Integration of metabolism

Seminar No. 6

The first law of thermodynamics

Energy can be converted from one form to another, but cannot be destroyed.

In the interaction between a closed system and its surroundings, the internal energy change of the system (ΔU) equals the **heat** exchanged by the system (ΔQ) plus the **work** done on or by the system (ΔW).

$$\Delta U = \Delta W + \Delta Q = \textbf{work} + \textbf{heat}$$

Although work can be transformed completely into heat, it does not follow that heat can be transformed completely to work.

$\Rightarrow$ **heat is taken as a less utilizable form of energy**.

Transformation of energy in human body

energy input → chemical energy of nutrients

energy output → work + heat

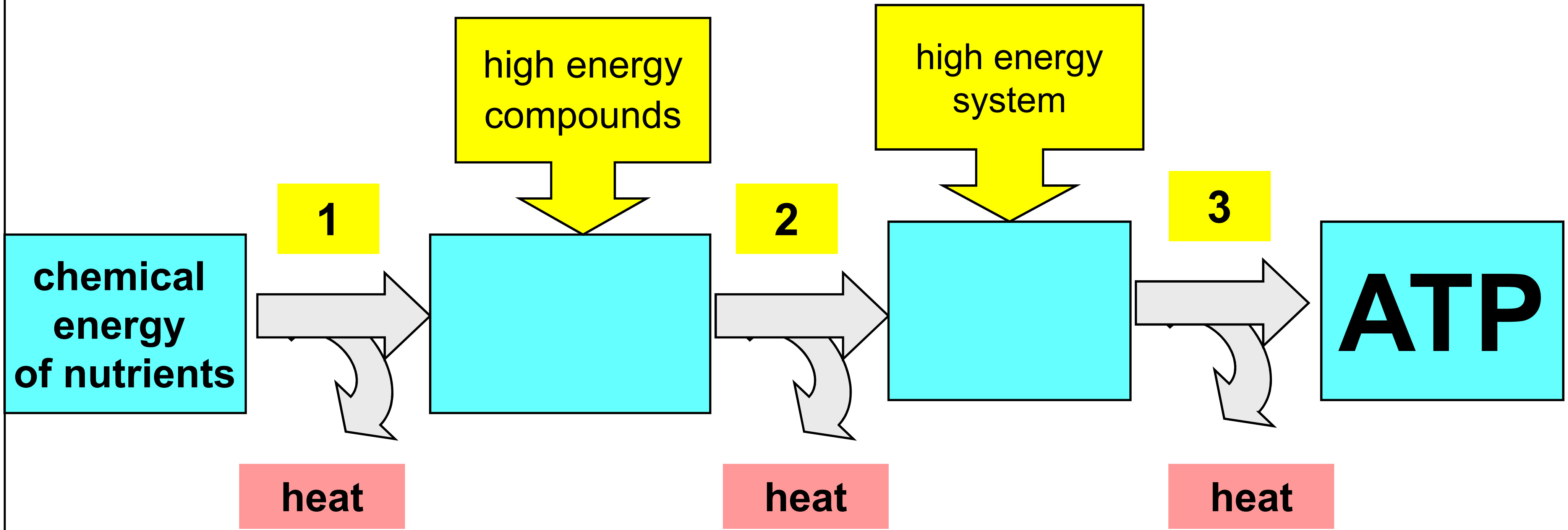
chemical energy of nutrients = **work** + **heat**

$$\text{energy of nutrients} = \underbrace{\textbf{BM + phys. activity + reserves}}_{\textbf{any work requires ATP}} + \textbf{heat}$$

BM = basal metabolism

Reserves = chemical energy of adip. tissue, liver/muscle glycogen, and cca ⅓ of muscle proteins

Energy transformations in the human body are accompanied with continuous production of heat

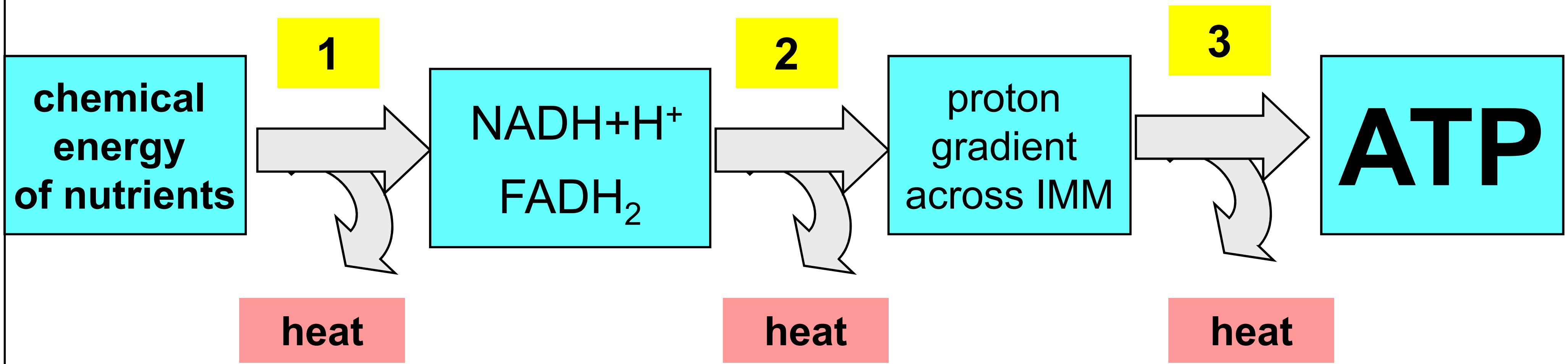


1 ....

2 ....

3 ....

Energy transformations in the human body are accompanied with continuous production of heat



1 .... metabolic dehydrogenations

2 .... respiratory chain = oxidation of reduced cofactors = reduction of O_2 to H_2O

3 .... aerobic phosphorylation ($ADP + P_i \rightarrow ATP$)

IMM .... inner mitochondrial membrane

Q. 2

A. 2

Basal metabolism is the amount of energy expended while at rest in a neutrally temperate environment, in the post-absorptive state (no digestion).

The release of energy in this state is sufficient only for the functioning of vital organs, such as the heart, lungs, brain.

