Biochemistry

Lec:2

Dr.Radhwan M. Asal

Bsc. Pharmacy

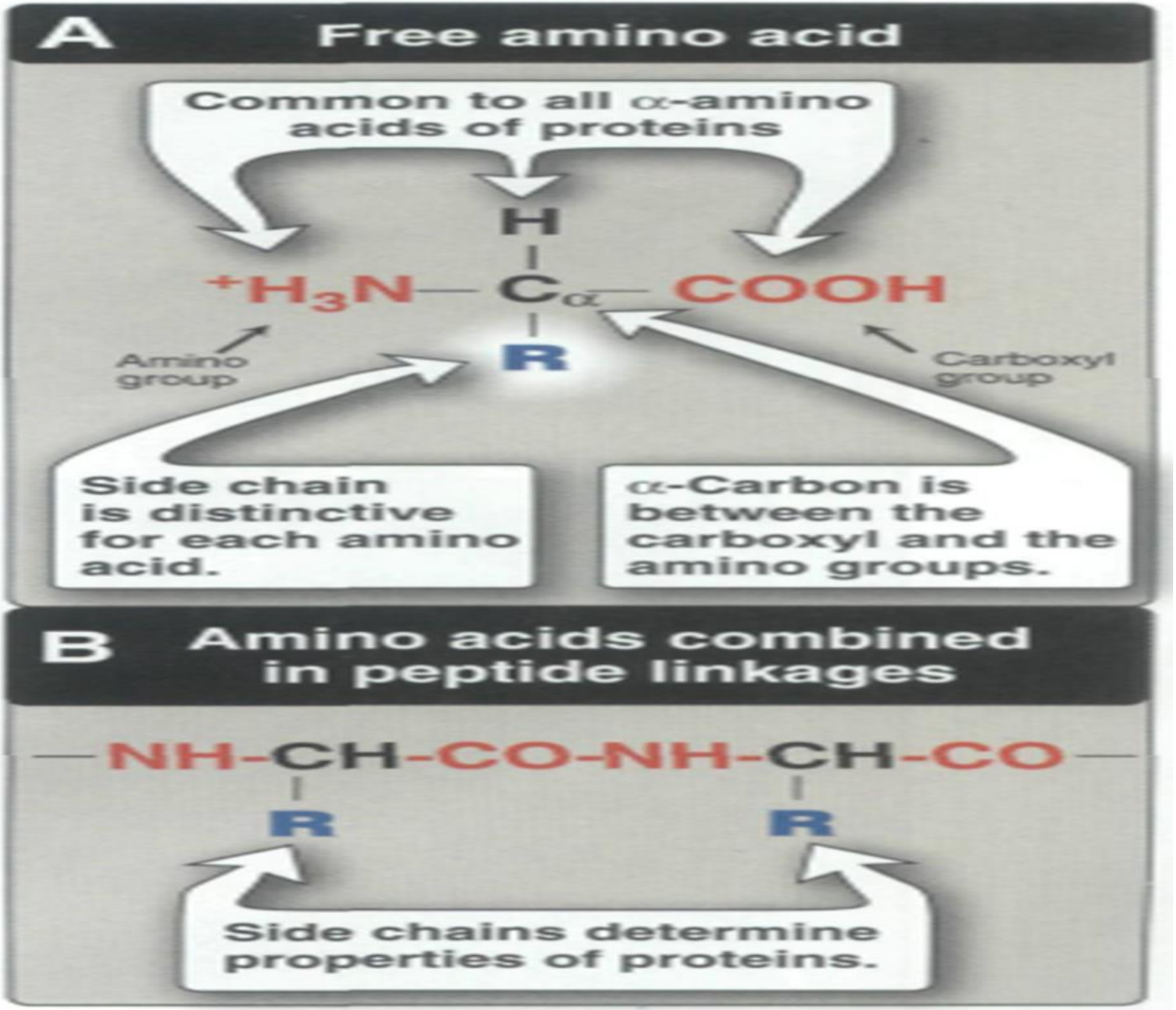
MSC ,PhD Clinical Biochemistry

Amino Acids

Proteins are the most abundant and functionally diverse molecules in living systems. Virtually every life process depends on this class of molecules. For example, enzymes and polypeptide hormones direct and regulate metabolism in the body, whereas contractile proteins in muscle permit movement. In bone, the protein collagen forms a framework for the deposition of calcium phosphate crystals, acting like the steel cables in reinforced concrete. In the bloodstream, proteins, such as hemoglobin and plasma albumin, whereas immunoglobulins fight infectious bacteria and viruses. All proteins share the common structural feature of being linear polymers of amino acids.

STRUCTURE OF THE AMINO ACIDS

Although more than 300 different amino acids have been described in nature, only twenty are commonly found as constituents of mammalian proteins. [Note: These are the only amino acids that are coded for by DNA] Each amino acid (except for proline) has a **carboxyl group,** an **amino group,** and a distinctive side chain **("R-group")** bonded to the α-carbon atom . At physiologic pH (approximately pH = 7.4), the carboxyl group is dissociated, forming the negatively charged carboxylate ion (–COO-) and the amino group is protonated (-NH3+) proteins, almost all of these carboxyl and amino groups are combined in peptide linkage and, in general, are not available for chemical reaction except for hydrogen bond formation .


