Disorders of Acid Base Balance (ABB),

influenced by lung, kidney and other organs

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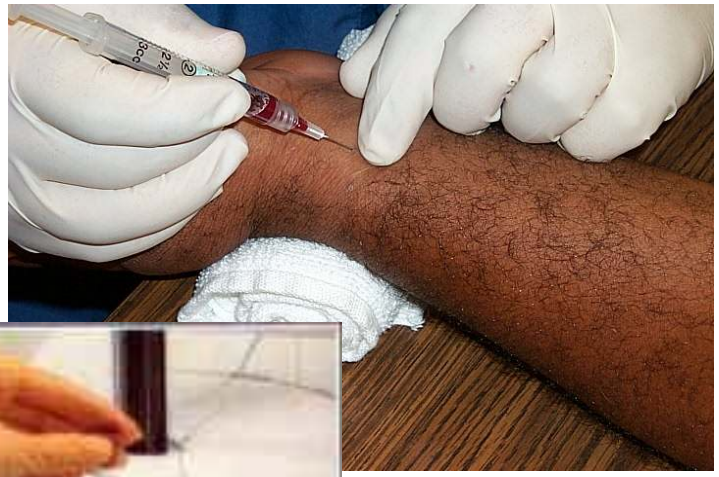
Bundesleistungszentrum Kienbaum, Kienbaum, Ostdeutschland, =
State Sport Training Facility, Kienbaum, Eastern Germany (founded in 1952), =
HYPOBARIC, i.e. low oxygen pressure facility, in year 2013 it was still in use.
Low pO2 smaller size cabins are in use even nowadays.

Outline

- Bicarbonate buffer
- Four basic types of disturbances
  - R.AC., R.AL., M.AC. and M.AL.
- Compensation of each disturbance
- Other buffers: BE, standard HCO_3^-
- (Extras: Stewart theory or dilution acidosis)

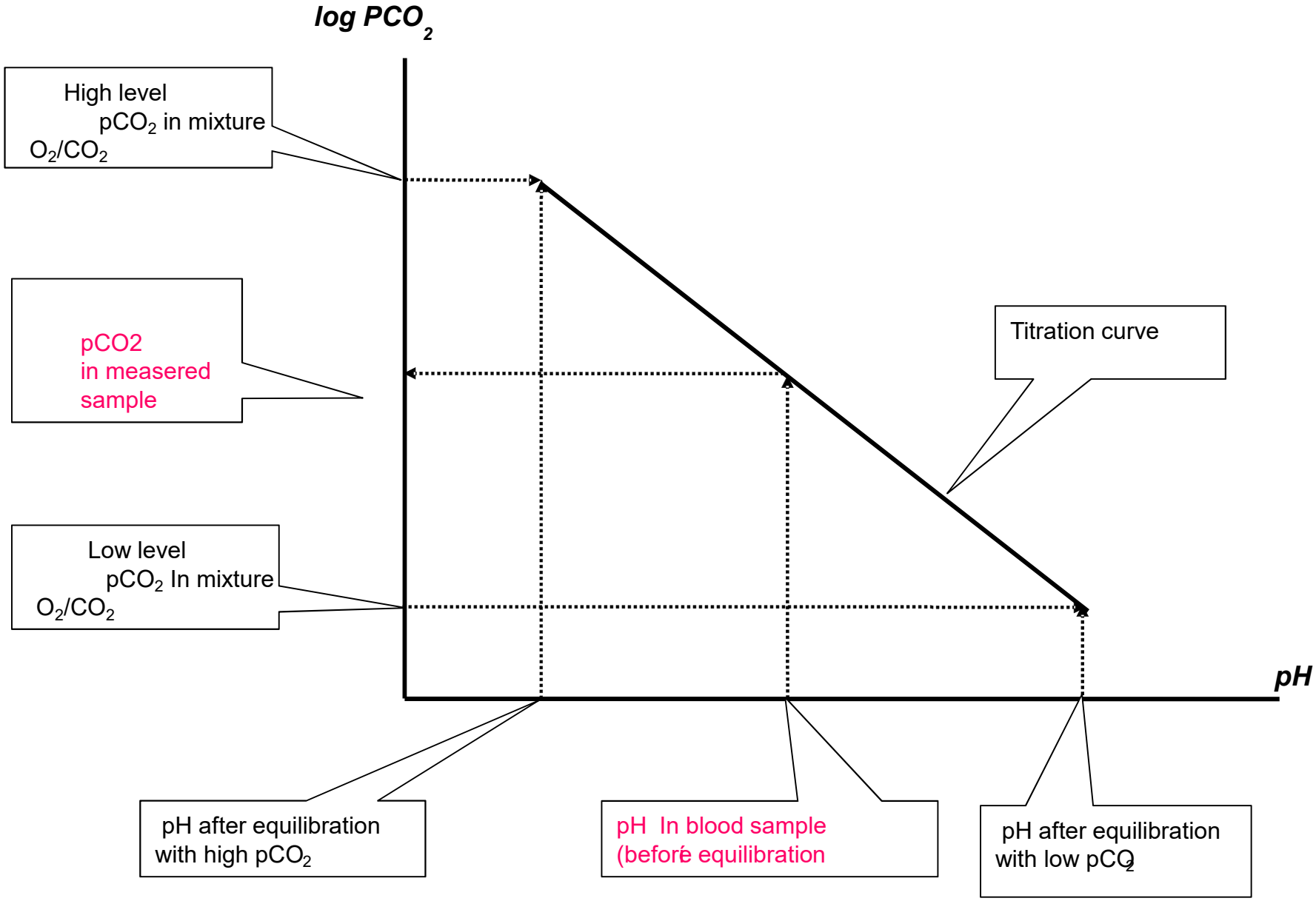
Do we take arterial/ capillary/ or ~~venous~~ blood?

- Arterial blood gas measurement ("Astrup method")
- Serum electrolytes
- Other (Albumin, hemoglobin)



Poul Bjorndahl Astrup (1915–2000), Danish clinical chemist

Equilibration method for pCO2 measurement by Astrup



Arterial blood gases measurement

Apparatus measures:

- **pH** (7.35 – 7.45)
  Or analogous value: H+ = 35 – 45 **nmol/ L**
- **pCO2** (40 Torr = 5.3 kPa)
- **pO2** (100 Torr = 13.3 kPa)

Apparatus calculates:

- **HCO_3^-** (24 mmol/ L) *From Henderson-Hasselbalch Equation*
- **BE** (0 mmol/ L) *From in-built Siggaard-Andersen nomogram*

Possible problems:

/ Visible air bubble stays in the syringe and dissolves in the sample.

/ The sample is not analyzed right away. Metabolic processes cause changes in AB parameters. (If immediate analysis is not possible, the sample should be kept in ice-bath.)

ABB parameters

Blood gases (Astrup method)

- pH 7.36-7.44
- (PaO_2 9.9-14.4 kPa)
- $PaCO_2$ 4.8-5.9 kPa
- BE ±2 mmol/ L
- BBS (Buffer Base) 48 ±2 mmol/ L
- NBB (Normal Buffer base)
- Standard bicarbonates 24 mmol/ L
- Actual bicarbonates 24 mmol/ L

ABB parameters, sex differences…

Normal range of acid–base parameters in plasma

	Women	Men
$[H^+]$ (nmol/L)	39.8 ± 1.4	40.7 ± 1.4
pH	7.40 ± 0.015	7.39 ± 0.015
P_{CO_2} (kPa)	5.07 ± 0.3	5.47 ± 0.3
(mmHg)	38.9 ± 2.3	41.0 ± 2.3
$[HCO_3^-]$ (mmol/L)	24 ± 2.5	24 ± 2.5

Serum electrolytes

- **Na+ (135 – 145 mmol/ L)**
- **Cl- (97 – 108 mmol/ L)**
- **Total CO2 or HCO_3^- (24 +- 2 mmol/ L)** …..should be equal to **HCO_3^-** from Astrup – this can check the measurement validity

Additional:

- Phosphates >> $H_2PO_4^-$ => HPO_4^{2-} (1 – 1.5 mmol/ L)
- K+ (3.5 – 5 mmol/ L)
- Ca++ (2.4 mmol/ L)
- SO_4^{2-}

Other biochemistry tests

- **Albumin** (35 – 50 g/ L)
- **Hb** (120 – 170 g/ L)

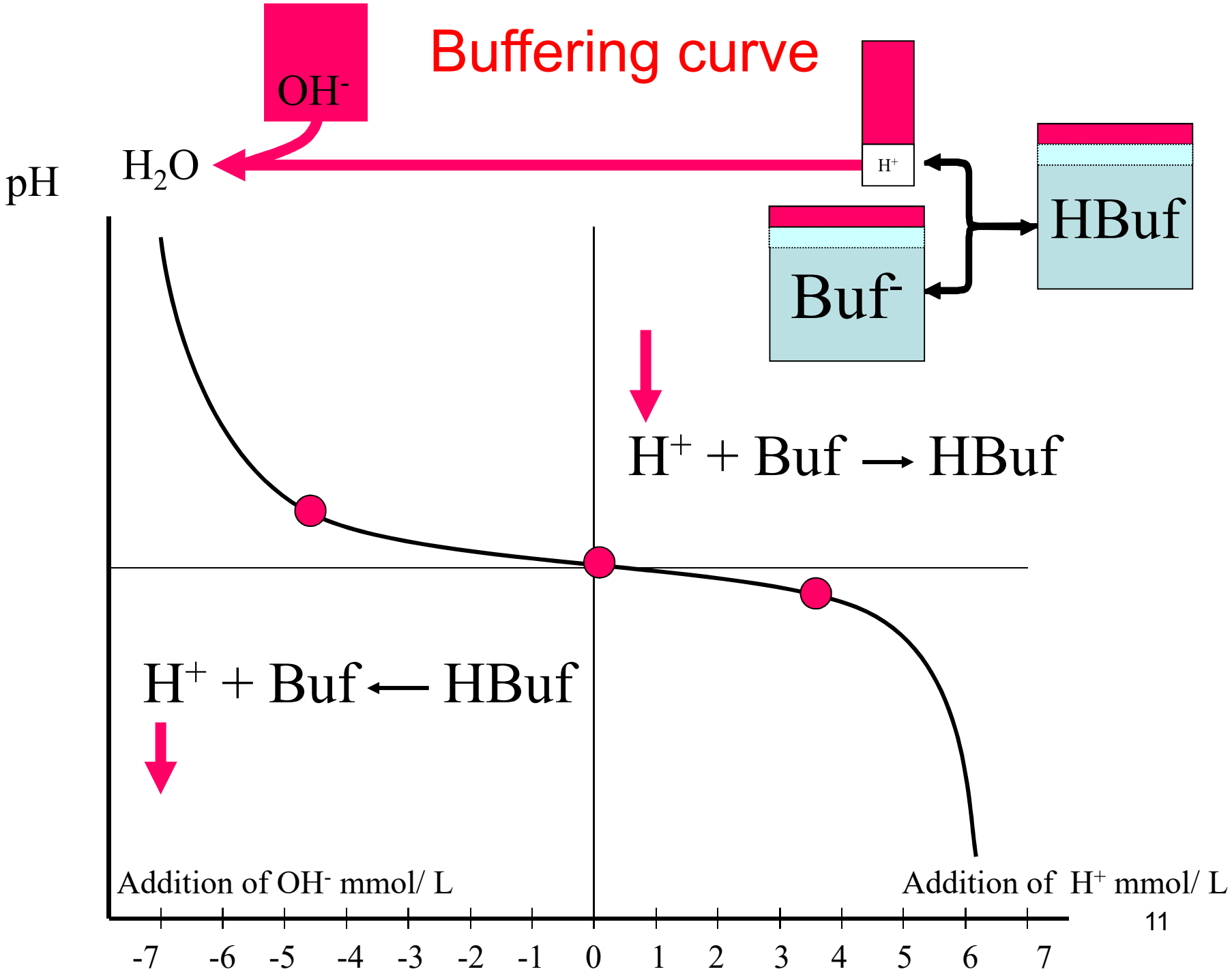
Additional:

