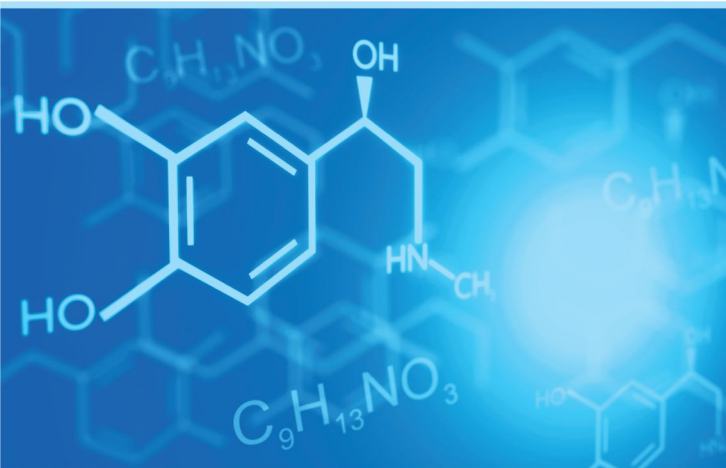


MEDICAL BIOCHEMISTRY

FOR STUDENTS OF GENERAL MEDICINE

Lecture notes



Gustáv Kováč, Anna Porubenová
Katarína Černá, Tatiana Bulíková



MEDICAL BIOCHEMISTRY

FOR STUDENTS OF GENERAL MEDICINE

Lecture notes

**Gustáv Kováč, Anna Porubenová
Katarína Černá, Tatiana Bulíková**

RAABE

Dr. Josef Raabe Slovakia, s.r.o

Professional publishing

A member of the KLETT group

Heydukova 12 – 14, 811 08 Bratislava

Phone: 02/32 66 18 40

E-mail address: raabe@raabe.sk

www.raabe.sk

Executive Director: Mgr. Miroslava Bianchi Schrimpelová

Copyright:

© Dr. Josef Raabe Slovakia, s. r. o., 2018

© Authors

All rights reserved.

No part of this work may be reproduced or transmitted in any form or by any means, electronic or mechanical, including photocopying, uploading or any available transfer of information without permission of the publisher Dr. Josef Raabe Slovakia, s. r. o.

Authors:

prof. MUDr. RNDr. Gustáv Kováč, CSc., MBA., MUDr. Anna Porubenová, MPH.,
MUDr. Katarína Černá, MBA., MPH., MHA., MUDr. Tatiana Bulíková PhD.

Institute of Chemistry, Clinical Biochemistry and Laboratory Medicine, SZU.

Project managers: Mgr. Monika Šerá, Ing. Vladimír Hudák

Graphic designer: Lucia Horineková

Photos on the title: Pixabay

Year of publication: 2018

ISBN: 978-80-8140-358-3

PREFACE

Medical biochemistry is not about chemical patterns or about metabolic pathways, but mainly about biochemical thinking: looking at the human body in health and disease from the molecular angle of vision. Anatomy deals with organs, histology with tissues, physiology with functions. Knowledge from these disciplines is a prerequisite for teaching medical biochemistry that unifies anatomical, physiological and histological knowledge by translating them into a common language of molecules.

We have divided the content into four parts: „Substances“ (molecules), „Metabolism“, „Biochemistry of organs and functions“ and „Biochemistry of systems and processes“.

Each part consists of ten chapters and each chapter of six subchapters: „Introduction“ (which describes the topic of the chapter's focus), „Biochemical Principles“ (viewing the subject of the chapter from the point of view of molecules), „Clinical Context“ (examples demonstrating the use of biochemical principles in clinical practice), „Remember“ (a summary of biochemical principles), „Realize“ (a summary of clinical examples), „Formulas and Schemes“ (the minimum of the formulas and schemes necessary to understand the problem).

The text is written in the form of lecture notes: it is intended to help the student to recall the lectures and impressions of lectures as easy as possible and also as a tool for the promotion of biochemical thinking. That is why the text is structured as strictly as it can be: subchapters: „Introduction“, „Remember“, „Realize“ use the hierarchy of bold and italics directly in the text, subchapters „Biochemical Principles“ and „Clinical Context“ also use the gray band on margins (marginalia), where the headings are placed to indicate the „focus“ of the information. The text in the subchapters is not fluent but in the form of bullets and points: the idea is to emphasize the basic idea that needs to be focused and to avoid dispersion and distraction: these are the main obstacles to understanding the essence and development of biochemical thinking.

