

# Introduction

- A diuretic is defined as drug that increases the rate of urine formation.
- The primary action of most diuretics is the direct **inhibition of Na<sup>+</sup> reabsorption** (increased excretion) at one or more of the four major sites along the nephron.
- An increased Na<sup>+</sup> excretion is accompanied by anion like Cl<sup>-</sup>. Since NaCl is the major determinant of extracellular fluid volume.
- Diuretics **reduce** extracellular fluid volume (decrease in oedema) by decreasing total body NaCl content.

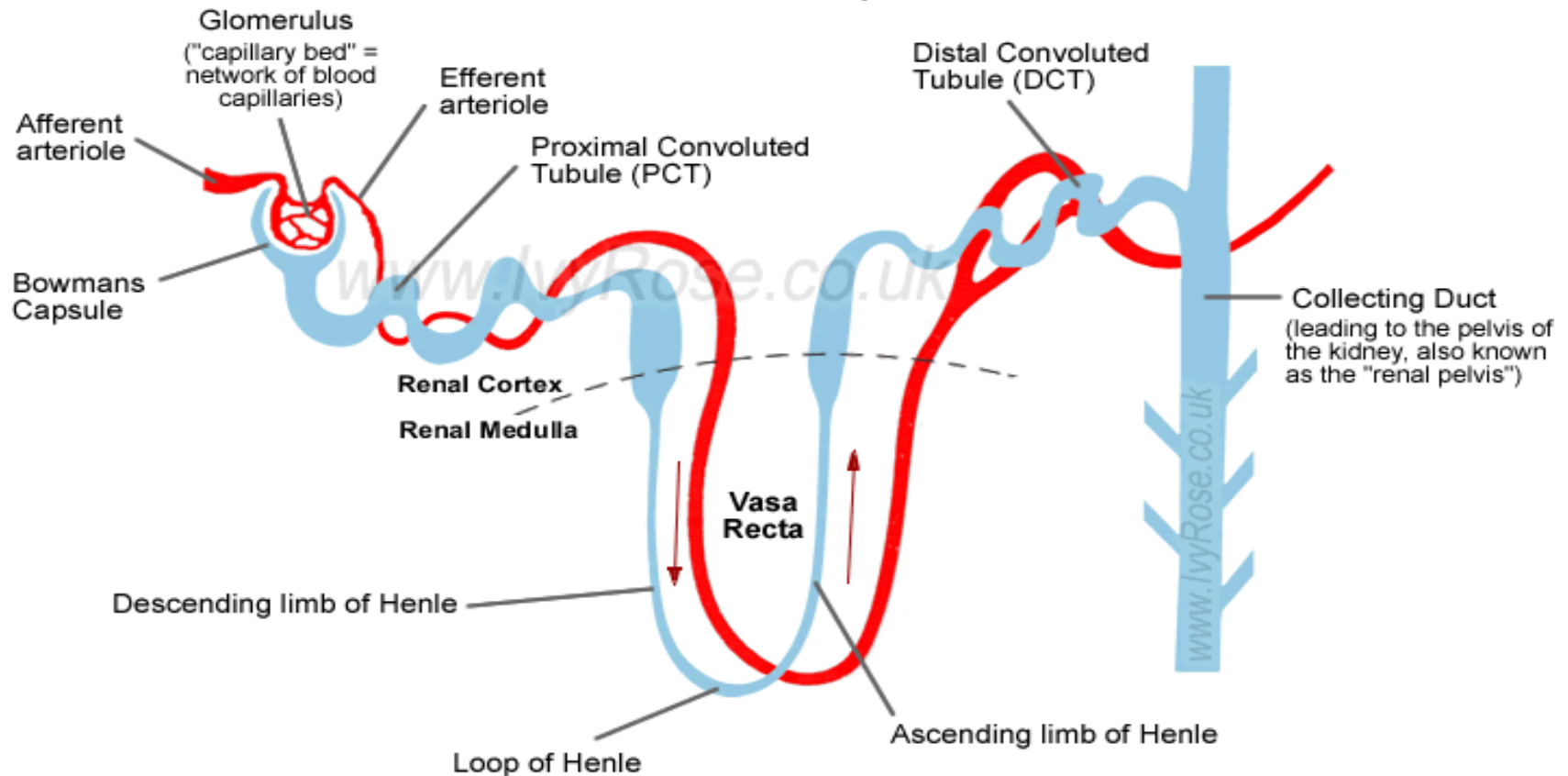
There are **four major sites** along the nephron that are responsible for reabsorption:

Site 1: Proximal Convoluted Tubule (PCT)

Site 2: Ascending Loop of Henle

Site 3: Distal Convoluted Tubule (DCT)

Site 4: Late Distal Tubule and Collecting Duct



## Classification of Diuretics

### 1) Site 1 Diuretics : Carbonic Anhydrase Inhibitors

Acetazolamide, Methazolamide, Dichlorphenamide,  
Chloraminophenamide.

### 2) Site 2 Diuretics : Loop diuretics (High Ceiling Diuretics)

Furosemide, Bumetanide and Ethacrynic acid

### 3) Site 3 Diuretics : Thiazides

Chlorothiazide, Benzthiazide, Hydrochlorothiazide,  
Hydroflumethiazide, Bendroflumethiazide.

### 4) Site 4 Diuretics : Potassium Sparing Diuretics

a. Na<sup>+</sup> Channel Inhibitors: Triamterene, Amiloride

b. Aldosterone Antagonists: Spironolactone

## 1) Site 1 Diuretics : Carbonic Anhydrase Inhibitors

- Carbonic anhydrase (CA) inhibitors are derived from the **sulfonamide antibacterials**.
- The carbonic anhydrase inhibitors have an **unsubstituted sulfamoyl ( $-\text{SO}_2\text{NH}_2$ )** group.
- Some CA inhibitors have a **heterocyclic ring** and some have **benzene ring** attached to sulfamoyl group.
- Accordingly CA inhibitors have been divided into two groups:
  - i) Simple heterocyclic sulfonamides
  - ii) *meta*-disulfamoylbenzene derivatives

## **Mechanism of action**

This class of diuretics inhibit **carbonic anhydrase enzyme** in the membrane and intracellularly in proximal tubules that causes the decreased reabsorption and increased excretion of Sodium, Bicarbonates and Potassium.

## **Adverse Effects**

Metabolic acidosis, Hypokalemia (decreased potassium), decreased glomerular filtration rate, hypersensitivity reactions

## **Uses**

Major use is in the treatment of Glaucoma because it reduces the rate of formation of aqueous humor, thereby reducing the intraocular pressure.