Acid-Base Balance

H+ concentrations are regulated a very low levels:

$$[H+] = 0.00004 \text{ mEq/L}$$

$$pH = -\log[H^+]$$

mEq one thousandth (10^{-3}) of a gram equivalent of a chemical element, an ion, a radical, or a compound.

$$[Na+] = 142 \text{ mEq/L}$$

ACID-BASE REGULATION

Metabolic reactions are very sensitive to changes of ambient pH and the body fluids are maintained within a very narrow range of values.

The extracellular pH is generally in the range 7.35 - 7.45

Several mechanisms are available to keep pH within these limits

1. Extracellular buffering
2. Adjustments to blood P_{CO2} by altering the ventilatory capacity of the lungs
3. Adjustments to renal acid excretion or base reabsorption

Very Basics (and Acidics)

Acid: proton donor
Base: proton acceptor
Weak acid or base: acid or base that incompletely dissociates
Buffer: Reduces changes in pH resulting from
the addition of strong acides or bases

Quantifying acidity:
$pH = -\log[H^+]$

Sources of acid

Metabolism (volatile acid)

CO_2 is greatest source of H^+ via oxidation of glucose and fatty acids

Fixed or non-volatile acids produced during metabolism

H_2SO_4 from sulfur-containing amino acids

Phosphoric acid

Hydrochloric acid

Lactic acid (anaerobic metabolism product) some of this is converted to CO_2

Buffering

Bicarbonate
Phosphate
Proteins

Henderson-Hasselbalch Equation

$HA \leftrightarrow H^+ + A^-$

$$pH = pK_A + \log \frac{[A^-]}{[HA]}$$

The pK_A is the negative log of the dissociation constant.

The carbonic anhydrase reaction is:

$$CO_2 + H_2O \underset{CA}{\longleftrightarrow} H_2CO_3 \longleftrightarrow H^+ + HCO_3^-$$

The first step is relatively slow and requires catalysis by the enzyme carbonic anhydrase (CA).

The buffer system is under the dual regulation of the lungs and the kidneys

Normal $[H^+]$ = 0.00004 mEq/L or 40 nEq/L

Normal variation in $[H^+]$ is 3-5 nEq/L
Extreme variation is 10 nEq/L

$[H^+]$ is expressed in log scale using pH units
$$pH = -\log[H^+]$$

Bicarbonate System

Buffer value = $\Delta[HCO_3^-]/\Delta pH$

In the presence of carbonic anhydrase

Then,

$$CO_2 + H_2O \xleftarrow{} CA \xrightarrow{} H_2CO_3 \leftrightarrow H^+ + HCO_3^-$$

$$pH = pK_{HCO3} + \log \frac{[HCO_3^-]}{[CO_2]}$$

$$pH = 6.1 + \log \frac{[HCO_3^-]}{[0.03 \cdot P_{CO2}]}$$

Pa_{CO2}=40 mmHg

$[HCO_3^-]$=24 mEq/L

$$pH = 6.1 + \log \frac{[HCO_3^-]}{[0.03 \cdot P_{CO2}]}$$

$$pH = 6.1 + \log \frac{24}{0.03 * 40}$$

$$pH = 6.1 + \log 20$$

$$pH = 6.1 + 1.3$$

$$pH = \mathbf{7.4}$$

What happens when acid is added?

$$CO_2 + H_2O \underset{CA}{\longleftrightarrow} H_2CO_3 \longleftrightarrow H^+ + HCO_3^-$$

Lungs

The $[CO_2]$, or PCO_2 will increase and removed by increased ventilation.

What would happen if the CO_2 were increased?

$$CO_2 + H_2O \underset{CA}{\longleftrightarrow} H_2CO_3 \longleftrightarrow H^+ + HCO_3^-$$

The HCO_3^- will rise removed by the kidneys.

Kidneys

$$pH = 6.1 + \log \frac{[HCO_3^-]}{[0.03 \cdot P_{CO2}]}$$

Kidneys

Lungs

$$pH = \text{Constant} + \frac{\text{Kidneys}}{\text{Lung}}$$

Phosphates

$H_2PO_4 \leftrightarrow H^+ + HPO_4^=$

pK = 6.8

Other organic phosphates can act as buffers

glucose-1-phosphate

ATP

Proteins

pKs range from 5.5 to 8.5

Hb has histidine residues (pKs 7 to 8)

Deoxyhemoglobin is a weaker acid than oxyhemoglobin

As O_2 leaves Hb, more H^+ attaches to Hb, allowing increased CO_2 to be transferred as bicarbonate