A Chinese saying is: I listen and forget, I watch and remember, I do and I understand. That is our approach. The aim of our lectures is to get acquainted with the issue: you listen to the lecture and forget about it. The aim of the lecture notes is to recall a lecture: if you look at the text repeatedly, you remember it. There is also something to be done: look into other textbooks and monographs, to attend laboratory classes and confront what you remember with what you did: you will understand. Knowledge itself does not come into the head: it requires an effort and an active approach. We wish you a lot of interest, zest and perseverance.

In conclusion, we would like to thank Ms. Ľubica Kováčová for language editing, Mgr. Monika Šerá and Ing. Vladimír Hudák from publishers Dr. Josef Raabe for technical and editorial support. It was a pleasure to work with them.

Authors

PREFACE	3
OBSAH	4
I BIOCHEMISTRY OF SUBSTANCES	
1. Notes to the Biochemistry of Proteins	5
2. Notes to the Enzymes	9
3. Notes to the Carbohydrates	14
4. Notes to the Cholesterol	18
5. Notes to the Nucleic Acids	23
6. Notes to the Hemoglobin and Myoglobin	31
7. Notes to the Lipids and Lipoproteins	36
8. Notes to the Vitamins and the Trace elements	43
9. Notes to the Complex Lipids	49
10. Notes to the Complex Saccharides	53
II TRANSFORMATION OF SUBSTANCES	
11. Notes to the Glycolysis and Pentose Cycle	57
12. Notes to the Gluconeogenesis and Glycogen Metabolism	61
13. Notes to the Lipolysis	67
14. Notes to the Lipogenesis	72
15. Notes to the Metabolism of Amino Acids	77
16. Notes to the Krebs Cycle	83
17. Notes to the Bioenergetics	87
18. Notes to the Metabolism of Fuels	93
19. Notes to the Neurotransmitters	99
20. Notes to the Metabolism of Nucleotides	104
III BIOCHEMISTRY OF ORGANS AND FUNCTIONS	
21. Notes to the Extracellular Matrix	108
22. Notes to the Membranes	112
23. Notes to the Gastrointestinal Tract	117
24. Notes to the Biochemistry of the Blood	122
25. Notes to the Biochemistry of the Liver	126
26. Notes to the Biochemistry of the Endocrine System	132
27. Notes to the Biochemistry of the Bone	138
28. Notes to the Biochemistry of the Muscle	144
29. Notes to the Biochemistry of the Nervous System	149
30. Notes to the Biochemistry of the Kidney	154
IV BIOCHEMISTRY OF SYSTEMS AND PROCESSES	
31. Notes to the Acid Base Balance	162
32. Notes to the Recombinant DNA	166
33. Notes to the Biochemistry of the Gene Expression	172
34. Notes to the Biochemistry of the Hemostasis and Thrombosis	176
35. Notes to the Biochemistry of the Proteosynthesis	182
36. Notes to the Biochemistry of the Immunity	186
37. Notes to the Biochemistry of the Antioxidative Protection	193
38. Notes to the Biochemistry of the Biosignalling	197
39. Notes to the Biochemistry of Aging	200
40. Notes to the Biochemistry of the Cancer	203
EPILOGUE	207

1. NOTES TO THE BIOCHEMISTRY OF PROTEINS

1.1 Introductory Notes

Proteins

- polymers of aminoacids
- main structural and functional elements of living organism
- metabolism
- transport
- structure of tissues and organs

Aminoacids

- 300 aminoacids
- only 20 of them in the human body

1.2 Notes of the Biochemical Principles

Structure and stereochemistry

Alpha carbon substituents

- carboxyl group
- amino group
- hydrogen
- side chain

Classification of Aminoacids

Based on Chemical Structure

- Aliphatic (glycine)
- Aromatic (phenylalanine)
- Neutral (serine)
- Acidic (asparagin)
- Basic (lysine)
- Sulphuric (cystein)
- Imino amino acids (prolin)

