Acid-Base Balance

Seminar No. 11

Parameters of acid base balance

Measured in arterial blood

- pH = 7.40 ± 0.04 = 7.36 – 7.44
- pCO_2 = 4.8 – 5.8 kPa
- supporting data: pO_2, tHb, sO_2, HbO_2, COHb, MetHb

Calculated

- $[HCO_3^-]$ = 24 ± 3 mmol/l (from H.-H. eq.)
- BE = 0 ± 3 mmol/l (from S.-A. nomogram, see physilogy)
- BB_s = 42 ± 3 mmol/l
- BB_b = 48 ± 3 mmol/l

Q. 1

Buffer bases in (arterial) plasma

Buffer base	mmol/l
HCO_3^-	24
Protein-His	17*
HPO_4^{2-}	1
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Total	**42**

* Molarity of negative charge ≈ binding sites for H^+

Q. 2

A. 2

$BB_s = 42 \pm 3$ mmol/l

$BB_b = 48 \pm 3$ mmol/l

hemoglobin in erythrocytes

increases BB_b by 6-8 mmol/l

Q. 3

Oxygen parameters and hemoglobin derivatives

Abr.	Name	Reference values
sO_2		
tHb		
COHb		
MetHb		
HbA_{1c}		

Oxygen parameters and hemoglobin derivatives

Abr.	Name	Reference values
sO_2	saturation of Hb by oxygen	94 – 99 %
tHb	total Hb	2.15 – 2.65 mmol/l (tetramer) 120-175 g/l (diff. males × females)
COHb	carbonylHb	1-2 % (nonsmokers)
MetHb	methemoglobin	0.5 – 1.5 %
HbA_{1c}	glycated Hb	2.8 - 4 %

Tissue hypoxia of any origin leads to lactic acidosis

Q. 4

A. 4

$7.4 = 6.1 + \log [HCO_3^-] / 0.22 \times 5.3$

$1.3 = \log [HCO_3^-] / 1.2$

$10^{1.3} = [HCO_3^-] / 1.2$

$20 = [HCO_3^-] / 1.2$

$[HCO_3^-] =$ **24 mmol/l**

Four types of acid-base disorders

$$pH = 6.1 + \log \frac{[HCO_3^-]}{0.22 \times pCO_2}$$

Changes in $[HCO_3^-]$

↓ metabolic acidosis

↑ metabolic alkalosis

Changes in pCO_2

↓ respiratory alkalosis

↑ respiratory acidosis

Maintanance of constant pH in body

System / Organ	What is altered?	How quickly?
Buffers in ECF/ICF	pH	sec / min
Lungs	pCO_2	hours
Liver	way of NH_3 detoxication	days
Kidney	NH_4^+ / $H_2PO_4^-$ excretion HCO_3^- resorption	days

Responses to acute change

- compensation
- correction

Q. 6

A. 6

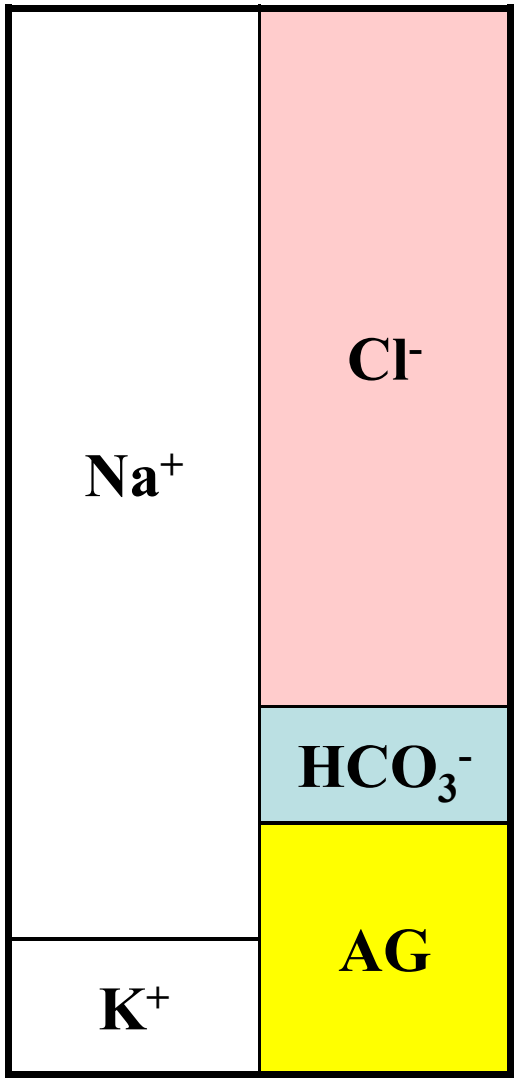
Feature	Plasma	ICF
Main cation	Na^+	K^+
Main anion	Cl^-	HPO_4^{2-}
Protein content	★	★ ★ ★
Main buffer base	**HCO_3^-**	**HPO_4^{2-}**