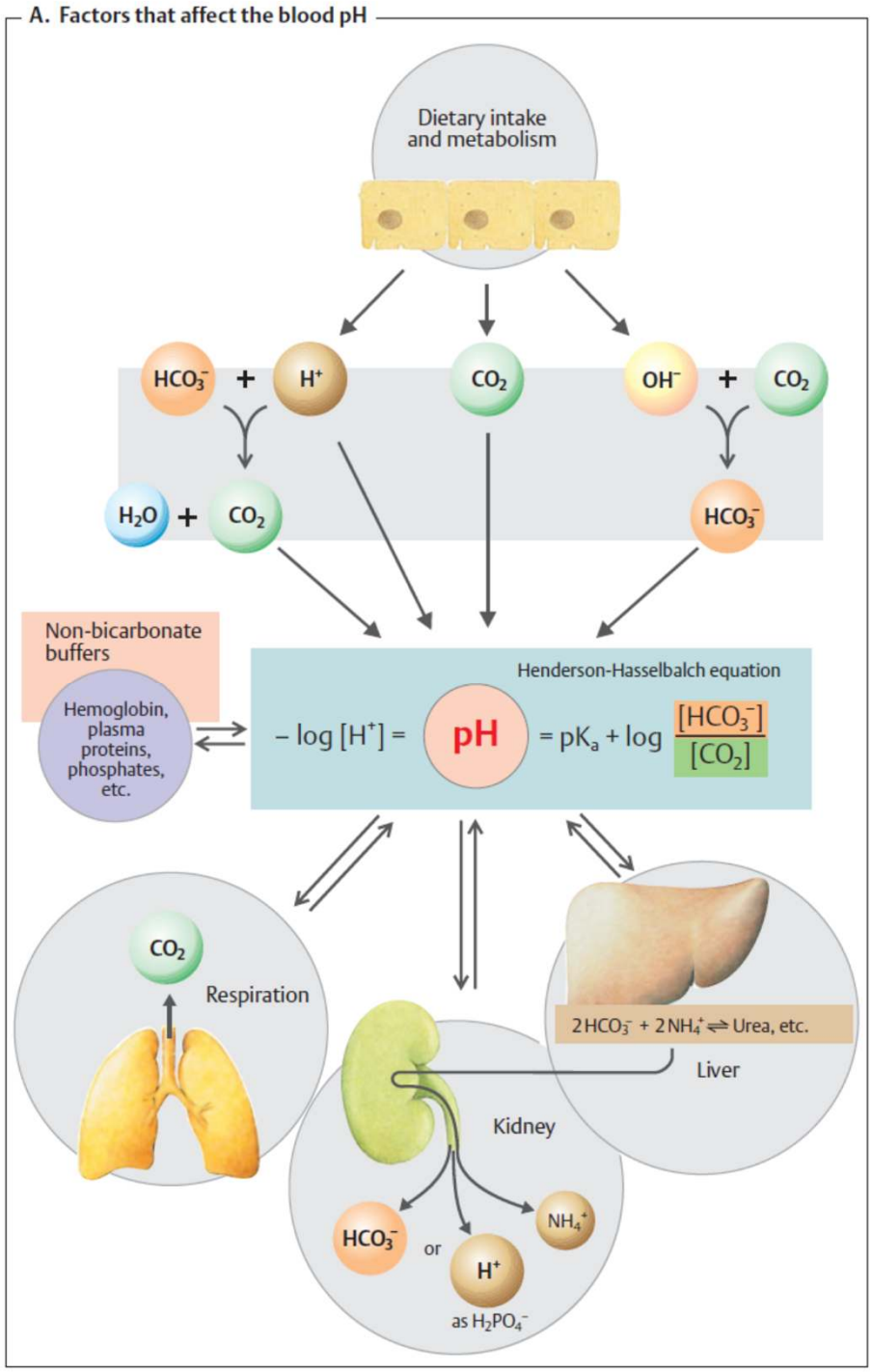
Albumins (35 – 50 g/ L)

Lactate (0.5 – 2.5 mmol/ L)

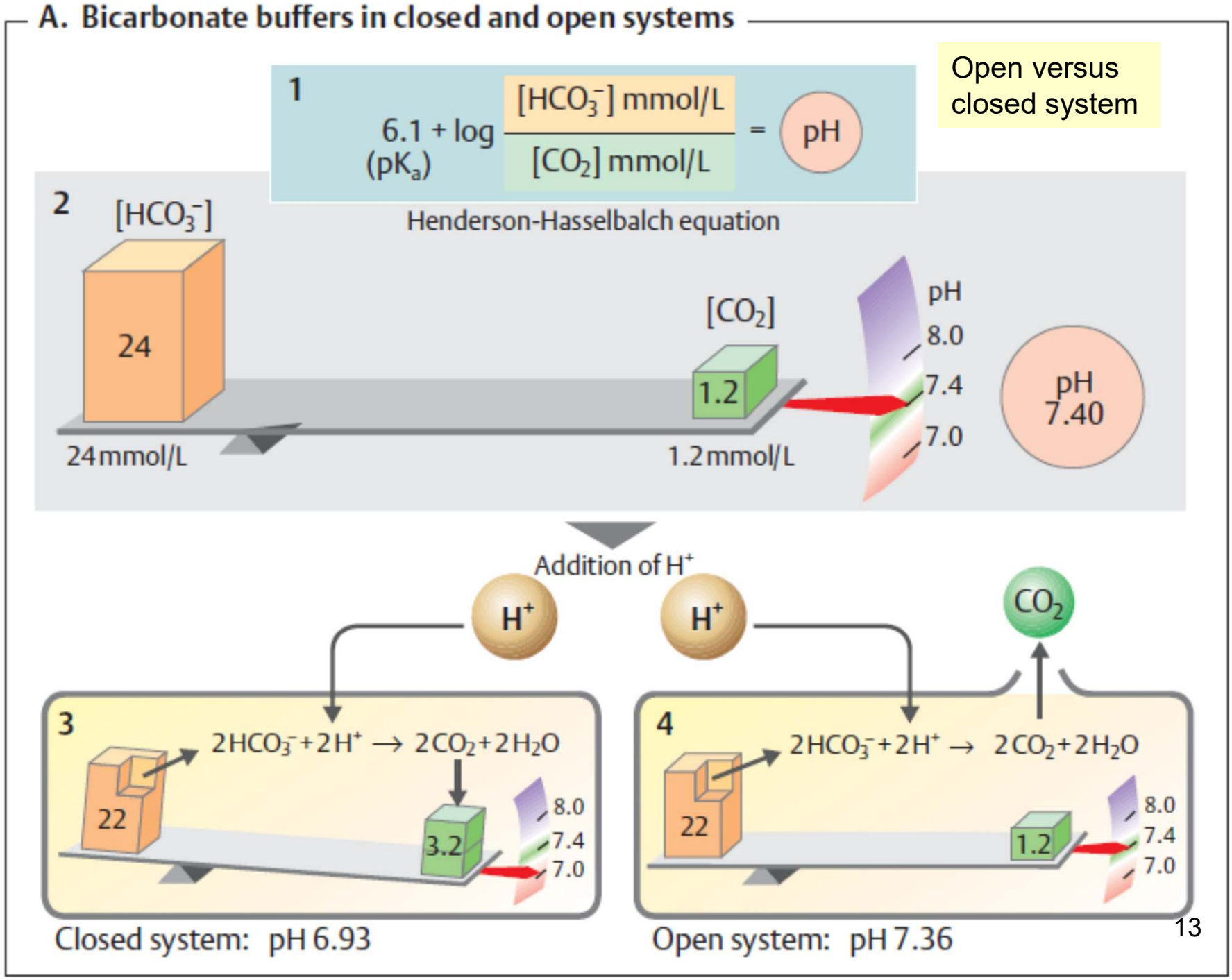
Keto- acids (0 mmol/ L)

Toxic substances: salicylates, methanol etc.


Buffering curve
OH-
H2O
pH
H+
HBuf
Buf-
H+ + Buf → HBuf
H+ + Buf ← HBuf
Addition of OH- mmol/ L
Addition of H+ mmol/ L
-7 -6 -5 -4 -3 -2 -1 0 1 2 3 4 5 6 7



Overall (AB) balance…



Open versus closed system

Henderson/ Hasselbalch/ Equation

$$K_B = \frac{[H^+][B^-]}{[HB]}.$$

Notation is a bit obscure: pH = - log10 [H+], pK_B is the base dissociation constant

$$pH = pK_B + \log \frac{[B^-]}{[HB]}.$$

Respiration and acid-base balance

$$pH = pK + \log \frac{[HCO_3^-]}{[H_2CO_3] = k \cdot pCO_2}$$

$$7{,}4 = 6{,}1 + \log \frac{24{,}0\ mM}{1{,}3\ mM} \ldots\ \underline{5{,}3\ kPa\ pCO_2}$$

Bicarbonate buffer action

$$CO_2 + H_2O \rightleftharpoons H_2CO_3 \rightleftharpoons H^+ + HCO_3^-$$

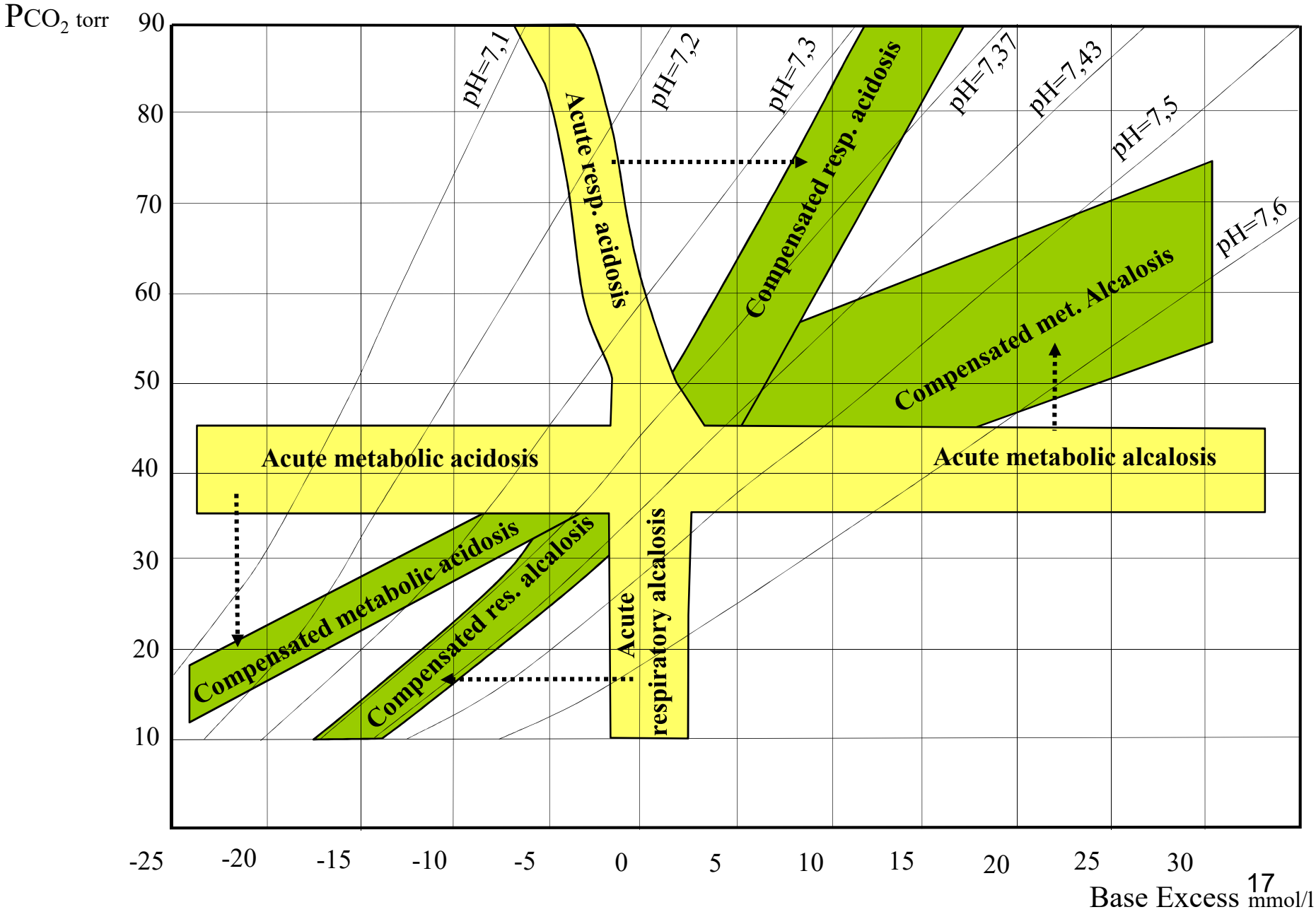
Hendersson- Hasselbalch equation:

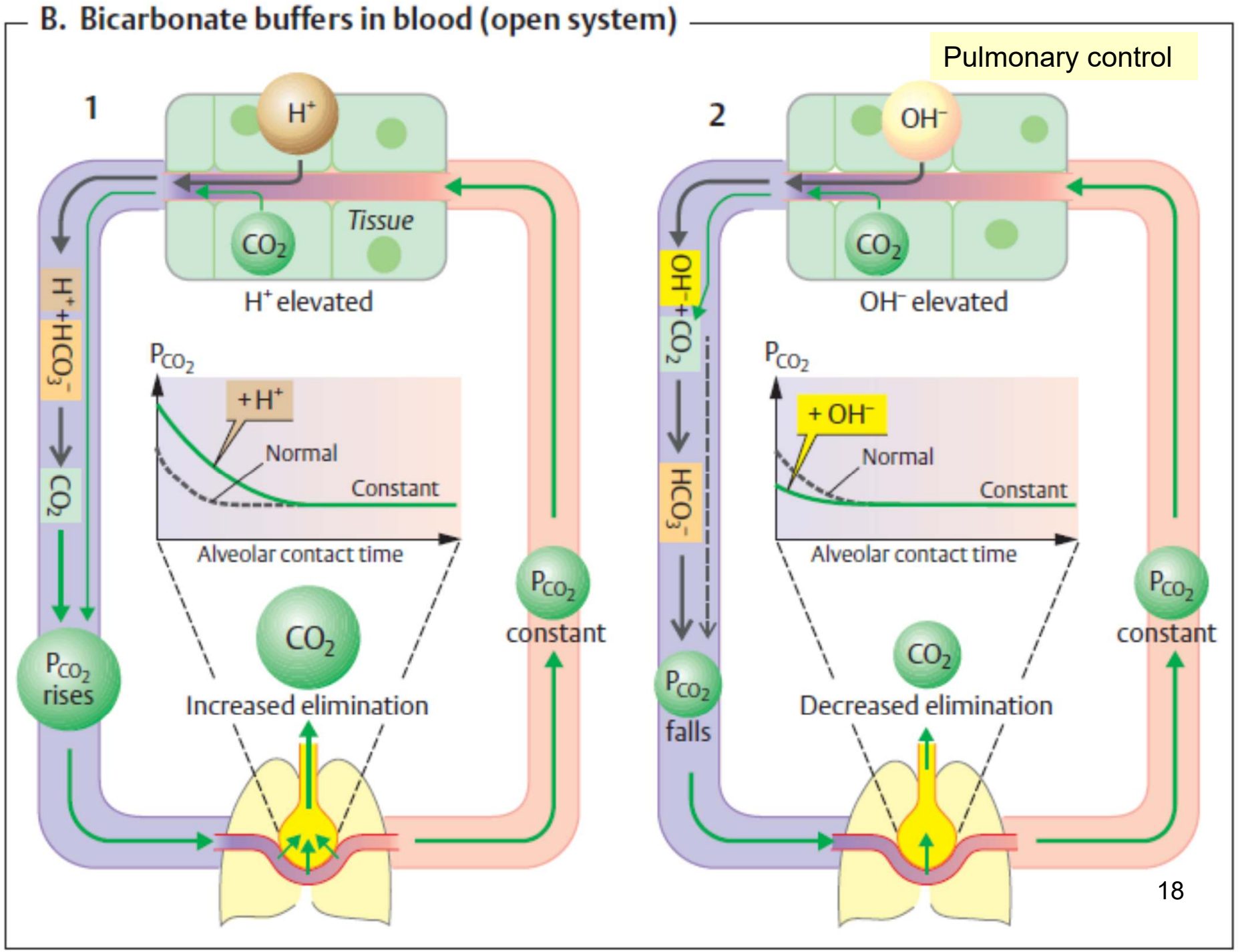
$[H^+] = 24 \cdot pCO2 / [HCO_3^-]$

or

$$pH = 6.1 + \log ([HCO_3^-] / [H_2CO_3])$$

$$= 6.1 + \log ([HCO_3^-] / 0.03\ pCO_2)$$


PCO2 torr
90
80
70
60
50
40
30
20
10
pH=7,1
Acute resp. acidosis
pH=7,2
pH=7,3
Compensated resp. acidosis
pH=7,37
pH=7,43
pH=7,5
pH=7,6
Compensated met. Alcalosis
Acute metabolic acidosis
Acute metabolic alcalosis
Compensated metabolic acidosis
Compensated res. alcalosis
Acute respiratory alcalosis
-25
-20
-15
-10
-5
0
5
10
15
20
25
30
Base Excess mmol/l


B. Bicarbonate buffers in blood (open system)
Pulmonary control
1
H+
Tissue
CO2
H+ elevated
H+ + HCO3−
CO2
PCO2
+H+
Normal
Constant
Alveolar contact time
PCO2 rises
CO2
Increased elimination
PCO2 constant
2
OH−
CO2
OH− elevated
OH− + CO2
HCO3−
PCO2
+ OH−
Normal
Constant
Alveolar contact time
PCO2 falls
CO2
Decreased elimination
PCO2 constant

Inner milieu: Why is pH (concentration of H^+) so important?

- Normal concentration of H^+ in plasma is 0.000 04 mmol/ L = 40 nmol/ L
- Very high chemical activity of hydrogen ions (protons) in solution
- Changes of pH influence spacial conformation of proteins

- however, in other fluids, it can different by many orders of magnitude
- **$pH = - \log_{10}(H^+)$**
- **40 nmol/ L = pH 7.4**

change 2x …. -0.3

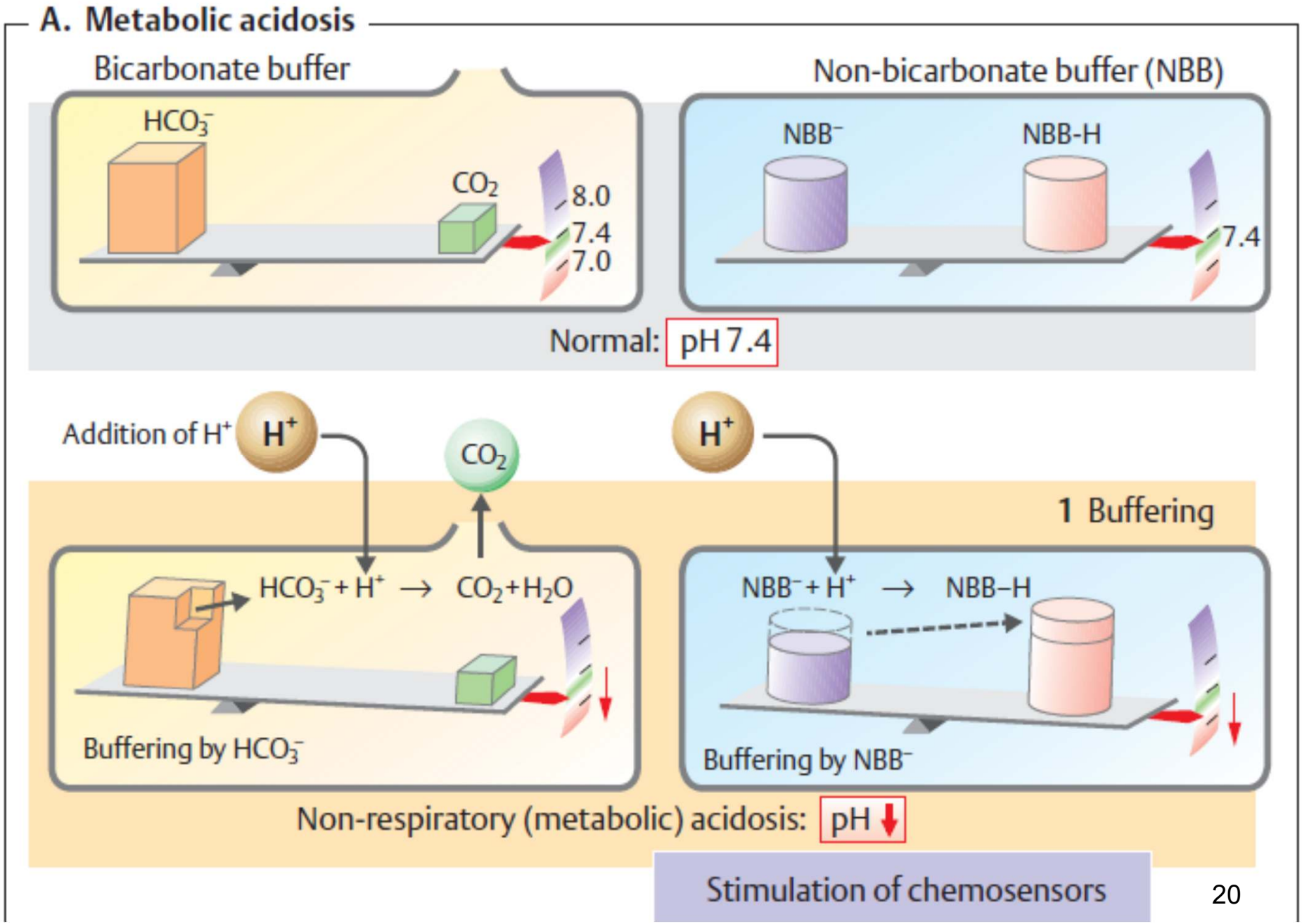
(change 1/2x…… +0.3)