A
Free amino acid
Common to all α-amino acids of proteins
H
+H3N— Cα —COOH
R
Amino group
Carboxyl group
Side chain is distinctive for each amino acid.
α-Carbon is between the carboxyl and the amino groups.
B
Amino acids combined in peptide linkages
—NH-CH-CO-NH-CH-CO—
R
R
Side chains determine properties of proteins.

Amino acids with nonpolar side chains

Each of these amino acids has a nonpolar side chain that does not bind or give off protons or participate in hydrogen or ionic bonds The side chains of these amino acids can be thought of as "oily" or Lipid like a property that promotes **hydrophobic interactions .**

-Location of nonpolar amino acids in proteins:

proteins found in aqueous solutions, the side chains of the nonpolar amino acids tend to cluster together in the interior of the protein . This phenomenon is the result of the hydrophobicity of the nonpolar R-groups which act much like droplets of oil that coalesce in an aqueous environment. The nonpolar R-groups thus fill up the interior of the folded protein and help give it its three-dimensional shape.

In proteins that are located in a hydrophobic environment, such as a membrane, the nonpolar R-groups are found on the outside surface of the protein, interacting with the lipid environment .

Proline: The side chain of proline and its α-amino group form a ring structure, and thus proline differs from other amino acids in that it contains an imino **group,** rather than an amino group .The unique geometry of proline contributes to the formation of the fibrous structure of collagen , and often interrupts the α-helices found in globular proteins

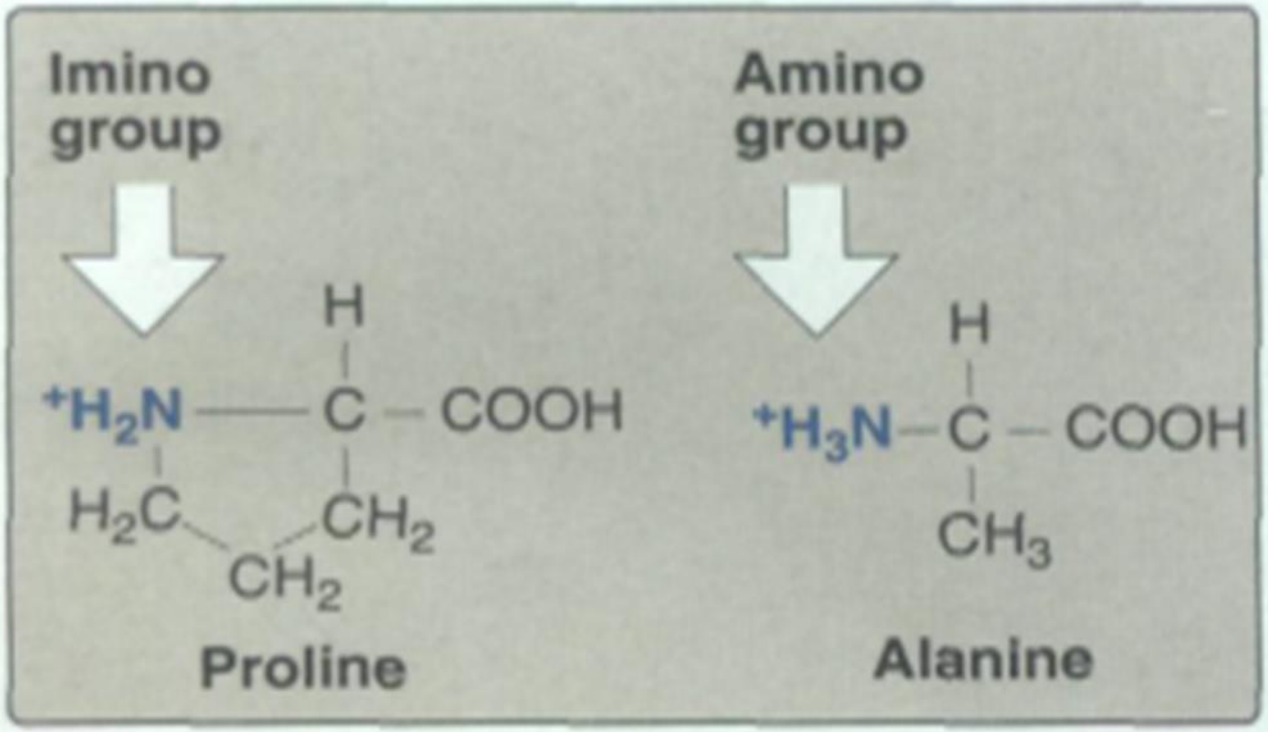
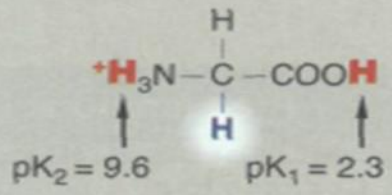


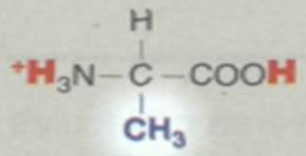
Figure 1.5

Comparison of the imino group found in proline with the α-amino group found in other amino acids, such as alanine.

