Metabolic relationships

Seminar No. 5

- Chapter 16 -

Transformation of energy in human body

energy input = chemical energy of nutrients = work + heat

energy of nutrients = BM + phys. activity + reserves + heat

work

BM = basal metabolism

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

Basal metabolism depends on

- sex (in females by cca 10 % lower)
- age (diminishes with age)
- body temperature (increase by 1 °C increases BM by 12 %)
- hormones thyroxine, adrenalin - increase BM
- long-term starvation – BM goes down (lowering diets, anorexia nervosa)

BM estimation (see p. 90)

4.2 MJ / m^2 / day

0.1 MJ / kg / day

Energy expenditure in various conditions (MJ/day)

BM - anorexia nervosa	1-2
BM - lowering diets	4-5
BM - females	6-7
BM - males	7-8
Light work	8-11
Medium hard work	11-14
Hard work	14-18

total energy expenditure

Main sources of nutrients

Nutrient	Food source
Saccharides	starch, sugar (sucrose)
Lipids	oils, lard, bacon, butter, margarines etc.
Proteins	meat, egg, milk, (cottage) cheese, beans

Energy content in nutrients

Nutrient	Heat of combustion (kJ/g)		
	Biological		Physical
Lipids	38		38
Saccharides	17		17
Proteins*	17	⟺	24

* In calorimeter, AA are oxidized to $CO_2 + H_2O + N_2$.

In human body, AA are catabolized to $CO_2 + H_2O$ + urea.

Recommended intake of nutrients

Saccharides 50-55 % (mainly starch)

Lipids 25-30 % (10 % PUFA)

Proteins 10-15 % (esenc. AA)

Essential FA:	linoleic, α-linolenic
Conditionally esent. FA:	arachidonic
Essential AA:	Phe, Trp, Val, Leu, Ile, Met, Thr, Lys
Conditionally esent. AA:	His, Arg, Ala, Gln

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. 1 (p. 95)

What is the performance of an active student in seminar if his body surface is 1.73 m^2 ?

Express it in Watts.

Use the data from the chart on p. 90.

A. 1

Energy expenditure of a student =

medium hard work
~ 4 MJ/d

basal expenditure (= BM) + activity in seminar =

$4.2 \times 1.73 + 4 = 11.266$ MJ/day =

11 266 000 J/day = $\frac{11266000}{86400}$ (J/s) = 130 J/s = **<u>130 W</u>**

Q.2 (p. 95)

The rate of energy expenditure in a fasting man (70 kg) without physical activity is 7 MJ/d.

How long do his energy stores last?

A. 2

Energy stores: (data from table p. 90)

$1.2 + 2.0 + 0.3 + 570.0 + 34.0 = \mathbf{607.5\ MJ}$

1/3 of total muscle energy

BM = 7 MJ/d

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

Body mass index

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

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

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 $\rightarrow$ oxalacetate $\rightarrow$ CAC
- glucose cannot be made from FA

