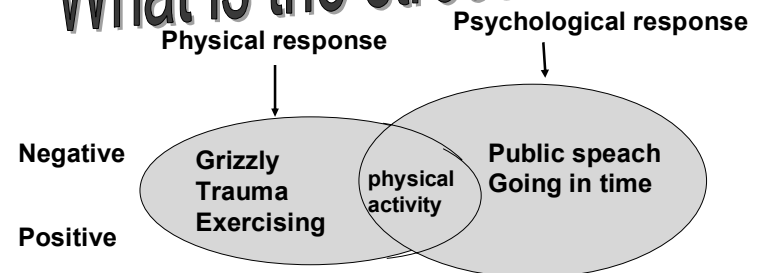


General adaptation syndrome

October 7, 2004

What is the stress?



stressor=any factor deflecting body homeostasis
stress response= body adaptation to homeostasis restoring
stress= the complexity of factors provoking stress response

Hans Selye

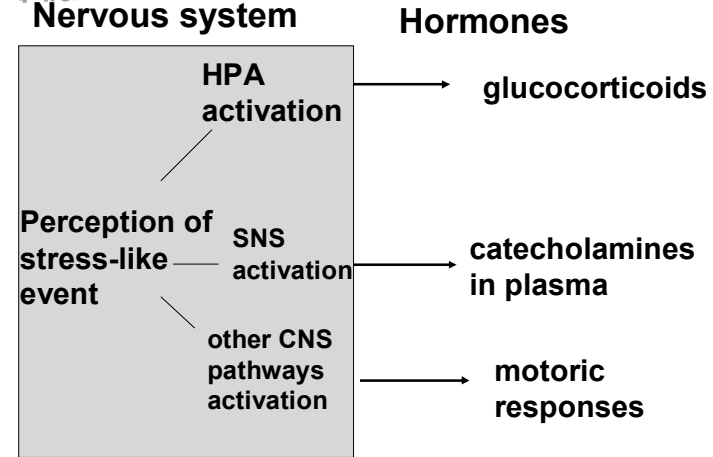
- *A syndrome produced by diverse nocuous agents, Nature 138, 32, 1936*
- General adaptation syndrome-stress reaction of organism:
- Experiments with animals showed that different toxic substances applied into the organisms led to stereotyped response explicable by suprarenal gland activation.

Stages of stress

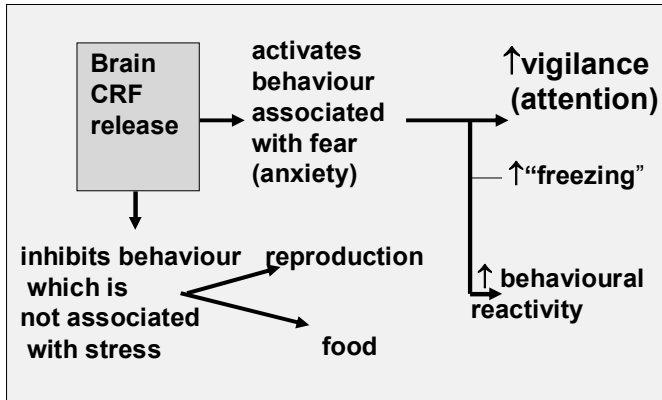
- ◎ **alarm reaction (fight and flight- Cannon's emergent reaction): shock, contra-shock**
- ◎ **stage of resistance**
- ◎ **stage of exhaustion**

- © Eustress- increases possibilities of the organism, healthy and life motivation
- © Distress- decreases possibilities, facilitates diseases development
- © Stressors= stress causes (frustrations, conflicts)
- © Factors influencing stress severity
 - stressor characteristics
 - subjective stress responsibility
- © Reactions to acute and chronic stress: physical and psychological