Basal metabolism can be estimated from

body mass: 0.1 MJ / kg / day

body surface: 4.2 MJ / m^2 / day

Example: 70 kg $\Rightarrow$ BM = 0.1 $\times$ 70 = 7 MJ/day

Q. 3

Statement	**TRUE**	**FALSE**
Females have higher BM than males		
Fever increases BM		
Hyperthyreosis increases BM		
Pregnancy increases BM		
BM increases with age		

Statement	TRUE	FALSE
Females have higher BM than males		×
Fever increases BM	×	
Hyperthyreosis increases BM	×	
Pregnancy increases BM	×	
BM increases with age		×

Recommended intake of nutrients

Nutrient	Percentage of energy intake / day
Starch	
Lipids	
Proteins	

Recommended intake of nutrients

Nutrient	Percentage of energy intake / day	
Starch	55 - 60 %	
Lipids	$\leq$ 30 %	SAFA $\approx$ 5 % MUFA $\approx$ 20 % PUFA $\approx$ 5 %
Proteins	10 - 15 %	

Q. 5

1) BM of student calculated from body surface (MJ/d) =

2) output of student (between light work and medium hard work)

estimated from graph (MJ/d) ≈

3) total energy output in MJ/d =

4) total energy output in J/s (= in W)

A. 5

1) BM of student (MJ/d) $= 4.2 \times 1.73 =$ **7.266 MJ/d**

2) activity of student estimated from graph (MJ/d) $\approx$ **4 MJ/d**

3) total energy output in MJ/d $= 7.266 + 4 =$ **11.266 MJ/d**

4) total energy output in J/s =

$$11\,266\,000 \text{ J/day} = \frac{11266000}{86400} \text{ (J/s)} = 130 \text{ J/s} = \underline{\mathbf{130\ W}}$$

Body mass index

$$\mathrm{BMI} = \frac{\text{mass (kg)}}{[\text{height (m)}]^2}$$

BMI	**Classification**
< 16	severe underweight
16-20	underweight
20-25	**optimal weight**
25-30	light obesity
30-40	marked obesity
> 40	severe obesity

Energy reserves in adult man (70 kg)

Nutrient	**Tissue**	**Mass (g)**	**Energy (MJ)**
Glycogen	liver	70	1,2
Glycogen	muscle	120	2,0
Glucose	ECF	20	0,3
Lipids	adip. t.	15 000	**570**
Proteins	muscle	6 000	102/3=34

Q. 6

energy stores =

$$\text{survival time} = \frac{\text{energy available}}{\text{BM}}$$

A. 6

Energy stores: (data from table p. 2)

$1.2 + 2.0 + 0.3 + 570.0 + 34.0 =$ **607.5 MJ**

1/3 of total muscle reserve

BM = 7 MJ/d

$$\text{survival time} = \frac{607.5(\text{MJ})}{7(\text{MJ/day})} = \underline{\textbf{86.8 days}}$$

Metabolic process	**Insulin**	**Glucagon**	**Adrenaline**	**Cortisol**
Gluconeogenesis				
Glycolysis in liver				
Glycolysis in muscle	↑	-		
Glycogenolysis in muscle	-	-		
Glycogenolysis in liver				
Glycogenesis liver + muscle				
Lipolysis in adipocytes				
Lipogenesis in liver/adip.t.	↑			
Cholesterol synthesis	↑	↓		
Proteosynthesis		-		
Proteolysis in liver		↑		
Proteolysis in muscles	-	-		

Metabolic process	Insulin	Glucagon	Adrenaline	Cortisol
Gluconeogenesis	↓	↑	↑	↑ (AA)
Glycolysis in liver	↑	↓	↓	-
Glycolysis in muscle	↑	-	↑↑↑	-
Glycogenolysis in muscle	-	-	↑↑↑	-
Glycogenolysis in liver	↓	↑	↑↑↑	-
Glycogenesis liver + muscle	↑	↓	↓↓	↑
Lipolysis in adipocytes	↓	↑	↑↑↑	↑
Lipogenesis in liver/adip.t.	↑	↓	↓	↓
Cholesterol synthesis	↑	↓	↓	↓
Proteosynthesis	↑	-	-	↑liver, ↓other
Proteolysis in liver	↓	↑	↑	↓
Proteolysis in muscles	-	-	↑	↑

no action on muscles

Basic facts on metabolism

- ATP is immediate source of energy in cells
- ATP is derived from metabolic oxidation of nutrients: glycolysis + β-oxidation of FA $\rightarrow$ acetyl-CoA $\rightarrow$ CAC $\rightarrow$ resp. chain $\rightarrow$ ATP
- ATP and glucose levels in body have to be reasonably constant
- glucose is necessary for brain and RBC
- **glucose is necessary for utilization of lipids for energy**: Glc $\rightarrow$ pyruvate $\rightarrow$ oxaloacetate $\rightarrow$ CAC
- glucose cannot be made from FA

Relationships between nutrients

!

glucose → lipids ✓

FA $\not\to$ glucose (PD reaction is irreversible)