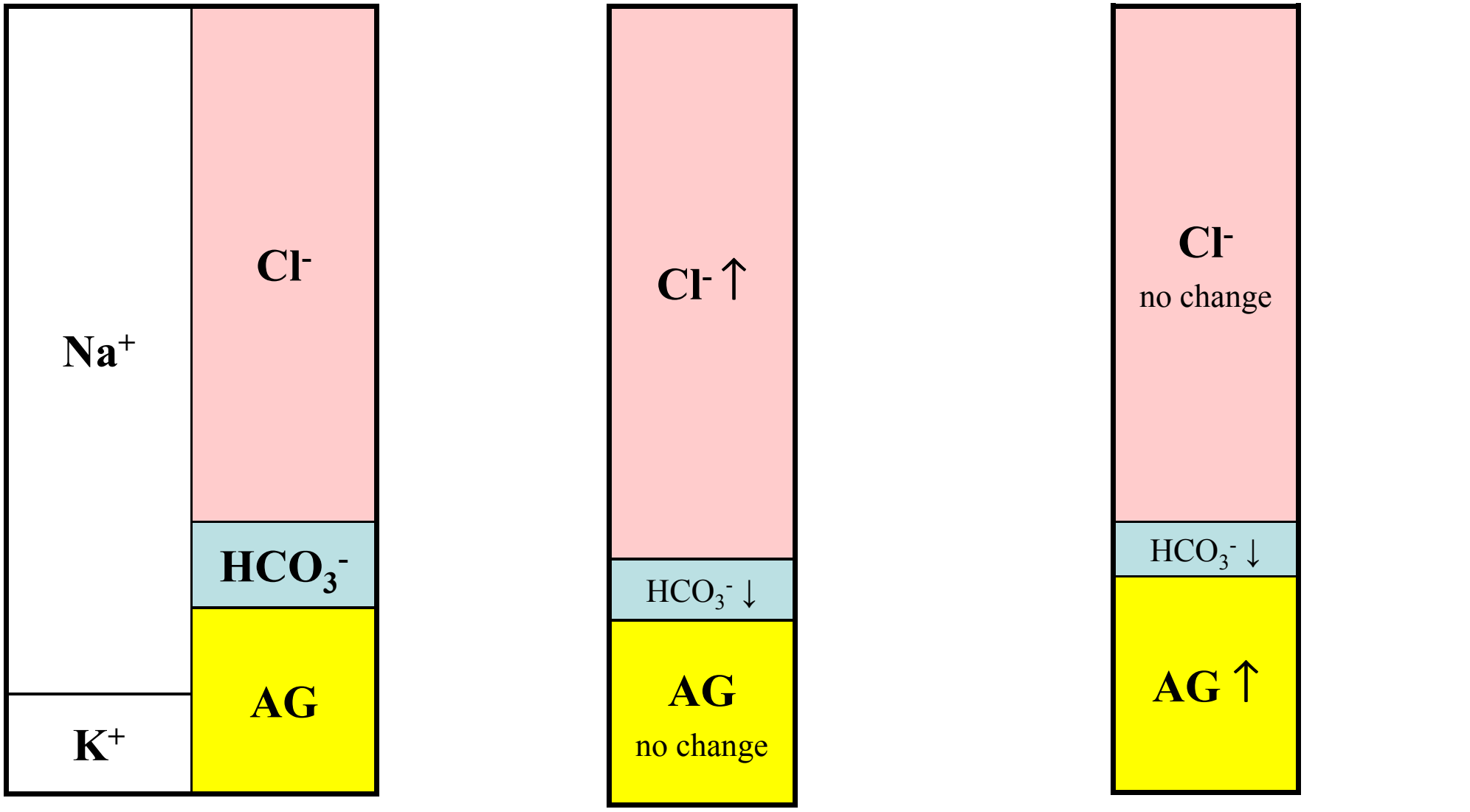
Metabolic acidosis is
the most common condition

Metabolic alkalosis is
the most dangerous condition

Q. 8

normal status **hyperchloremic MAC** **normochloremic MAC**





NaCl infusions

See Q. 11

Q. 9

A. 9 Excessive infusions of NaCl isotonic solution lead to metabolic acidosis

Blood plasma (mmol/l)	
Na^+	Cl^-
133-150	97-108
Ratio ~ 1 : 0.7	

Isotonic solution (mmol/l)	
Na^+	Cl^-
154	154
Ratio 1 : 1	

Isotonic solution of NaCl has elevated concentration of Cl^- compared to plasma

Blood plasma is diluted by infusion solution ⇒ **$[HCO_3^-]$ decreases**

pCO_2 in alveolar air is **the same**

the ratio $[A^-] / [HA]$ in H.-H. equation decreases ⇒ pH < 7.40 (acidosis)