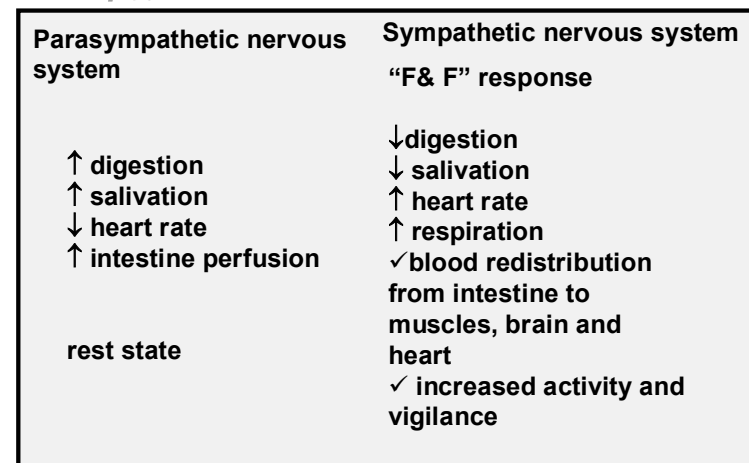
Alarm reaction "fight or flight"

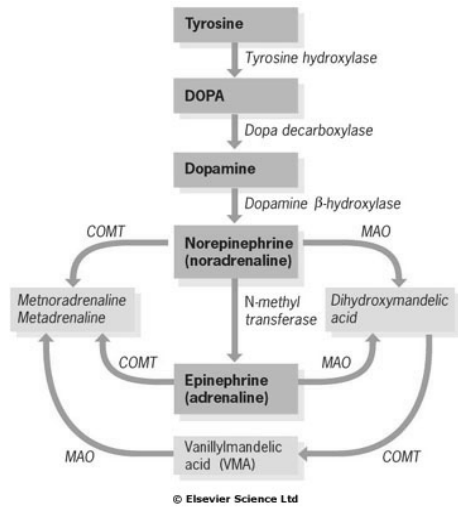


Acute stress response: behavioral alterations caused by CRF release



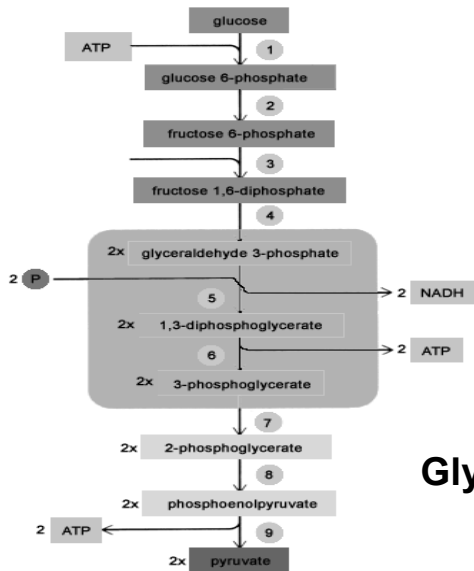
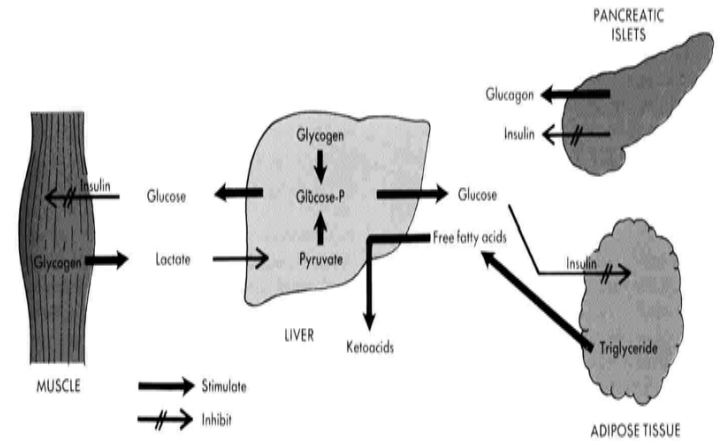
Autonomic nervous system