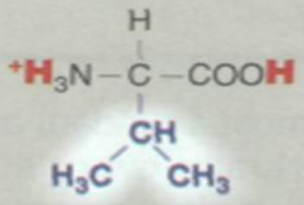
NONPOLAR SIDE CHAINS



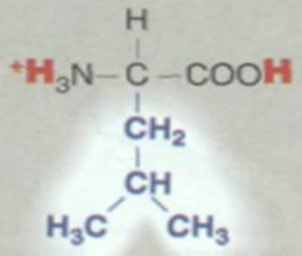
Glycine



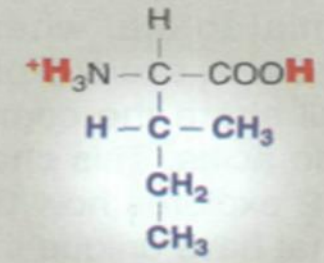
Alanine



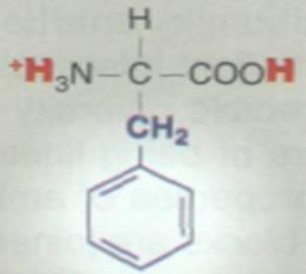
Valine



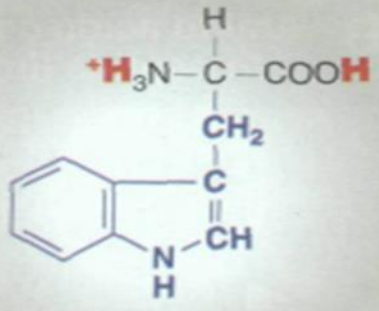
Leucine



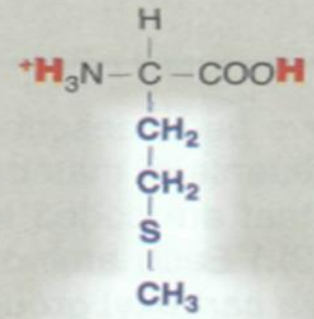
Isoleucine



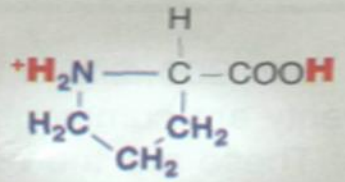
Phenylalanine



Tryptophan



Methionine



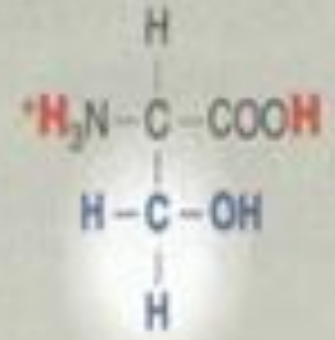
Proline

Amino acids with uncharged polar side chains

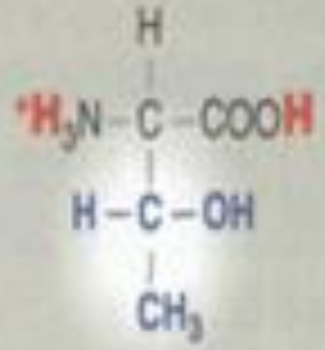
These amino acids have zero net charge at neutral PH although the side chains of cysteine and tyrosine can lose a proton at an alkaline PH Serine, threonine, and tyrosine each contain a polar hydroxyl group that can participate in **hydrogen bond** formation. The side chains of asparagine and glutamine each contain a carbonyl group and an amide group, both of which can also participate in hydrogen bonds.

--Disulfide bond: The side chain of **cysteine** contains a **sulfhydryl group** (-SH), which is an important component of the active site of many enzymes. In proteins, the -SH groups of two cysteines can become oxidized to form a dimer **cystine,** which contains a covalent cross-link called a disulfide bond (-S-S-).