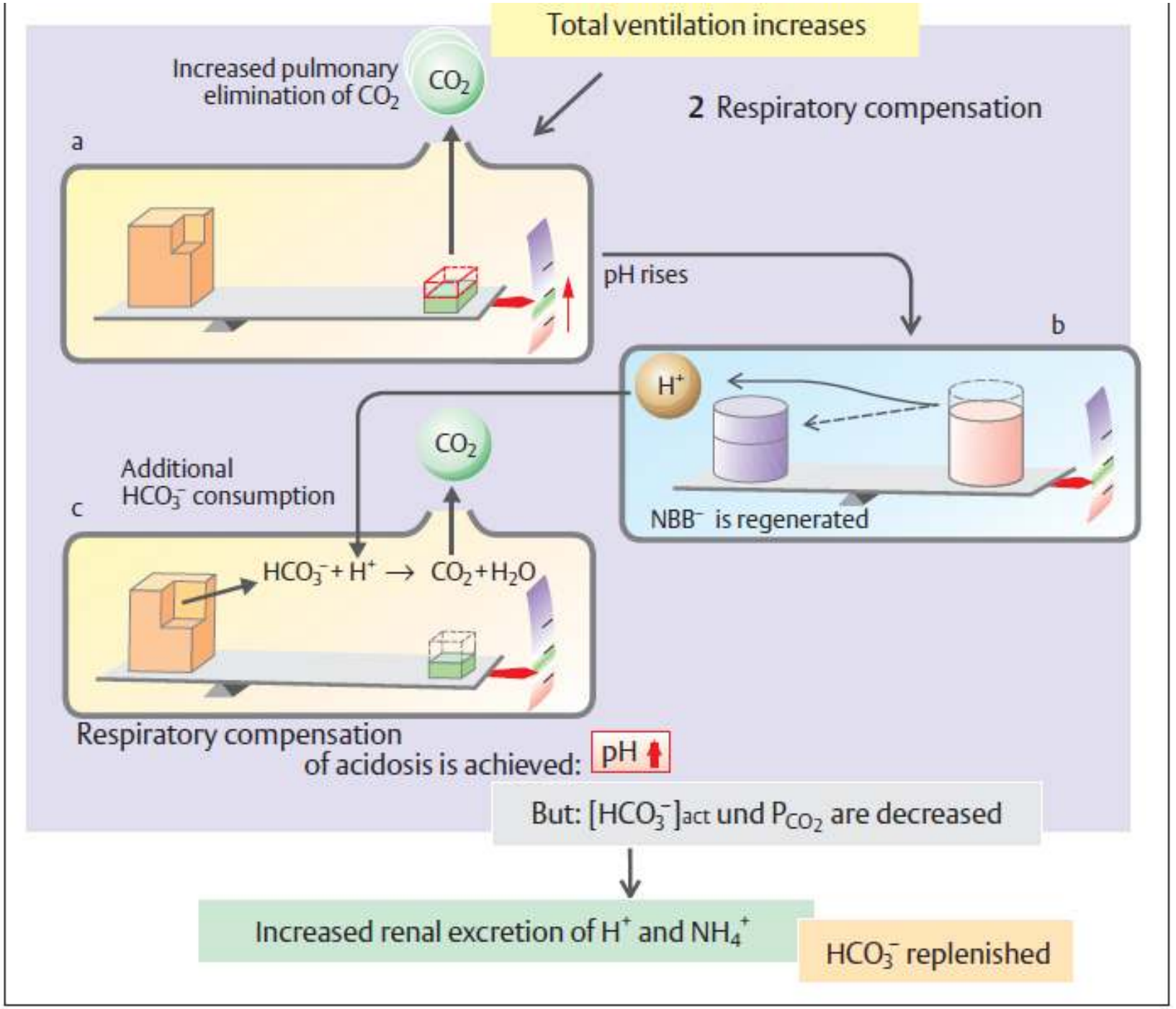
change 4x …. -0.6

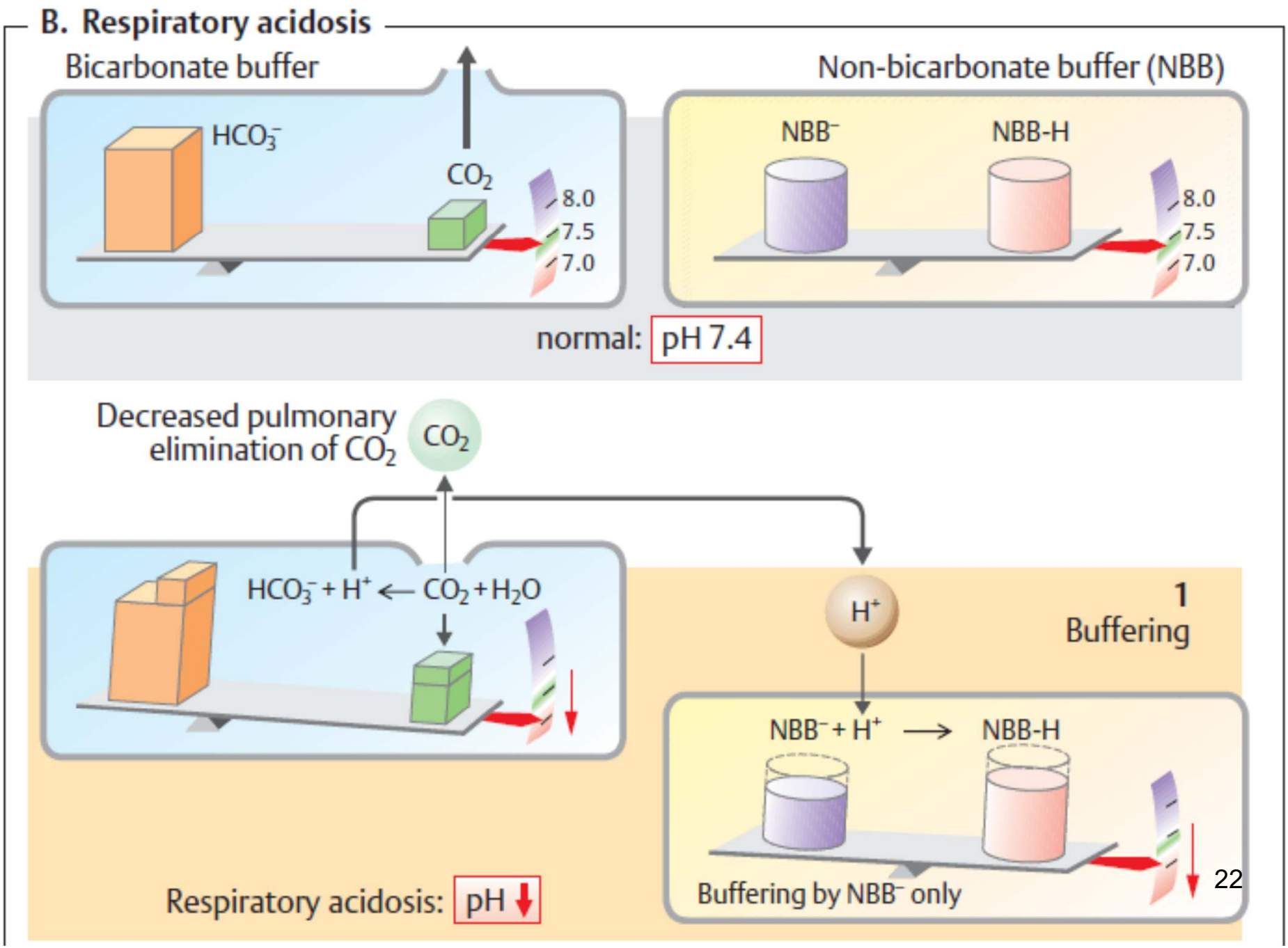
change 8x …… -0.9

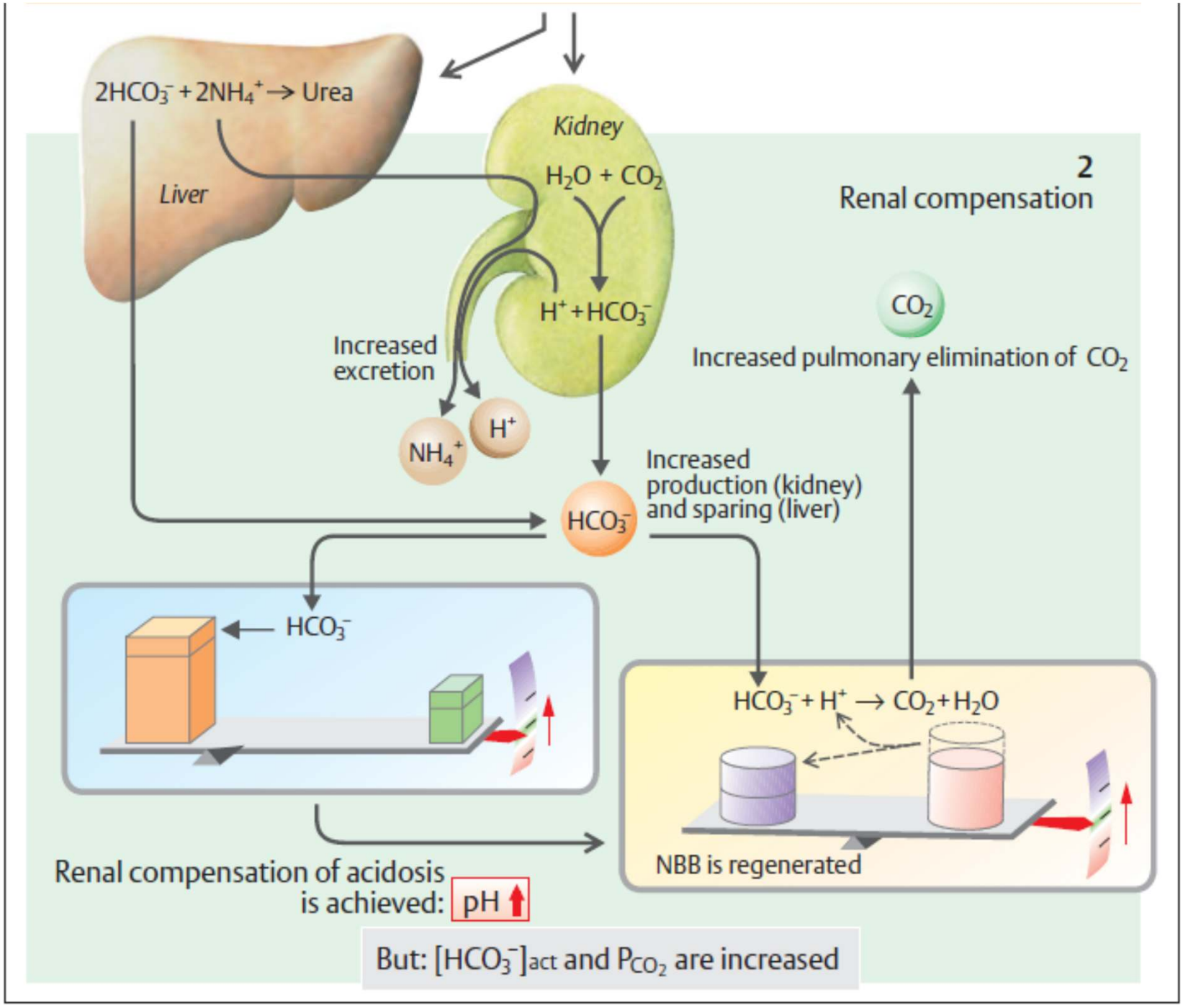
change 10x …….- 1.0

How is $[H^+]$ determined?