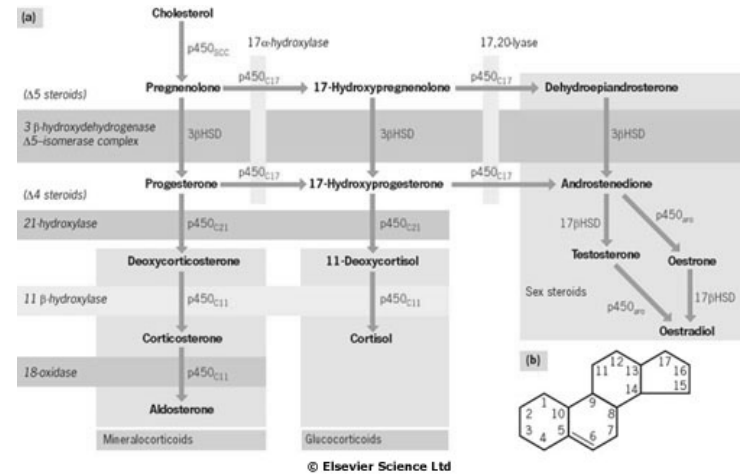


Catecholamines synthesis and metabolism

Metabolic effects of epinephrine



Glycolysis



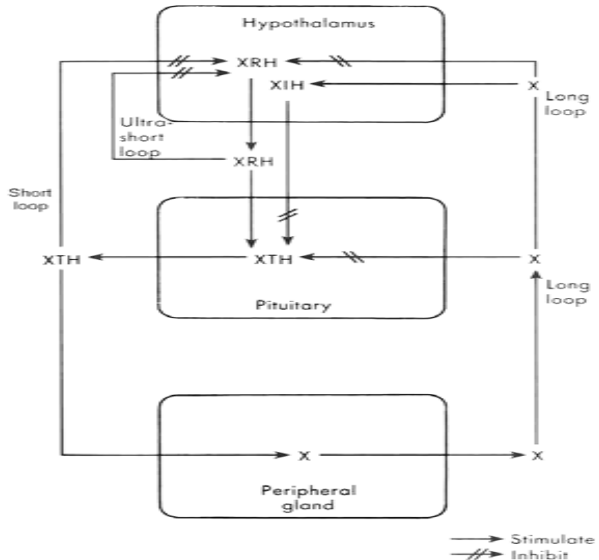
(a) The major steroid biosynthetic pathways. Enzymes catalysing reactions are in red: p450 enzymes are in mitochondria and each catalyses several reaction steps; 3βHSD (hydroxysteroid dehydrogenase) is in cytoplasm, bound to endoplasmic reticulum; 17βHSD and p450_{ar} are found mainly in gonads. **(b) The steroid molecule.**

Table 18.27

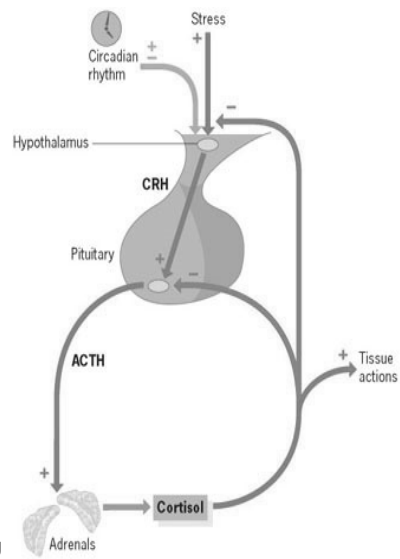
The major actions of glucocorticoids

Increased or stimulated	Decreased or inhibited
Gluconeogenesis	Protein synthesis
Glycogen deposition	Host response to infection
Protein catabolism	Lymphocyte transformation
Fat deposition	Delayed hypersensitivity
Sodium retention	Circulating lymphocytes
Potassium loss	Circulating eosinophils
Free water clearance	
Uric acid production	
Circulating neutrophils	