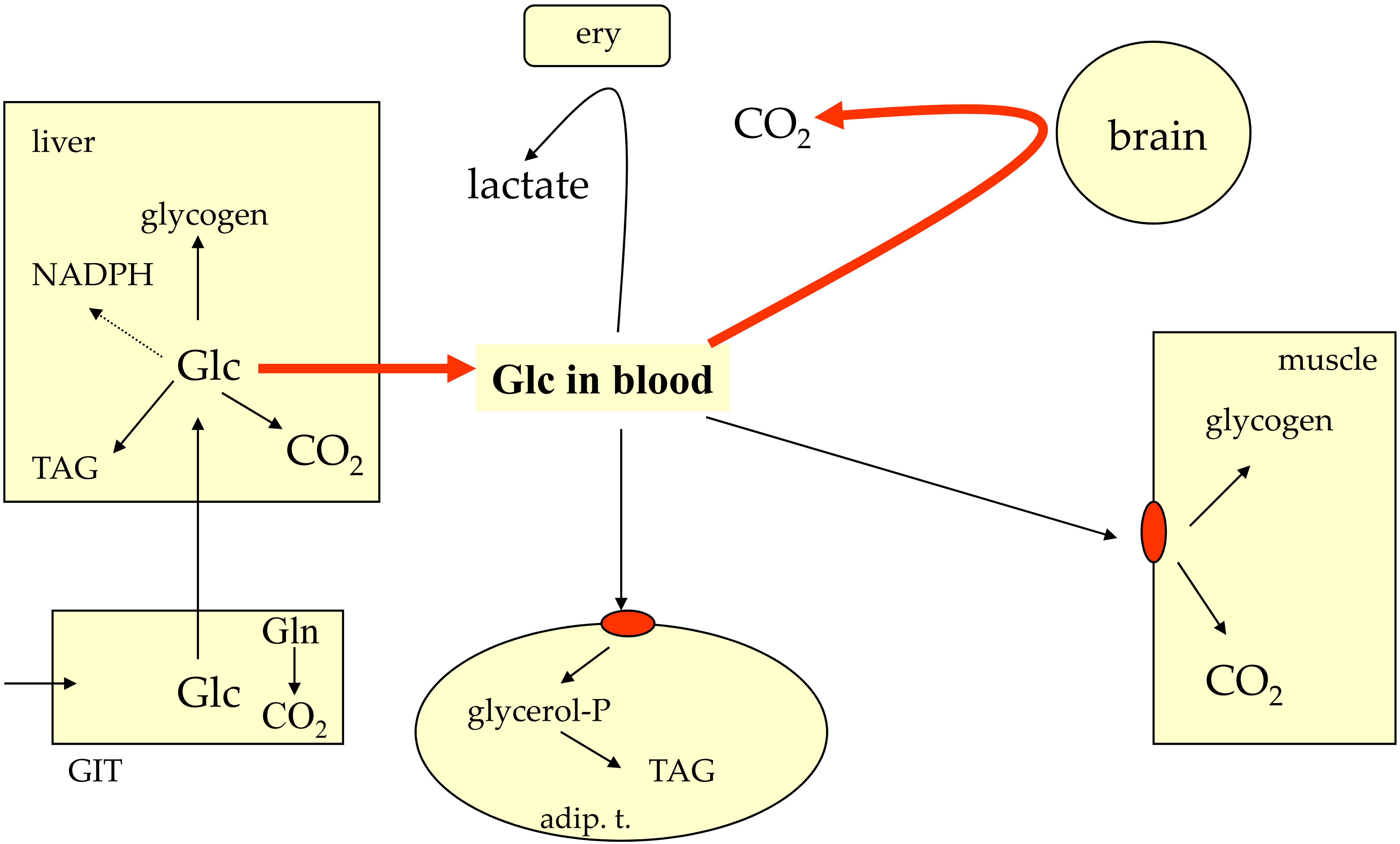
glucogenic AA → glucose ✓

Glc (pyruvate, CAC intermed) → C skeleton of non-essential AA ✓

AA → lipids ✓

lipids $\not\to$ AA (most ketogenic + mixed AA are essential)

Saccharides after meal (insulin)



GLUT 4 insulin dependent transporter

Glucose (Glc) in liver after meal

- Glc → glycogen
- Glc → pyruvate → acetyl-CoA → CAC → energy
- Glc → pyruvate → acetyl-CoA → FA → TAG (VLDL)
- considerable amount of Glc just passes through into blood
- small portion of Glc is converted into specialized products (pentoses + NADPH, galactose, glucuronate)
- excess of Glc → lipids (VLDL) → blood → adipose tissue → obesity

Glc in other tissues after meal

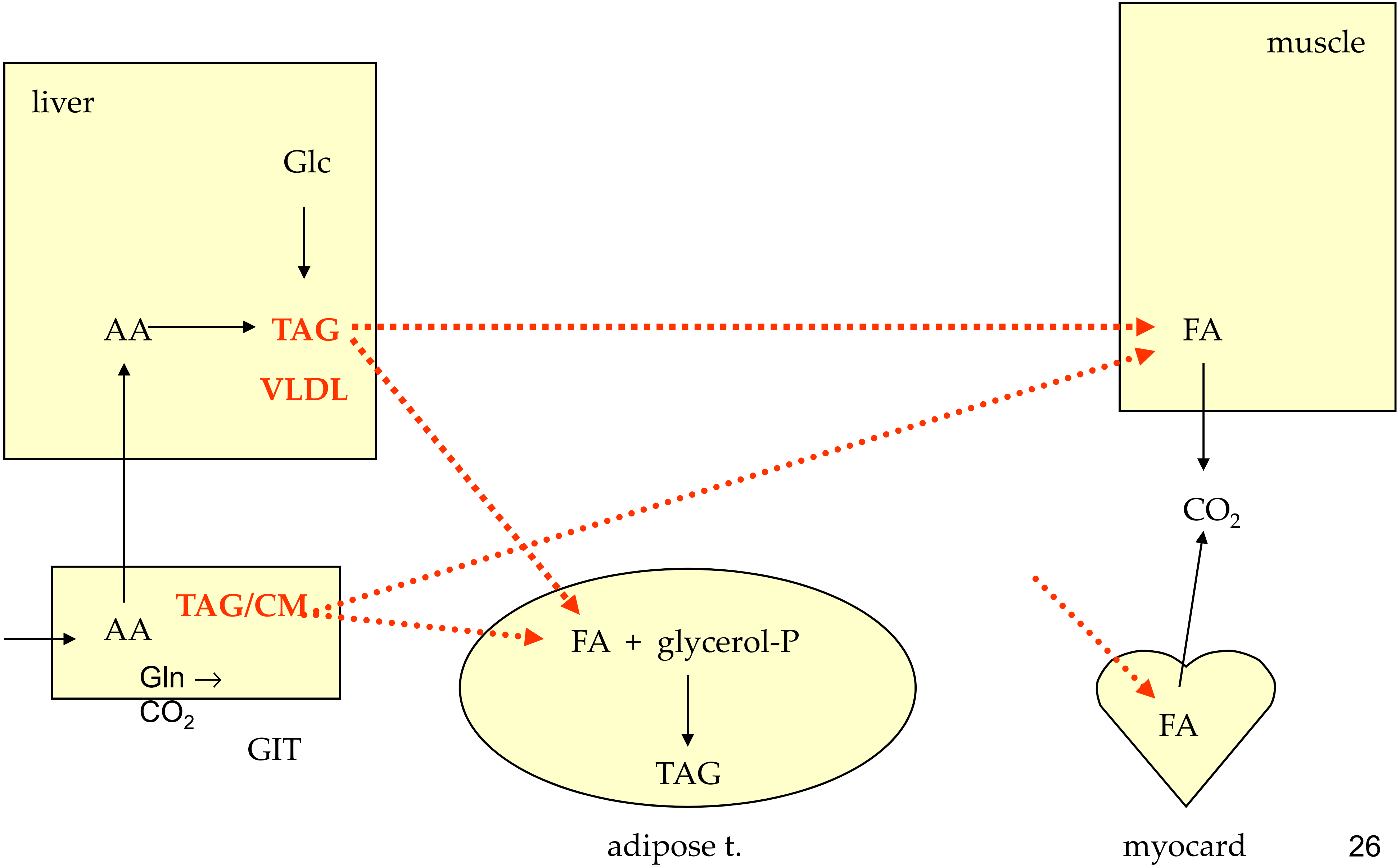
- Glc is the only fuel for RBC (anaerobic glycolysis)
- Glc is prominent fuel for brain (aerobic glycolysis)
- Glc is source of energy + reserves (glycogen) in muscles
- Glc is source of glycerol-3-P for TAG synthesis in adip. tissue