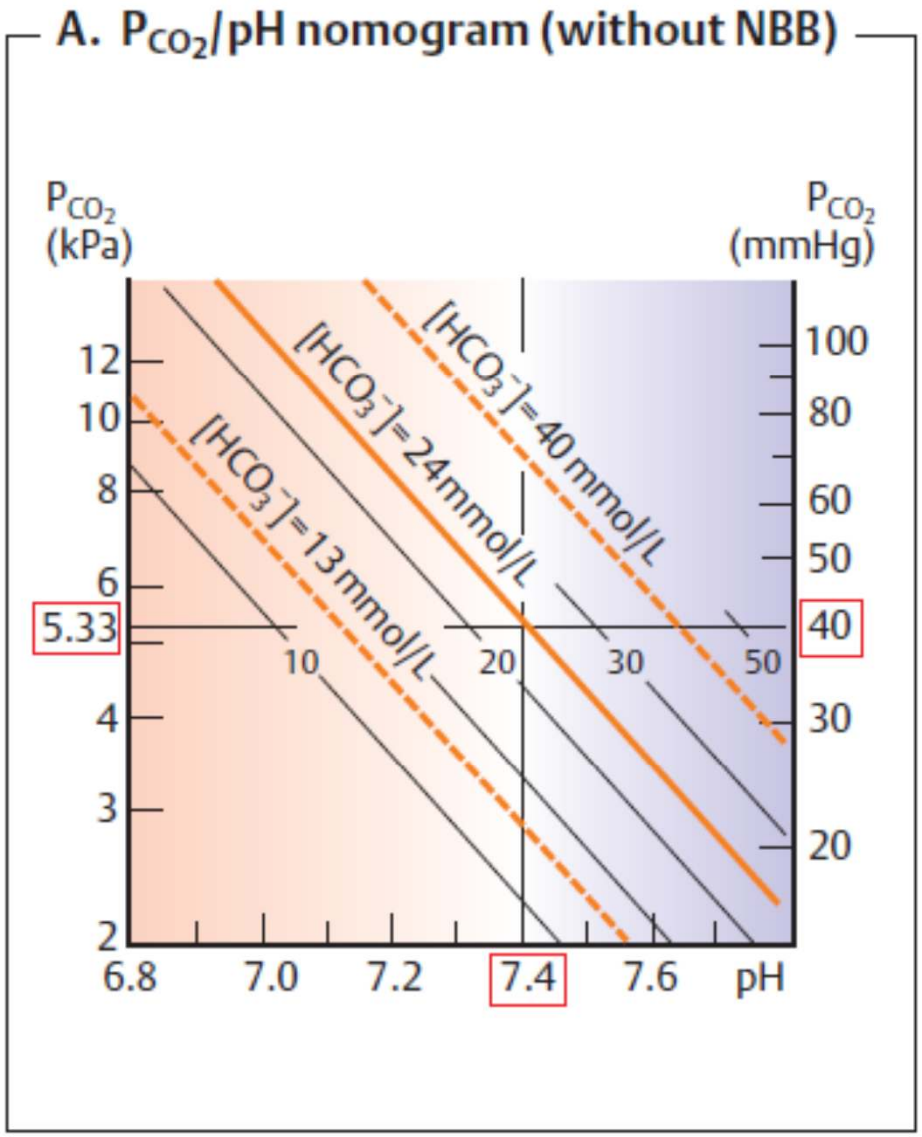

A. Metabolic acidosis
Bicarbonate buffer
Non-bicarbonate buffer (NBB)
HCO_3^-
CO_2
8.0
7.4
7.0
NBB^-
NBB-H
7.4
Normal: pH 7.4
Addition of H^+
H^+
CO_2
H^+
1 Buffering
$HCO_3^- + H^+ \rightarrow CO_2 + H_2O$
$NBB^- + H^+ \rightarrow$ NBB–H
Buffering by HCO_3^-
Buffering by NBB^-
Non-respiratory (metabolic) acidosis: pH ↓
Stimulation of chemosensors

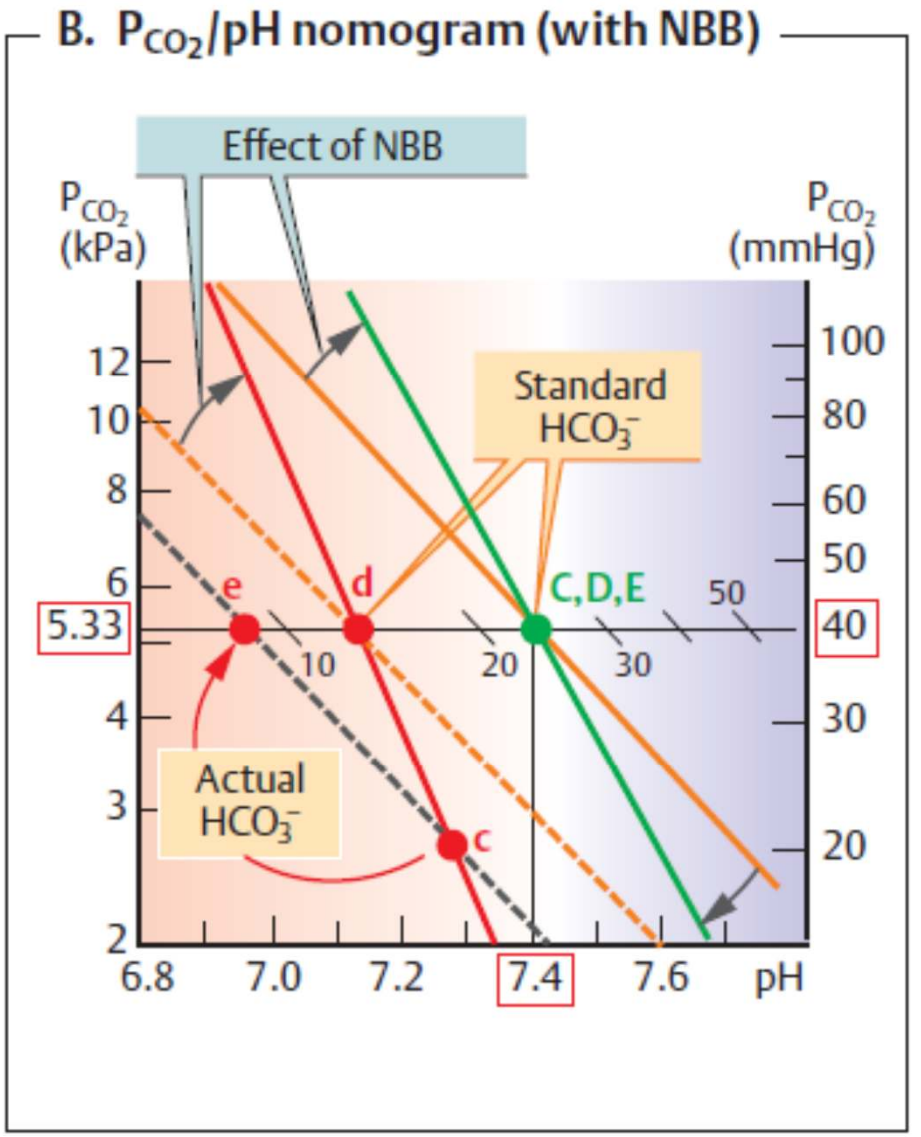

Total ventilation increases
Increased pulmonary elimination of CO_2
CO_2
2 Respiratory compensation
a
pH rises
b
H^+
CO_2
Additional HCO_3^- consumption
c
$HCO_3^- + H^+ \rightarrow CO_2 + H_2O$
NBB^- is regenerated
Respiratory compensation of acidosis is achieved: pH ↑
But: $[HCO_3^-]_{act}$ und P_{CO_2} are decreased
Increased renal excretion of H^+ and NH_4^+
HCO_3^- replenished


B. Respiratory acidosis
Bicarbonate buffer
Non-bicarbonate buffer (NBB)
HCO_3^-
CO_2
NBB⁻
NBB-H
8.0
7.5
7.0
normal: pH 7.4
Decreased pulmonary elimination of CO_2
CO_2
$HCO_3^- + H^+ \leftarrow CO_2 + H_2O$
H^+
1
Buffering
$NBB^- + H^+ \rightarrow$ NBB-H
Buffering by NBB^- only
Respiratory acidosis: pH ↓


2HCO3- + 2NH4+ → Urea
Liver
Kidney
H2O + CO2
2
Renal compensation
H+ + HCO3-
CO2
Increased pulmonary elimination of CO2
Increased excretion
NH4+
H+
Increased production (kidney) and sparing (liver)
HCO3-
HCO3-
HCO3- + H+ → CO2 + H2O
NBB is regenerated
Renal compensation of acidosis is achieved: pH
But: [HCO3-]act and PCO2 are increased