Relationships between nutrients

glucose → lipids ✓

FA → glucose ✘

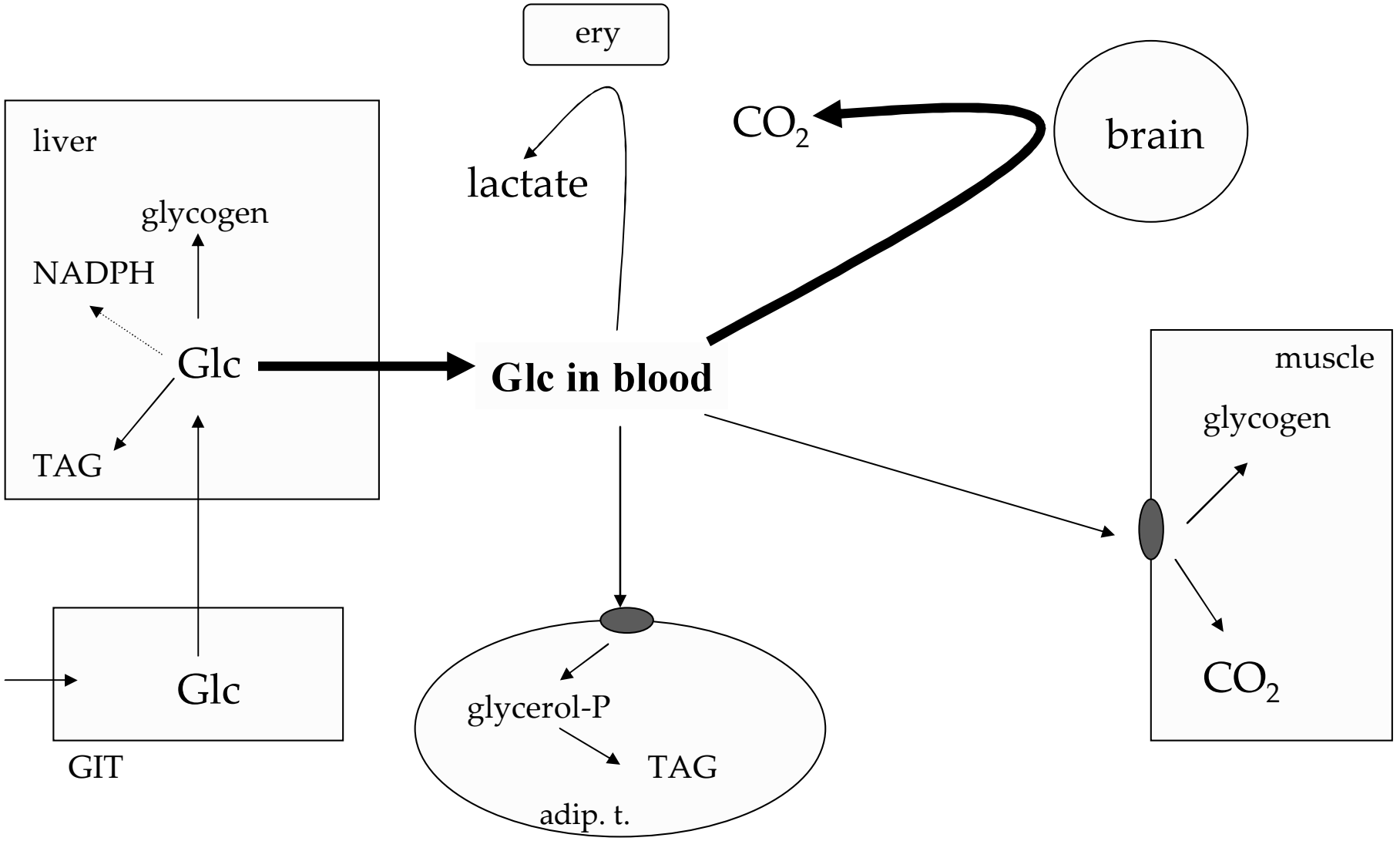
glucogenic AA → glucose ✓

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

AA → lipids ✓

lipids → AA ✘