Amphophatic/amphibic molecules

- contain at the same time the basic and the acidic groups

Titration curve

- demonstrates the equivalency of titration reagent to the titration progress/process from pH 0 to pH 12

Dissociation

- amino and carboxy groups dissociate in dependency on pH

Buffers

- concentration is possible to calculate according the Henderson – Hasselbalch equation

Definition

Macromolecules

- polymers of aminoacids bound by peptid bond

Structure

Primary structure

- aminoacid sequence

Secondary structure

- geometry of peptidic bond
- alphahelix: peptidic bond rotates
- folded sheet: peptic bond does not rotate

Aminoacids

Proteins

Tertiary Structure

- three dimensional space arrangement

Ternary Structure

- mutual arrangement of subunits with tertiary structure

Methodology

- Ammonium Sulphate
- Dialysis, Ultrafiltration, Gel Filtration
- Exchange Chromatography
- Affinity Chromatography
- Electrophoresis
- Edman Degradation (Aminoacid Sequence)
- X Ray Diffraction
- MALDI TOF
- SELDI TOF

1.3 Notes to the Clinical Context**Non Protein Aminoacids***Some aminoacids*

- which are not found in proteins
- represent biologically important intermediates
- citrulline (urea cycle)
- creatinine (muscle metabolism)

Glutathion*Tripeptide*

- which is present in the cells in high concentration
- antioxidant defense

Collagen*Collagen*

- contains glycine, alanine and hydroxyproline
- polymerised in left oriented alpha helix
- represent the most wide spread protein family
- 1/3 of body weight represent collagen molecules

Posttranslational Modifications*The most common reaction:*

- Glycosylation
- Phosphorylation
- Amidation
- Sulphatation
- Acetylation
- Disulphidic bonds

Creutzfeldt – Jacob Disease*Demmition*

- caused by prions
- brain neurodegeneration
- amyloid encephalopathy

Prions

- abnormal proteins
- protein isoforms coded by host codon
- located in brain
- abnormal configuration of normally coded proteins

Stanley Prusiner

- Nobel Prize 1997

HPLC*High Performance Liquid Chromatography**Differentiation/division*

- according to the electrostatic load and hydrophobicity

Chromatographic column

- matrix of small round particles

Protein blend

- „flows through“ the column

Eluate is monitored by

- UV
 - fluorescence
- detector

1.4 Summary

There exist

- thousands of proteins in the human body cells

Each protein

- has its own structure and function

First step

- in proteins structure study there is division/dissociation/differentiation of proteins

There exist differences in

- solubility, electrostatic load, binding capacity: that is principle of chromatographic and electrophoretic techniques

It is possible

- to define the molecule mass by SDS PAGE electrophoresis

Primary structure

- is defined by hydrolysis

Higher structures

- are defined by X ray diffraction

1.5 Remember

After studying this chapter you should be able to define the importance of

- aminoacids not found in human body proteins

functions of

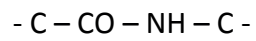
- glutathion
- collagens
- posttranslational modification of proteins

Importance of

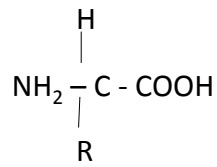
- Creutzfeldt – Jacob Disease
- HPLC

for clinical practice

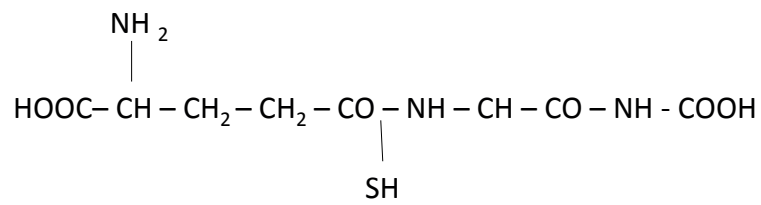
1.6 Formulas and Schemes



Peptidic Bond



Aminoacid



Peptide (Glutathion)