Improvements by Siggaard-Andersen follow…



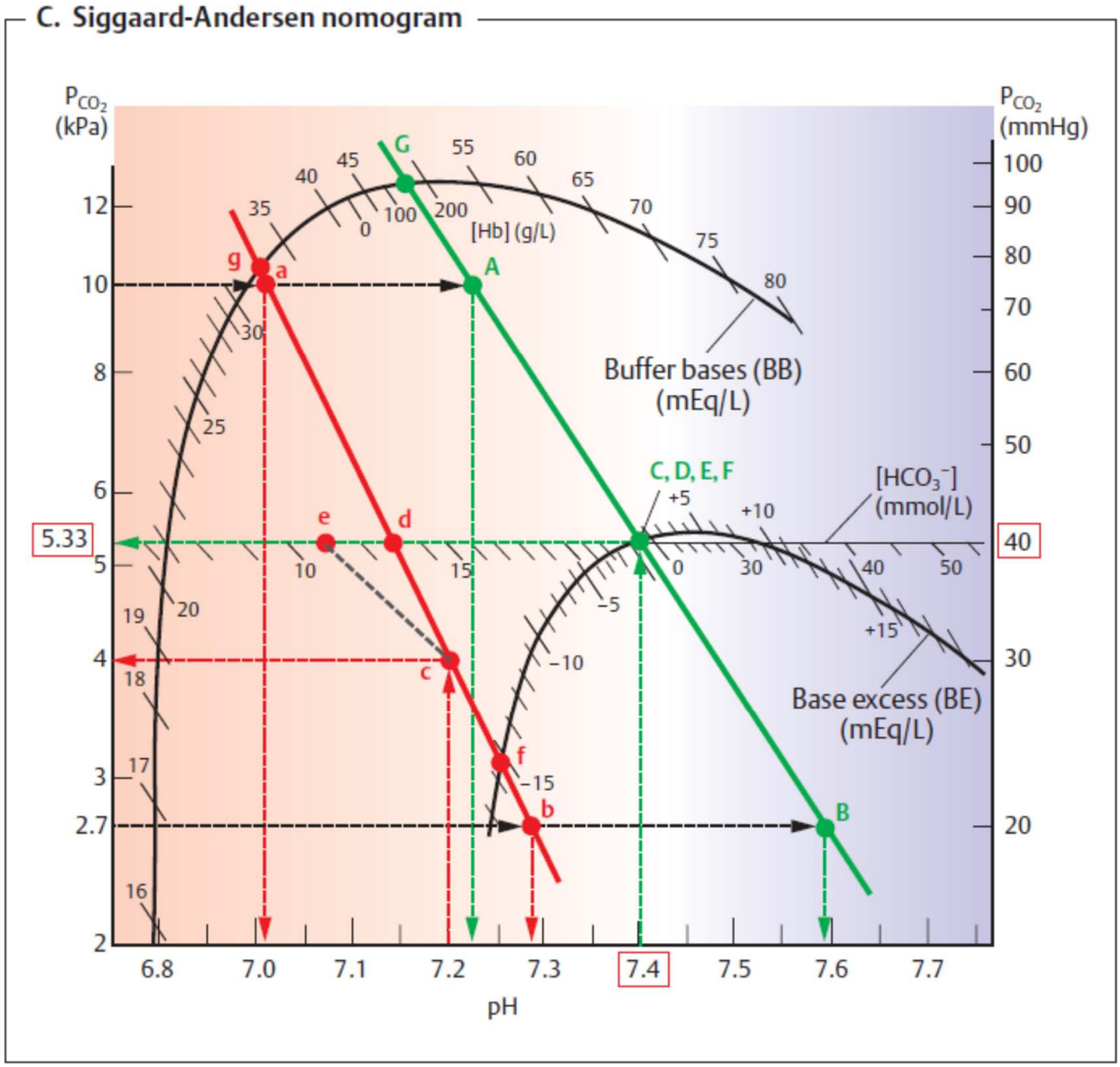


Base Excess - Solution by Siggaard-Andersen

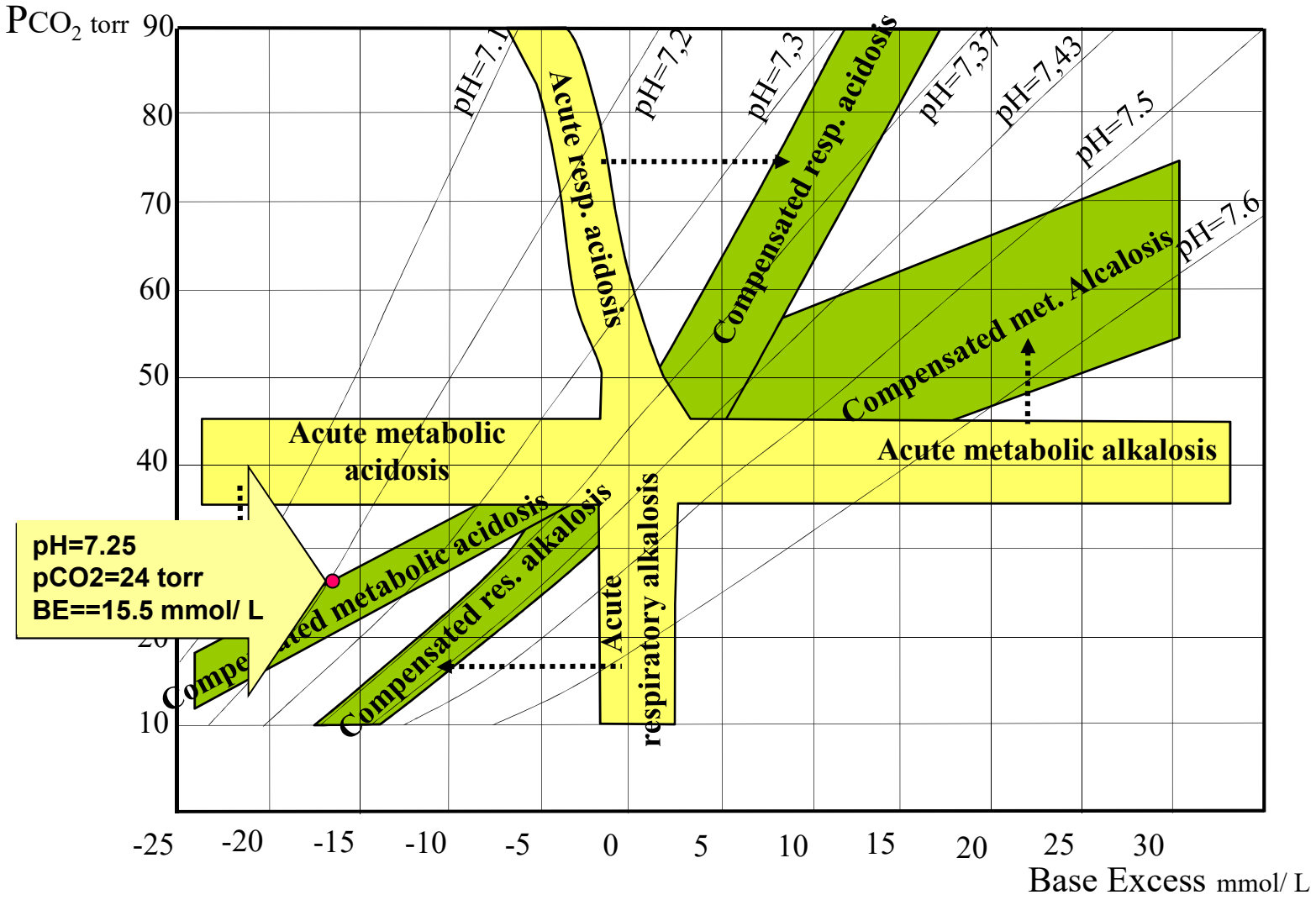
BE = BB - normalBB

- **Normal BB** is the buffer base that the given **blood would have at pH=7.4** It varies with hemoglobin level (anemia, polycythemia), albumin content etc.
- BE then only represents changes in BB due to changes in pH
- **BE** is independent of pCO2 (= 2D system)

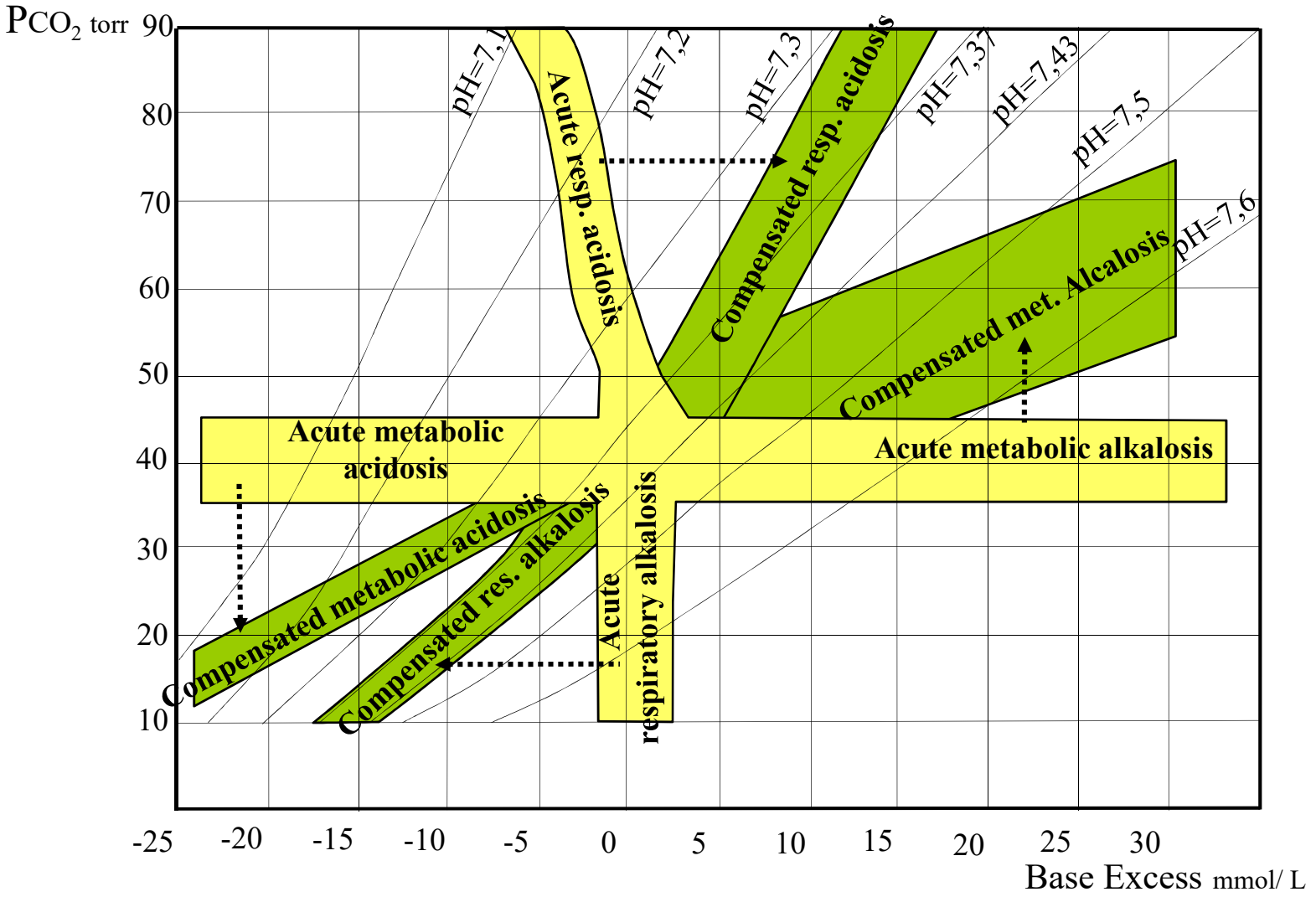
Ole Siggaard-Andersen (born 10 Dec 1932 -)
Danish physician, clinical chemist


C. Siggaard-Andersen nomogram
P_{CO_2} (kPa)
P_{CO_2} (mmHg)
[Hb] (g/L)
Buffer bases (BB) (mEq/L)
$[HCO_3^-]$ (mmol/L)
Base excess (BE) (mEq/L)
C, D, E, F
pH
5.33
7.4
G
A
B
a
b
c
d
e
f
g

Compensated metabolic acidosis



Other compensated ABB disturbances



Basic division of acid-base disturbances

- **Respiratory acidosis**

  ↑ pCO_2 - alveolar hypoventilation

- **Respiratory alcalosis**

  ↓pCO_2 - alveolar hyperventilation

- **Metabolic acidosis**

  ↓ HCO_3^-

- **Metabolic alcalosis**

  ↑ HCO_3^-

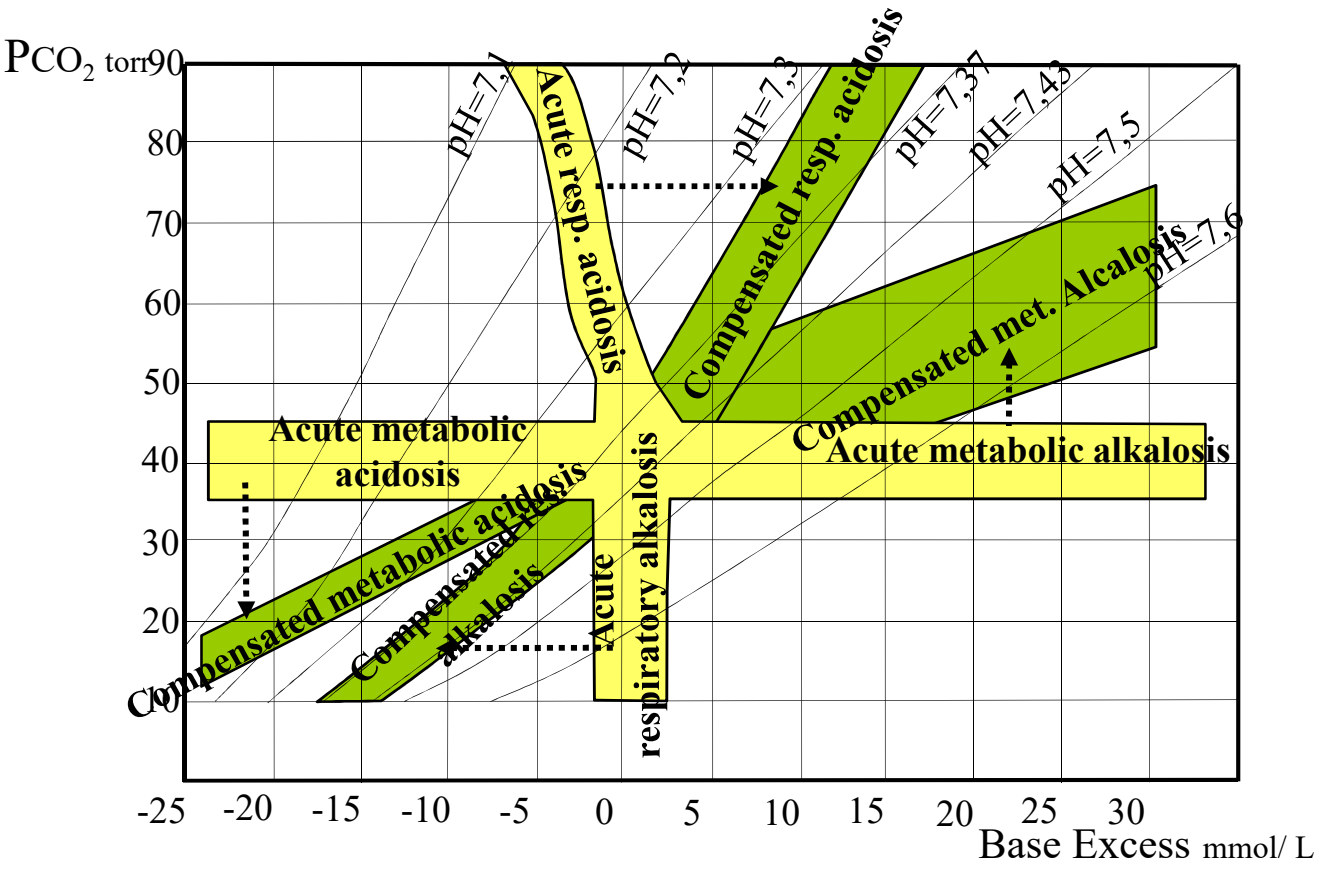
Metabolic compensation of respiratory disorder

- Is carried out by **kidneys** that **increase** plasma concentration of **bicarbonate in respiratory acidosis**. Kidneys also decrease bicarbonate reabsorption and their concentration in plasma in respiratory alkalosis.
- It takes about **2.5 days** to develop fully.

