Adrenal Steroid Hormones

(Chapter 15)

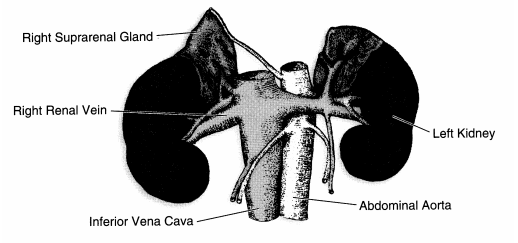
I. glucocorticoids
- cortisol
- corticosterone

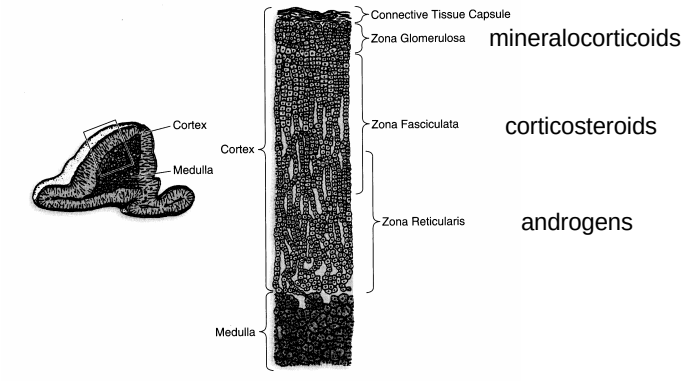
II. mineralocorticoids
- aldosterone

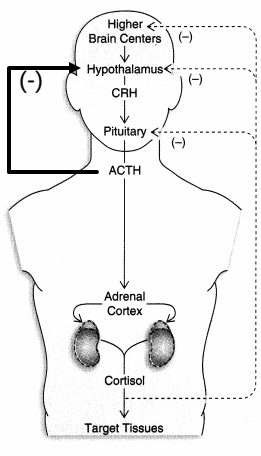
III. androgenic steroids
- dehydroepiandrosterone
- testosterone

IV. estrogenic steroids
- estradiol

V. progestins
- pregnenolone
- progesterone







Corticotropin-Releasing Hormone

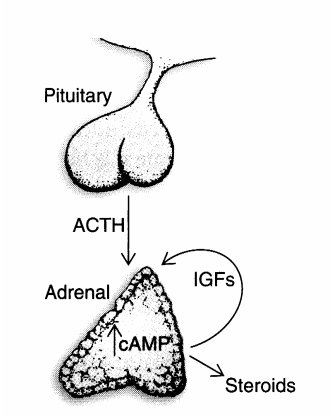
Adrenocorticotropin Hormone

Negative feedbacks

A) cortisol dual negative feedback

1) inhibit hypothalamic neuronal activity: decrease CRH
2) decreases sensitivity of anterior pituitary to CRH: decrease ACTH
3) inhibits stimulus from higher brain centers

B) ACTH negative feedback on hypothalamus: decrease CRH



Primary cultures

human fetal adrenal cells

ACTH or cAMP → Insulin-like growth factor II mRNA

I. SECRETION/ACTION OF GLUCOCORTICOIDS

A) Inputs from various brain centers regulates hypothalamus
B) release CRH (hypothalamus)
C) zona fasciculata secrete glucocorticoids
1) circadian pattern during the 24-hr period
a) highest at morning when awakening
b) lowest around midnight
c) due to circadian variations of CRH/ACTH secretions
d) individual sleep/wake patterns not environmental light/dark cycles
e) change in sleep/wake cycles (working night shift) result in temporal
f) shift in daily rhythm of cortisol secretion
g) dips/increases within the circadian pattern
h) buffered by specific carrier proteins in plasma to prevent rapid changes in free cortisol in plasma

2) increased cortisol secretion response to a specific stimuli
a) physical stress
1) hypoglycemia (low blood glucose) during fasting
2) trauma
a) broken bones
b) burns
c) surgery
d) cold exposures
e) infection
3) heavy exercise (competitive athletics)

b) psychological stress
**1) acute anxiety (prior to surgical operations/final exams)
*2) novel situations
3) chronic anxiety