Saccharides in well-fed state (insulin)



GLUT 4 insulin dependent

Glucose in liver (well fed state)

- 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

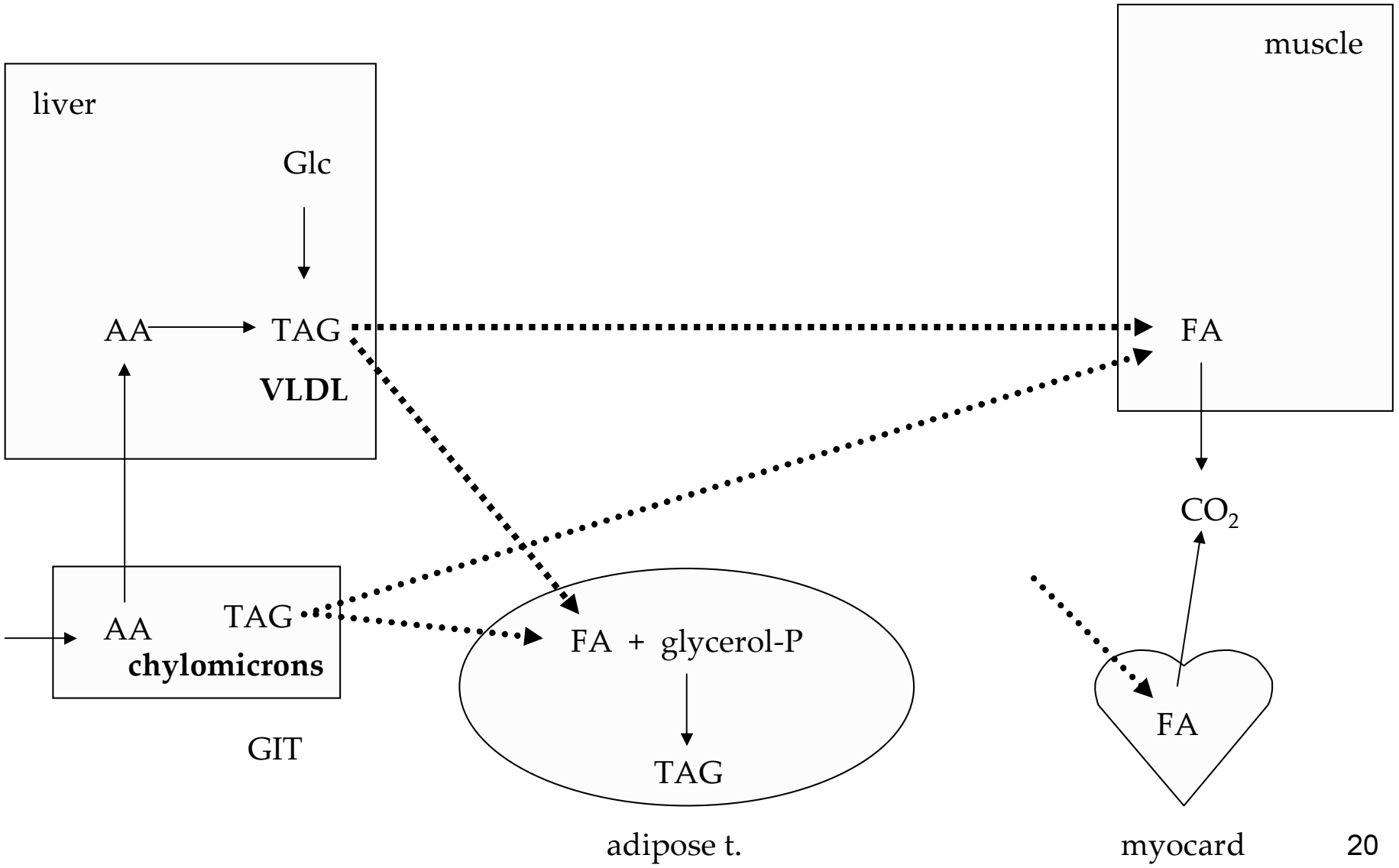
Glc in other tissues (well fed state)