Respiratory compensation of metabolic disorder

- In **metabolic acidosis**, **lungs eliminate more pCO2** by deeper and faster breathing. This is called **Kussmaul breathing.**
- The respiratory compensation of the metabolic alkalosis is limited, because slower and more shallow breathing is limited by hypoxemia.
- Full compensation takes about ½ **day** to develop.

How fast are ABB disturbances compensated?



- **Respiratory** disorders are compensated by **Kidney**

  in 3 to 5 days

- **Metabolic** disorders are compensated by **Lung**

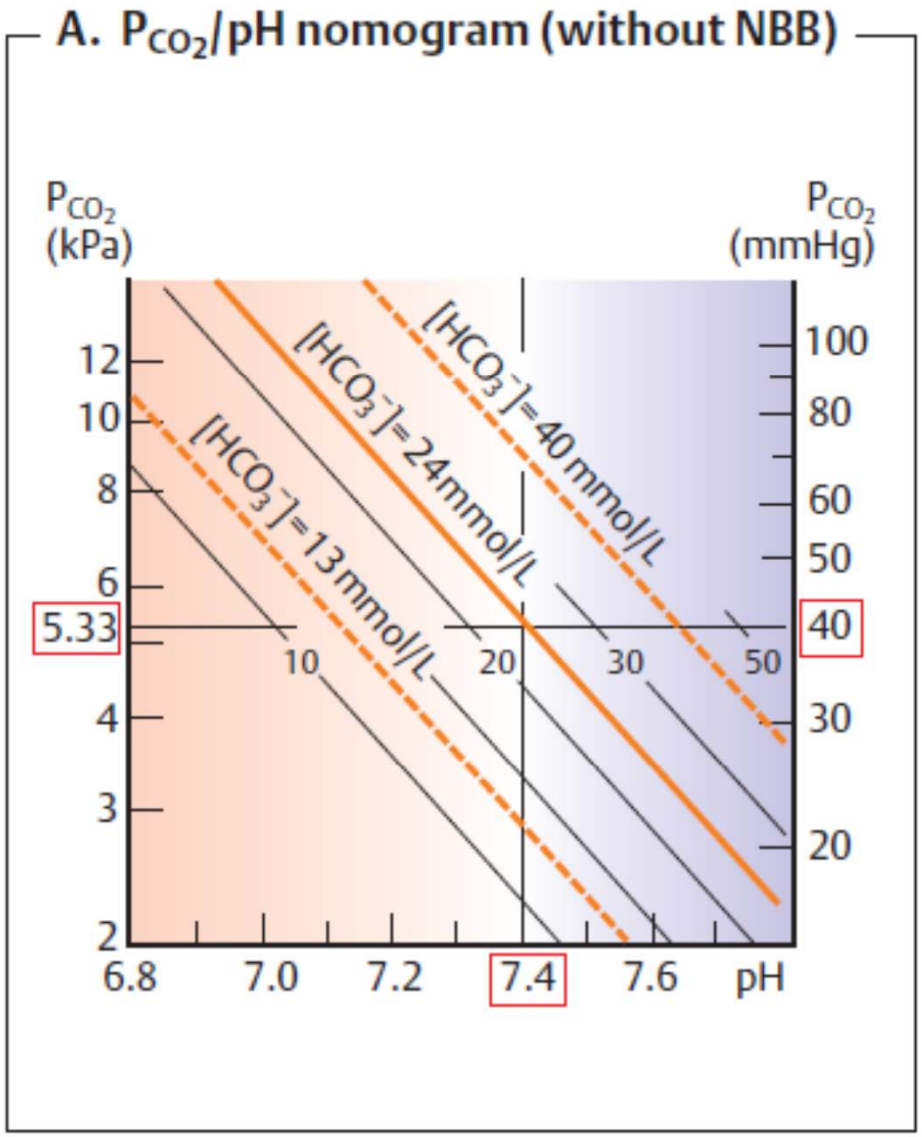
in 6 to 12 hours

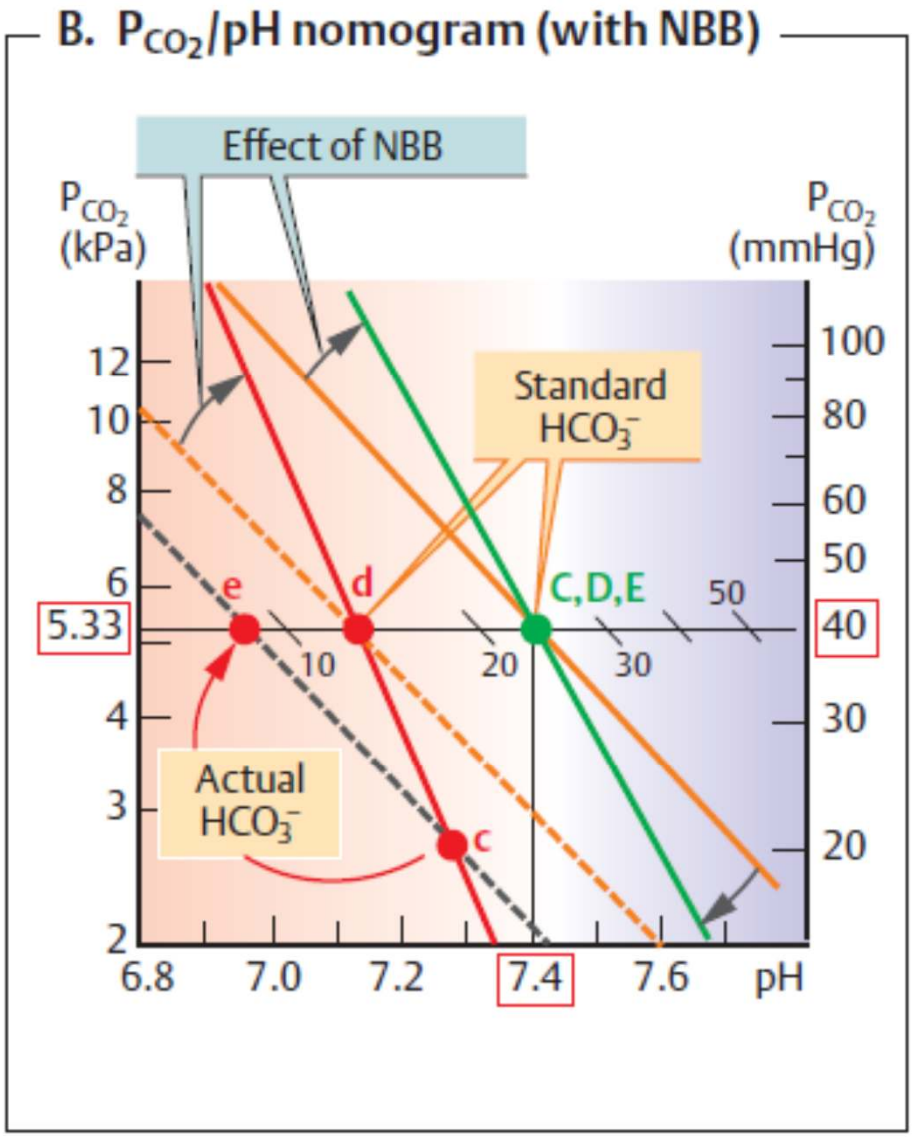
Measures of metabolic disturbances

- Independently changing variable: Only bicarbonate buffer => Change in pCO2 causes no change in HCO_3^-
- Other buffers present => **Increase** in **pCO2** causes an **increase** in **HCO_3^-** as well, but at the same time as a chain reaction **decrease** in **Buf^-** (non-bicarbonate buffers) =>

  BB (buffer base) = HCO_3^- + Buf^- stays constant
- Two possible approaches to the description of metabolic disturbances (2D system):
  - USA: **Standard Bicarbonates** - measure of metabolic disturbances independent of pCO2
  - EU: **Base Excess** – measure derived from BB, thus independent of pCO2

National differences…





Base excess

- At **pH = 7.4** different blood samples can have different total BB (depending on Hb, albumin, phosphates), but **BE = 0**
- Amount of BB a sample has at pH 7.4 is called its normal buffer base (nBB)
- BE = BB – nBB
- If we add to all these samples 10 mmol/ L of acid, the BB of each sample will decrease by 10 mmol/ L. **Now** each **BE = - 10.**

Is “direct” correction of AB imbalance a good idea? No it is not!