Reversed in the lungs

pH

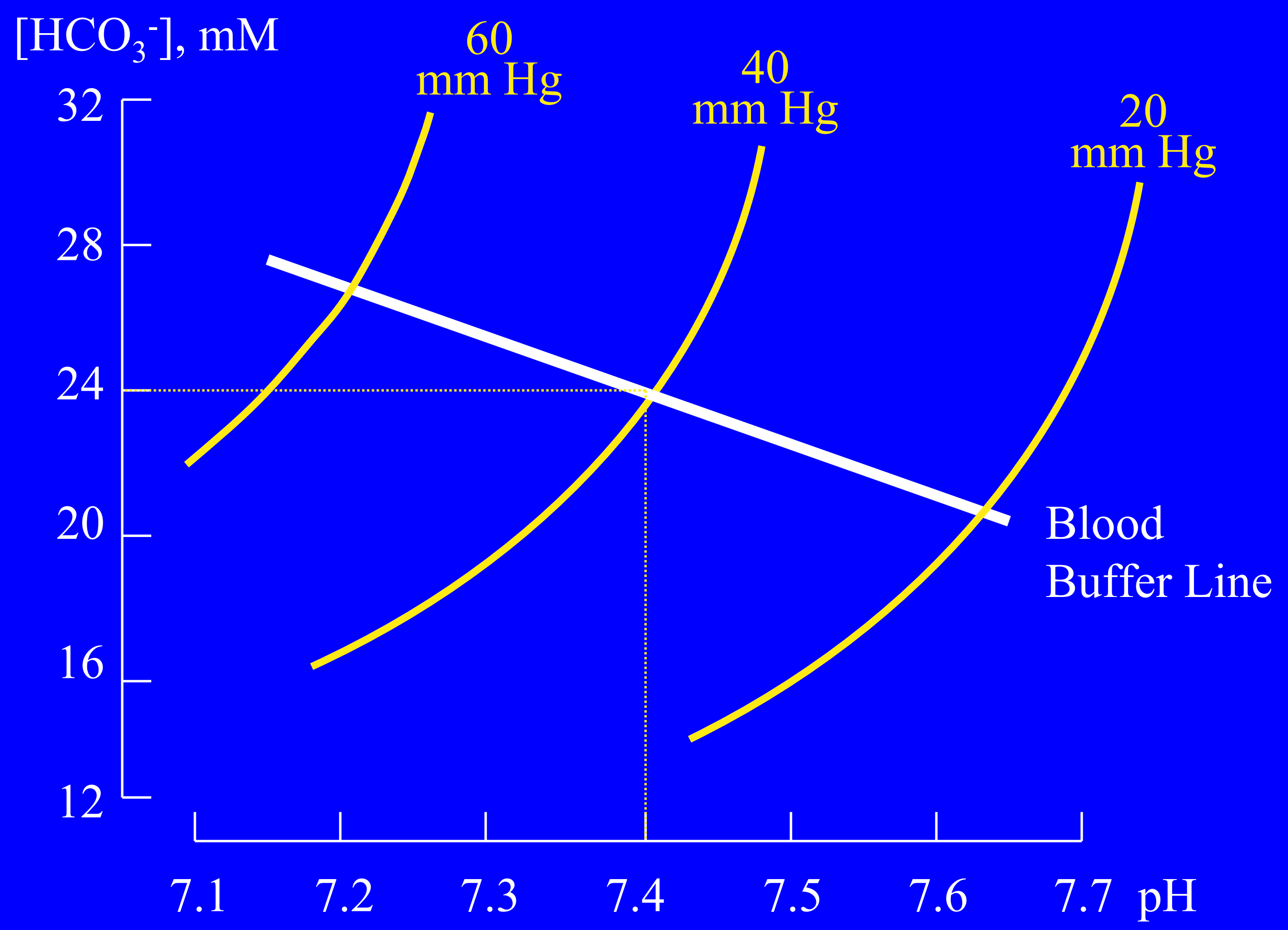
1.0---------------<7.35 – 7.45 <---------------10.0