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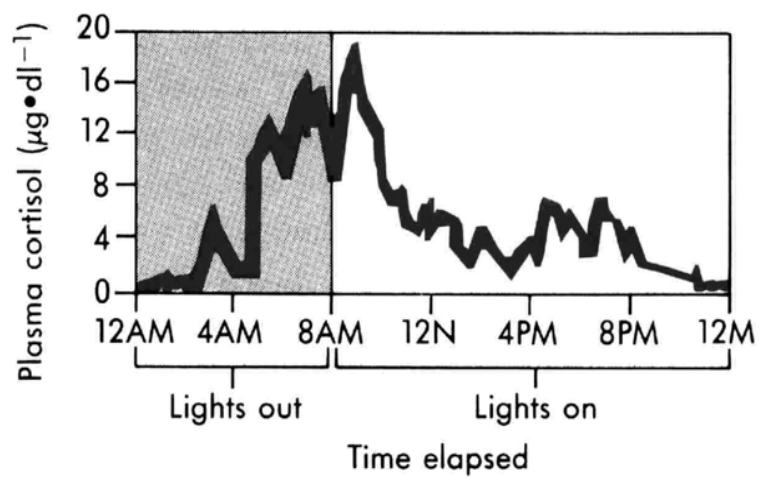
→ Stimulate
 // Inhibit

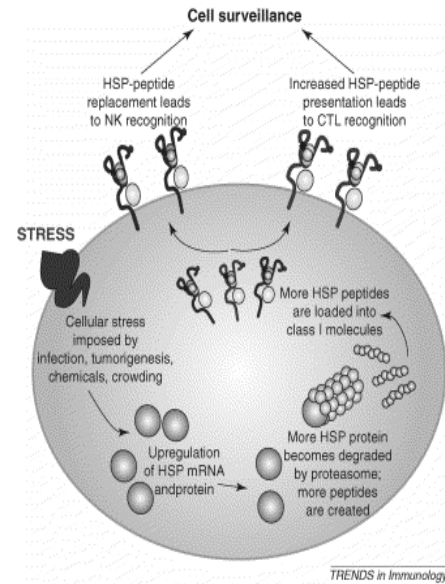
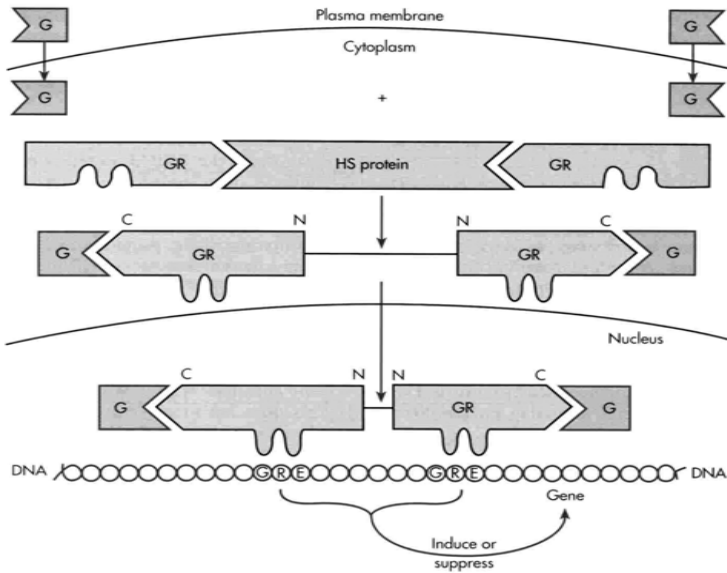
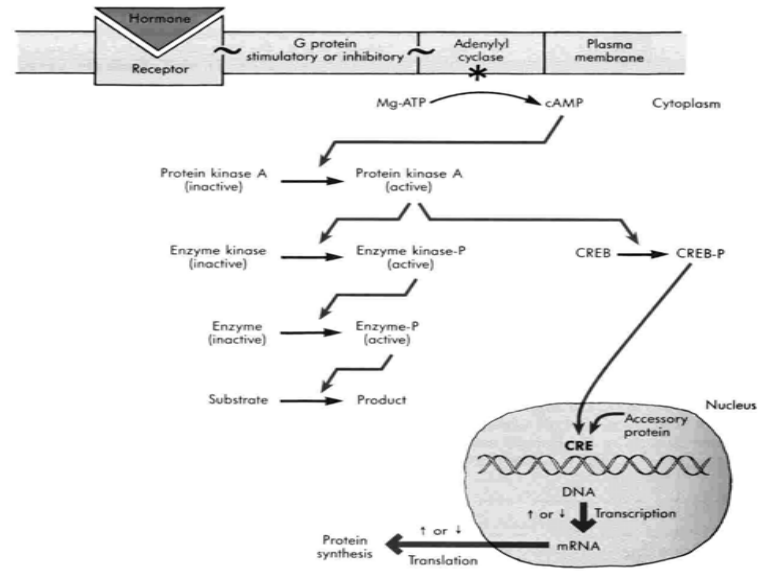
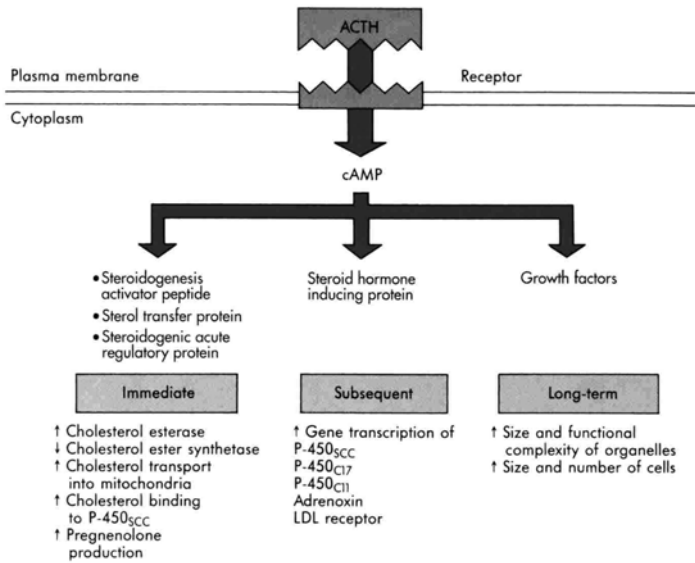