Glc $\rightarrow$ glyceraldehyde-3-P + DHAP

$\downarrow$ Reaction type?

glycerol-3-P

Lipids after meal (insulin)



Lipids after meal

- Exogen. TAG (CM) and endogen. lipids (VLDL) supply peripheral tissues (muscles, myocard, kidney, adip. t.)
- FA are released from TAG by the action of LPL
- FA are fuel for muscles

  FA $\rightarrow$ acetyl-CoA $\rightarrow$ CAC $\rightarrow$ CO_2 + energy
- In adipose tiss., FA are substrates for TAG synthesis

Q. 8

A. 8

- Glc is metabolic fuel in most tissues:
- ERCS + brain (exclusively in well-fed state)
- muscles + adipose tissue + some other ...

- insulin stimulates the exposition of GLUT4 in muscles and adipose tissue cell membranes
- Glc can massively enter these organs

Q. 10

A. 10

1. Glc is the source of **energy** (aerobic glycolysis)
2. Glc is the source of **NADPH+H$^+$** for FA synthesis (pentose cycle)
3. Glc is the source of **glycerol-3-P** for TAG synthesis

glycerol-3-P $\rightarrow$ 1-acylglycerol-3-P $\rightarrow$ 1,2-diacylglycerol-3-P $\rightarrow$

1,2-diacylglycerol $\rightarrow$ TAG

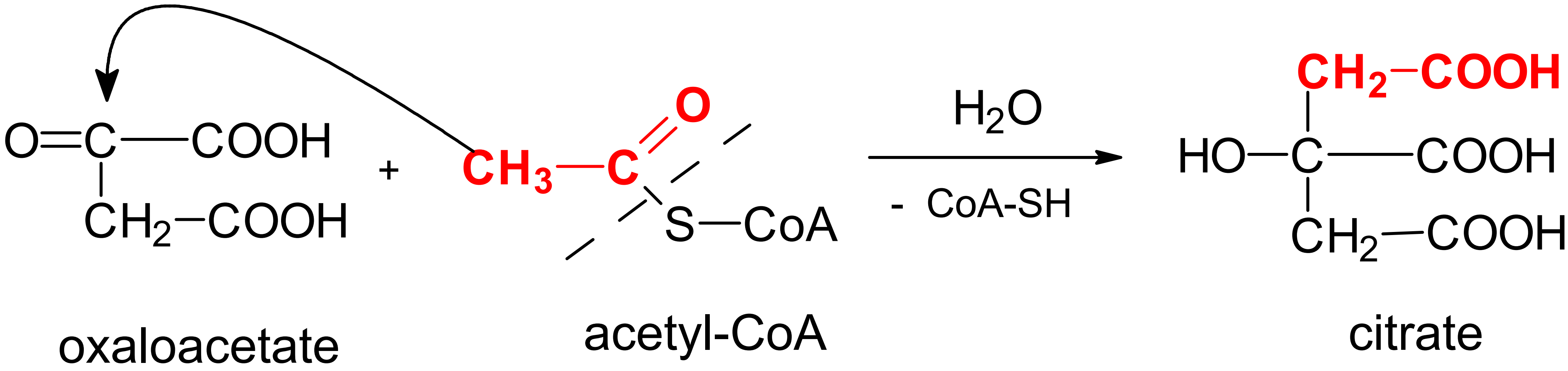
Q. 11

A. 11

- **Glc** $\rightarrow$ 2 pyruvate (aerobic glycolysis)
- pyruvate $\rightarrow$ acetyl-CoA (oxidative decarboxylation)
- acetyl-CoA + CO_2-biotin $\rightarrow$ malonyl-CoA (activation)
- [malonyl-CoA + acetyl-CoA]$_{nx}$ $\rightarrow \rightarrow$ **FA**

Q. 12

A. 12 in the form of citrate: condensation of oxaloacetate with s acetyl-CoA



Q. 13

A. 13

- LPL – lipoprotein lipase
- Insulin is the inducer of LPL synthesis

Q. 14

Why are KB **not** made after meal?