Acidosis Alkalosis

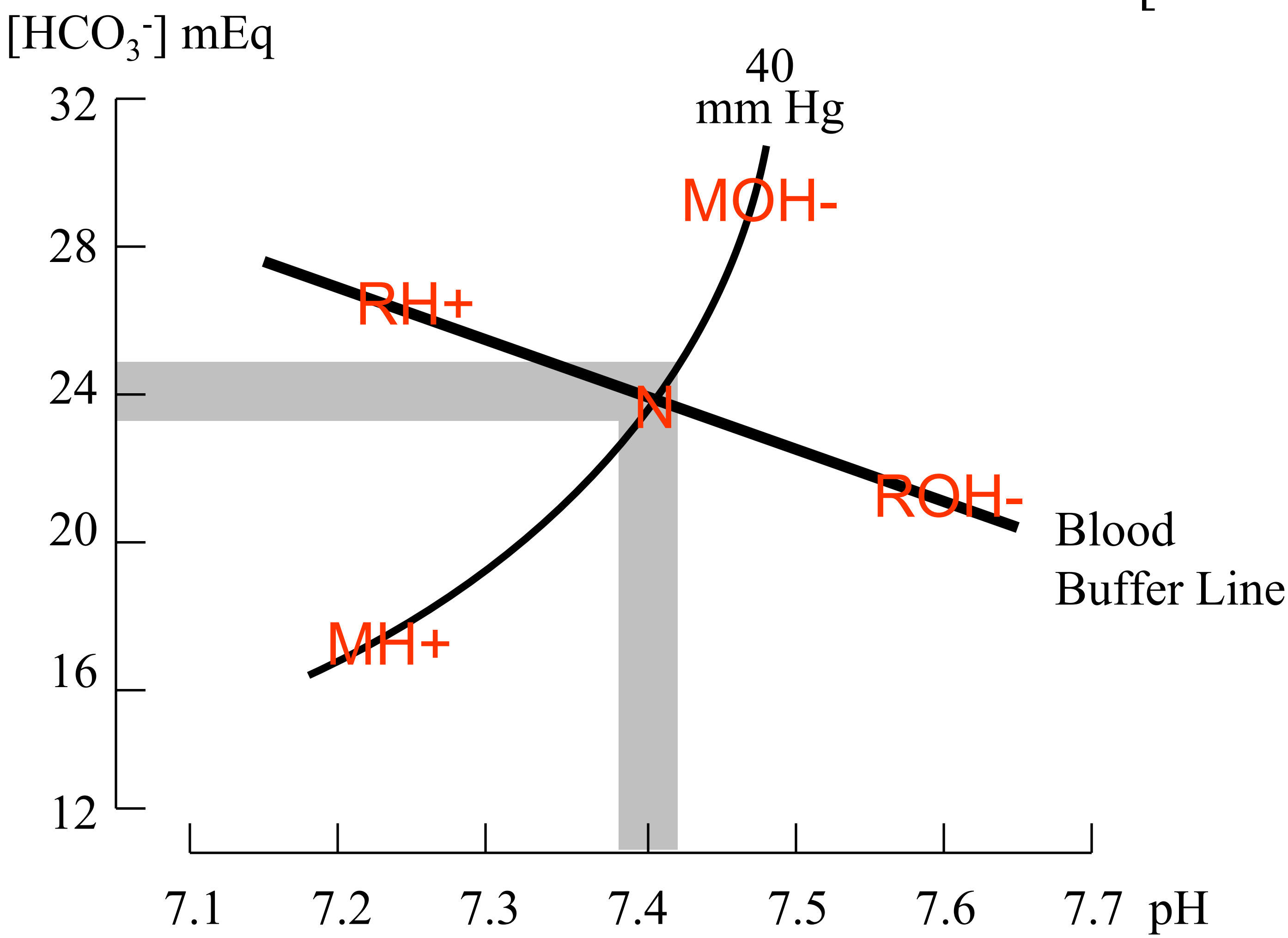
	pH	$[H^+]$	Pa_{CO2}	$[HCO3^-]$
Normal	7.4	40 nEq/L	40 mmHg	24 mEq/l
Respiratory Acidemia	↓	↑	↑	↑
Respiratory Alkalemia	↑	↓	↓	↓
Metabolic Acidemia	↓	↑	↓	↓
Metabolic Alkalemia	↑	↓	↑	↑