Q. 10

Hyperchloremic MAc

- **excessive infusions of NaCl solution**

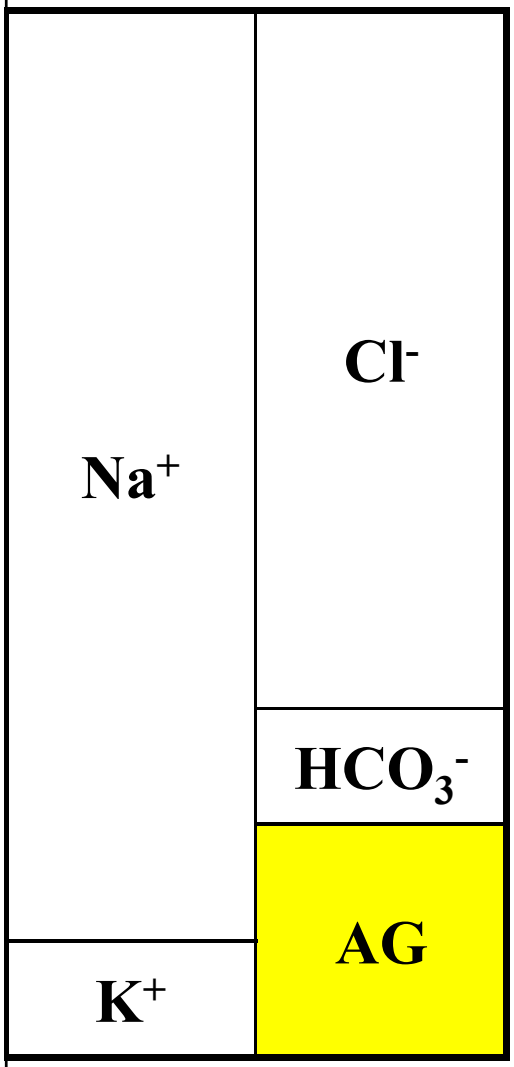
- **the loss of HCO_3^- + Na^+ + water** (diarrhoea, renal disorders)

  $\Rightarrow$ relative higher concentration of chlorides in plasma

Q. 11

How is AG calculated?

AG



AG calculation = $[Na^+] + [K^+] - [Cl^-] - [HCO_3^-]$

AG composition = $HPO_4^{2-} + Prot^- + SO_4^{2-} + OA$

A. 11 MAc with increased AG

- **Hypoxia of tissues** – insufficient supply of O_2 ⇒ anaerobic glycolysis: glucose → 2 lactate
- elevated AG – lactoacidosis

- **Starvation, diabetes**
- TAG → FA (β-oxidation in liver)→ acetyl-CoA (excess, over the capacity of CAC) ⇒ KB production
- elevated AG - ketoacidosis

- **Renal insufficiency** – elevated phosphates, sulfates
- Various intoxications

Q. 12

A. 12

- AG – normal values
- SID – buffer bases (mainly HCO_3^-) – decreased
- compare Q. 8a)

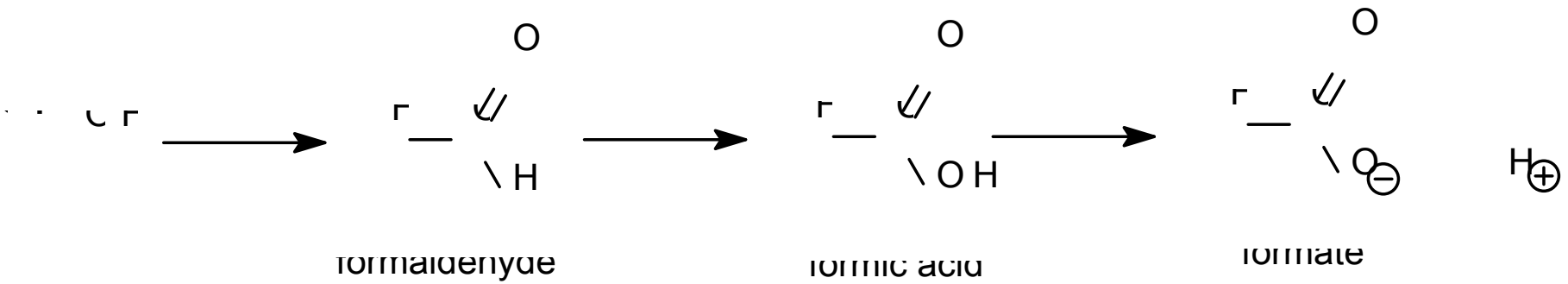
Q. 13 Metabolic acidosis

Parameter	Physiol. st.	Ac. change	Compensation	Correction
$[HCO_3^-]$	24 mmol/l	↓		→ **N**
pCO_2	5.3 kPa	**N**	↓	
$[A^-] / [HA]$	20 : 1	< 20 : 1		
pH	7.40 ± 0.04	< 7.36		
		System	**lungs**	**kidney**
		Process	hyperventilation	↑ HCO_3^- resorption ↑ NH_4^+ / $H_2PO_4^-$ excr.