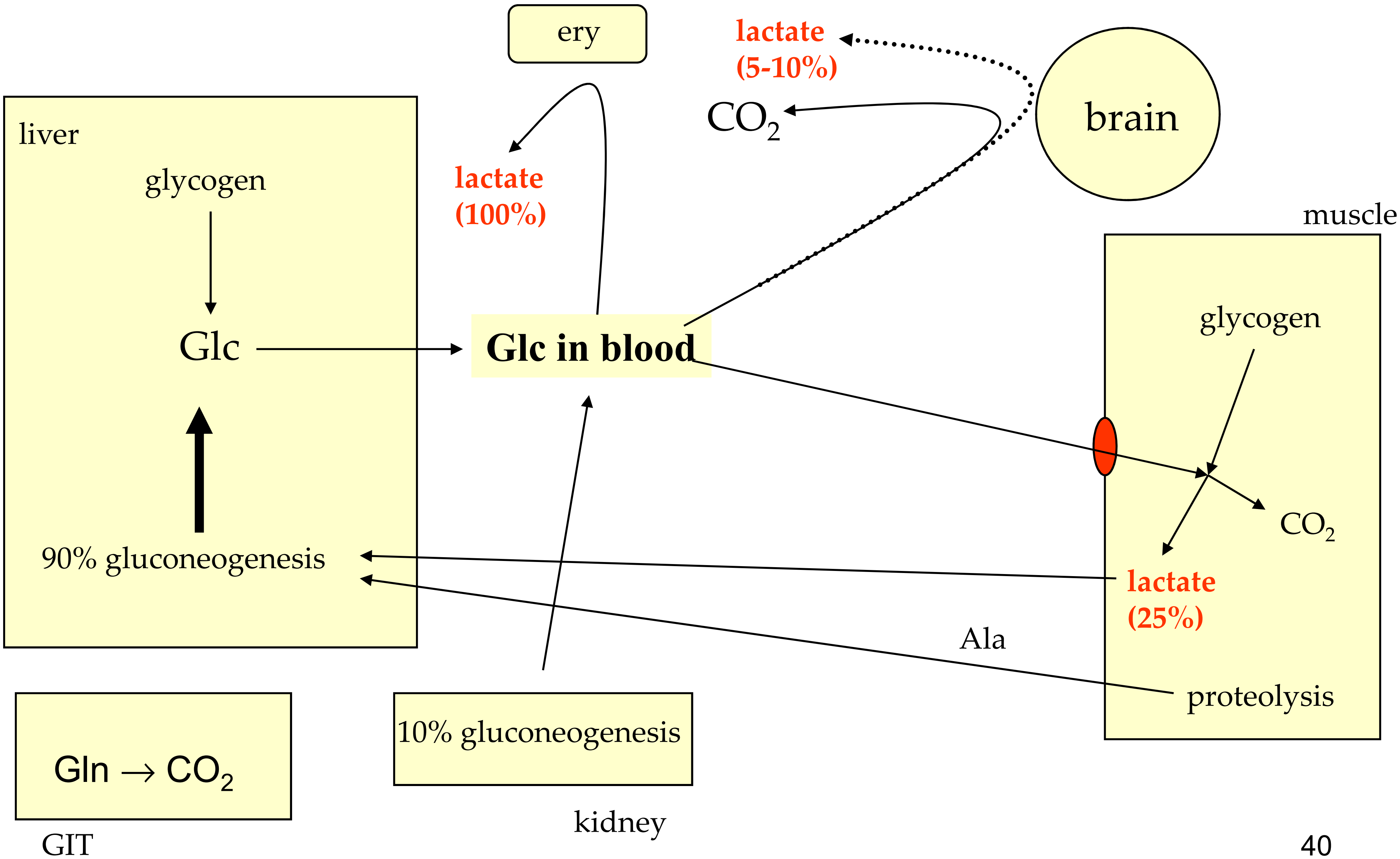
A. 14

- there is not enough substrate for KB synthesis

- insulin has **anti-lipolytic action**

  $\Rightarrow$ not enough FA and acetyl-CoA

Saccharides in fasting (glucagon)



Glucose in fasting (glucagon)

- blood Glc level is maintained by two processes:
- **(1) liver glycogenolysis**

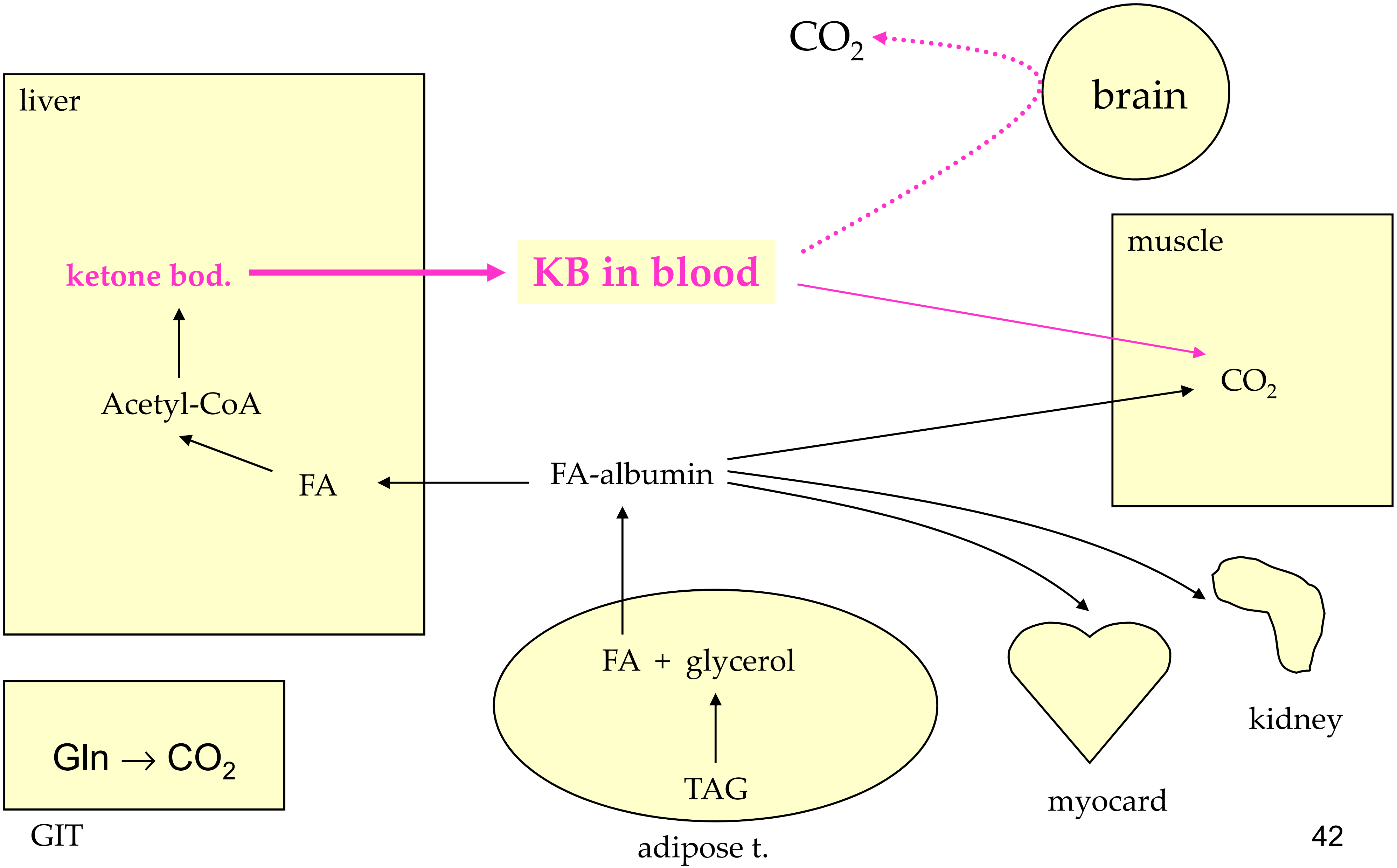
$$(\mathrm{Glc})_n + P_i \rightarrow (\mathrm{Glc})_{n-1} + \text{Glc-1-P}$$