3) recent studies ACTH promotes learning
- a) new learning/challenging situations: ↑ ACTH/cortisol
- b) anterior pituitary--> ACTH
  ACTH part of large proopiomelanocortin (POMC) peptide: precursor to ACTH/opioids/melanocyte stimulating hormone (MSH)
- c) opioid peptides are produced (e.g. morphine-like ß-endorphin) peptides acts as endogenous analgesic & ↑ pain threshold

4) Cortisol transport in blood
- a) 80% bound to corticosteroid-binding globulin (CBG specific carrier protein) which protects cortisol from breakdown/excretion
  biological half-life 80 minutes
- b) 15% bound to albumin
- c) 5% free---> bind to receptors produce physiological effects

III. Physiological Effects of Glucocorticoids -primarily 3 tissues

A. Liver: ↑ blood glucose
1) ↑ gluconeogenesis : AA-->glucose
   a. ↑ activity of enzymes catalyze key steps in gluconeogenic pathway
   b. ↑ activity of enzymes involved in AA metabolism → facilitating AA as substrates of gluconeogenesis
   c. stimulate activity of enzymes of urea cycle → disposition of N during metabolism of AA

2) ↑ glycogen synthesis
   a. ↑ glucose from above steps
   b. stimulation of enzymes involved in glycogen formation

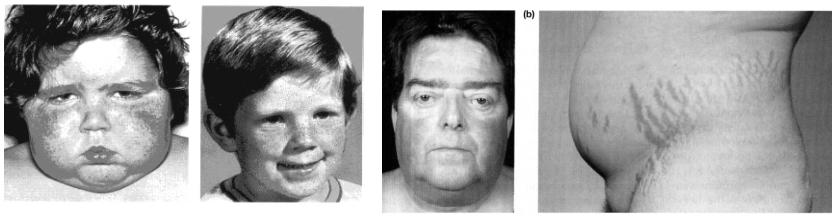
B. Skeletal Muscle:

Net loss of proteins: catabolic activity of cortisol unlike anabolic steroids (androgens) → ↑muscle mass

1) decreased protein synthesis
   reduction of blood AA uptake and incorporation into muscle
2) ↑protein degradation
   a. ↑AA from muscle into blood
   b. liver can utilize the extra blood AA for gluconeogenesis
3) decrease glucose uptake → anti-insulin effect

C. Adipose tissue (fat storing tissues)

1) decreases glucose uptake → anti-insulin effect
2) ↑lipid mobilization from stores within differential adipose tissues
   a. ↑↑cortisol: fat stores in legs/arms decrease & redistributed to trunk & shoulder blade region
   b. ***Cushing syndrome*** (hypersecretion of cortisol)
      1. thin arms/legs: ↑↑ lipids in face, neck, base of trunk, shoulder:
      2. blood vessel surface-red complexion/reddish → purplish streaks → stretch marks



Cushing syndrome **after treatment** **reddish** **stretch marks**

3. loss connective tissues in small blood vessels -fractures=>bruising
4. hypertension-primary cause of death
5. increased susceptibility to infection
6. lead to diabetes

IV. Permissive Actions of Glucocorticoids

A. cortisol amplifying effect with other hormones

1) epinephrine stimulates break down of adipose lipids: enhanced with cortisol

2) glucagon effect enhanced during hypoglycemic challenge

3) catecholamine synthesis within sympathetic nerve terminal and its reuptake

B. exact nature of cortisol permissiveness* ??

*permissiveness=required presence of a hormone for another hormone to have its effect

V. Glucocorticoid Effects on Blood Vessels/Blood Cells

A. enhance responsiveness of blood vessels (**vascular reactivity**)

Arterioles small diameter in the absence of cortisol during stress:

Blood pressure can fall-->death

B. ↑neutrophils , red blood cells, platelets

C. decreases esoinophils and basophils

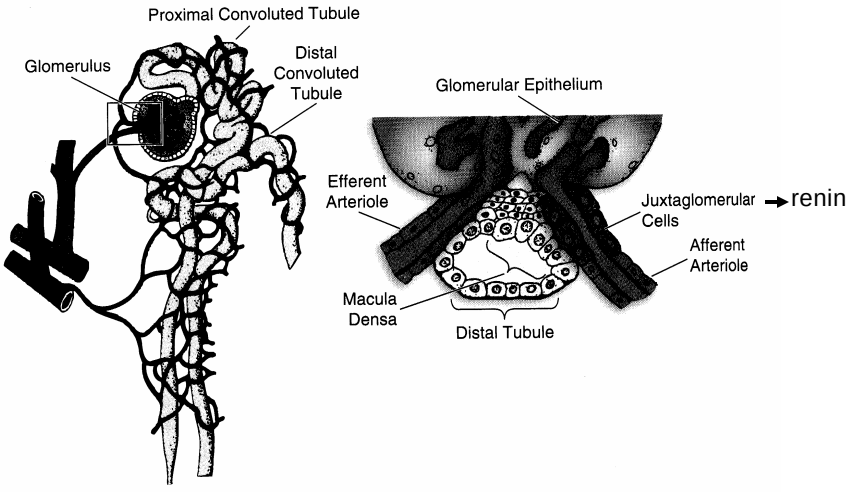
VI. Pharmacological Effects

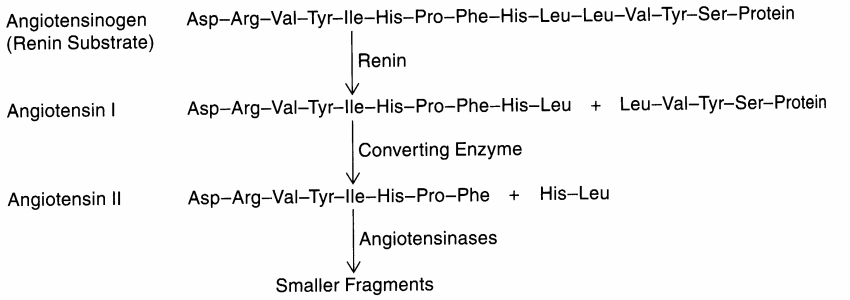
A. Anti-inflammatory-Injury tissues

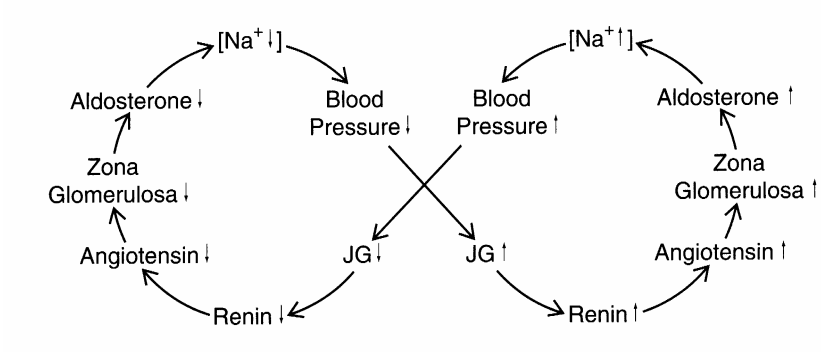
1) inhibit vasodialation
2) inhibit capillary permeability
3) inhibit increased phagocytosis

B. Immunosuppressive-Lymphoid tissues

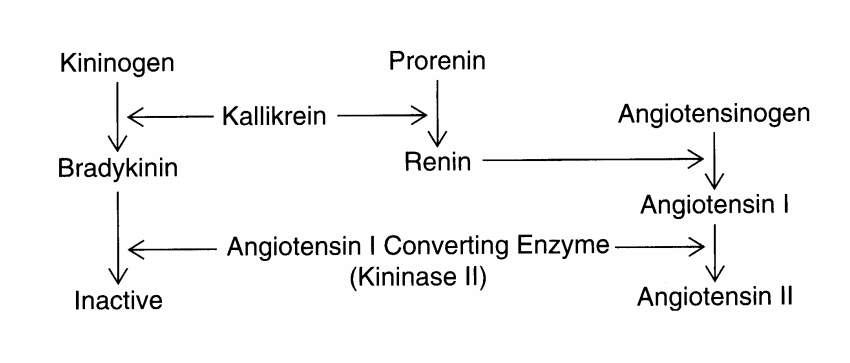
1) decreased antibody production
2) decrease circulating lymphocyte:
   ↑lymphocyte destruction/decrease lymphoid nodes
3) important in organ transplant but leads susceptibility to infections requiring antibiotics