Direct acidification

in vitro/ in vivo:
adding NH_4Cl

Direct alcalisation

in vitro/ in vivo:
adding $NaHCO_3$

Causes of metabolic acidosis

- Extensive disequilibrating load on buffering system
  - Loss of bicarbonate from extensive buffering of acids
    - Ketoacidosis
      - Diabetic
      - Alcoholic
      - Starvation
    - Lactic Acidosis
    - Toxic substances
      - Salicylates
      - Ethylen glycol
      - methanol
  - Loss of bicarbonate by GIT
    - By diarrhea
    - By fistula and stomia
- Impairment of kidney regulation
  - Renal tubular acidoses
  - Kidney failure

Causes of respiratory acidosis

- ↓ alveolar ventilation
  - Respiratory center depression
    - Drugs, medicaments
    - Respiratory centre hypoxia or damage
      - Trauma
      - Stroke
      - Tumor
      - Cerebral edema / increased intracranial pressure
  - Nerve of muscle disease
    - Myasthenia gravis
    - Polyradiculoneuritis
    - Serious obesity
  - Lung disease
    - Restrictive
      - ARDS
      - Fibroses
    - Trauma, pneumothorax, serial rib fractures
    - Obstructive
      - Astma
      - Tumor
      - Foreign body
    - Increase in dead space
      - Embolism
      - Emphysema
- Breathing CO2 in the inspired air

Causes of respiratory alcalosis

- Hyperventilation
  - in mechanical ventilation
  - With hypoxemia
    - High altitude disease
    - Right-left shunting
- Respiratory centre irritation
  - Trauma, salicylates, inflammation

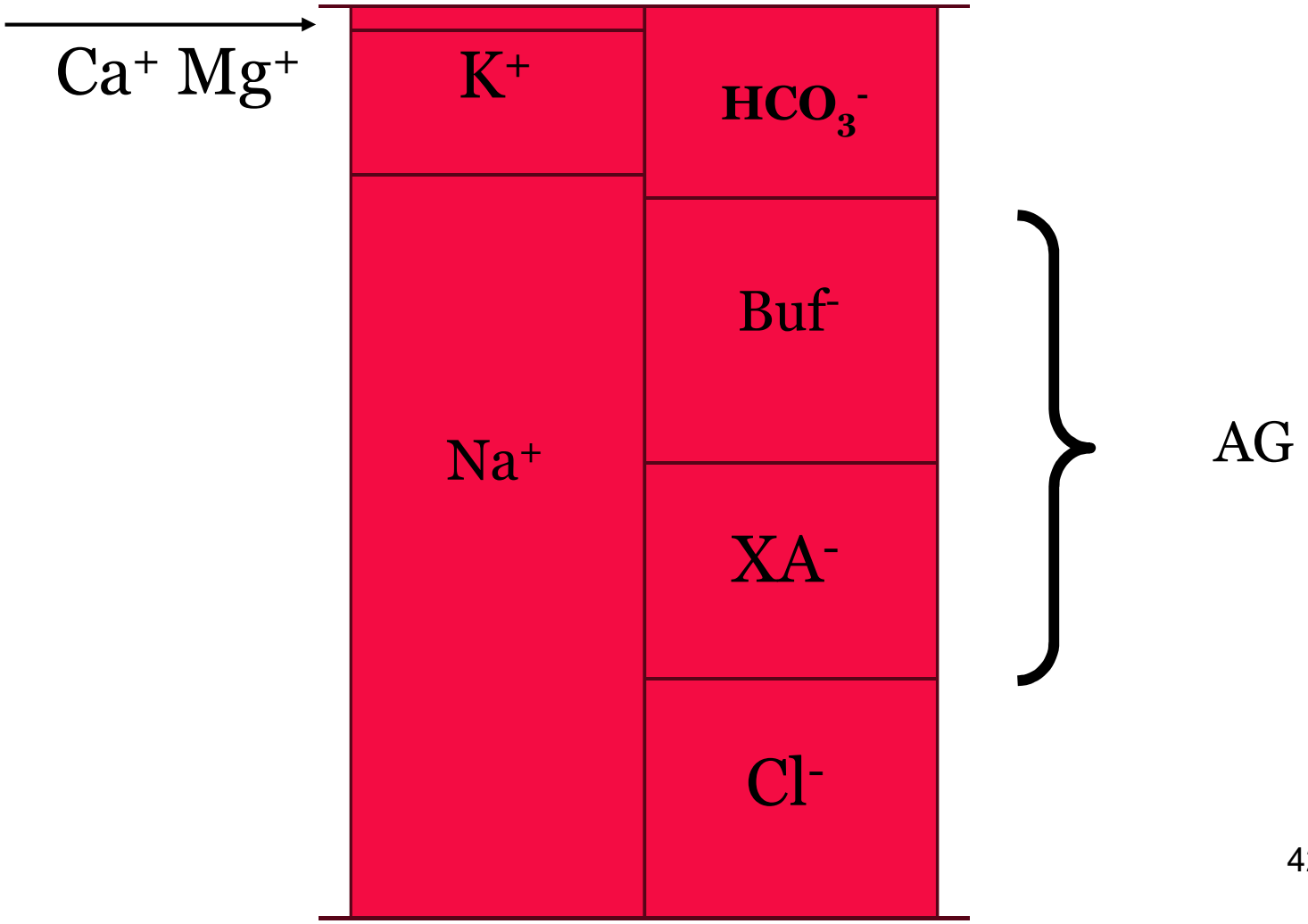
Causes of metabolic alcalosis

- Vomiting – losses of hydrochloric acid
- Hyper-aldosteronism
- Liver failure and insufficiency
- Kidney disorders
- Incorrect infusion therapy

Anion gap

- Metabolic acidoses may be distinguished according the strong acids participation
- These are **lactate, substances of ketoacidosis, sulfates,** etc
- AG = Na^+ - HCO_3^- - Cl^-
- norm: **10+/- 2** mmol/ L

Anion gap



END
OF THE LECTURE

Thanks for your attention

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Contact: Petr.Marsalek@LF1.CUNI.CZ

First Medical Faculty, Institute of Pathological Physiology

Side comment: ABB founders in Czechoslovakia and in world

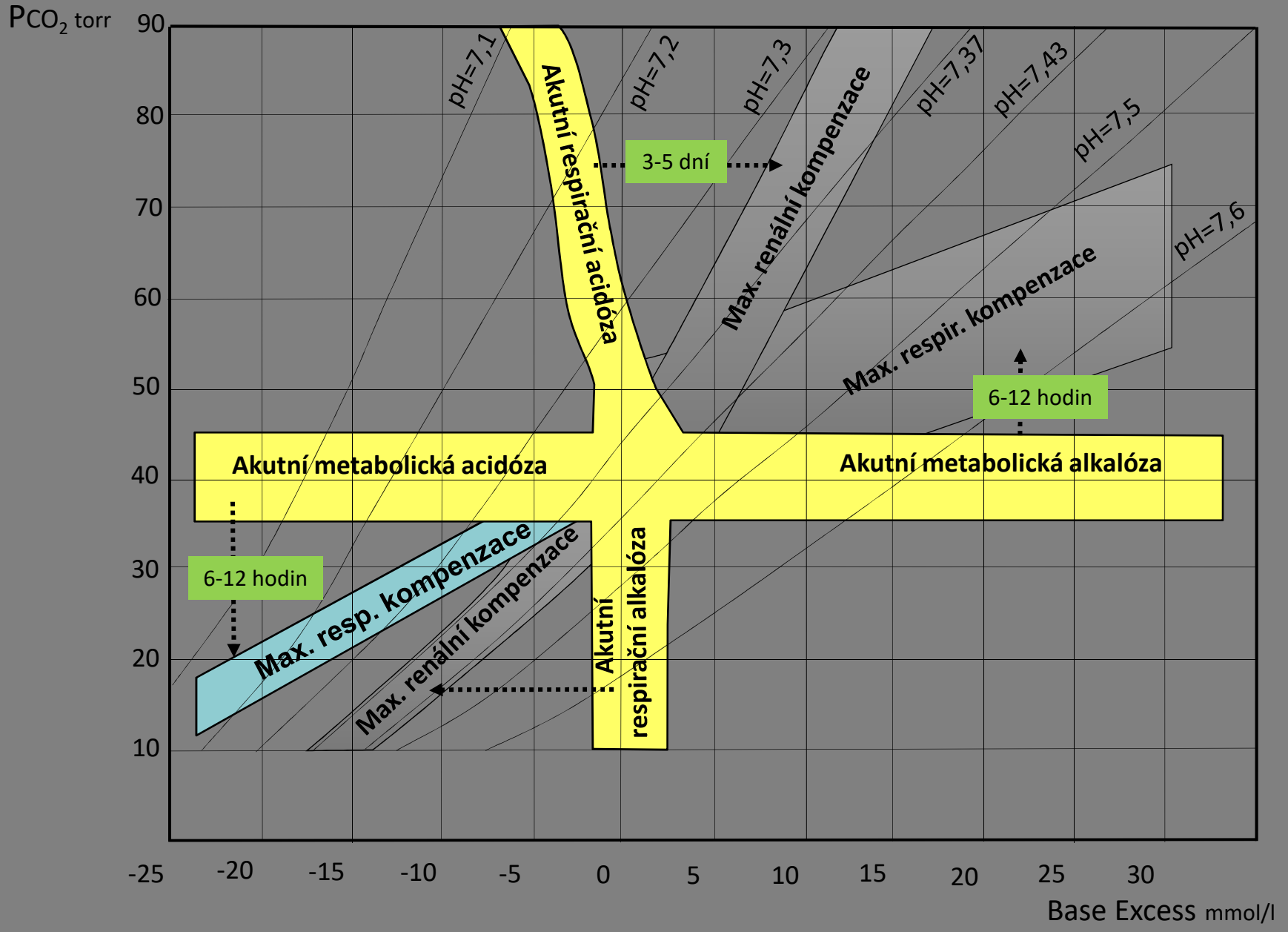
Poul (Paul) Bjørndahl Astrup (* 4 August 1915 – [+] 30 November 2000) was a Danish clinical chemist

Ole Siggaard-Andersen, * 1932, another Danish professor

Antonín Kazda, * 1934, in 2020 aged 86

Marie Brodanová, * 1933, aged 87

Miroslav Engliš, (*1932 - [+] 2014)


PCO2 torr
90
80
70
60
50
40
30
20
10
-25
-20
-15
-10
-5
0
5
10
15
20
25
30
Base Excess mmol/l
pH=7,1
pH=7,2
pH=7,3
pH=7,37
pH=7,43
pH=7,5
pH=7,6
Akutní respirační acidóza
Max. renální kompenzace
3-5 dní
Max. respir. kompenzace
6-12 hodin
Akutní metabolická acidóza
Akutní metabolická alkalóza
6-12 hodin
Max. resp. kompenzace
Max. renální kompenzace
Akutní respirační alkalóza

Přepočty tlaků: 101 kPA~100 kPa

760 mmHg = 101 kPa = 1000 cmH_2O = 100%

(1). (aktuální) kyselost;
(↔). pH = 7,4 ± 0,04;
(2). parciální tlak CO_2 v alveolech;
(↔). p_{CO_2} = 5,3 ± 0,8 kPa (40 ± 6 mmHg);
(3). standardní bikarbonáty, koncentrace $[HCO_3^-]_{STD}$, při standardním p_{CO_2} = 5,3 kPa a nasycení krve O_2;
(↔). $[HCO_3^-]_{STD}$ = 24 ± 2 mmol/l;
(4). aktuální bikarbonáty, koncentrace $[HCO_3^-]_{ACT}$, při aktuálním p_{CO_2} a nasycení krve O_2;
(↔). normálně $[HCO_3^-]_{ACT} = [HCO_3^-]_{STD}$;
(5). NBB (normal buffer base), souhrn nárazníkových bazí, při standardním p_{CO_2} a nasycení krve O_2;
(↔). NBB = 48 ± 2 mmol/l; viz rovnice;
(6). BB (buffer base), souhrn nárazníkových bazí při aktuálním p_{CO_2};
(↔). normálně BB = NBB;
(7). BE (base excess), množství bazí, které je třeba přidat/ubrat za standardních podmínek, aby pH = 7,4;
(↔). BE = 0± 2 mmol/l.

Vědět rozdíly acidóza vs. acidémie, alkalóza vs. alkalémie, ...

Je možné užít kapilární krev, venózní krev? ...

Souhrn – budeme po této přednášce patofyziologie umět odpovědět na tyto otázky?

1. Jak se vyšetřuje ABR?
2. Proč se používá arteriální/ arterializovaná krev?
3. Proč používáme STD., či AKT. hodnoty, jaký je rozdíl?
4. Víme ještě z fyziologie/ patobiochemie, co jsou základní pufry?
5. Proč je pufrování CO2 otevřený systém (také fyziologie)?
6. Jaká je souvislost plicních poruch a ABR?
7. Jaká je souvislost poruch ledvin a ABR?
8. Znáte rychlost kompenzace poruchy ABR plícemi a ledvinami?
9. Proč diskutujeme alkalizaci/ nebo acidifikaci vnitřního prostředí?
10. Jak poznáme kombinovanou poruchu acidobazické rovnováhy?