- 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 adipose tissues

Glc → glyceraldehyde-3-P + DHAP

glycerol-3-P

Lipids in well-fed state (insulin)



Lipids in well-fed state (insulin)

- 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.

Which extrahepatal tissues utilize glucose in well-fed state?

What is the role of insulin in this process?

A.

- most tissues:
- RBC + brain (exclusively in well-fed state)
- muscles + adipose tissue + some other ...

- insulin stimulates the exposition of GLUT4 in muscles and adip. tiss. cell membranes
- Glc can enter these organs

Q.

Why is glucose needed for adipose tissue?

A.

- Glc is the source of **energy** (aerobic glycolysis)
- Glc is the source of **NADPH +H$^+$** for FA synthesis (pentose cycle)
- 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.

How can FA be formed from glucose?

A.

- **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. (p. 91)

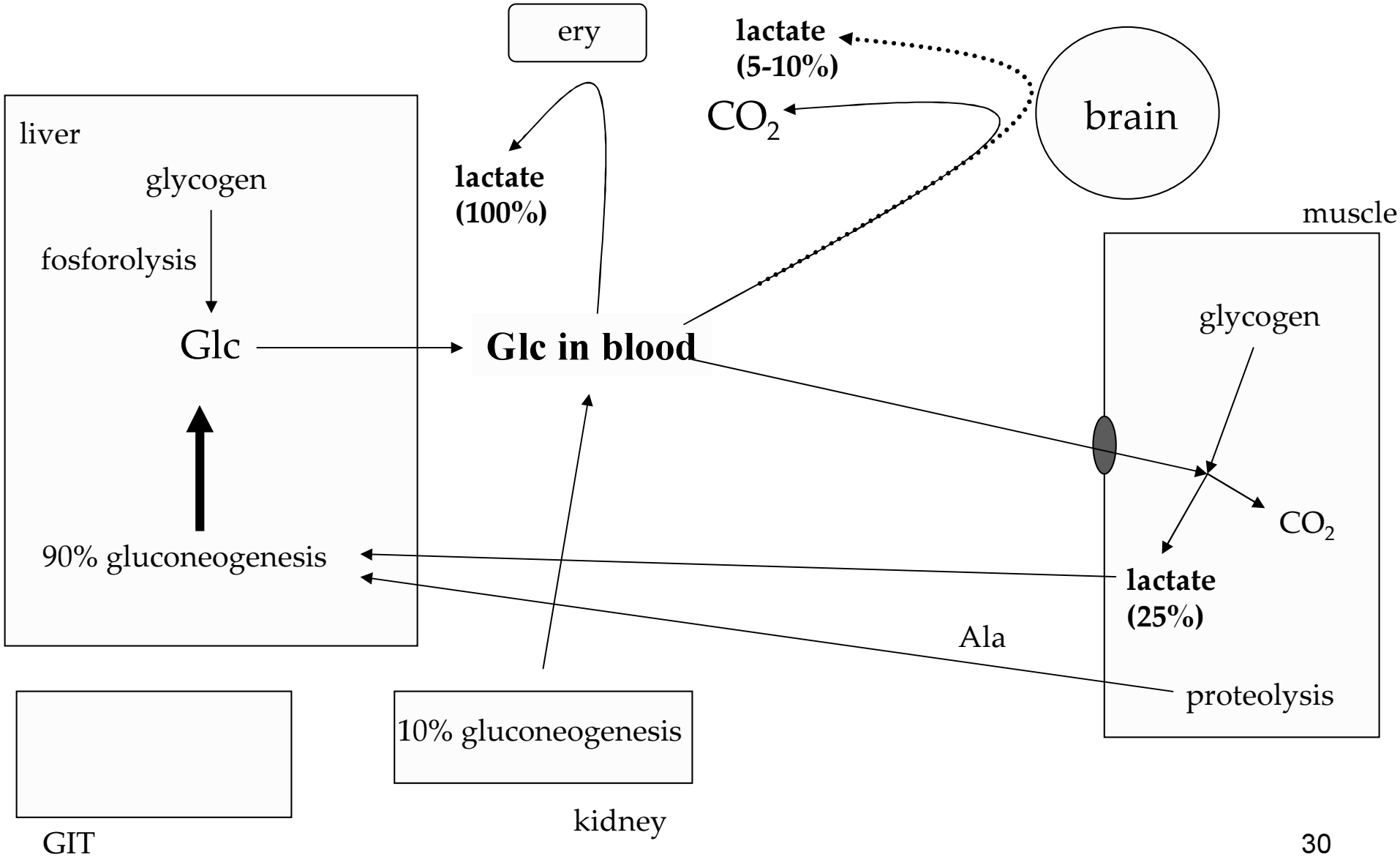
Why are KB **not** formed during resorption state?

A.

- 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 <u>two</u> processes:
- **(1) liver glycogenolysis**

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

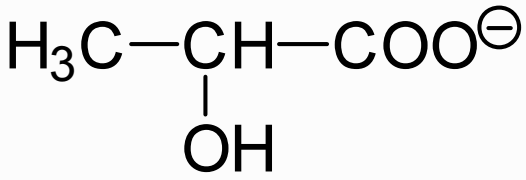
$$\text{Glc-1-P} \downarrow$$

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

- **(2) liver gluconeogenesis** from lactate, AA, glycerol
- in muscles + brain, glycolysis is partly anaerobic
  Glc (6C) $\rightarrow$ 2 lactate (3C)
- the body starts to save glucose

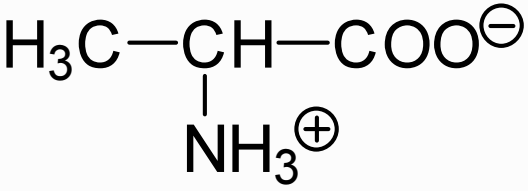
Substrates of gluconeogenesis

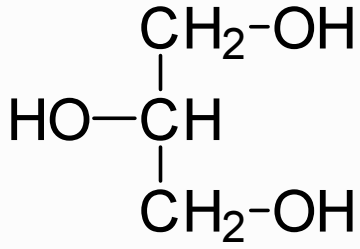
Lactate(60 %)



