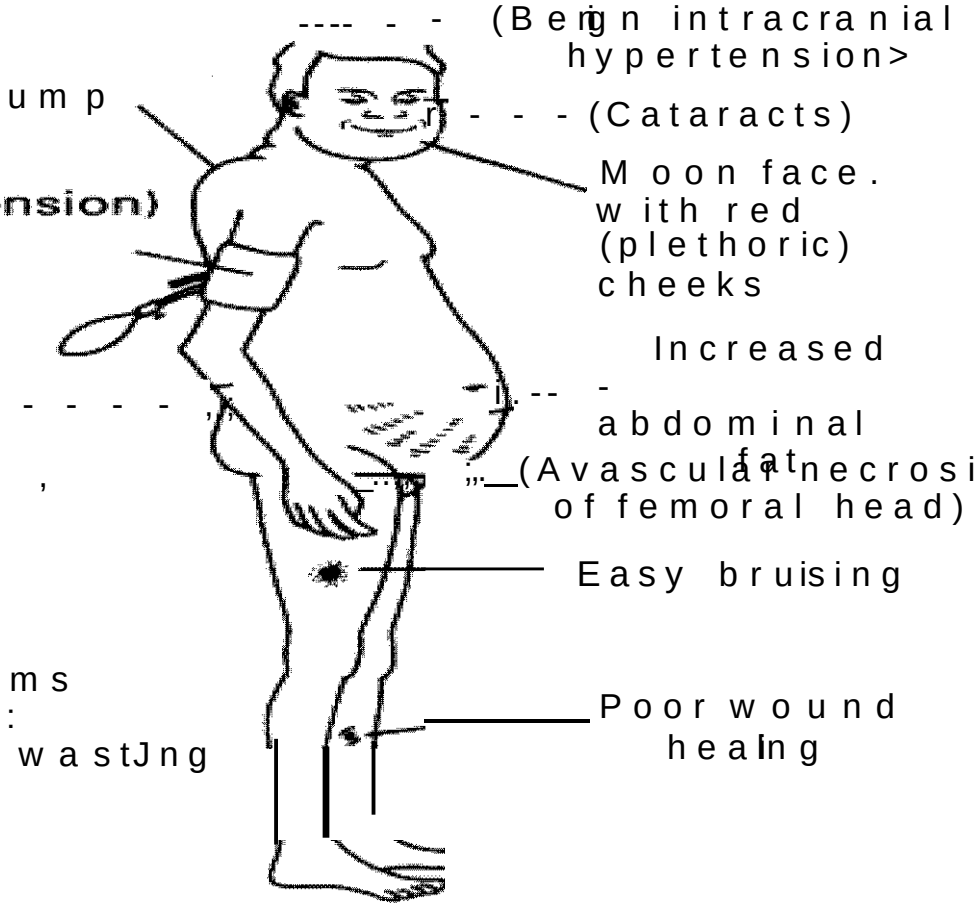
Unwanted Effects

- growth suppression
- diabetes mellitus
- muscle wasting
- osteoporosis
- fat redistribution
- skin atrophy
- hirsutism
- acne
- hypertension
- hypokalaemia
- menstrual irregularities
- adrenal suppression

Unwanted Effects

- Other:
  - infection
  - emotional disturbances (psychosis, depression, mania)
  - cataract, glaucoma
  - GI bleeding, perforation
- Withdrawal
  - Addisonian crisis
  - raised intracranial pressure
  - arthralgia/myalgia
  - pustular rash

Euphoria
(though sometimes depression or psychotic symptoms. and emotional lability)



Also:

Osteoporosis
Tendency to hyperglycaemia.
Negative nitrogen balance
Increased appetite
Increased susceptibility to infection
Obesity

Alternate-day therapy

- In 1963, Harter & Haugen suggested this method
- To minimize ACTH-suppressing ability, and its tissue and anti-inflammatory effects
- Alternate-day steroid therapy should be tried in any condition likely to last more than one month
- Many steroid-responsive chronic diseases may be maintained in remission with alternate day steroid therapy

Avoiding unwanted effects

- Modification of dose/dose regimen
  - Use short courses/low doses if possible
  - Use steroid sparing drugs
  - Withdraw ‘chronic’ steroids slowly
  - Give dose once daily and in morning
  - Give on alternate days if possible
  - Give prophylactics if possible (e.g. Bronchial Asthma)
  - Give product locally if possible
  - Remember contraindications

Caution with Topical Steroid

- No more frequently than twice daily, apply thinly to the affected area only
- Use the least potent formulation which is fully effective
- Avoid prolonged use on the face and keep away from eyes
- Suppression of pituitary adrenal axis and even cause Cushing's syndrome with prolonged use in large area

Monitoring hydrocortisone replacement

- In general, therapy for 3 weeks or less, or a dose of prednisolone less than 1 0 mg per day, will not result in significant long-term suppression of the normal adrenal axis
- Biochemical monitoring enables detection of minor degrees of under- or over-replacement
- 24 h urine free cortisol measurement should be in the normal range; mid-day and evening plasma cortisol should be > 50nmol/l
- Dexa scan monitoring for those on steroid for duration exceeded 6 months.