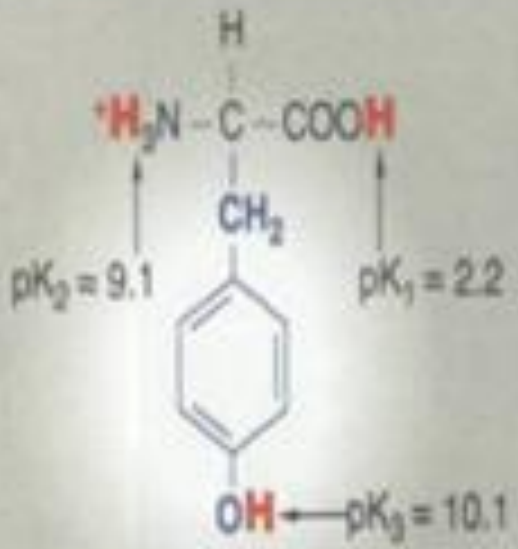
UNCHARGED POLAR SIDE CHAINS



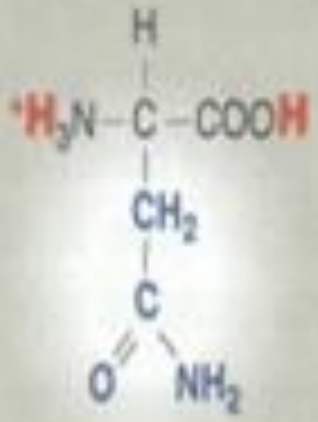
Serine



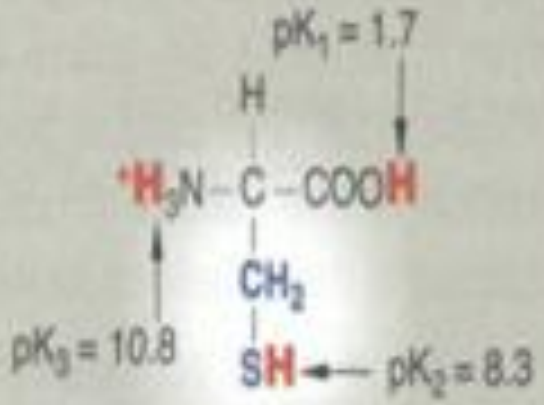
Threonine



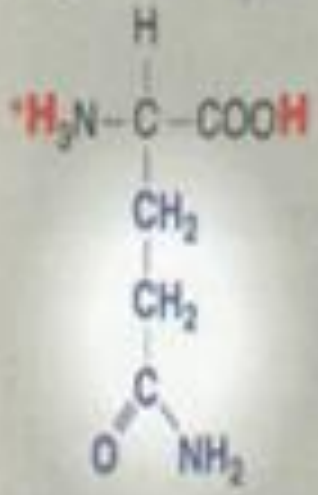
Tyrosine



Asparagine



Cysteine



Glutamine

---Side chains as sites of attachment for other compounds: Serine, threonine, and, rarely, tyrosine contain a **polar hydroxyl group** that can serve as a site of attachment for structures such as a phosphate group. [Note: The side chain of serine is an important component of the active site of many enzymes.] .In addition, the **amide group** of asparagine, as well as the hydroxyl group of serine or threonine, can serve as a site of attachment for oligosaccharide chains in glycoproteins .

---Amino acids with acidic side chains

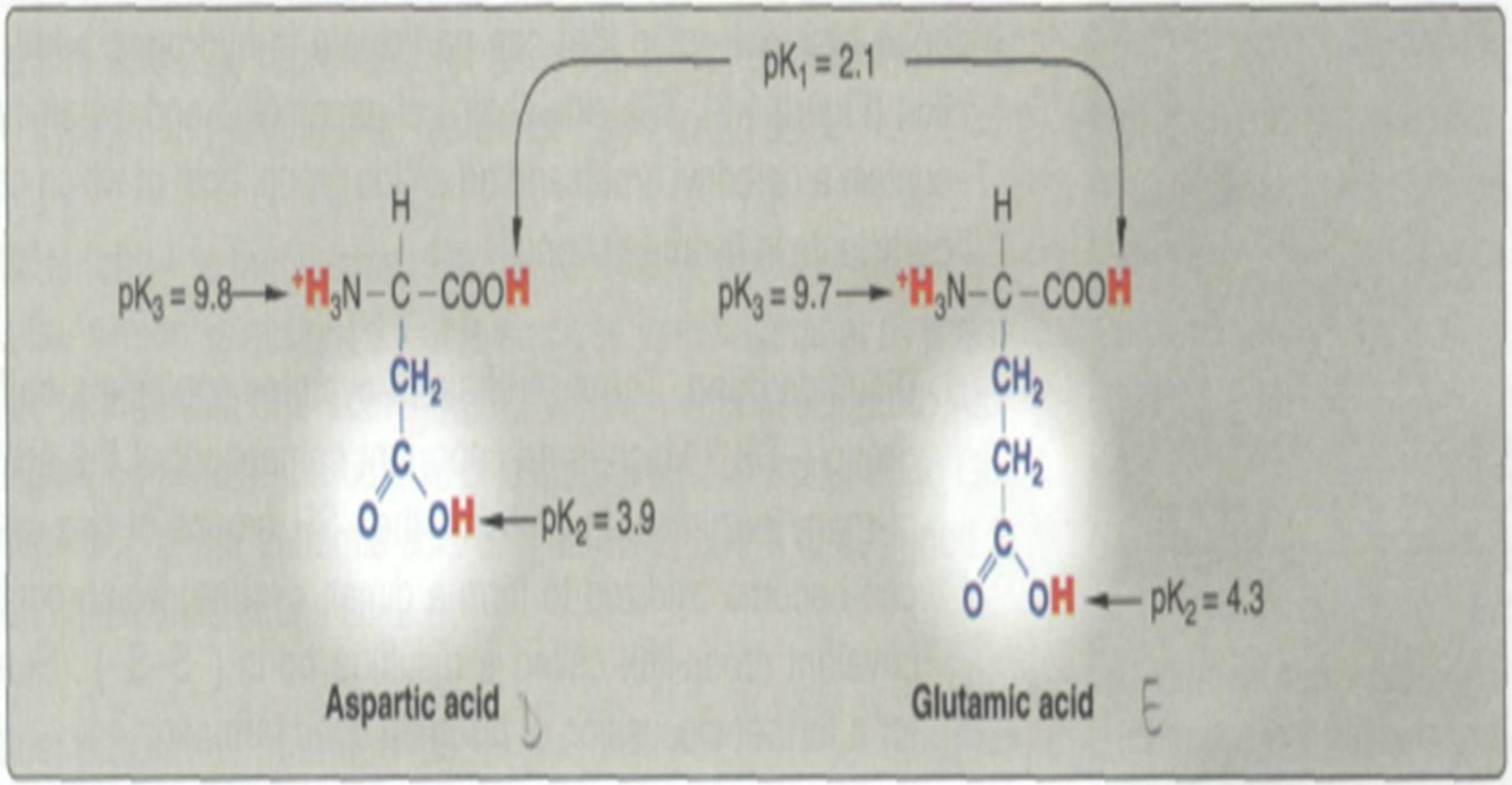
The amino acids aspartic and glutamic acid are **proton donors.** At neutral PH the side chains of these amino acids are fully ionized, containing a negatively charged **carboxylate group** (-C00^{-}).

They are, therefore, called aspartate or glutamate to emphasize that these amino acids are negatively charged at physiologic PH.