Q. 15

Methanol intoxication

Metabolic oxidation of methanol provides a rather strong formic acid

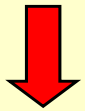


Consequences:

- formate in plasma ⇒ elevated AG ⇒ acidosis
- excess of NADH ⇒ lactoacidosis

Compare two acids

ethanol

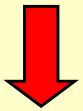


acetic acid

$pK_A = 4.75$

$K_A = 1.8 \times 10^{-5}$

methanol



formic acid

$pK_A = 3.75$

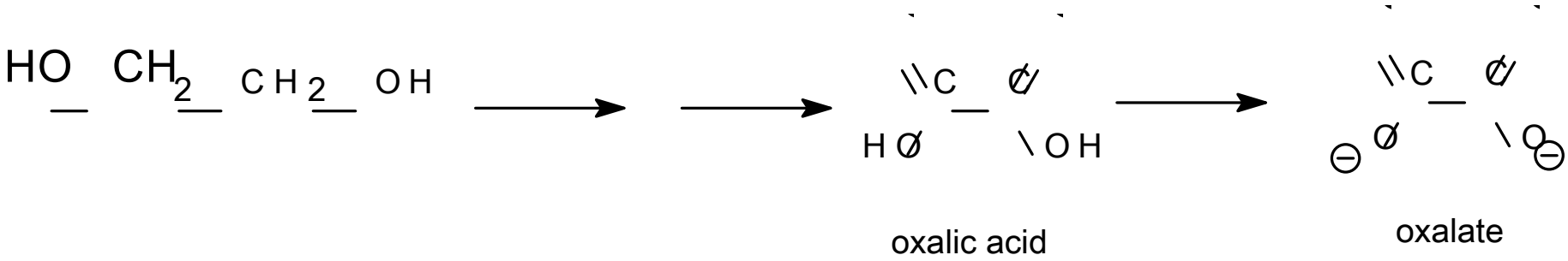
$K_A = 1.8 \times 10^{-4}$

K_A (formic ac.) : K_A (acetic ac.) = 10 : 1

formic acid is 10 × stronger than acetic acid

ethylene glycol intoxication

Intoxication by ethylene glycol



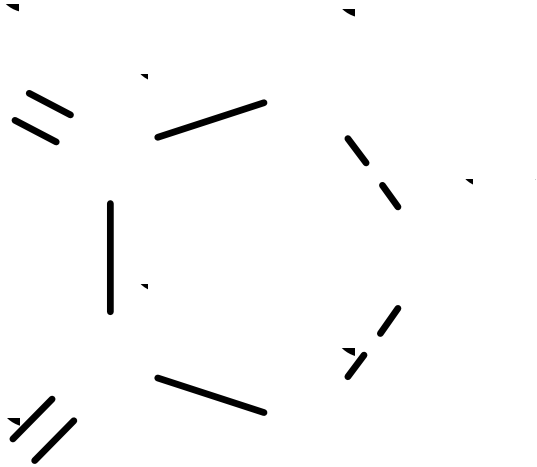
Consequences:

- oxalic acid is rather strong acid ($pK_{A1} = 1.25$, $pK_{A2} = 4.29$)
- oxalate in plasma ⇒ elevated AG ⇒ acidosis
- excess of NADH ⇒ lactoacidosis
- in urine ⇒ calcium oxalate concrements

Calcium oxalate is insoluble chelate

Draw formula

Calcium oxalate is insoluble chelate



Why MAc occurs in anemia?

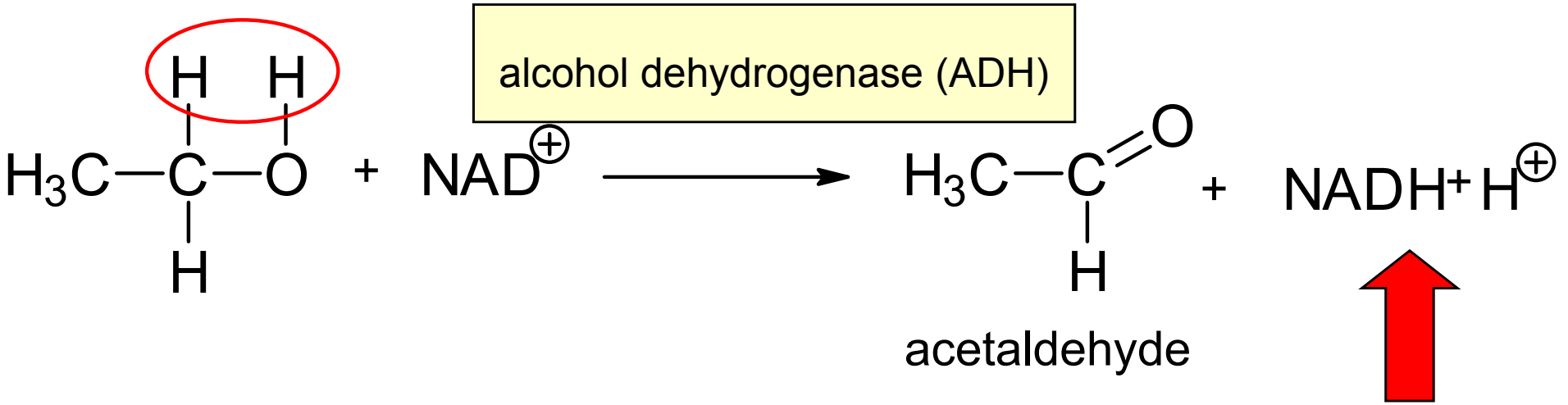
Not enough hemoglobin $\Rightarrow$ insufficient supply of O_2