2. NOTES TO THE ENZYMES

2.1 Introductory Notes

Enzymes Characteristics

- all biological functions are mediated by chemical reactions which are catalyzed by enzymes
- metabolism is controlled and governed by metabolic routes
- enzymes catalyze biochemical reactions at neutral pH and 37 °C
- enzymes do not change chemical balance of reaction, they only decrease its activation energy

2.2 Notes to the Biochemical Principles

Factors influencing enzyme reactions

- temperature
- pH

Definition of the unit of enzyme activity

- catal = mol/s

Specificity of substrate

- active site

Prosthetic groups

- tightly bound to enzyme body

Coenzymes helper molecules

- soluble
- some of coenzymes need for their activity presence of double loaded cations
- not tightly bound to enzyme body

Classification

- oxidoreductases
- transferases
- hydrolases
- lyases
- ligases
- isomerases

Prerequisites

- $E + S \rightleftharpoons ES \rightleftharpoons E + P$
- $v = k \cdot ES$
- E, S and ES are all in the status of chemical balance
- there exist no other forms of enzyme: only E or ES,
- conversion $ES \rightarrow E + P$ is irreversible

Michaelis Menten Equation (MME) describes relationship between

- speed of the reaction
- and the concentration of the substrate

$$V = V_{\max} \cdot S / (K_m + S)$$

MME Equation has several modifications

- Lineweaver – Burk
- Eadie – Hofstede

Based on

- reaction speed
- and substrate concentration

Basics

Kinetics

it is possible to differentiate between

- competitive
- non competitive
- acompetitive

course of reaction catalysis.

Regulation of activity

Several levels of regulation

- gene expression
- enzyme (reversible/irreversible) inhibition
- allosteric modulation
- enzyme degradation by proteases

Proteolytic activity of digestive enzymes

- some enzymes are pooled as inactive zymogens

Zymogens are via proteolysis transformed to active forms like

- trypsinogen to trypsin
- chymotrypsinogen to chymotrypsin
- coagulation cascade
- fibrinolytic reactions

Allosteric regulation

Saturation

- is the prerequisite

Hyperbolic dependency

- allosteric enzymes show sigmoid shape of dependency
- allosteric effector molecule is bound on other site than active site

Homeotropic effect

- if substrate plays at the same time also the role of effector molecule

Heterotropic effect

- if substrate and effector molecule are different molecules,

Cooperativity (positive or negative)

- is the term which is used in connection with degree of affinity of the active site of the enzyme and that of the substrate

2.3 Notes to the Clinical Context

Tissue specificity of LDH

Lactat dehydrogenase (LDH)

2 subunits:

- H (heart)
- M (muscle)

LDH Isoenzymes

- LDH 1 = HHHH (heart)
- LDH 2 = HHMM (brain)
- LDH 3 = HMMM (liver)
- LDH 4 = MMMM (muscle)

Each isoenzyme is organ specific

Isoenzymes: glucokinase and hexokinase

Hexokinase

- catalyzes glucose phosphorylation

Glucokinase

- catalyzes the same reaction as hexokinase

The enzymes

- differ from each other by different balance constant

*That means for practice**Glucokinase*

- is active by higher concentration of glucose

Hexokinase

- phosphorylates by lower concentration of glucose

Differences

- play an important role by the regulation of glucose metabolism

In clinical laboratories

- is obviously used as indicator of the damage of different organs

Principle of clinical use

- enzyme is located in the cell
- if the organ/cell are damaged, enzyme is present in the extracellular fluid: that is the indication of organ damage

Enzymes

- are markers of organ damage

Renine

- catalyzes the conversion of angiotensin I to angiotensin II
- in the kidney

Angiotensin II

- is the most potent vasoconstrictor in the human body
- it causes retention of sodium

Inhibition

- of the angiotensin converting enzyme
- has very strong hypotensive effect

Captopril

- is an example of such an inhibitor and is used as a very effective hypotensive agent

Methanol intoxication

- is very dangerous
- (risk of blindness)

Clinical symptoms

- ebrietas (patient is drunken)
- blindness
- metabolic acidosis

Methanol

- is metabolised to formic acid:
- this reaction is catalysed by alcohol dehydrogenase

Formic acid

- is the direct cause of clinical symptoms and consequences

Drinking ethanol

- in the case of methanol intoxication is the therapeutic measure
- based on principle of competitive inhibition of the alcoholdehydrogenase