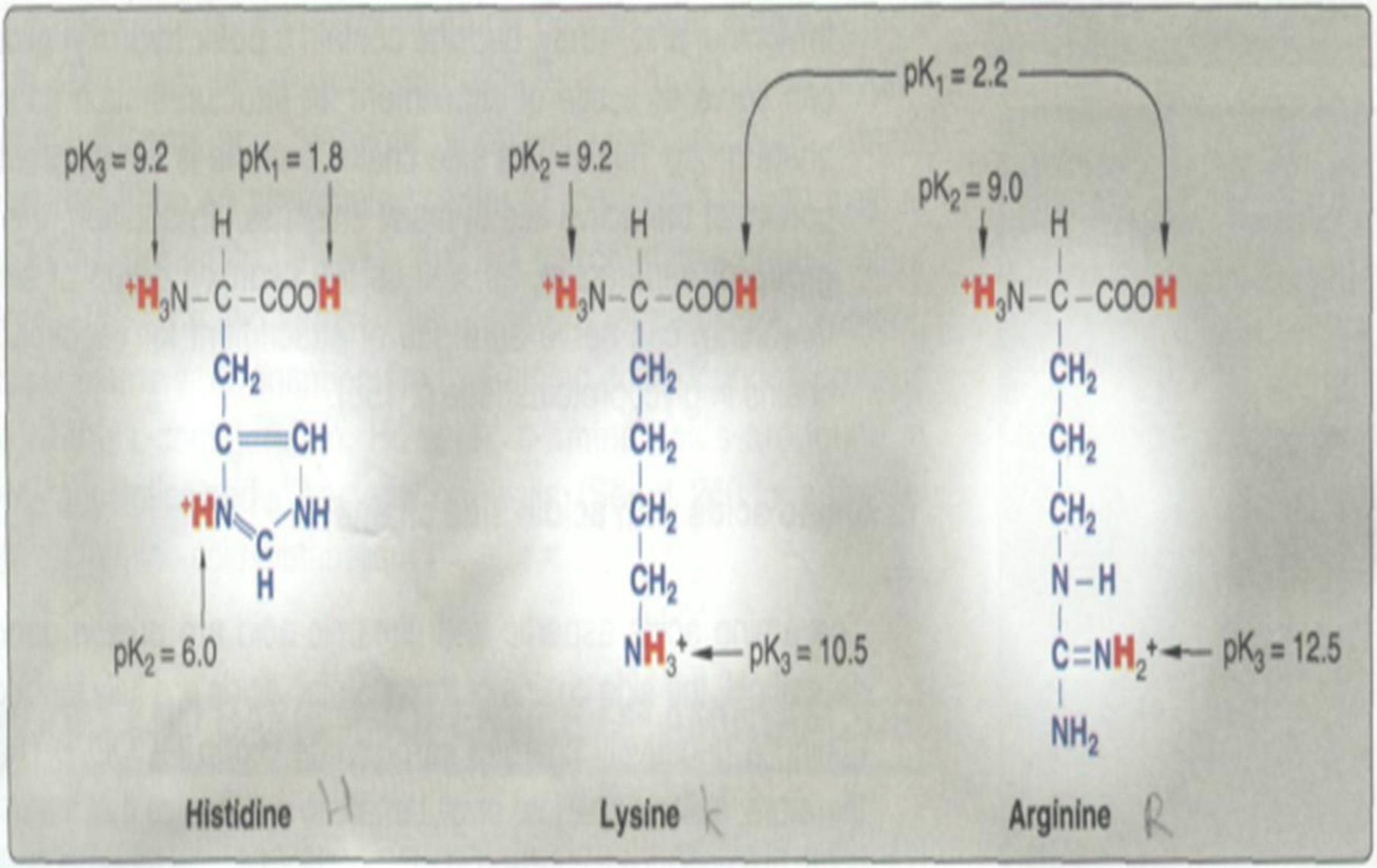
---Amino acids with basic side chains

The side chains of the basic amino acids **accept protons.** At physiologic PH the side chains of lysine and arginine are fully ionized and positively charged. In contrast, histidine is weakly basic, and the free amino acid is largely uncharged at physiologic PH. However, when histidine is incorporated into a protein, its side chain can be either positively charged or neutral, depending on the ionic environment provided by the polypeptide chains of the protein. Note: This is an important property of histidine that contributes to the role it plays in the functioning of proteins such as hemoglobin.

ACIDIC SIDE CHAINS



BASIC SIDE CHAINS



Optical properties of amino acids

The α-carbon of each amino acid is attached to four different chemical groups and is, therefore, a **chiral** or **optically active** carbon atom. Glycine is the exception because its α-carbon has two hydrogen substituents and, therefore, is optically inactive. [Note: Amino acids that have an asymmetric center at the α-carbon can exist in two forms, designated D and L, that are mirror images of each other. The two forms in each pair are termed **stereoisomers, optical isomers,** or **enantiomers.** All amino acids found in proteins are of the L-configuration. However, **D-amino acids** are found in some antibiotics and in bacterial cell walls.