$$\text{Glc-1-P} \downarrow$$

$$\text{Glc-6-P} \rightarrow \text{free glucose}$$

- **(2) liver gluconeogenesis** from lactate, AA, glycerol

Lipids in fasting (glucagon)



Q. 17

A. 17

- glucagon stimulates lipolysis in adip. tiss. (HSL)

  TAG $\rightarrow$ 3 FA + glycerol

- FA are released to blood, bound to albumin, and trasferred to

  muscles ($\rightarrow$ CO_2 + energy)

  to liver ($\rightarrow$ partly CO_2 + energy for liver, partly KB for export)

- KB are metabolic fuel for muscles and partly for brain

Q. 19

A. 19

mostly branched AA – Val, Ile, Leu

Q. 21

A. 21

Alanine, glutamine

Originate from:

- Muscle proteolysis $\rightarrow$ alanine + glutamine
- Transamination of pyruvate $\rightarrow$ alanine
- Ammonia detoxication $\rightarrow$ glutamine

Q. 22

A. 22

in muscles + brain, glycolysis is partly anaerobic

Glc (6C) $\rightarrow$ 2 lactate (3C) ...... **recycling three carbon atoms**

the body starts to save glucose

Q. 23

Compare two different degradation processes

Feature	Glycogen	Starch
Where in body		
Enzyme		
Reagent		
Type of reaction		
Product		

Compare two different degradation processes

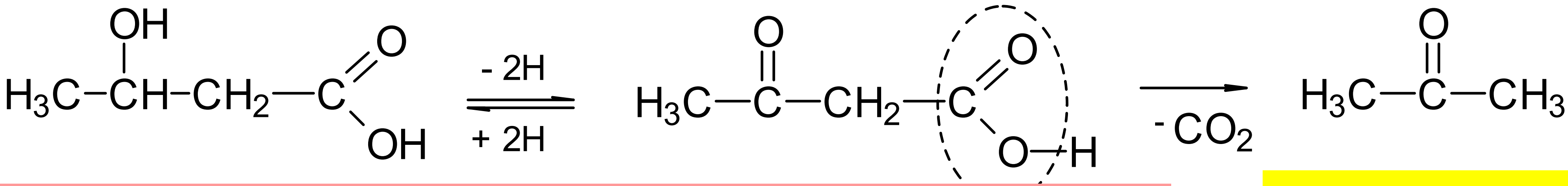
Feature	**Glycogen**	**Starch**
Where in body	liver / muscles	intestine
Enzyme	glycogen phosphorylase	pancreatic amylase
Reagent	P_i	H_2O
Type of reaction	phosporolysis	hydrolysis
Product	glucose-1-P	maltose

Q. 28

A. 28

- KB are produced only in **liver** from acetyl-CoA
- the metabolic cause:

  the shortage of oxaloacetate and excess of acetyl-CoA



β-hydroxybutyric acid

weak electrolyte

acetoacetic acid

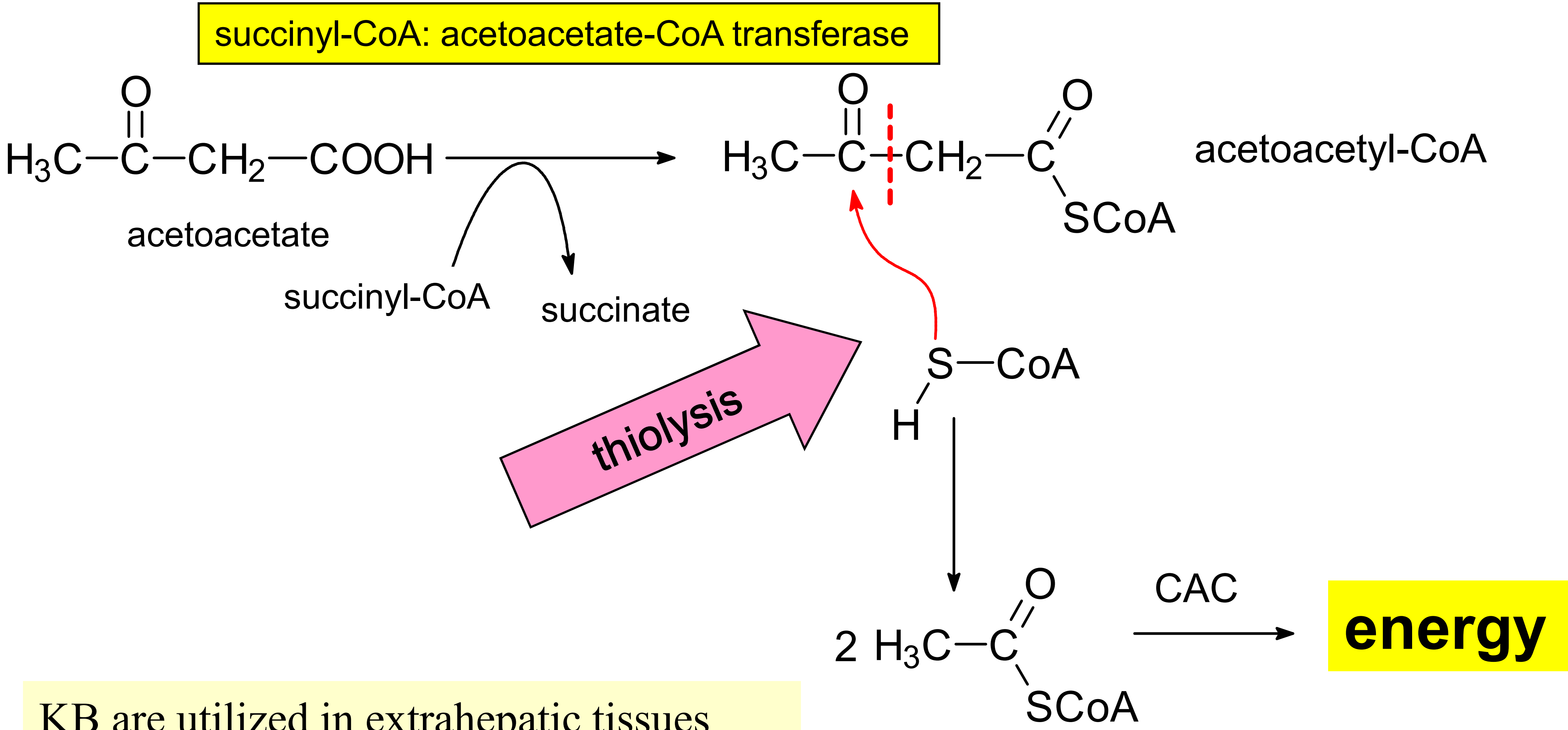
weak electrolyte

acetone

non electrolyte

Q. 29

A. 29



KB are utilized in extrahepatic tissues

not in liver

Q. 30

A. 30

succinyl-CoA: acetoacetate-CoA transferase

does not occur in the liver

Q. 31

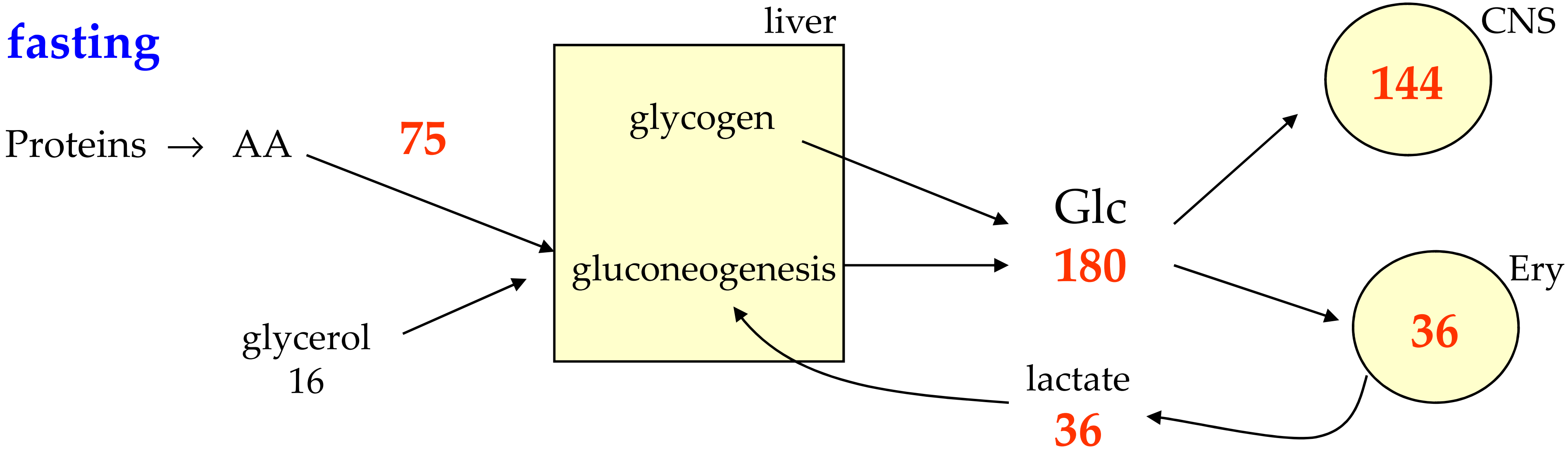
A. 31

KB ..... small soluble molecules, enter brain

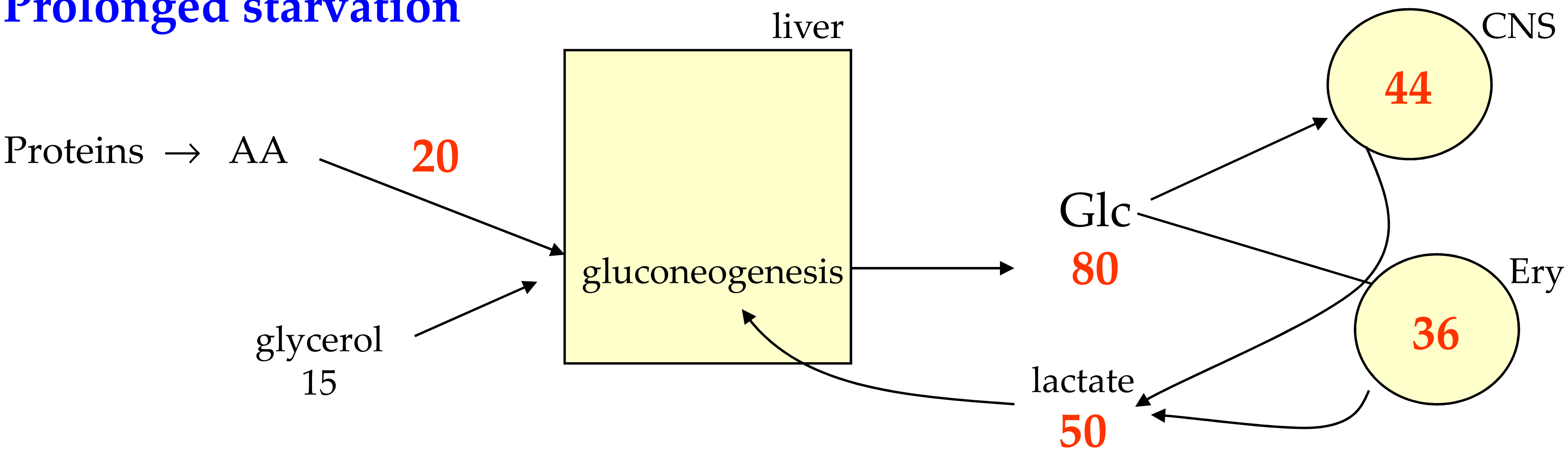
FA .... big molecules, cannot get across blood-brain barrier