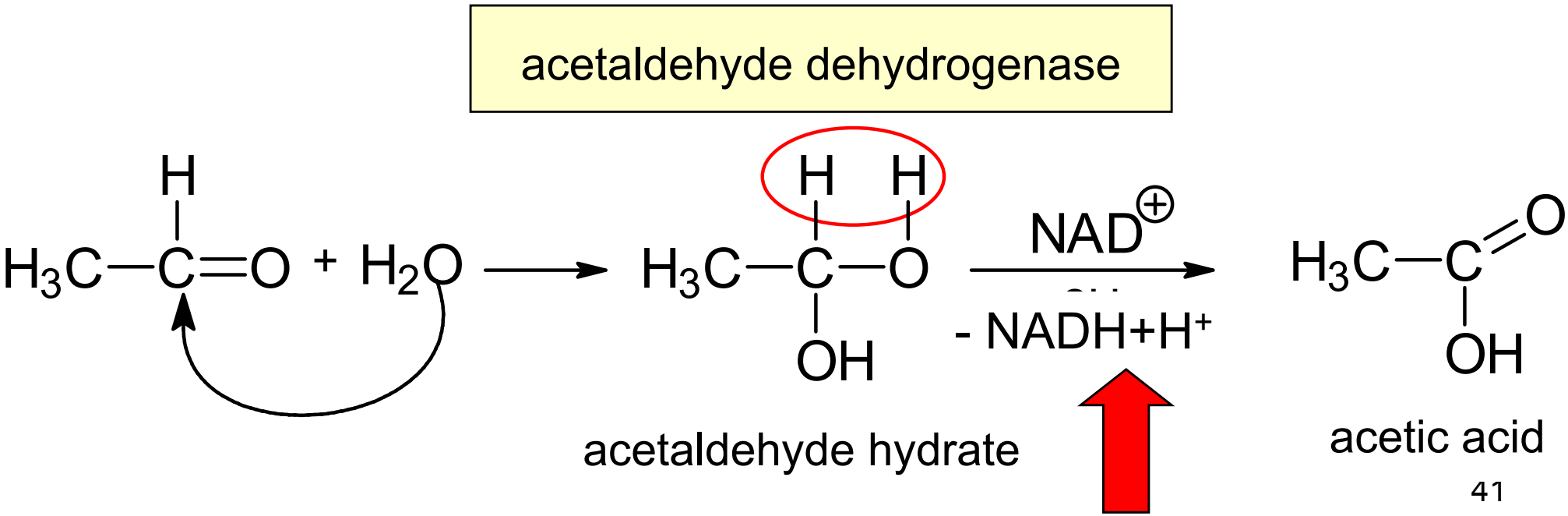
$\Rightarrow$ hypoxia $\Rightarrow$ anaerobic glycolysis to lactate