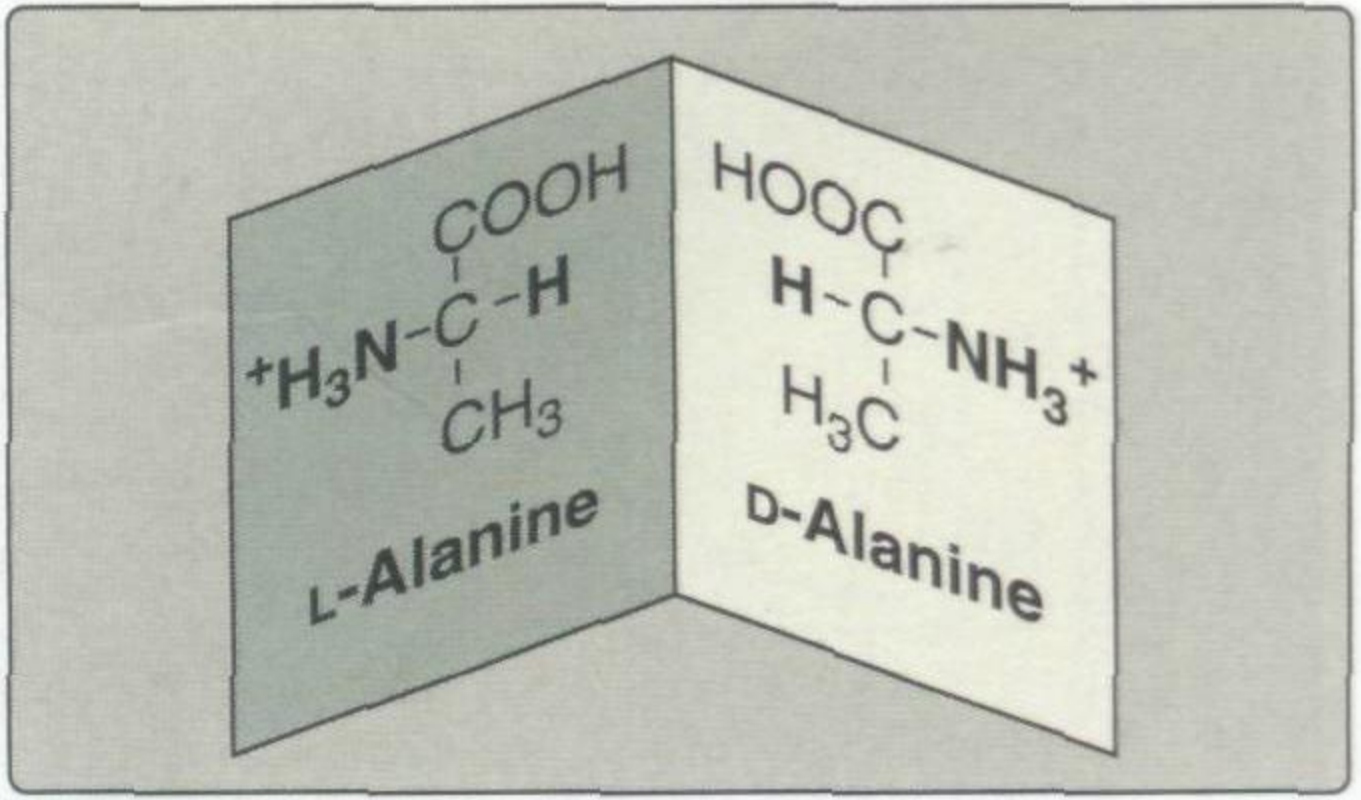


Figure 1.8

D and L forms of alanine are mirror images.

ACIDIC AND BASIC PROPERTIES OF AMINO ACIDS

Amino acids in aqueous solution contain weakly acidic α-carboxyl groups and weakly basic α-amino groups. In addition, each of the acidic and basic amino acids contains an ionizable group in its side chain. Thus, both free amino acids and some amino acids combined in peptide linkages can act as **buffers.** The quantitative relationship between the concentration of a weak acid (HA) and its conjugate base (A^-)is described by the **Henderson-Hasselbalch equation.**

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

Titration of an amino acid

Dissociation of the carboxyl group: The titration curve of an amino acid can be analyzed in the same way as described for acetic acid. Consider alanine, for example, which contains both an α-carboxyl and an α-amino group. At a low (acidic) pH, both of these groups are protonated . As the pH of the solution is raised, the -COOH group of form I can dissociate by donating a proton to the medium. The release of a proton results in the formation of the carboxylate group –COO-, This structure is shown as form II, which is the **dipolar form** of the molecule [Note: This form, also called a zwitterion, is the **isoelectric form** of alanine is, it has an overall charge of zero.]