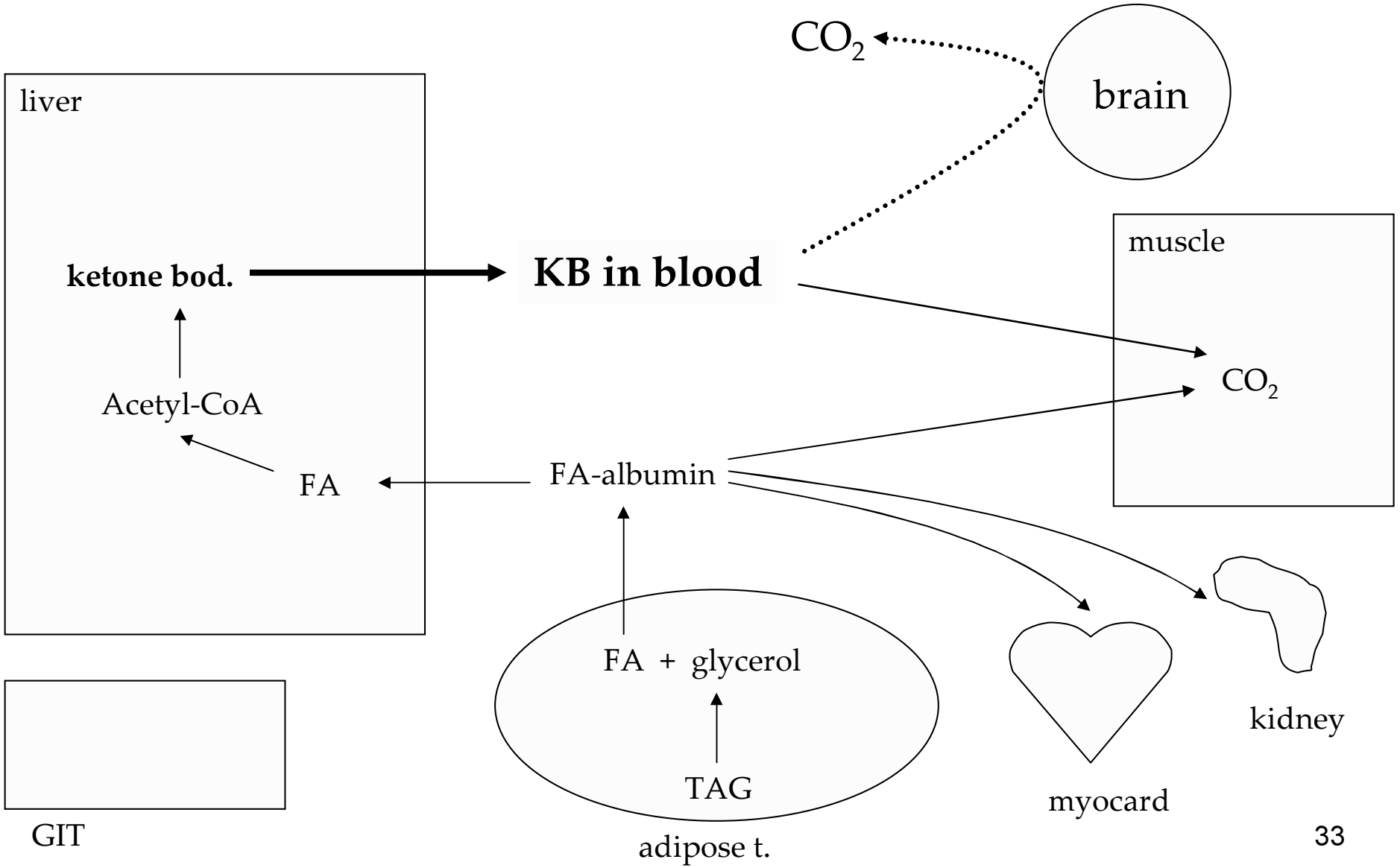
Alanine + other glucogennic AA (30 %)

Glycerol (10 %)





Lipids in fasting (glucagon)



Lipids in fasting (glucagon)

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

  TAG $\rightarrow$ 3 FA + glycerol

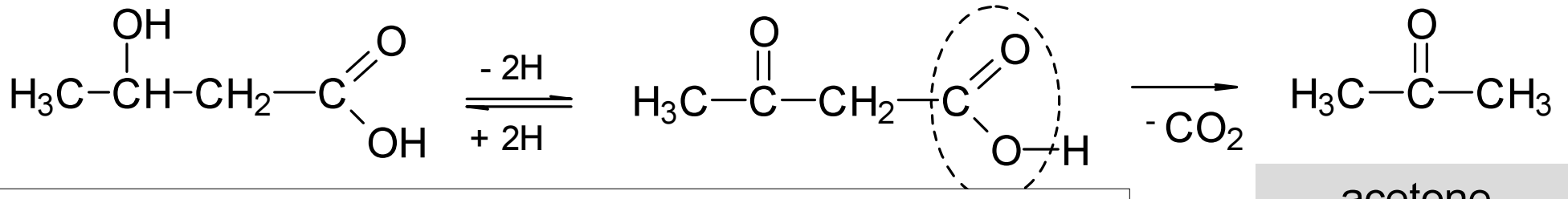
- FA are released to blood, bound to albumin, and trasferred to