Control of the hypothalamic-pituitary adrenal axis. CRH, corticotropin-releasing hormone.

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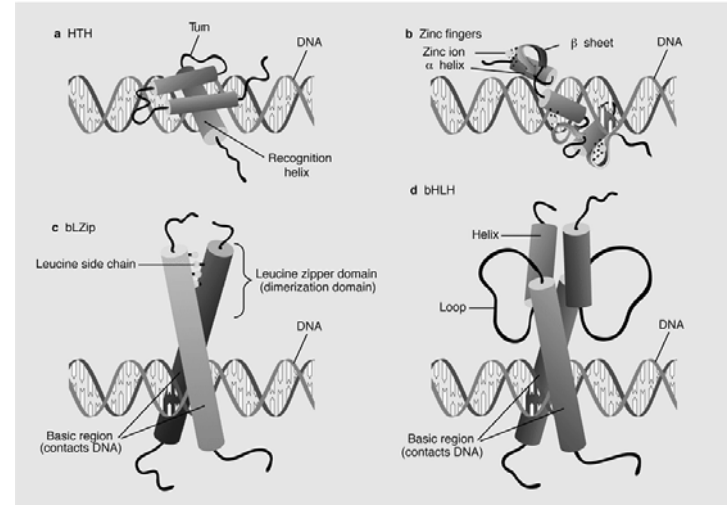
Pulsatile and diurnal character of glucocorticoid secretion