THE RELATIONSHIP BETWEEN PLASMA pH, [HCO_3^-] and PCO_2

The Davenport diagram expresses the relationship between these variables

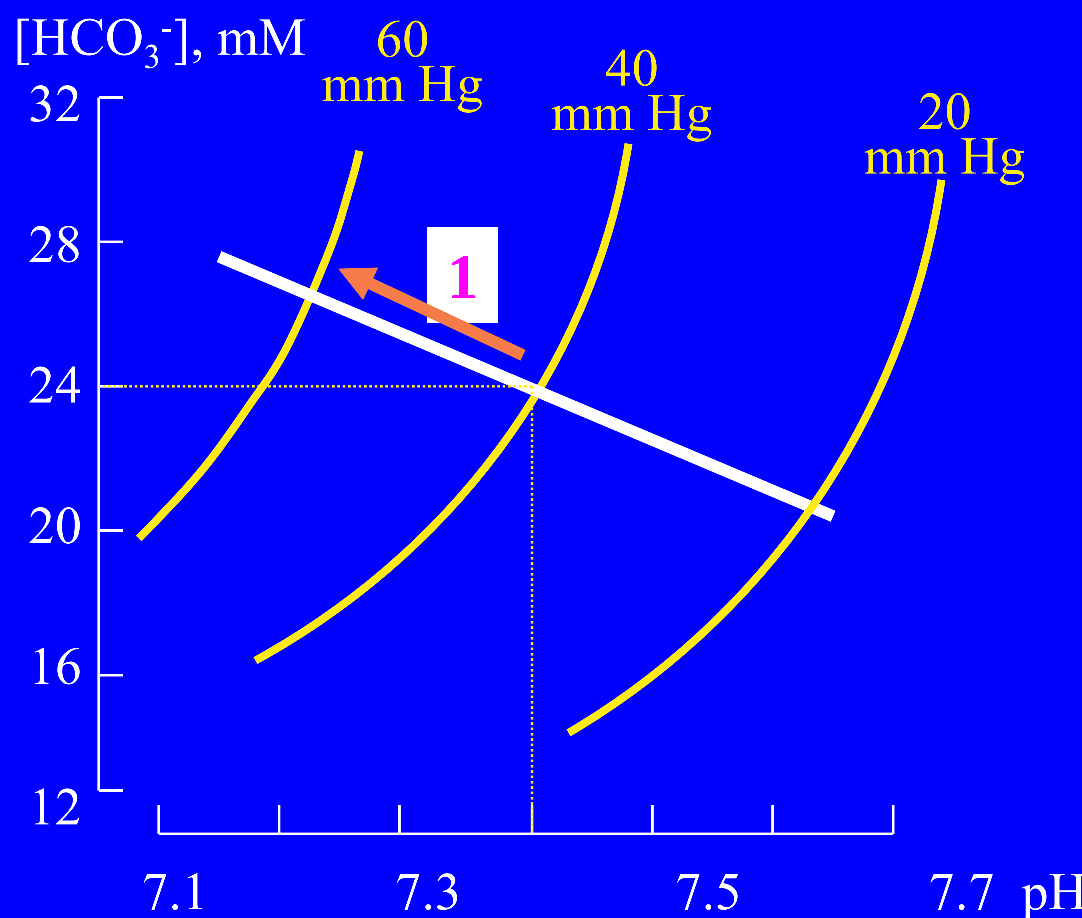


$$pH = 6.1 + \log \frac{[HCO_3^-]}{[0.03 \cdot P_{CO2}]}$$



RESPIRATORY ACIDEMIA

A retention of CO_2 generally caused by respiratory problems, **hypoventilation**