elevated AG – lactoacidosis

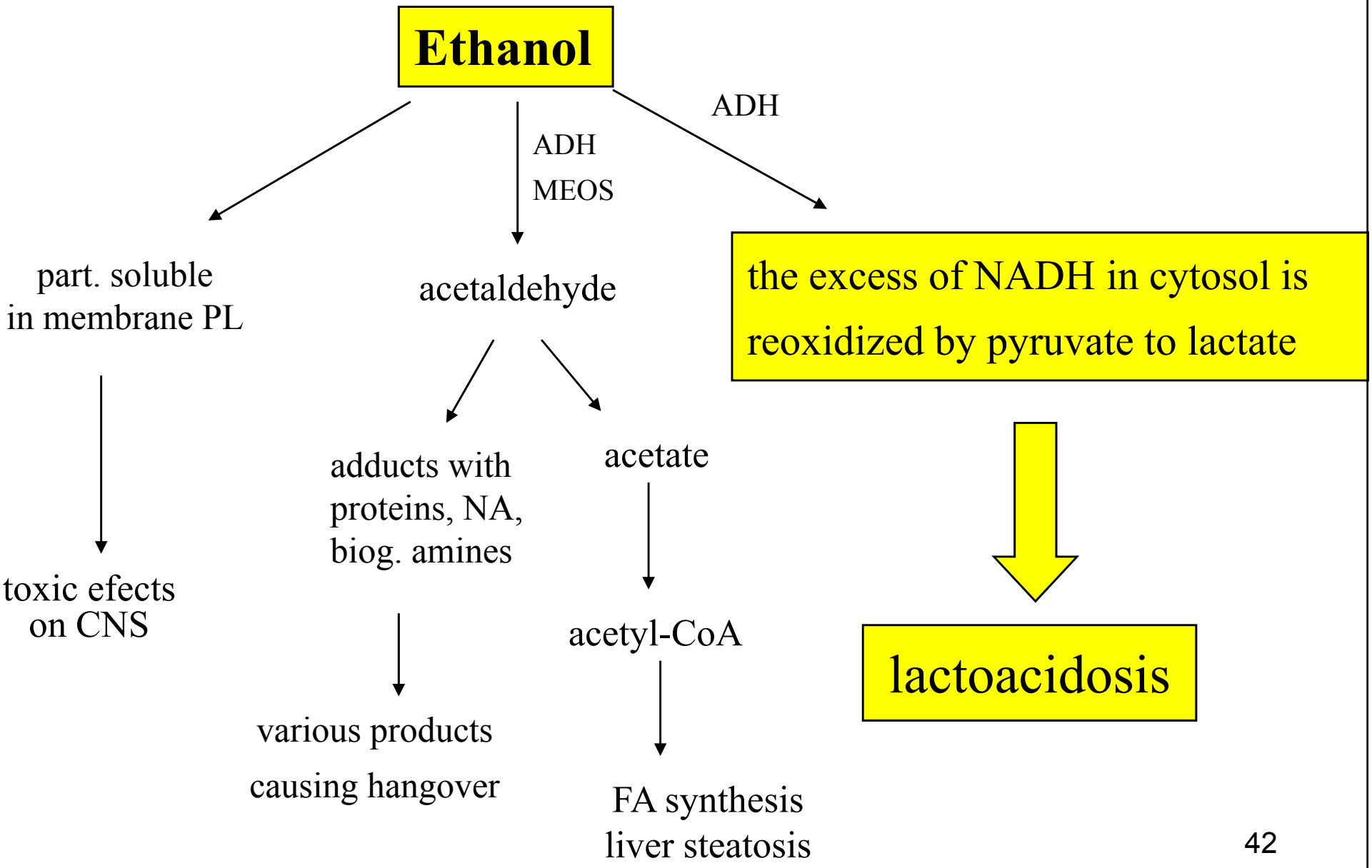
Q. 16

Metabolic oxidation of ethanol leads to excess of NADH





Metabolic consequences of EtOH biotransformation



Q. 17

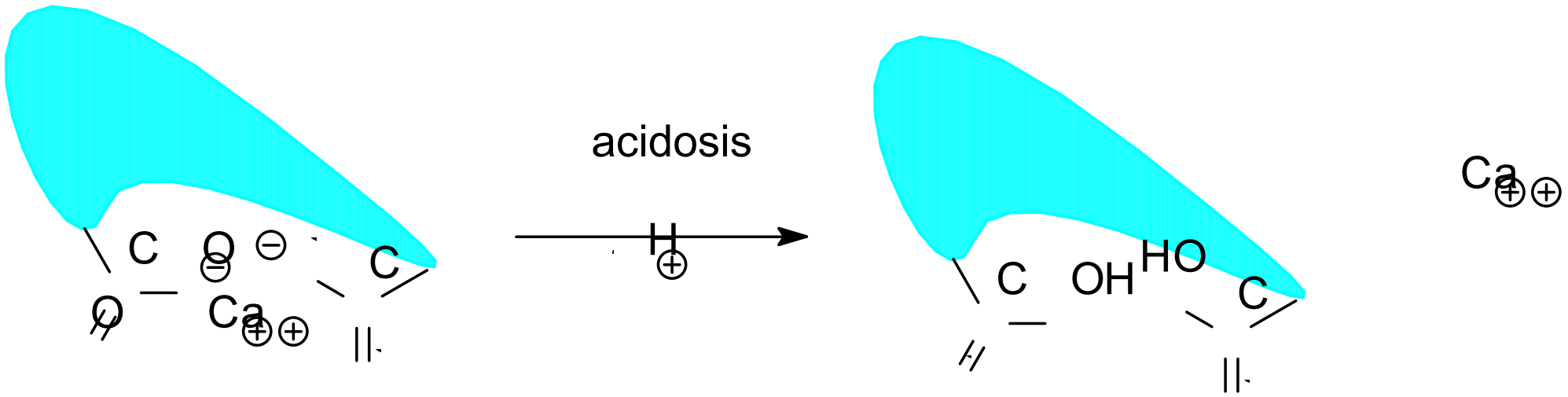
CH_3-CO-COOH + CoA-SH + NAD^+ → CO_2 + CH_3-CO-S-CoA + $NADH+H^+$

- thiamine is the cofactor of aerobic decarboxylation of pyruvate
- thiamine deficit ⇒ pyruvate cannot be converted to acetyl-CoA
- therefore pyruvate is hydrogenated to lactate
- **even in aerobic conditions: glucose → lactate**
- increased plasma lactate ⇒ elevated AG ⇒ lactoacidosis

1. Thiamin diphosphate
2. Lipoate
3. Coenzym A
4. FAD
5. NAD^+

Q. 18

A. 18



- calcium cations make electrostatic interactions with carboxylate anions in side chains of glutamate and aspartate (in various proteins)
- increased [H^+] (= decreased pH) of plasma leads to a partial cation exchange
- one calcium ion is liberated and replaced by two protons

Causes of metabolic alkalosis

- **Repeated vomiting** – the loss of chloride (Cl^-) anion ⇒ hypochloremic alkalosis

- **Direct administration of buffer base HCO_3^-**

  per os: baking soda, some mineral waters

  intravenous infusions of sodium bicarbonate

- **Hypoalbuminemia**

  severe malnutrition

  liver damage, kidney damage

What is baking soda?

A.