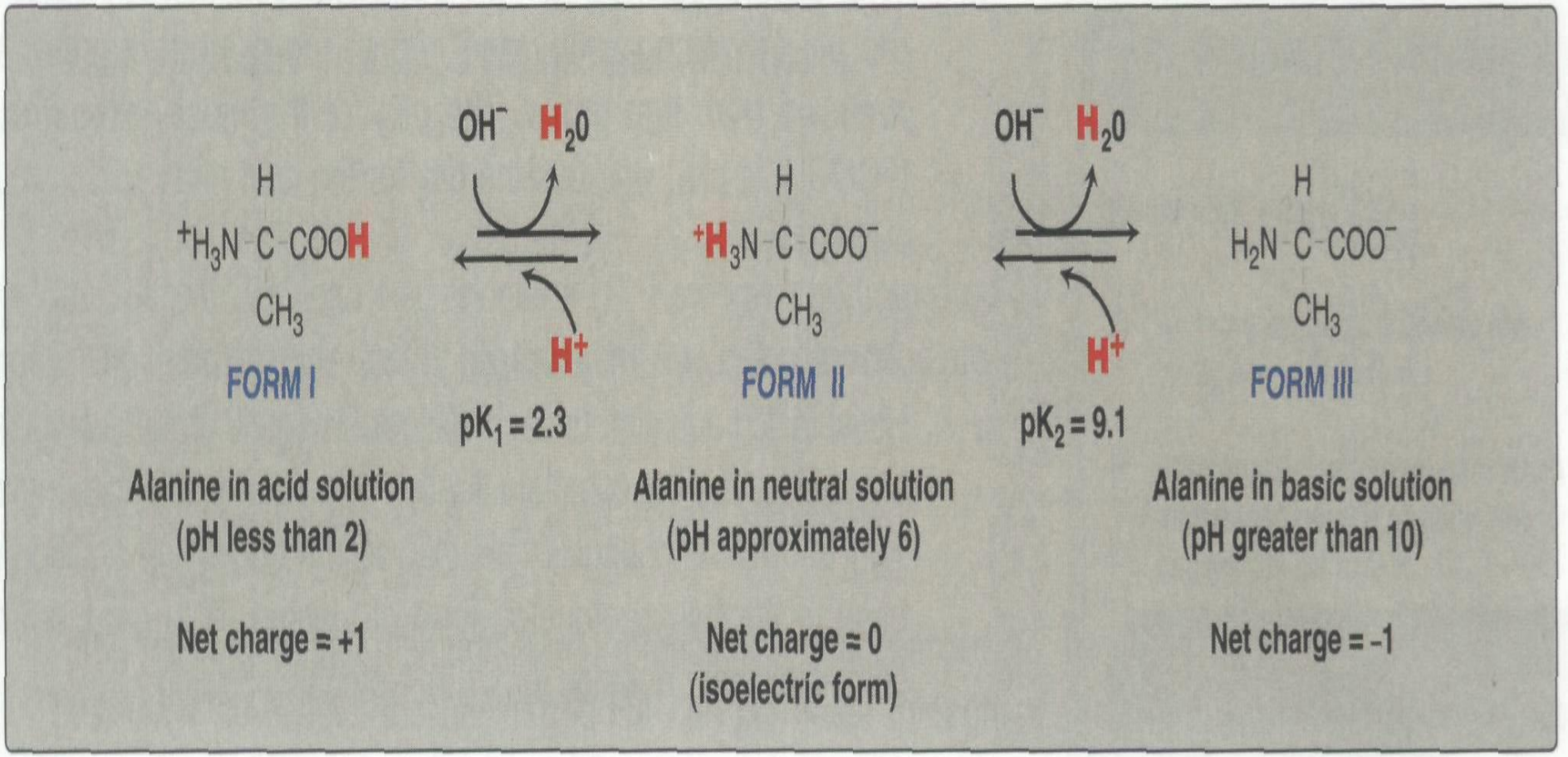


Figure 1.10
Ionic forms of alanine in acidic, neutral, and basic solutions.

Isoelectric point: At neutral pH, alanine exists predominantly as the dipolar form II in which the amino and carboxyl groups are ionized, but the net charge is zero. The isoelectric point (PI) is the pH at which an amino acid is electrically neutral that is, in which the sum of the positive charges equals the sum of the negative charges. [Note: For an amino acid, such as alanine, that has only two dissociable hydrogens (one from the α-carboxyl and one from the α-amino group), the PI is the average of PK1and PK2.

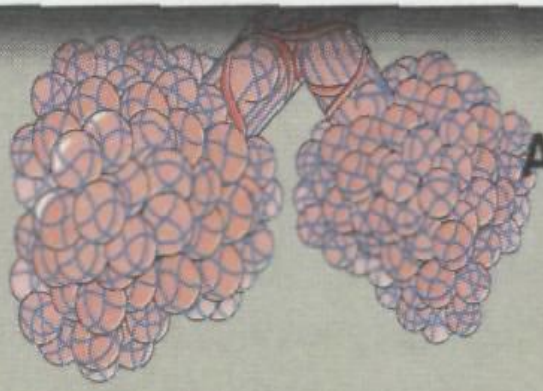
Net charge of amino acids at neutral pH: At physiologic pH, all amino acids have a negatively charged group –COO- and a positively charged group – NH3+ both attached to the α-carbon.

[Note: Glutamate, aspartate, histidine, arginine, and lysine have additional potentially charged groups in their side chains.] Substances, such as amino acids, that can act either as an acid or a base are defined as **amphoteric,** and are referred to as **ampholytes (amphoteric electrolytes).**

The Henderson-Hasselbalch equation can be used to calculate how the pH of a physiologic solution responds to changes in the concentration of weak acid and/or its corresponding "salt" form. For example, in the **bicarbonate buffer system,** the Henderson-Hasselbalch equation predicts how shifts in HCO_3^- and PCO_2 and influence PH .

A BICARBONATE AS A BUFFER

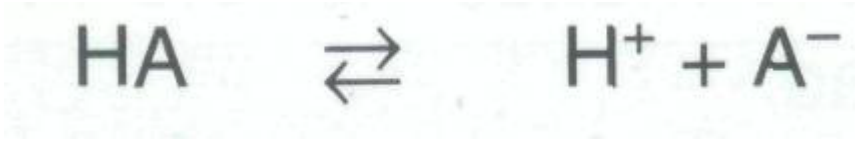
- $pH = pK + \log \frac{[HCO_3^-]}{[H_2CO_3]}$
- An increase in bicarbonate ion causes the pH to rise.
- Pulmonary obstruction causes an increase in carbon dioxide and causes the pH to fall.