Metabolic turn-over of saccharides in fasting (g/d)

Early fasting

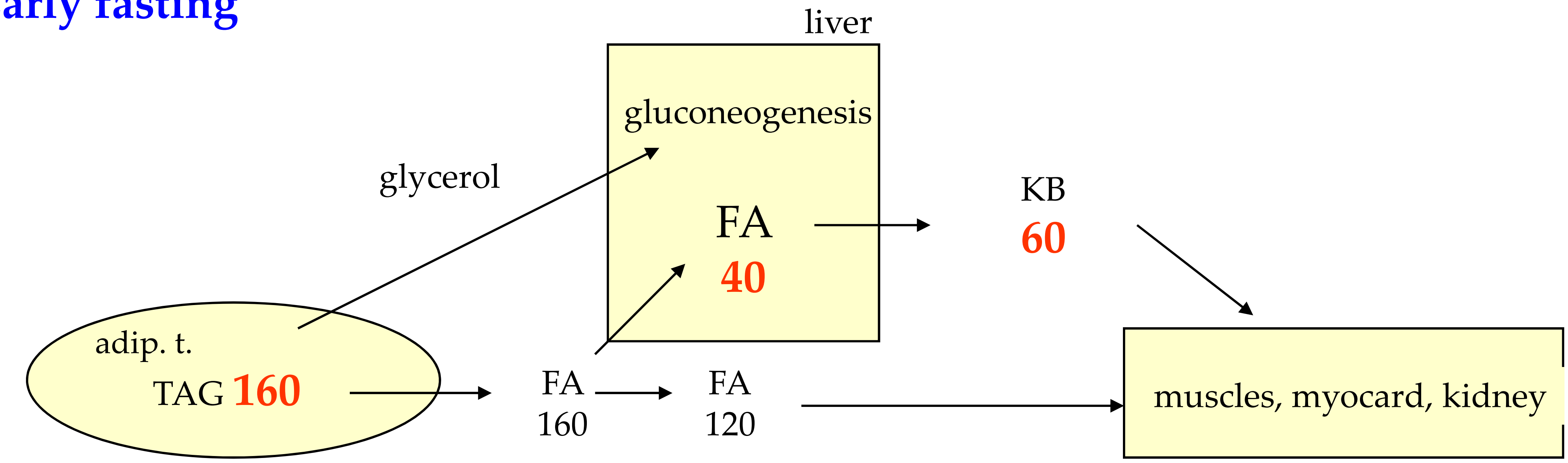


Prolonged starvation

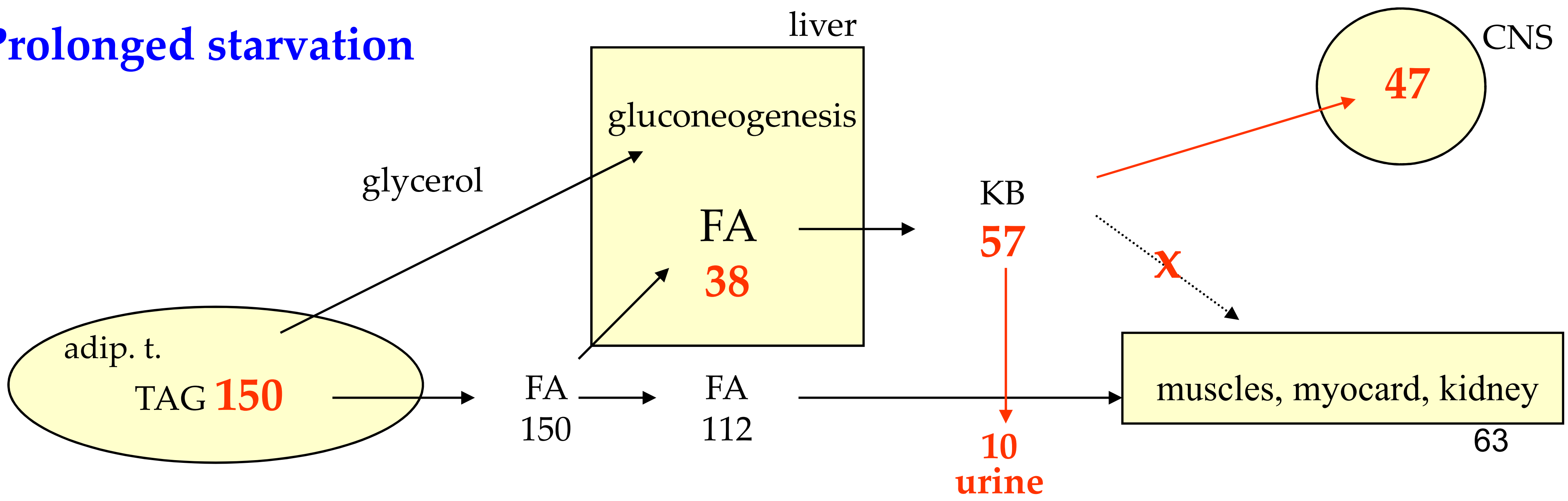


Metabolic turn-over of lipids in fasting (g/d)

Early fasting



Prolonged starvation



Q. 32

A. 32

- muscle proteolysis: 75 $\rightarrow$ 20 g/d $\Rightarrow$ decreases
- liver gluconeogenesis: 180 $\rightarrow$ 80 g/d $\Rightarrow$ decreases
- lipolysis: 160 $\rightarrow$ 150 g/d $\Rightarrow$ approx. the same
- KB production: 60 $\rightarrow$ 57 g/d $\Rightarrow$ approx. the same (dif. utilization)
- energy for brain: Glc (44 g/d) + KB (47 g/d)
- energy for muscle: FA

Q. 33

A. 33

1. sparing glucose
2. sparing proteins

Q. 36

A. 36

1. The capacity of brain to utilize KB is limited
2. The protection of body against excessive acidification of internal environment

Q. 37

A. 37

the accumulation of acetoacetate and β-hydroxybutyrate

anions in ECF leads to the decrease of main buffer base [HCO_3^-]

$\Rightarrow$ decrease of pH $\Rightarrow$ **metabolic acidosis (ketoacidosis)**