Basic biochemical examination in endocrinology

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Diabetes mellitus

Endocrinology of reproduction
Hormones - definition

Hormones are endogenous substances produced by specialized cells

Secretion: continuous (thyroid hormones) with diurnal rhythm (cortisol) with monatial rhythm (menstrual cycle hormones) seasonal rhythm (parathormon)
Hormones - types

Proteohormones and peptides

Steroid hormones

Low molecular weight hormones derived from modified amino acids

Prostanoids
Action of hormones

Autocrine
Paracrine
Endocrine
Diabetes mellitus
DM definition

WHO 1985

Status characterized by chronic elevation of blood glucose, that could be connected with clinical syndromes and could lead to death without proper care.
Langerhans islets

- Delta cell
- Islet of Langerhans
- Pancreatic acini
- Alpha cell
- Red blood cells
- Beta cell
B (beta) cells

70%
Produce insulin
Insulin

Men and other mammals 1 gen on chromosome 11 (rodents, 2 genes)

51 AA, 2 strands

Homology between species high: pig, dog, hare 1 AA; cow 3 AA; sheep, horse 4 AA.

Secretion increased: elevation of blood sugar, aminoacids, parasympaticus system action, glukagon, glucocorticoides, growth hormone, placental lactogen,estrogenes, gestagenes (during pregnancy)

Secretion decreased: fats, sympaticus action, somatostatin, adrenalin
Insulin

PREPROINSULIN

C peptid

PROINSULIN

INSULIN
Insulin

Daily production:
40-50 units
(15-20% of pancreatic depot)
50% basal secretion
50% postprandial secretion

Plasmatic halftime:
3-5 minutes, no transport protein

First-pass effect:
50% used during first passage through liver
C peptid

Function unknown

Variable length

Used as marker of endogenous insulin production (produced in equimolar proportion, can be used in patients on insulin therapy as well)

No first-pass effect
Insulin like growth factors

IGF-I
70 AMK

62 % homology (IGF-I and IGF-II)
50 % homology with insulin

IGF-II
67 AMK

More stimulate growth than insulin
Have less metabolic effect than insulin
A (alpha) cells

25%
Produce glucagon
Glucagon

29 amino acids

Synthetized as proglukagon

Plasmatic halftime 5 minutes

No transport protein

Inactivation in liver
Glucagon

Enhances

glycogenolysis
lipolysis
gluconeogenesis
ketogenesis

Receptors mainly in liver
D (delta) cells

5%
Produce somatostatin
Somatostatin

cyclic peptide, 14 amino acids

in CNS – neurotransmitter function

synthesized also in other places in GIT

Inhibition of insulin and glucagon secretion

Slows gastric emptying, lowers gastrin secretion, pancreatic exocrine secretion, …
Blood glucose regulation

- INSULIN
  glucagon like peptid
  utilization in CNS
  muscle work

+ GLUCAGON
  catecholamins
  glucocorticoides
  growth hormone

FOOD INTAKE
Blood glucose regulation

- INSULIN
  glucagon like peptid
  utilization in CNS
  Muscle work

+ GLUCAGON
  catecholamins
  glucocorticoides
  growth hormone
DM diagnosis

Fasting glycemia (venous and capillary blood)

<5.6 mmol/l  no DM
5.7-7.0 mmol/l  impaired fasting glycemia
>7 mmol/l  DM present

Glycemia in random sample

Several times >10mmol/l  DM present
DM diagnosis

OGTT (oral glucose tolerance test)

75 g of glucose in 400 ml water (tea)

Measurement at time 0 and 120 min (60 min and 180 min sometimes added)

7.8

NORMAL
DM diagnosis

OGTT

Impaired glucose tolerance

repeat OGTT every 2-3 years
DM diagnosis

OGTT

7.7

11.1

DM
DM

Insulin secretion

Glycemia

Insulin sensitivity

11.1

7.7

8-10 years
Lab tests in DM

BLOOD GLUCOSE
  fasting
  random
  oral glucose tolerance test (OGTT)
  glycemic profile