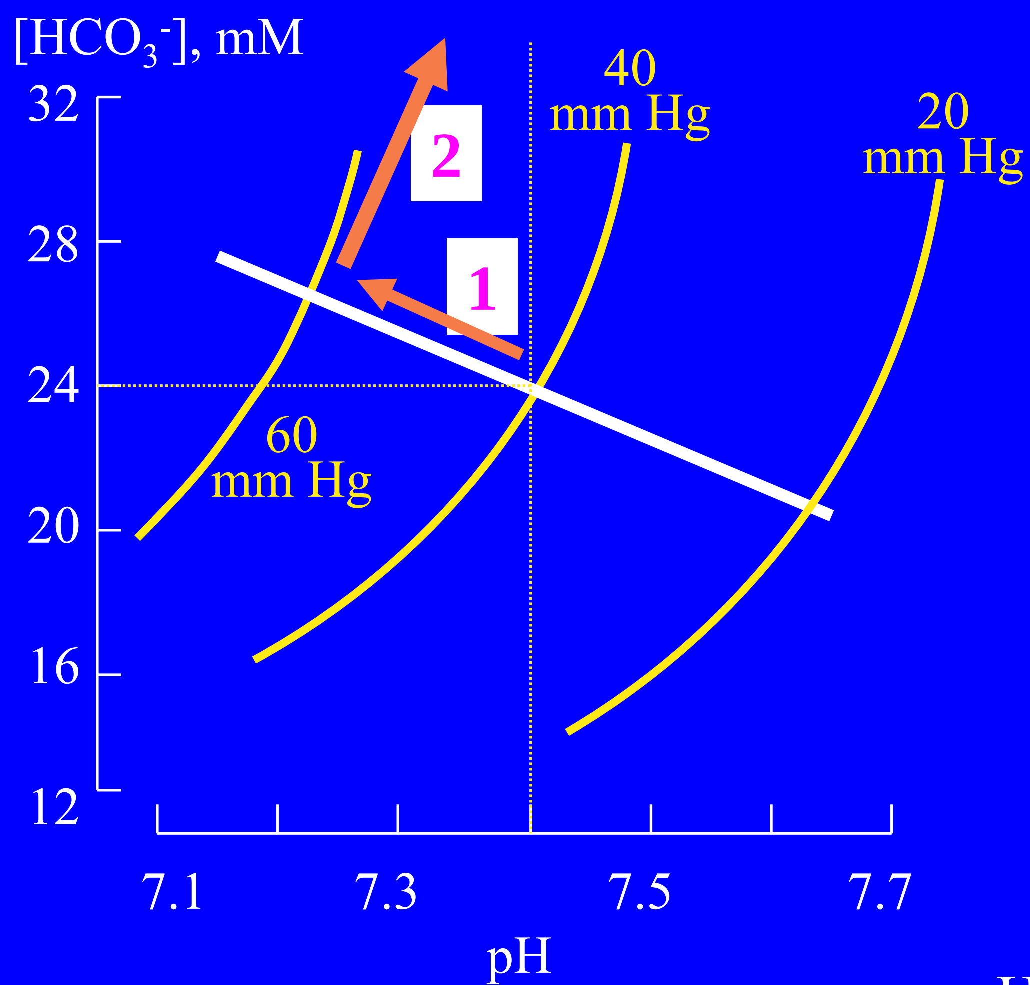


$$pH = 6.1 + \log \frac{[HCO_3^-]}{[0.03 \cdot P_{CO2}]}$$

PCO_2 is raised, pH is reduced
HCO_3^- is normal

COMPENSATED RESPIRATORY ACIDEMIA

Compensation attempts to restore the pH towards normal



The kidney retains base, i.e. HCO_3^-

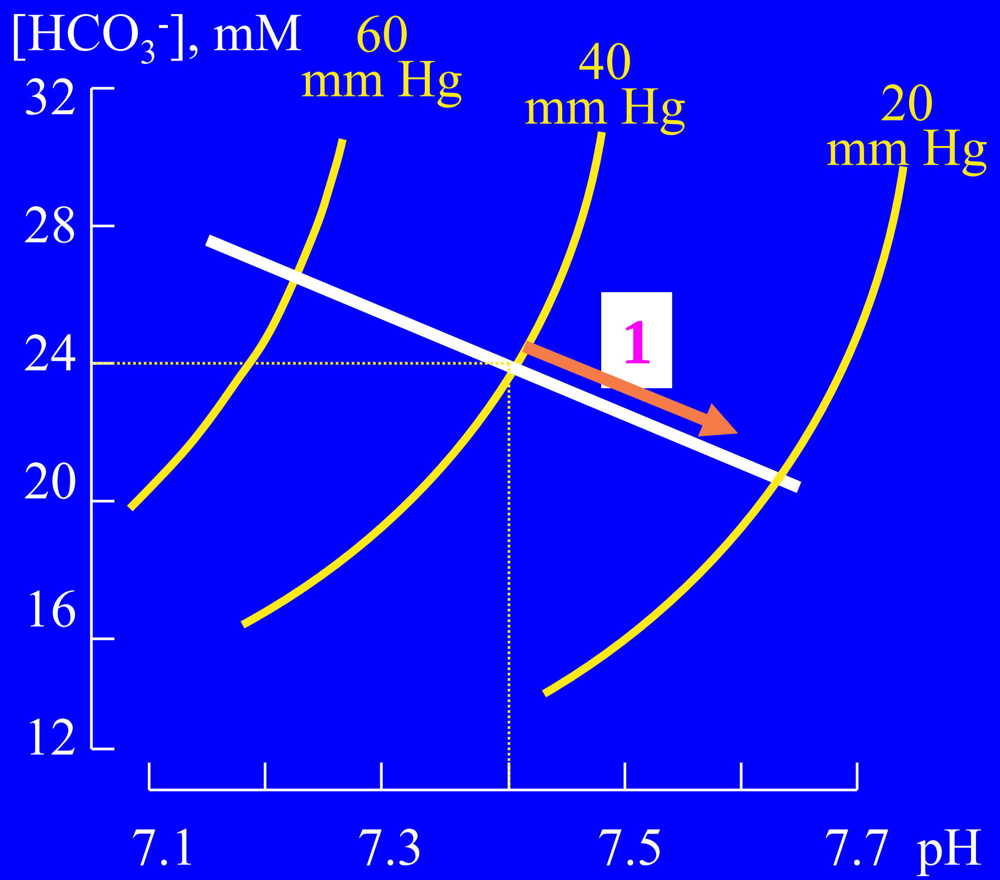
Although the PCO_2 remains elevated the pH approaches a normal value

PCO_2 is raised,
pH is normalised
HCO_3^- is raised

$$pH = 6.1 + \log \frac{[HCO_3^-]}{[0.03 \cdot P_{CO2}]}$$

RESPIRATORY ALKALEMIA

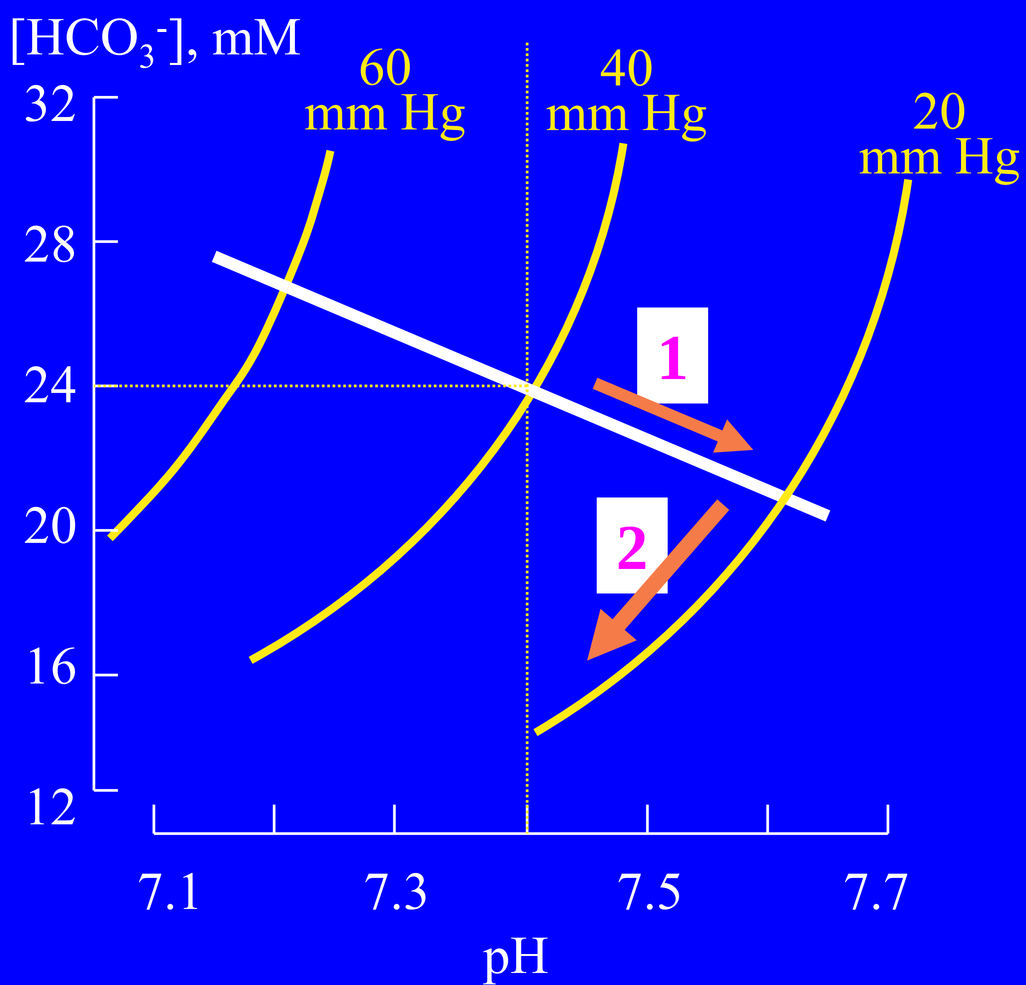
Excessive loss of CO_2 generally caused by **hyperventilation**