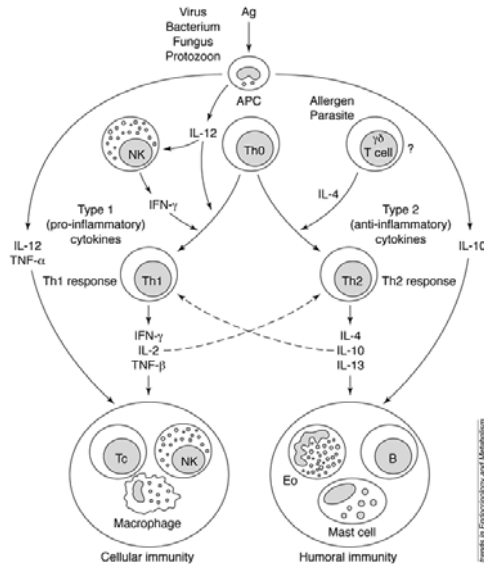


Glossary to the figure

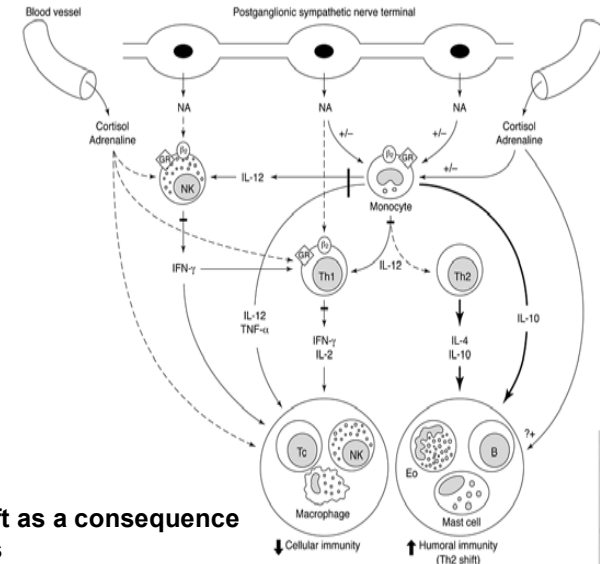
- A putative model for the presentation of heat-shock protein (HSP)-derived class I peptides. Stress on the cell causes increased levels of HSP transcription and translation. HSPs are degraded by the proteasome and subsequently loaded into the peptide-binding groove of MHC class I molecules. Increased or novel HSP-peptide-MHC complexes are present on the cell surface for interaction with innate [natural killer (NK) cells] and adaptive [cytotoxic T lymphocytes (CTLs)] immune effectors. Individual or synergistic recognition by various effectors results in the destruction of stressed cells.



Balance of Th1/Th2 immune responses

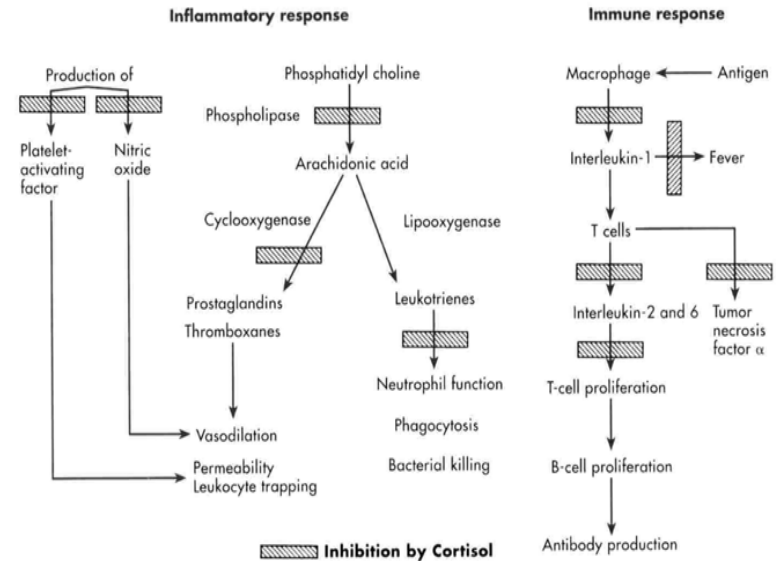
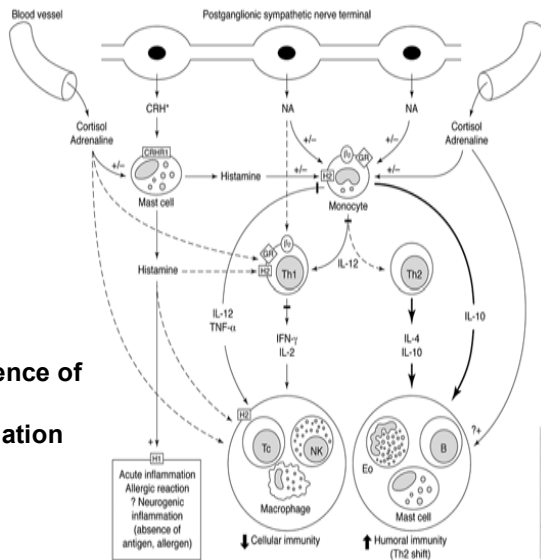