  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

Ketone bodies



β-hydroxybutyric acid — acetoacetic acid

acetone

non electrolyte

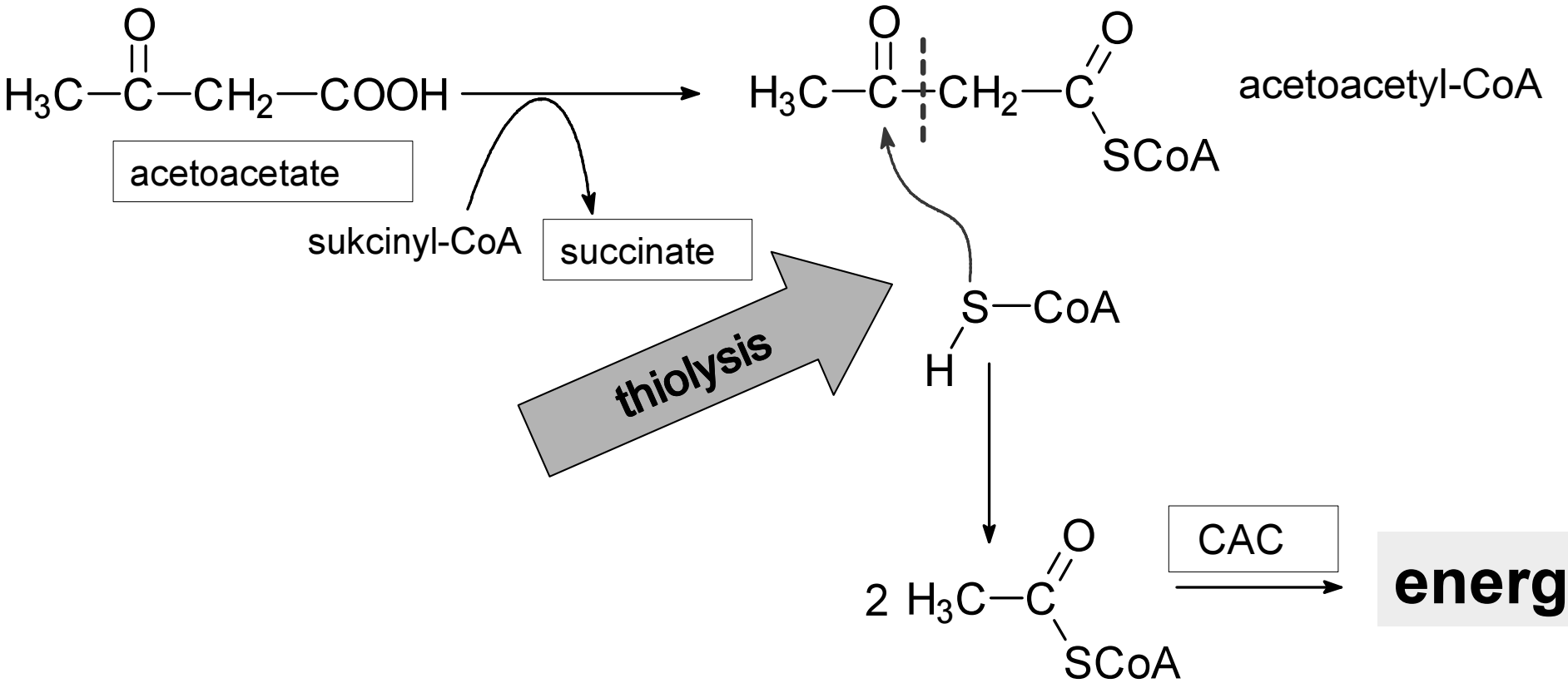
Acid	**pK_A**
Acetoacetic	3.52
β-Hydroxybutyric	4.70

which is stronger acid?

Compare:

acetic acid	pK_A = 4.75
formic acid	pK_A = 3.75

Ketone bodies as the source of energy



Q.

In which tissue are KB produced?

Which substrate is the source?

What is the cause of increased synthesis of KB?

A.

- KB are produced **only in liver** from acetyl-CoA
- liver is not able to utilize KB
- the metabolic cause:
  the shortage of oxaloacetate and excess of acetyl-CoA

Q.