Measuring
the enzyme
activity

Angiotensin
converting
enzyme

Managing
methanol
intoxication

**Insecticides
intoxication***Organophosphates*

- develop inhibiting activity to acetylcholinesterase

Acetylcholin esterase

- plays an important role in acetylcholine metabolism and neuronal function

Inhibition of acetylcholin esterase

- develops the cumulation of acetylcholine
- and the prevalence of parasympathetic activity is the consequence (as acetylcholine is neurotransmitter of parasympathetic nervous system)

Atropine

- is used as antidotum

Penicillin*Penicillin*

- inhibits transpeptidase in the bacterial wall

Transpeptidase

- is an element present in the metabolic sequence of the bacterial wall synthesis

Penicillin

- acts as a strong bactericidal agent

Protein kinase A*Cyclic AMP*

- is second messenger in signalling pathways
- it is modulated by protein kinase A

Protein kinase A

- influences a lot of proteins
- which are phosphorylated via protein kinase activity
- to the different degree of each other

**Serpines
(Serine Proteases)***Specific serpin rest*

- creates catalytic centres for amino acid binding

That is used in activation of

- elastase
- trypsin
- and chymotrypsin

Hemophilia A*Hemophilia A*

- coagulation disease
- caused by inherited lack of coagulation factor VIII

Synthesis

- of coagulation factor VIII
- is determined by serine protease (serpin)

Enzyme insufficiency

- or its lack is the direct cause of the disease

2.4 Summary*All metabolic reactions*

- are catalyzed by enzymes

Catalytic activities of enzymes

- are strictly regulated by body temperature

Chemical bonds

- are effective tools of the regulation of enzyme activity

Influencing enzyme activity

- (activation or inhibition) is possible via different agents

One example of it

- represent allosteric agents

Enzyme kinetics

- helps in studying the mechanism of enzyme action

Measuring enzyme activity

- is an important clinical diagnostic tool

Uncontrolled and unregulated

- enzyme activity can lead sometimes to severe problems
- in the above mentioned case the enzyme inhibition is indicated

2.5 Remember**Examples as**

- tissue specificity of LDH
- glucose concentration dependency on glucokinase and hexokinase activity
- measuring enzyme activities as a diagnostic tool for organ damage indication
- using ACE inhibitors as a potent hypotensive agent
- mechanism of methanol intoxication management via ethanol competitive inhibition of alcohol dehydrogenase
- clinical role of serpins
- understanding the „enzyme“ basis of hemophilia A

illustrate the importance of the knowledge of enzyme biochemistry for clinical practice.

2.6 Formulas and Schemes

Enzyme Substrate EquaGon

$$V = k \cdot ES$$

EquaGon of the Speed of Enzyme Reaction

$$V = v \cdot S / K + S$$

Michaelis – Menten EquaGon

3. NOTES TO THE CARBOHYDRATES

3.1 Introductory Notes

Carbohydrate (s)

is the common name for

- a group of optical active polyhydroxyderivatives
- with the carbonyl functional group

They are present in

- living organisms and
- viruses
- (some of them however were synthesized out of them)
- represent so called primer metabolites

3.2 Notes to the Biochemical Principles

Function

Source of energy

- (glucose, glycogen)

Structural elements

- (cellulose, chitin)

Pool

- (starch in plants/glykogen in animals)

Component of molecules

- enzymes, nucleic acids

Components of structures

- membranes (glycoproteins, glycolipids)

Composition

Carbohydrates are organic compounds composited from

- carbon (C)
- hydrogen (H)
- oxygen (O)

Derivatives of carbohydrates may contain also

- phosphorus (P)
- nitrogen (N) or
- sulphur (S)

The name carbohydrates originates from three basic elements:

- carbon
- hydrogen and oxygen
- consolidated in the ratio: $C_n(H_2O)_n$

Formulas

Fischer's Formula

- according to Fischer, carbohydrates represent polyhydroxylated compounds: that represent Fischer's formula

Tollens Formula describes saccharides as heterocyclic compounds:

- by other investigations cyclic character of compounds was revealed: saccharides are heterocyclic compounds
- their creation was described as addition of carbonyl group to the last chiralic carbon so called hemiacetal reaction
- the last carbonyl binds four different functional groups: in that situation there exists no chirality but special cis or trans stereoisomerism or epimerism (alpha over/beta beneath) the virtual plan

- heterocycle with five elements is called furanosis, heterocycle with six elements is called pyranosis
- it is not very useful/practical

Haworth formula

- has view of substituted heterocycle
- its transformation is achieved by rewriting functional groups as on the right side over the virtual plan soon the left under the virtual plan

According to number of carbons

- trioses
- tetroses
- pentoses
- hexoses
- heptoses
- ect

According to functional group

- ketoses
- aldoses

Oligosaccharides categorisation

According to the number of monosaccharide units

- disaccharides (2 units)
- trisaccharides (3 units)
- ect

According to the free hemiacetal group

- reductive – free hemiacetal group – oxidation is possible
- non reductive – no free hemiacetal functional group – oxidation is impossible

Polysaccharides categorisation

Present

- in plants
- in organisms

3.3 Notes to the Clinical Context

Monosaccharides are simple carbohydrates – basic units of saccharides

- can develop polymers by chaining process from several monosaccharides
- have no color
- are soluble in water, not soluble in organic solvents
- have typical sweet taste

From chemical point of view

- polyhydroxyketones or polyhydroxyaldehydes
- functional keto or aldehyde group
- aldoses or ketoses with the same number of carbons have identical molecular but different structural formulas
- most important monosaccharide: glucose and fructose

Oligosaccharides

- are chains of monosaccharides built from two to ten units
- the monosaccharide units are bound by the glycosidic bond

The most important oligosaccharides

Disaccharides

- sucrose – (glucose + fructose)
- lactose – (galactose + glucose)
- maltose – (glucose + glucose)

Categories

Monosaccharides

Oligosaccharides

Polysaccharides*Trisaccharides*

- raphinose – (galactose + fructose + glucose)

Oligosaccharides

- inulins – contain 2 – 140 fructose units

Polysaccharides

- are polymers from the monosaccharides
- the chains contain large number of monosaccharide units
- building unit is mostly glucose

Chemical properties

- do not crystallize,
- not soluble in water
- develop colloidal solutions
- in acid environment or by the action of enzymes cleave to oligosaccharides and monosaccharides

Plant polysaccharides

- cellulose
- starch
- inulins
- pectins

Organism polysaccharides

- glycogen
- chitin
- hyaluronic acid
- heparin

3.4 Summary*The main function of saccharides is*

- a source of energy
- and structural element

Main elements of saccharides are

- carbon
- hydrogen
- and oxygen

Types of saccharides formulas

- Fischer
- Tollens
- and Haworth

Categorisation of saccharides is based

- either on number of carbon
- or on type of functional groups

3.5 Remember*Monosaccharides*

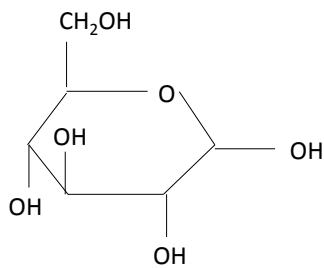
- have typical sweet taste

The most important oligosaccharides are

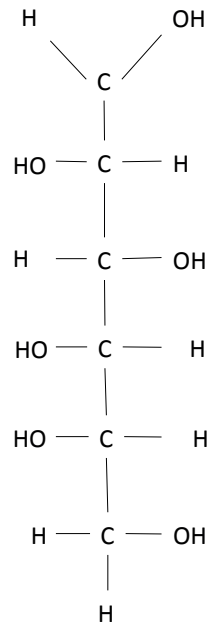
- sucrose
- lactose
- maltose

Polysaccharides

- do not crystalize
- are not soluble in water
- and develop colloidal solutions

3.6 Formulas and Schemes

Glucose
(Haworth Formula)



Glucose
Fischer Formula

4. NOTES TO THE CHOLESTEROL

4.1 Introductory Notes

Cholesterol

- is steroid (isoprenoid lipid) representing the essential component of cellular membranes in mammals
- it is also the precursor of bile acids, steroid hormones and vitamin D