From: In Endocrinology and Metabolism



Th2 shift as a consequence of stress

From: In Endocrinology and Metabolism



Treatment by glucocorticoids

Respiratory diseases

- Asthma
- Chronic obstructive pulmonary disease
- Sarcoidosis
- Prevention/treatment of ARDS

Cardiac diseases

- Post-myocardial infarction syndrome

Renal diseases

- Some nephrotic syndromes
- Some glomerulonephritides
- Gastrointestinal disease
- Ulcerative colitis
- Crohn's disease
- Autoimmune hepatitis

Treatment by glucocorticoids

Rheumatological diseases

- Systemic lupus erythematosus
- Polymyalgia rheumatica
- Cranial arteritis
- Juvenile idiopathic arthritis
- Vasculitides
- Rheumatoid arthritis

Neurological diseases

- Cerebral oedema

Skin diseases

- Pemphigus, eczema

Tumours

- Hodgkin's lymphoma
- Other lymphomas

Transplantation

- Immunosuppression

Major adverse effects of corticosteroid therapy

Physiological

- Adrenal and/or pituitary suppression

Pathophysiological

Cardiovascular

- Increased blood pressure

Gastrointestinal

- Peptic ulceration exacerbation (possibly)
- Pancreatitis

Renal

- Polyuria
- Nocturia

Central nervous

- **Depression**
- **Euphoria**
- **Psychosis**
- **Insomnia**

Endocrine

- **Weight gain**
- **Glycosuria/hyperglycaemia/diabetes**
- **Impaired growth**
- **Amenorrhoea**

Major adverse effects of corticosteroid therapy

Bone and muscles

- Osteoporosis
- Proximal myopathy and wasting
- Aseptic necrosis of the hip
- Pathological fractures

Skin

- Thinning
- Easy bruising

Eyes

- Cataracts (including inhaled drug)

Increased susceptibility to infection

- (signs and fever are frequently masked)
- **Septicaemia**
- **Reactivation of TB**
- **Skin (e.g. fungi)**

Table 18.32

Causes of Cushing's syndrome

ACTH-dependent disease


- Pituitary-dependent (Cushing's disease)
- Ectopic ACTH-producing tumours
- ACTH administration

Non-ACTH-dependent causes

- Adrenal adenomas
- Adrenal carcinomas
- Glucocorticoid administration

Others

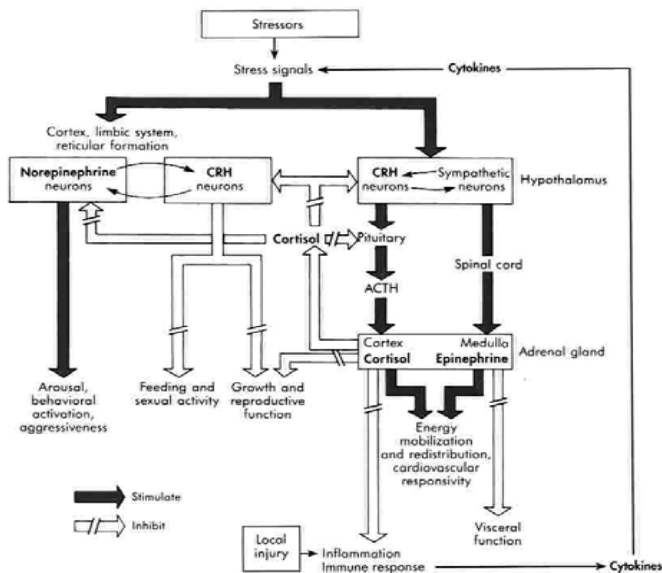
- Alcohol-induced pseudo-Cushing's syndrome