$NaHCO_3$

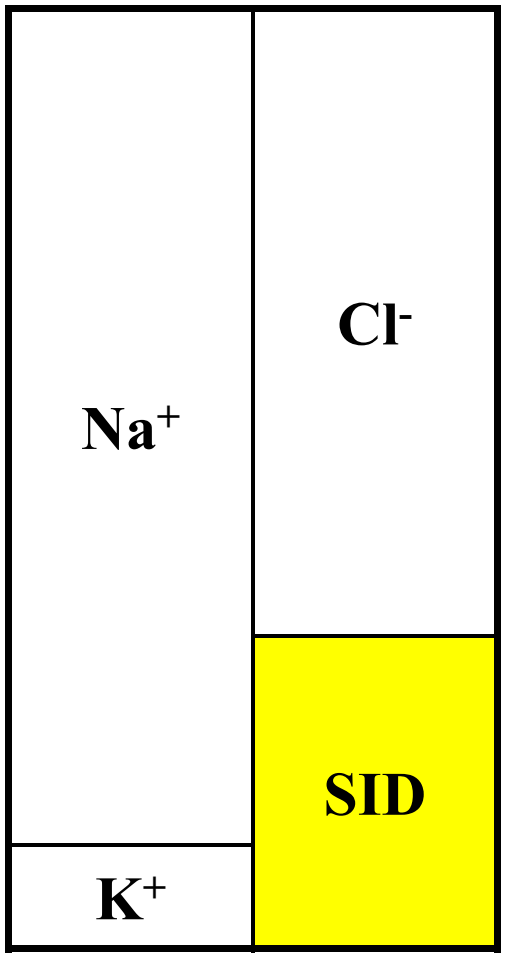
sodium hydrogen carbonate (sodium bicarbonate)

sold in pharmacy

Q. 19

How is SID calculated?

SID corresponds to buffer bases of plasma

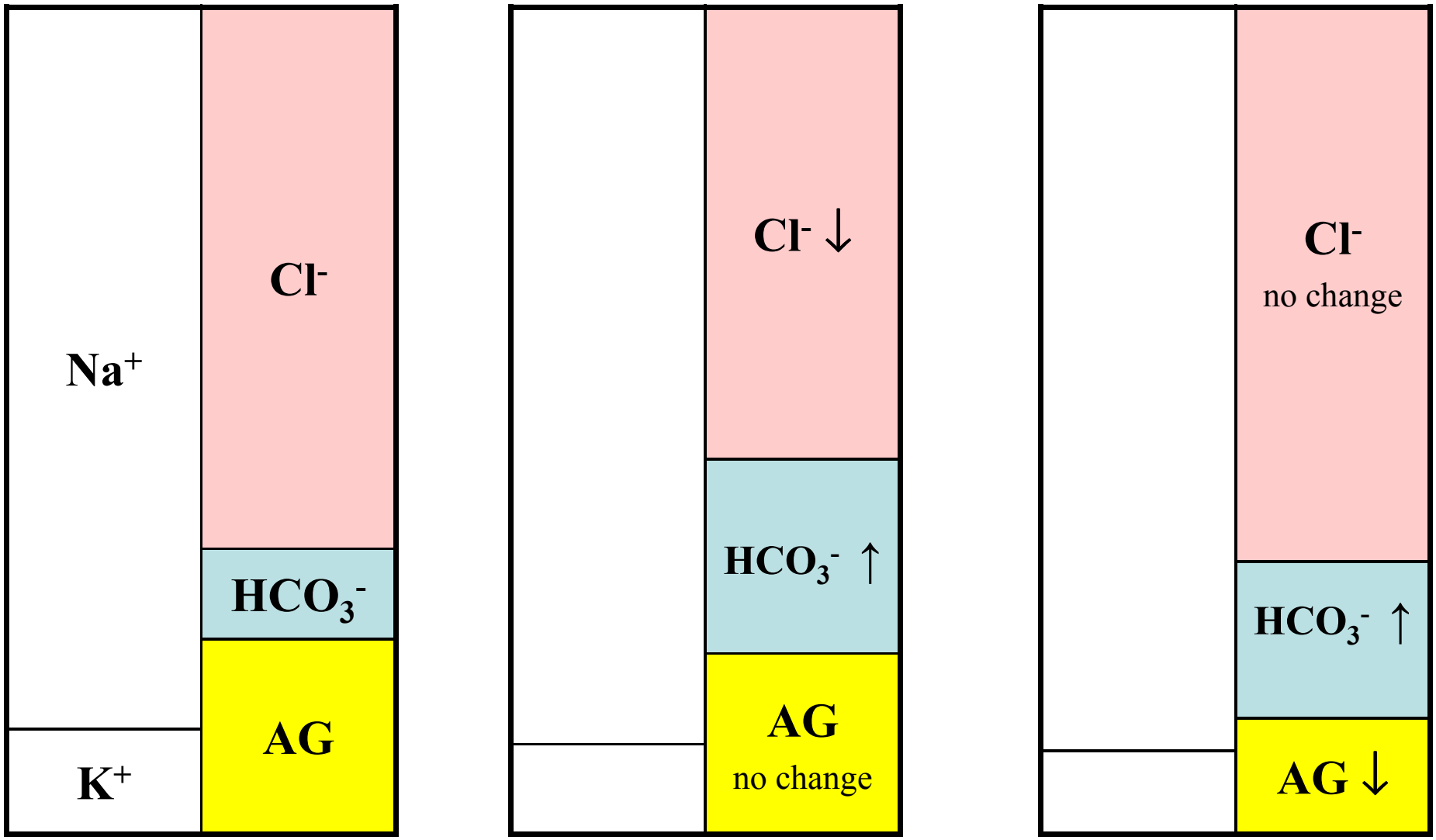


SID calculation = $[Na^+] + [K^+] - [Cl^-]$

SID composition = $HCO_3^- + HPO_4^{2-} + Prot^-$

In MAlk ⇒ SID increases

Q. 20


normal status
hypochloremic MAlk
normochloremic MAlk
Na+
Cl-
HCO3-
K+
AG
Cl- ↓
HCO3- ↑
AG
no change
Cl-
no change
HCO3- ↑
AG ↓
vomiting
hypoalbuminemia