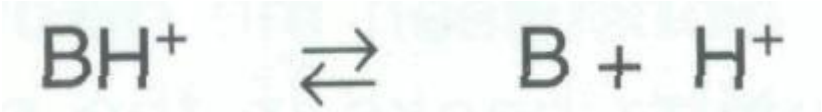
LUNG ALVEOLI

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

The equation is also useful for calculating the abundance of ionic forms of acidic and basic drugs. For example, most drugs are either weak acids or weak bases . Acidic drugs (HA)release a proton H+ causing a charged anion (A") to form.



Weak bases BH+ can also release a H+ However, the protonated form of basic drugs is usually charged, and the loss of a proton produces the uncharged base (B).



A drug passes through membranes more readily if it is uncharged. Thus, for a weak acid, the uncharged HA can permeate through membranes and A^- cannot. For a weak base, such as morphine, the uncharged form, B, penetrates through the cell membrane and BH+ does not. Therefore, the effective concentration of the permeable form of each drug at its absorption site is determined by the relative concentrations of the charged and uncharged forms. The ratio between the two forms is, in turn, determined by the pH at the site of absorption, and by the strength of the weak acid or base, which is represented by the Pka of the ionizable group.

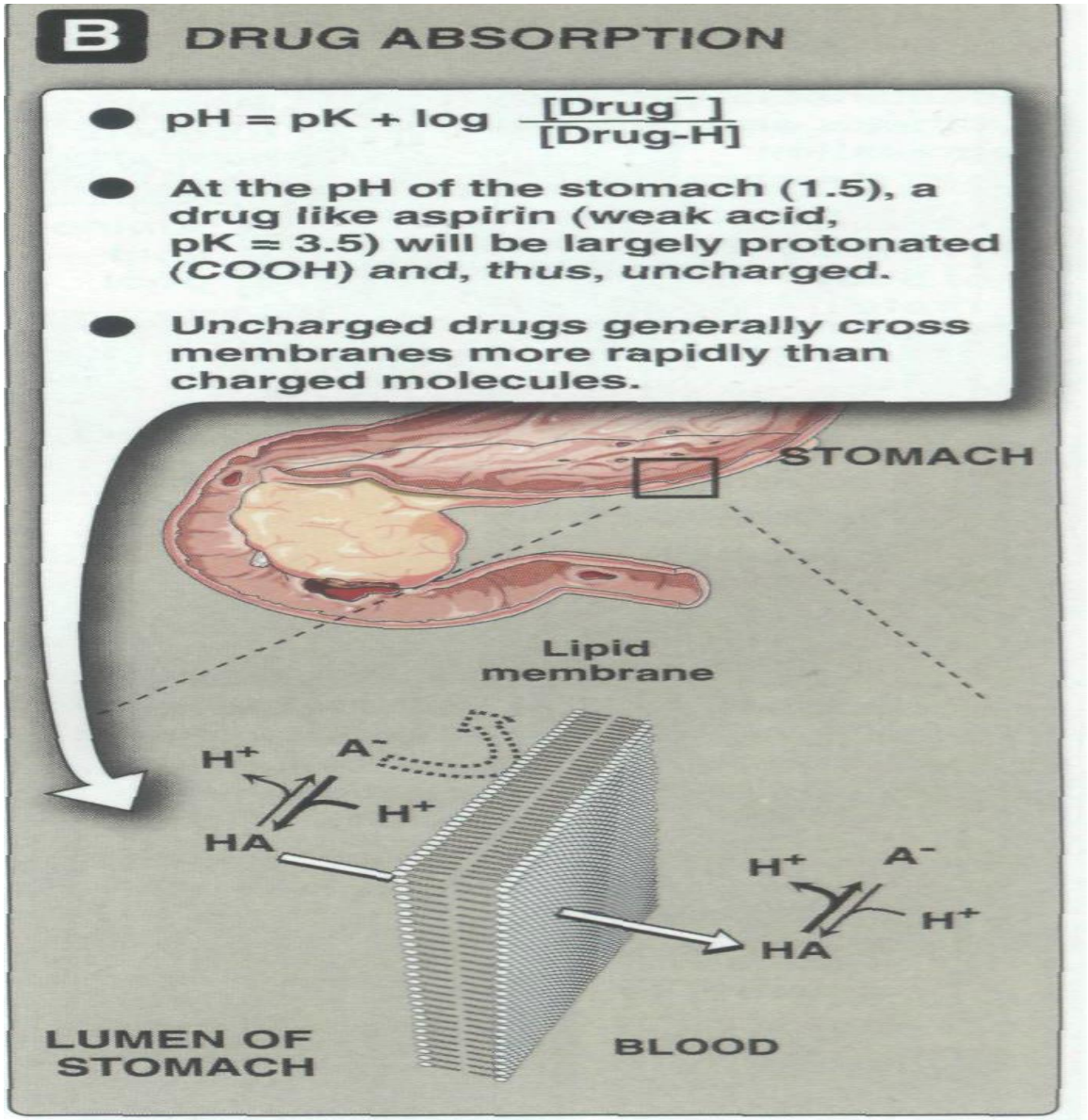


Figure 1.12
The Henderson-Hasselbalch equation is used to predict: A, changes in pH as the concentrations of HCO_3^- or CO_2 are altered; or B, the ionic forms of drugs.

The Henderson-Hasselbalch equation is useful in determining how much drug is found on either side of a membrane that separates two compartments that differ in pH, for example, the stomach (pH 1.0-1.5) and blood plasma (pH 7.4).