$$pH = 6.1 + \log \frac{[HCO_3^-]}{[0.03 \cdot P_{CO2}]}$$

PCO_2 is reduced, pH is raised
HCO_3^- is normal

COMPENSATED RESPIRATORY ALKALEMIA



The kidney loses net base, i.e. HCO_3^-

Although the PCO_2 remains reduced the pH approaches a normal value

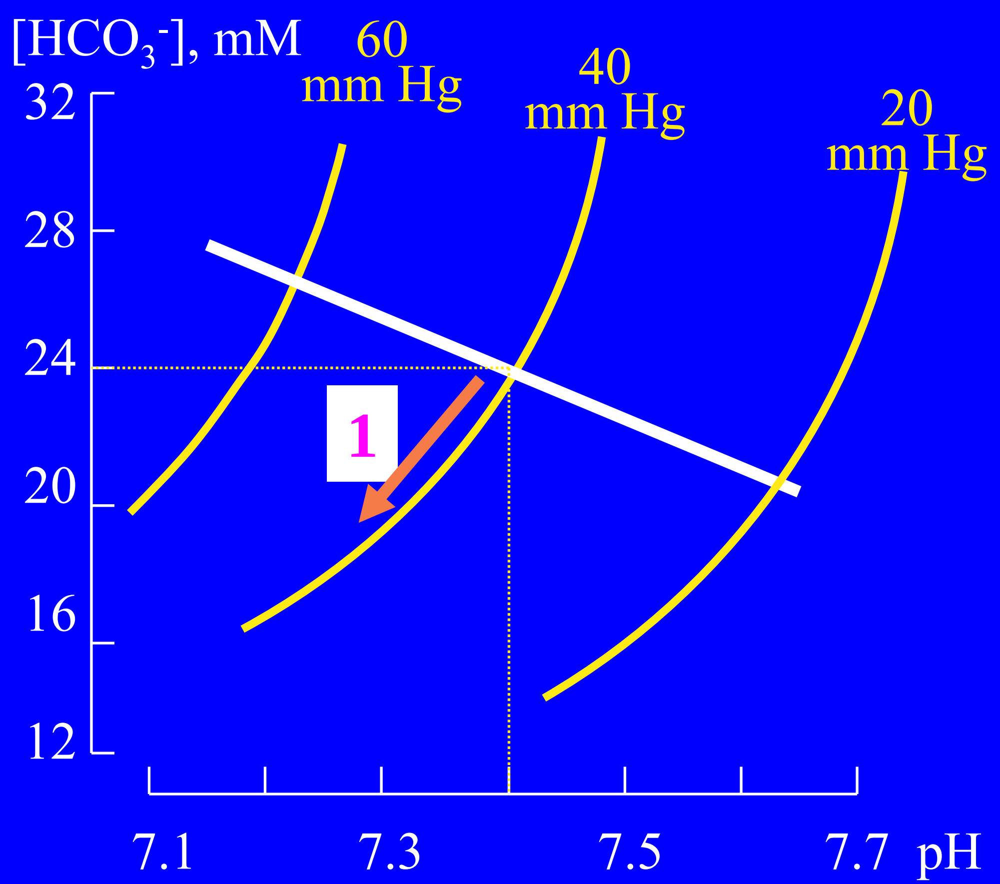
PCO_2 is reduced,
pH is normalised
HCO_3^- is lowered