Symptoms		Signs
Weight gain (central)		Oedema
Change of appearance		Plethora
Depression		Depression/psychosis
Insomnia		Acne
Amenorrhoea/oligomenorrhoea		Hirsutism
Poor libido		Frontal balding (female)
Thin skin/easy bruising		Thin skin
Hair growth/acne		Bruising
Muscular weakness		Poor wound healing
Growth arrest in children		Pigmentation
Back pain		Skin infections
Polyuria/polydipsia		Hypertension
Psychosis		Osteoporosis
Old photographs may be useful		Pathological fractures (especially vertebrae and ribs)
	Kyphosis	
	'Buffalo hump' (dorsal fat pad)	
	Central obesity	
	Striae (purple or red)	
	Rib fractures	
	Proximal muscle wasting	
	Glycosuria	

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The symptoms and signs of Cushing's syndrome.

Bold type indicates signs of most value in discriminating Cushing's syndrome from simple obesity and hirsutism.



Acute stress response

- ⊙ adaptive, enabling surveillance
- ⊙ although different reactions are used, the aim is always the same: = surveillance
- ⊙ *metabolic*: ↑glycemia
- ⊙ *cardiovaskular/respiratory*- glucose traffic to muscles, heart and brain
- ⊙ *analgesia*
- ⊙ *inhibition of processes decreasing surveillance chance* (reproduction, food).

Acute stress reaction-metabolic effects

- ⊙ Purpose: to increase glycemia using catecholamines and glucocorticoids
- ⊙ Glucose uptake is inhibited; proteins, fatty acids and glycogen synthesis is stopped. Lysis of lipids and proteins (immune system is „sacrificed“)
- ⊙ Glykogenolysis by catecholamines (short-time effects on glycemia), gluconeogenesis (glucocorticoids with long-time effects on glycemia).

Acute stress response-cardiovascular/ respiratory effects

- ⊙ Purpose: to increase cardiovascular tonus for a quick transport of mobilized glucose to the tissues with the highest oxygen consumption.
- ⊙ Vasopressin release from axon neurohypophysal terminals leading to reabsorption of water in the kidney vasopressinu z axonových terminál neurohypofýzy vede k reabsorbci vody v ledvinách. Purpose: to increase cardiovascular circulating volume

Acute stress response-analgesia

- ☺ Purpose: to decrease pain perception
 - ☺ Two forms of stress-induced analgesia can be distinguished (SIA)
 - ☺ -opiates-dependent SIA (enkephalins and β -endorphine)
 - ☺ -opiates independent SIA (glutamate)
- Both SIA can combine one to another.

Stress and multiplex factors role

- ☺ Dominant and subdominant primates (males):
- ☺ In stable conditions (no territorial emergency), dominant males have lower glucocorticoids levels than subdominant ones.
- ☺ But, in unstable conditions, these levels in dominant males increase and they are the same or higher than in subdominant males.
- ☺ “Personal power” of dominant male correlates with low GCs levels during rest conditions.

Chronic stress response

- ☹ maladaptive = impairing effects
- ☹ chronic stress can contribute to development of diseases as peptic ulcer, visceral obesity, lower growth, higher risk of CAD
- ☹ chronic stress influences behaviour:
- ☹ inhibition of reproduction
- ☹ depression, schizophrenia etc.

Stress and multiplex factors role

- ☺ „Good state of mind” is necessary !
- ☺ Social supporting groups forming- f.e. non sexually based friendship between men and women in the team
- ☺ Training of ability to anticipate stressful event and undertake the control.
- ☺ Transformation of aggression (sports)