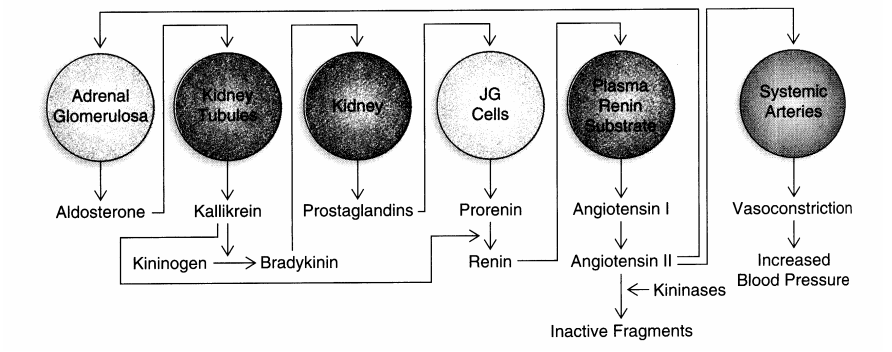


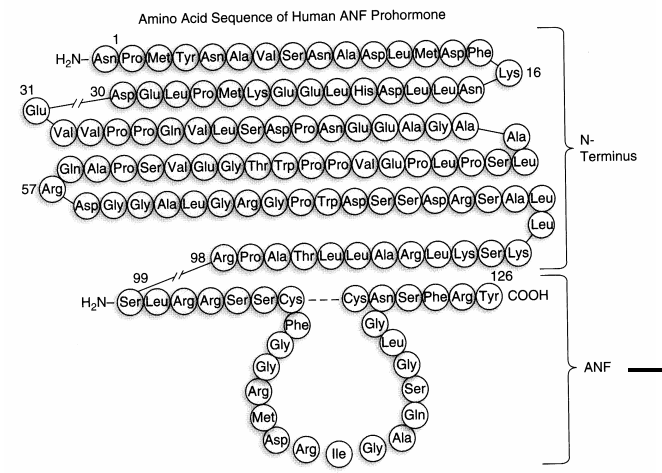

Angiotensinogen
(Renin Substrate)
Asp–Arg–Val–Tyr–Ile–His–Pro–Phe–His–Leu–Leu–Val–Tyr–Ser–Protein
Renin
Angiotensin I
Asp–Arg–Val–Tyr–Ile–His–Pro–Phe–His–Leu + Leu–Val–Tyr–Ser–Protein
Converting Enzyme
Angiotensin II
Asp–Arg–Val–Tyr–Ile–His–Pro–Phe + His–Leu
Angiotensinases
Smaller Fragments

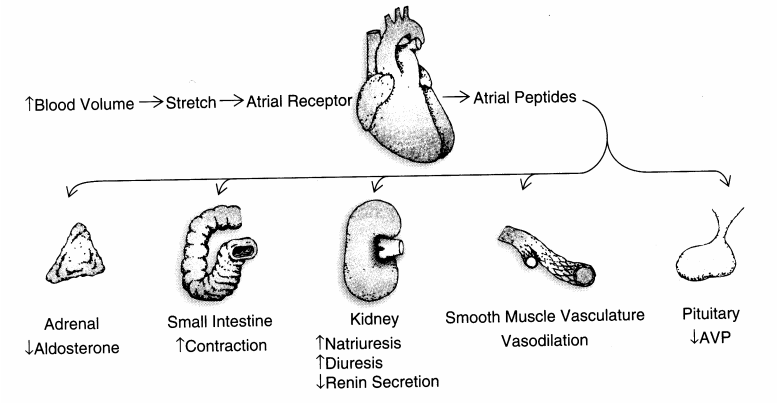

[Na+↓]
Aldosterone↓
Blood Pressure↓
Zona Glomerulosa↓
Angiotensin↓
JG↓
Renin↓
[Na+↑]
Blood Pressure↑
Aldosterone↑
Zona Glomerulosa↑
Angiotensin↑
JG↑
Renin↑