$$pH = 6.1 + \log \frac{[HCO_3^-]}{[0.03 \cdot P_{CO2}]}$$

METABOLIC ACIDEMIA

Many different diseases and medical conditions lead to metabolic acidosis

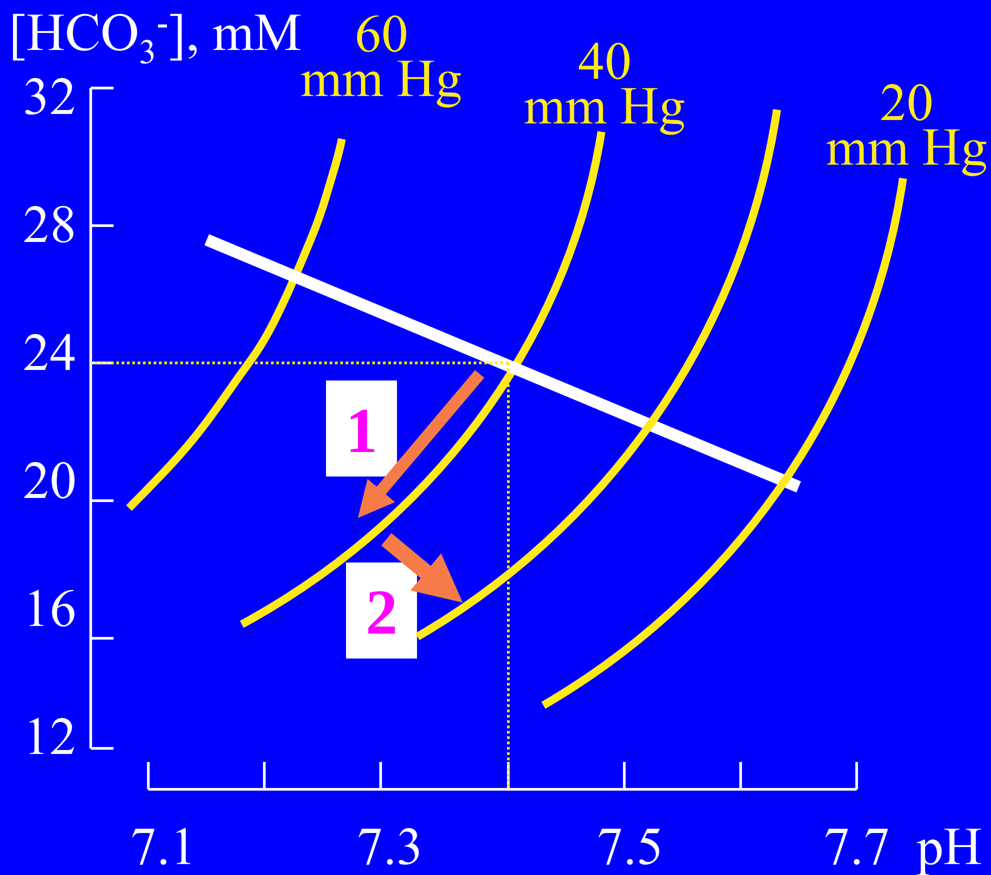
Diabetes
Heart failure
Renal failure
Diarrhoea



$$pH = 6.1 + \log \frac{[HCO_3^-]}{[0.03 \cdot P_{CO2}]}$$

PCO_2 is unchanged, pH is reduced
HCO_3^- is reduced

COMPENSATED METABOLIC ACIDEMIA



The lungs excrete more CO_2 hyperventilation

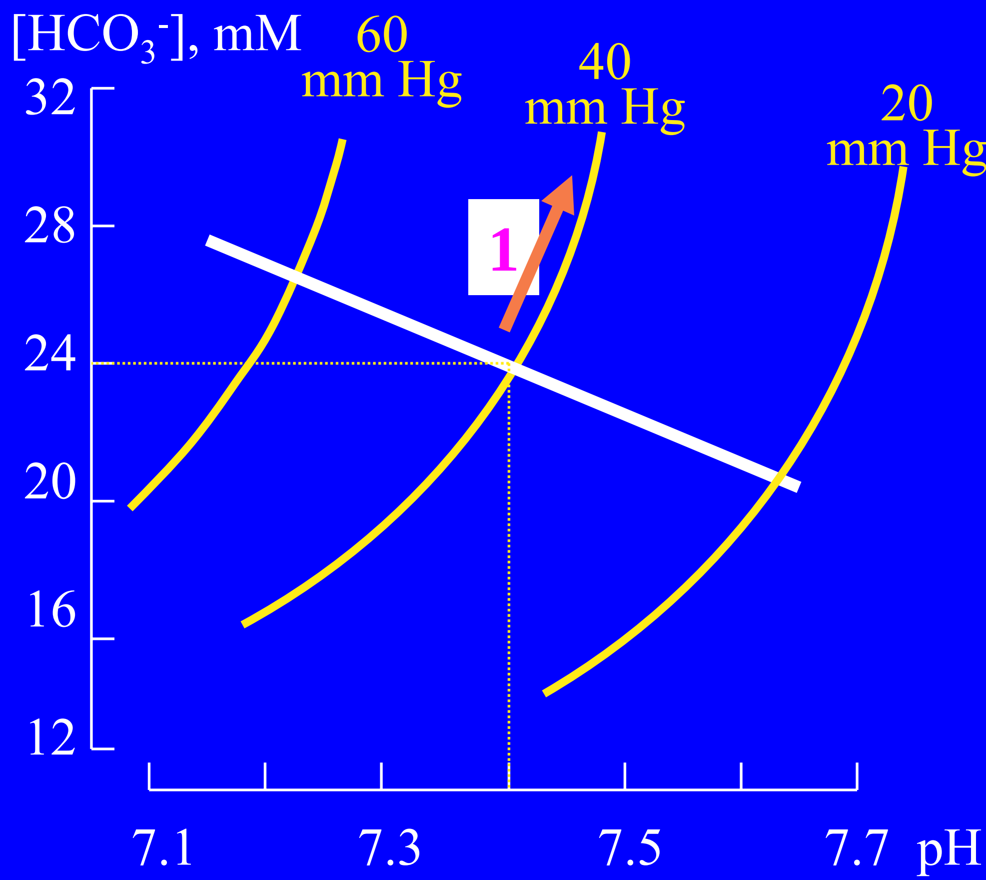
Although the HCO_3^- remains reduced the pH approaches a normal value