Q. 21 Metabolic alkalosis

Parameter	Physiol. st.	Ac. change	Compensation	Correction
$[HCO_3^-]$	24 mmol/l	↑		→ **N**
pCO_2	5.3 kPa	**N**	↑	
$[A^-] / [HA]$	20 : 1	> 20 : 1		
pH	7.40 ± 0.04	> 7.44		
		System	**lungs**	**kidney**
		Process	hypoventilation	↑ HCO_3^- excretion

Q. 23

A. 23

pCO_2 = 5.5 kPa ..... **OK**

$[HCO_3^-]$ = 39 mmol/l ..... ↑ **elevated**

pH = 7.6 ..... ↑ **elevated**

status: metabolic alkalosis

pCO_2 will increase during compensation (hypoventilation)

Q. 25

Solution	Effect	Explanation
NaCl		
$KHCO_3$		
NH_4Cl		
$NaHCO_3$		
Na lactate		

Solution	Effect	Explanation
NaCl	acid.	plasma dilution ⇒ $[HCO_3^-]$ ↓ while pCO_2 is constant
$KHCO_3$	alkal.	direct addition of the main buffer base
NH_4Cl	acid.	NH_4^+ excreted by urine, Cl^- remains in plasma ⇒ $[HCO_3^-]$ ↓
$NaHCO_3$	alkal.	direct addition of the main buffer base
Na lactate	alkal.	lactate anion goes from plasma to liver (gluconeogenesis), Na^+ remains in plasma ⇒ its pos. charge is balanced by extra HCO_3^- (similar effect like in vegetarian diet)

Q. 26 Respiratory acidosis

Parameter	Physiol. st.	Ac. change	Compensation	Correction
$[HCO_3^-]$	24 mmol/l	**N,** ↑	↑	-
pCO_2	5.3 kPa	↑		→ **N**
$[A^-] / [HA]$	20 : 1			
pH	7.40 ± 0.04			
		System	**kidney**	**lungs**
		Process	HCO_3^- resorption $NH_4^+ / H_2PO_4^-$ excr.	hyperventilation

Q. 27

Describe the scheme on p. 5

- Excess of CO_2 in the body produces more H_2CO_3 in blood
- Carbonic acid in buffering reaction with proteins gives HCO_3^- ion
- Hydrogen carbonate ion is driven to ICF
- Therefore the level of HCO_3^- in ECF is normal or slightly elevated

Q. 29

A. 29

pH 7.32 .....↓

pCO_2 9.3 kPa ..... ↑

$[HCO_3^-]$ = 39 mmol/l .....↑

$[Na^+]$ = 136 mmol/l .....OK

$[K^+]$ = 4.5 mmol/l .....OK

$[Cl^-]$ = 92 mmol/l .....↓

AG = 136 + 4.5 - 39 – 92 = 9.5 mmol/l .....↓ ⇒ no MAc

Conclusion: compensated RAc

Q. 30 Respiratory alkalosis

Parameter	Physiol. st.	Ac. change	Compensation	Correction
$[HCO_3^-]$	24 mmol/l	**N, ↓**	**↓**	**-**
pCO_2	5.3 kPa	**↓**	**-**	**→N**
$[A^-] / [HA]$	20 : 1			
pH	7.40 ± 0.04			
		System	**kidney**	**lungs**
		Process	Excretion of HCO_3^-	hypoventilation (if possible)

Combined disorders

Q. 33

A. 33

pH 7. 4 ..... **OK**

pCO_2 5.13 kPa .....**OK**

BE 1 mmol/l .....**OK** $\Rightarrow$ HCO_3^- = 25 mmol/l ..... **OK**

Na^+ 140 mmol/l .....**OK**

K^+ 4.6 mmol/l .....**OK**

Cl^- 89 mmol/l ..... ↓

AG = 140 + 4.6 – 25 – 89 = 30.6 mmol/l .....↑

SID = 140 + 4.6 – 89 = 55.6 mmol/l .....↑

Conclusion: MAc + MAlk

Q. 34

A. 34

Q.	Explanation
a)	MAc - lactoacidosis (alcohol) + loss of Cl^- (vomiting) - MAlk
b)	MAc - ketoacidosis (starvation) + loss of Cl^- (vomiting after overeating) - MAlk
c)	RAlk (stimulation of resp. centre) + MAc (salicylate – AG ↑)
d)	MAc (ketoacidosis) + RAc (heart failure – circulation insuff.)