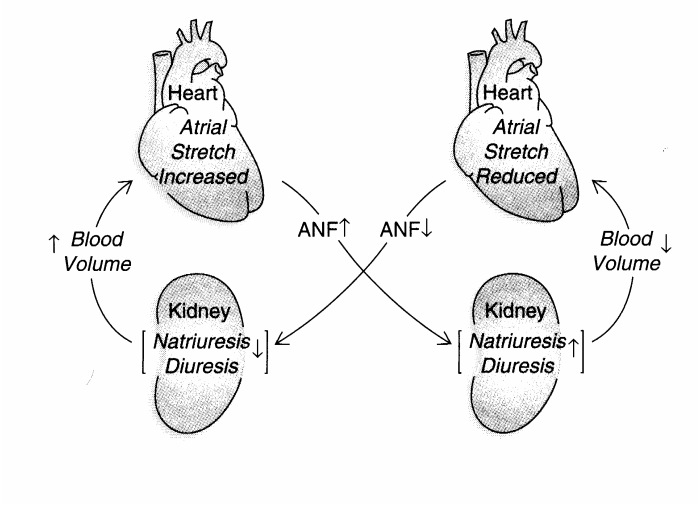
Kinins: peptide hormones from plasma proteins & tissue enzymes






Amino Acid Sequence of Human ANF Prohormone
N-Terminus
ANF
28 AA


↑Blood Volume → Stretch → Atrial Receptor → Atrial Peptides
Adrenal
↓Aldosterone
Small Intestine
↑Contraction
Kidney
↑Natriuresis
↑Diuresis
↓Renin Secretion
Smooth Muscle Vasculature
Vasodilation
Pituitary
↓AVP



Cortisol metabolism in liver to form water-soluble glucuronides

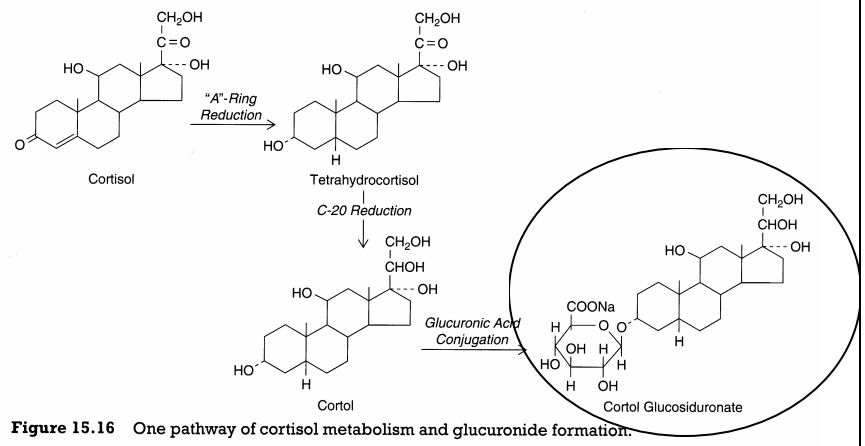
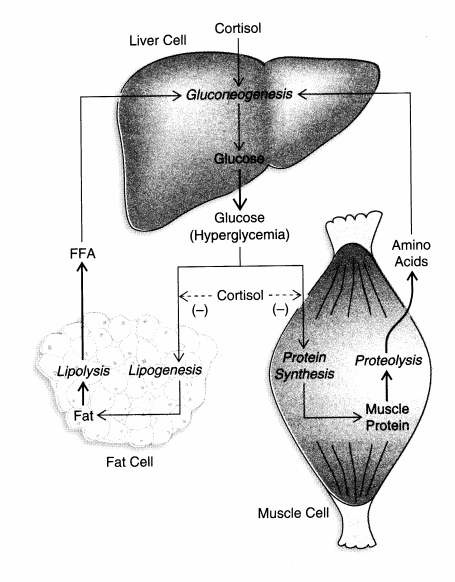


Figure 15.16 One pathway of cortisol metabolism and glucuronide formation.