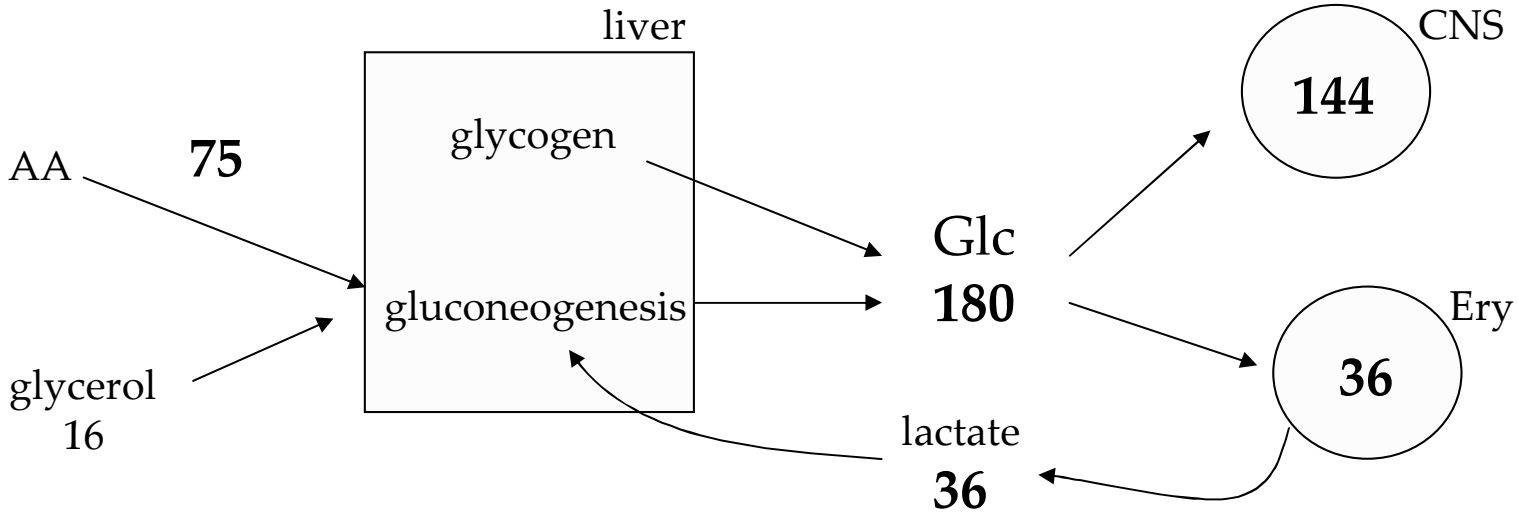
- How does lipoprotein lipase act on fat reserves in body?
- How does hormon sensitive lipase act on fat reserves in body?

A.

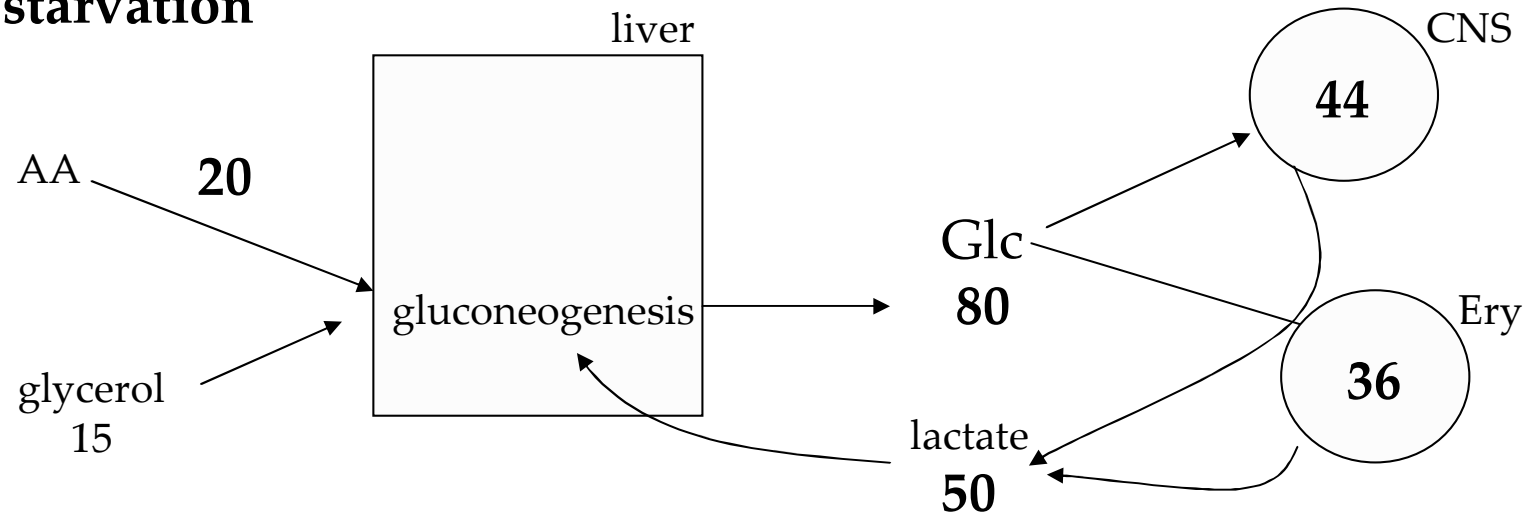
Feature	LPL	HSL
Substrate	TAG in blood	TAG in adipose tissue
Fat reserves are	increased	decreased
Stimulation by	insulin (inducer)	glucagon + adrenalin