HCO_3^- is reduced, pH is normalised PCO_2 is lowered

$$pH = 6.1 + \log \frac{[HCO_3^-]}{[0.03 \cdot P_{CO2}]}$$

METABOLIC ALKALEMIA

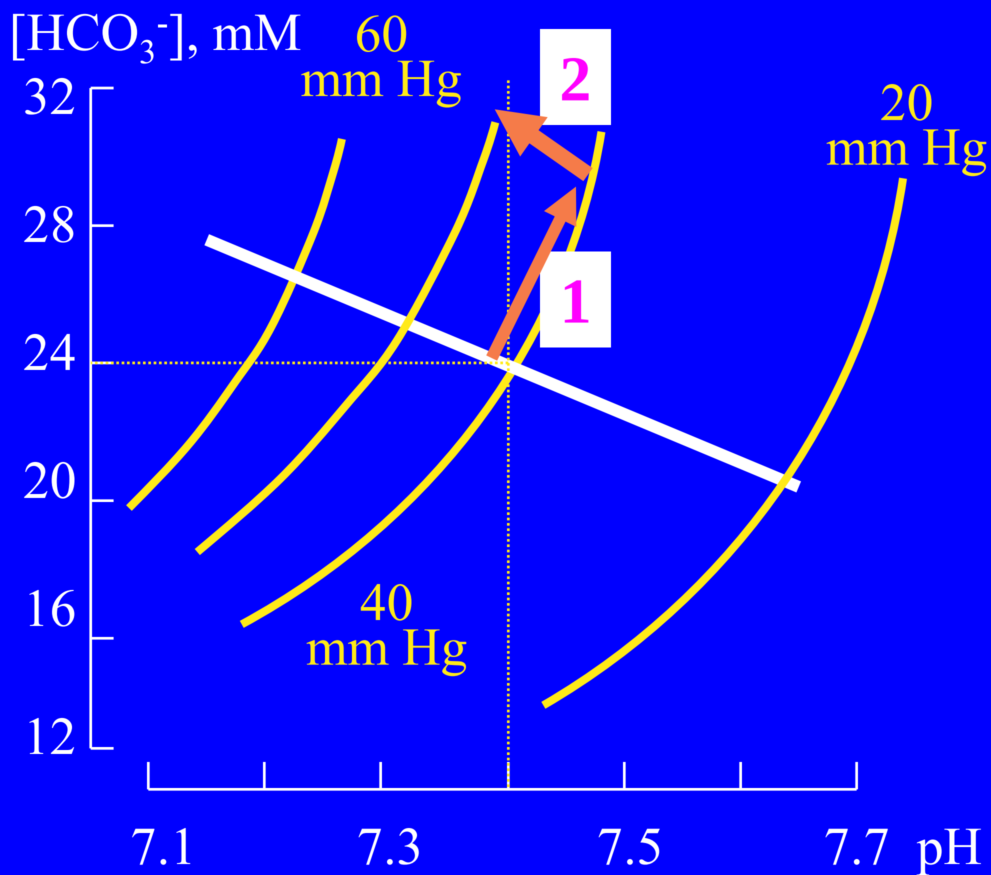
Example: net loss of H^+; e.g. through vomiting



$$pH = 6.1 + \log \frac{[HCO_3^-]}{[0.03 \cdot P_{CO2}]}$$

PCO_2 is unchanged, pH is increased
HCO_3^- is increased

COMPENSATED METABOLIC ALKALEMIA



The lungs excrete less CO_2 hypoventilation

Although the HCO_3^- remains increased the pH approaches a normal value

$$pH = 6.1 + \log \frac{[HCO_3^-]}{[0.03 \cdot P_{CO2}]}$$

HCO_3^- is raised,
pH is normalised
PCO_2 is raised