II. MINERALOCORTICOIDS

A. zona glomerulosa → aldosterone
B. regulators of aldosterone secretion
1) K^+
2) angiotensin II (peptide hormone)
3) kidney determines plasma levels of these two regulators
C. aldosterone affects kidney
D. not bound in blood—susceptible to breakdown/excretion
biological half life: 30 minutes

1) K^+
A. zona glomerulosa cells sensitive to ↑ K^+ plasma concentrations
B. aldosterone promote K^+ secretion by kidney

2) Angiotensin II
renin angiotensin system: amount of kidney renin in response to decrease in blood pressure or blood flow to kidney
A. zona glomerulosa cells --specific receptors for angiotensin II
B. binding stimulates production/secretion of aldosterone
C. exact mechanism ??-perhaps activation of secondary messengers (phosphatidylinositol)

3) Physiological Effects

A. ↑ extracellular fluid volume

a) ↑ blood volume

b) ↑ blood pressure

c) ↑ blood flow

B. regulation fluid balance

C. kidney

a) retain more Na^+

b) secrete more K^+

D. stimulate smooth muscle contraction blood vessels

E. activation of brain thirst centers

F. stimulation of antidiuretic hormone (ADH) release from posterior pituitary

4) Low Secretions of Adrenal Cortex Hormones

A. malfunction ACTH secretion → hyposecretion all adrenal steroid hormones

B. Addison's Disease

1) decreased plasma Na^+

2) ↑ plasma K^+

3) decreased blood pressure

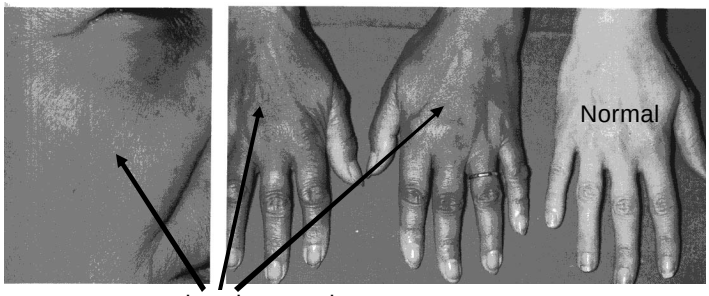
4) muscle weakness/fatigue

5) vomiting/loss of appetite

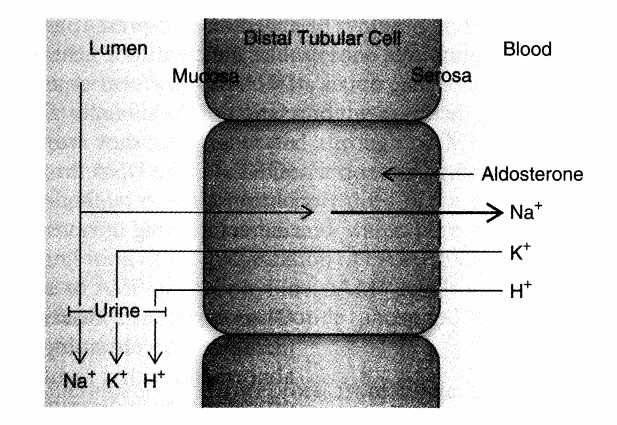
6) dehydration

7) decreased blood glucose

**8) excess pigmentation of skin: due to ACTH mimicking melanocyte stimulating hormone (MSH) structural similarities



excessive pigmentation



Effects of Aldosterone

1) Na^+ reabsorption
2) K^+ secretion
3) H^+ secretion