Disturbances

- of cholesterol metabolism play important role in the pathogenesis of cardiovascular diseases and bile stones formation

Typical western diet

- contains in average 500 mg cholesterol daily – mainly in eggs, meat and dairy products
- approximately the same amount is synthesized de novo daily mainly in liver
- controlling cholesterol intake and influencing its biosynthesis play important role in prevention of cardiovascular diseases

4.2 Notes to the Biochemical Principles

Structure

Cycles

- three (3) six carbon
- one (1) five carbon cycles
- aliphatic side chain

Atoms

- 27 carbons
- one hydroxyl group
- one double bond

Molecule

- the molecule of cholesterol is planar

Biosynthesis

Starting point:

- Acetyl Coenzyme A

Second step

Mevalonic Acid synthesis

- from 3 Acetyl CoA molecules

Third step

Farnesylpyrophosphate is synthesized

- from three molecules of mevalonic acid (via isopentenylpyrophosphate and geranylpyrophosphate)

Fourth step

Squalen is synthesized

- from 2 farnesylpyrophosphate molecules
- Squalen represents a linear molecule with all prerequisites to form cyclic formation

Fifth step

Lanosterol

- squalen cyclisation to

Sixth step

Cholesterol

- lanosterol „polishing“ to cholesterol

Clue/main regulatory enzyme

- Hydroxy-Methyl-Glutaryl-Coenzym A-reductase (HMG CoA)

Regulation*Circadian rythm*

- peak of synthesis is achieved six hours after darkness, minimum of sythesis during the sun light exposition

Insulin and thriodethyronin

- increase in the activity of HMG CoA-reductase

Glucagon and cortisol

- decrease the activity of HMG-CoA-reductase

Membranes

- cholesterol is the main component of cellular membranes and maintains their fluidity
- there exist differences between different types of membranes (organelles, nucleus, cell)
- the highest concentration of cholesterol is in cellular membranes

Function*Precursor*

Cholesterol is precursor of

- *bile acids*
- *vitamin D*
- *steroid hormones*

Structure

- similar to *cholesterol*
- *in addition: COOH group + 24 carbons (more than 1 OH groups)*

Bile acids*Synthesis*

- in the *liver*
- main enzymes: *carboxylase, hydroxylase*

Function

- *fat emulgation* during the digestion process

Types

- *glycocholic* and *taurocholic* acid
- *deoxycholic* and *lithocholic* acid

Structure

- cholesterol is the precursor of steroid hormones

Hormones*21 carbons*

- progesteron
- cortizol
- aldosteron
- gestagens
- glucokroticoids
- mineralocortikoids

19 carbons

- testosteron

18 carbons

- estrogens
- estradiol

Biosyntheses

Conversion from cholesterol to steroid hormones:

Cortex

- glucocorticoids
- mineralocorticoids

Testes

- androgens

Ovarium

- esterogens
- gestagens

Clue enzyme:

- P 450-monoxygenase

Action and elimination

- nucleus receptors
- urin

Vitamin D₃*Delivery (cholecalciferol)*

- it develops from cholesterol in the Malpigi layer of *epidermis via nonenzymic photolysis*
- smaller part is supplemented via *food* intake (eggs, fish oil)

Transport

- from epidermis via plasma to organs (kidney)

Kidney

- *hydroxylation* catalyzed by cytochrom P 450-enzyme system to 1.25 dihydroxycholecalciferol (important in calcium metabolism regulation)

4.3 Notes to the Clinical Context**Regulation of metabolism***In general*

- activity modulation of clue enzyme
- *hydroxy-metyl-glutharyl-coenzyme A-reductase*

HMG CoA-reductase inhibitors*Statins*

- decrease cholesterol level up to 40%

Isolated

- from *Penicillium citrinum*

Trans-methyl-glutaconate bypass*Metabolic sequence*

- *conversion of mevalonic acid back to the acetyl coenzyme A*

Activated

- in the case of „higher metabolic priority“
- e.g.: if the *lack of fatty acids* jeopardizes the existence of human body

Bile stones*Characteristics*

- develop from *bile acids*
- 20% prevalence in *Caucasians*

Treatment

- surgical (*lithotripsy*)
- conservative: *solution* via bile acids