Hans Selye

- A syndrome produced by diverse nocos 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

What is the stress?

- Physical response
- Psychological response
- Negative
- Positive

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

Hans Selye

October 7, 2004
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"
Nervous system
Hormones

Perception of stress-like event
HPA activation
→ glucocorticoids
catecholamines in plasma
other CNS pathways activation
motoric responses

Acute stress response: behavioral alterations caused by CRF release

Autonomic nervous system

Brain CRF release activates behaviour associated with fear (anxiety)
hits behaviour which is not associated with stress

↑ vigilance (attention)
↑“freezing”
↑ behavioural reactivity

Parasympathetic nervous system
Sympathetic nervous system

"F& F" response

↑ digestion
↑ salivation
↑ heart rate
↑ intestine perfusion
rest state

↓ digestion
↓ salivation
↓ heart rate
↑ respiration
✓ blood redistribution from intestine to muscles, brain and heart
✓ increased activity and vigilance
Catecholamines synthesis and metabolism

Glycolysis

Metabolic effects of epinephrine

(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 arom are found mainly in gonads. (b) The steroid molecule.
### Table 18.27
The major actions of glucocorticoids

<table>
<thead>
<tr>
<th>Increased or stimulated</th>
<th>Decreased or inhibited</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gluconeogenesis</td>
<td>Protein synthesis</td>
</tr>
<tr>
<td>Glycogen deposition</td>
<td>Host response to infection</td>
</tr>
<tr>
<td>Protein catabolism</td>
<td>Lymphocyte transformation</td>
</tr>
<tr>
<td>Fat deposition</td>
<td>Delayed hypersensitivity</td>
</tr>
<tr>
<td>Sodium retention</td>
<td>Circulating lymphocytes</td>
</tr>
<tr>
<td>Potassium loss</td>
<td>Circulating eosinophils</td>
</tr>
<tr>
<td>Free water clearance</td>
<td></td>
</tr>
<tr>
<td>Uric acid production</td>
<td></td>
</tr>
<tr>
<td>Circulating neutrophils</td>
<td></td>
</tr>
</tbody>
</table>

**Control of the hypothalamic-pituitary adrenal axis.** CRH, corticotropin-releasing hormone.
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.
Th2 shift as a consequence of stress and acute inflammation

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

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

- 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

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

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
- cardiovascular/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“)
- Glycogenolysis 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 neurohypophysial terminals leading to reabsorption of water in the kidney vasopresinu 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.

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

✿ 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.

✿ „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 agresivity (sports)