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

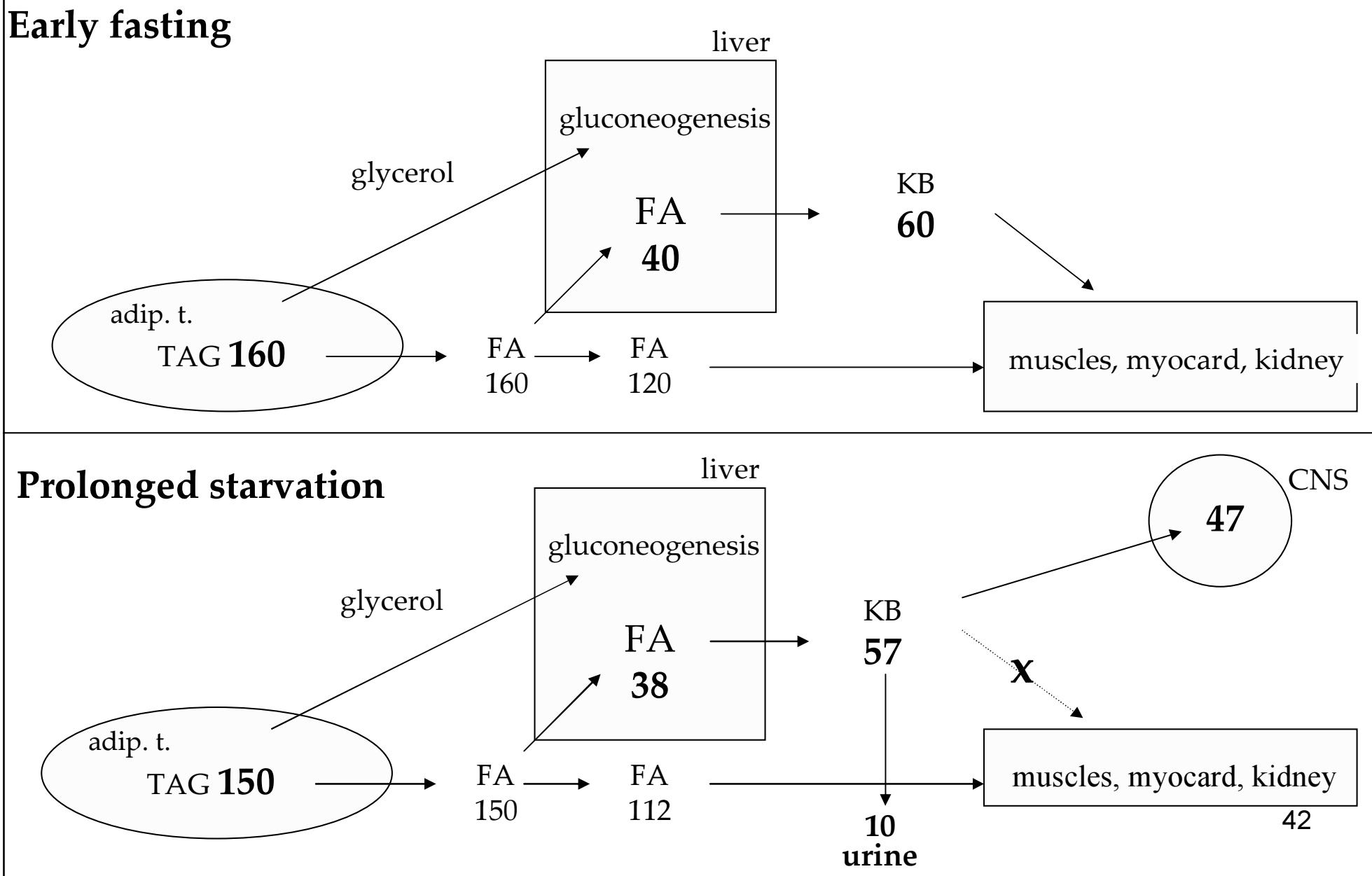
Early fasting



Prolonged starvation



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



Adaptation to prolonged starvation

- 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. utiliz.)
- energy for brain: Glc (44 g/d) + KB (47 g/d)
- energy for muscle: FA

Q.

Which are the main priorities of metabolism during long starvation?

A.

1. sparing glucose
2. sparing proteins

Q.

How does a long term fasting affect the acid-base balance?

A.

- the accumulation of acetoacetate and β-hydroxybutyrate in ECF leads to the decresase of pH $\Rightarrow$ acidosis

Acid	**pK_A**
Acetoacetic	3.52
β-Hydroxybutyric	4.70