GLYCATED HAEMOGLOBIN, PEPTIDES, AGEs

INSULIN, C PEPTID, anti-GAD antibodies, antibodies against insulin, antibodies against B cells (ICA, IA2)
haemoglobin glycation

\[
\begin{align*}
\text{HC} = \text{O} & \quad \text{HC} = \text{N-ß} & \quad \text{CH}_2\text{-NH-ß} \\
\text{} & \quad \text{} & \quad \\
\text{HCOH} & \quad \text{HCOH} & \quad \text{C} = \text{O} \\
\text{} & \quad \text{} & \quad \\
\text{HOCH} & \quad \text{HOCH} & \quad \text{HOCH} \\
\beta\text{-NH}_2 & + & \\
\text{HCOH} & \quad \text{fast} & \quad \text{HCOH} & \quad \text{slow} & \quad \text{HCOH} \\
\text{} & \quad \text{} & \quad \\
\text{HCOH} & \quad \text{HCOH} & \quad \text{HCOH} \\
\text{} & \quad \text{} & \quad \\
\text{CH}_2\text{OH} & \quad \text{CH}_2\text{OH} & \quad \text{CH}_2\text{OH} \\
\end{align*}
\]

Aldimin (labile HbA\textsubscript{1c})

Ketoamin (stabile HbA\textsubscript{1c})
### Haemoglobin - types

<table>
<thead>
<tr>
<th>Haemoglobin and derivates</th>
<th>Subunits present</th>
<th>Sugar</th>
<th>Content</th>
</tr>
</thead>
<tbody>
<tr>
<td>HbA₀</td>
<td>$\alpha_2\beta_2$</td>
<td>-</td>
<td>&gt; 90%</td>
</tr>
<tr>
<td>HbA₂</td>
<td>$\alpha_2\delta_2$</td>
<td>-</td>
<td>2%</td>
</tr>
<tr>
<td>HbF</td>
<td>$\alpha_2\gamma_2$</td>
<td>-</td>
<td>0.5%</td>
</tr>
<tr>
<td>HbA₁₁a₁</td>
<td>$\alpha_2(\beta$-F-D-P)$_2$</td>
<td>Fructose-1,6-diphosphate</td>
<td>&lt;1%</td>
</tr>
<tr>
<td>HbA₁₁a₂</td>
<td>$\alpha_2(\beta$-G-6-P)$_2$</td>
<td>Glucose-6-phosphate</td>
<td>&lt;1%</td>
</tr>
<tr>
<td>HbA₁₁b</td>
<td>?</td>
<td>?</td>
<td>&lt;1%</td>
</tr>
<tr>
<td>HbA₁₁c</td>
<td>$\alpha_2(\beta$-G)$_2$</td>
<td>Glucose</td>
<td>&lt;4%</td>
</tr>
<tr>
<td>HbA₁₁d</td>
<td>?</td>
<td>?</td>
<td>traces</td>
</tr>
<tr>
<td>HbA₁₁e</td>
<td>?</td>
<td>?</td>
<td>traces</td>
</tr>
</tbody>
</table>
Haemoglobin $A_{1c}$

*Reference values 28 – 40 (95 % interval)*

<table>
<thead>
<tr>
<th>DM compensation</th>
<th>Values given by IFCC applicable from 1. 1. 2004</th>
</tr>
</thead>
<tbody>
<tr>
<td>excellent</td>
<td>&lt; 45</td>
</tr>
<tr>
<td>good</td>
<td>45 – 60</td>
</tr>
<tr>
<td>bad</td>
<td>&gt; 60</td>
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</table>
Endocrinology of reproduction
Female hormonal system

Gonadotropic hormones

FSH
LH
prolactin
Female hormonal system

Gonadotropic hormones

FSH

function: follicles growth, stimulation of estrogens secretion

structure: proteohormon, 207 amino acids, subunits alpha and beta

Lab assessment: immunoanalysis
Female hormonal system

Gonadotropic hormones

LH

function: peak precedes ovulation, afterwards stimulation of both estrogen and gestagen secretion

structure: proteohormon, 205 amino acids, alpha and beta subunits

lab: immunoanalysis
Female hormonal system

Gonadotropic hormones

**prolaktin**

function: mainly milk production, acts also on ovaries

structure: proteohormon, 198 amino acids, 1 band

lab: immunoanalysis
Female hormonal system

Native estrogens

structure: 18C steroids
aromatic A circle

lab: immunochemistry
Female hormonal system

Native estrogens

estrone 17β-estradiol estriol (−3, 16α, 17β)
Female hormonal system

Native gestagens

structure: 21C steroids

Lab: immunochemistry
Native gestagens
ERROR: stackunderflow

OFFENDING COMMAND: ~

ERROR: stackunderflow