

# تفريغ بيوفارما

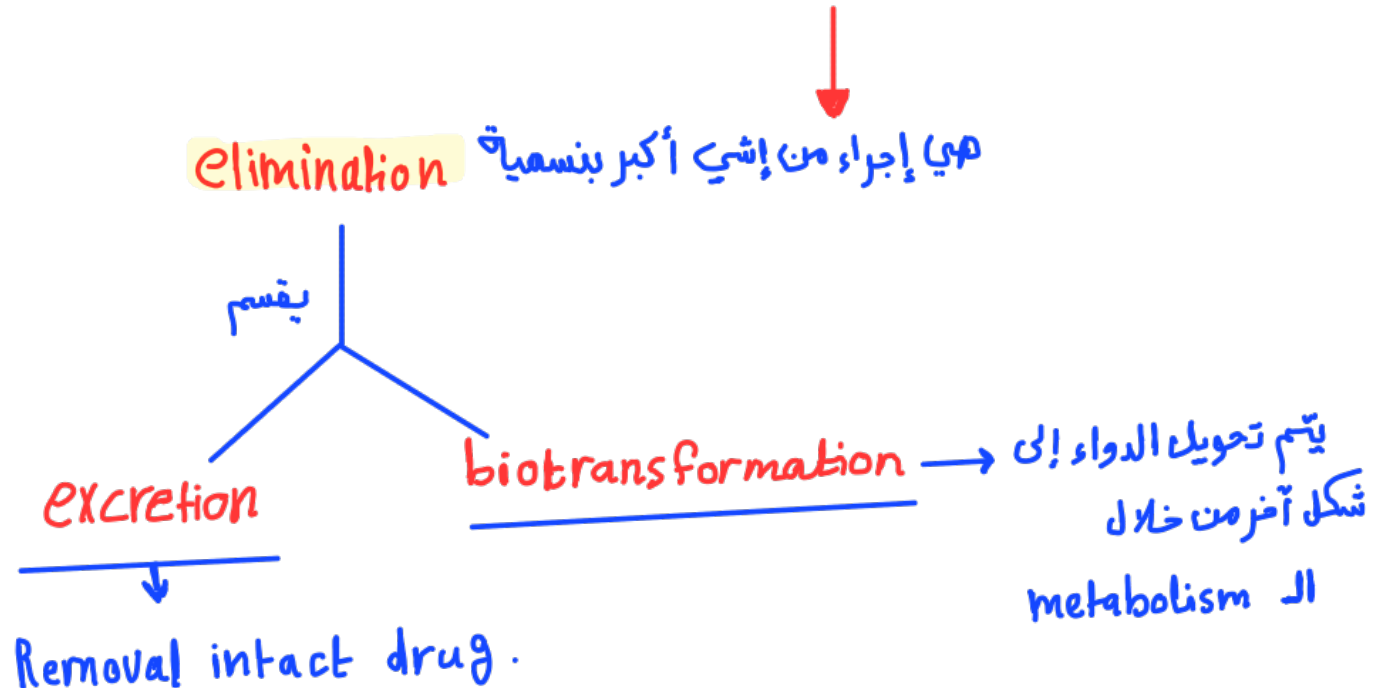


## Excretion Part 1

اسم الموضوع:

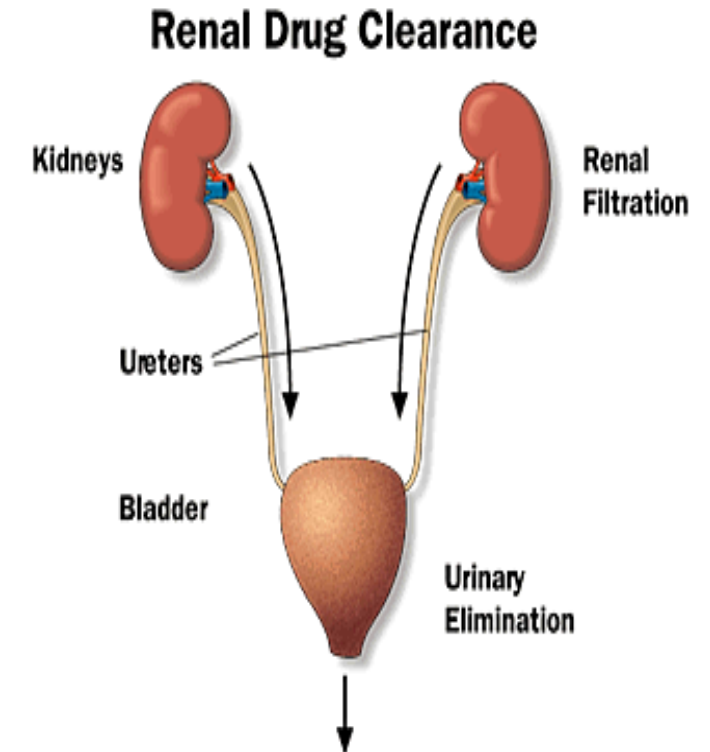
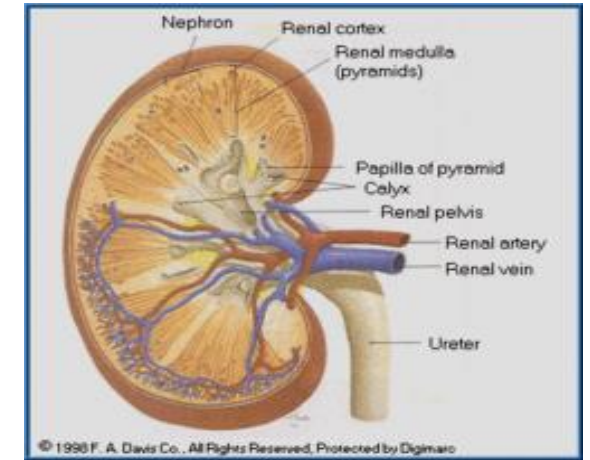
إعداد الصيدلاني/ة: Ghada Kasasbeh

# Excretion of drugs



# Excretion :

- **Drug elimination** refers to the irreversible removal of drug from the body by all routes of elimination
- **Drug elimination** is usually divided into two major components: **excretion** and **biotransformation**.
- **Drug excretion** is the removal of the intact drug.
- Nonvolatile and polar drugs are excreted **mainly by renal excretion**, a process in which the drug passes through the kidney to the bladder and ultimately into the urine.



# Excretion

- في طرق غير ال Kidney رغم إنها هي <sup>main</sup> ال
- Other pathways for drug excretion may include the excretion of drug into bile, sweat, saliva, milk (via lactation), or other body fluids.
  - ⊕ • Volatile drugs, such as gaseous anesthetics, alcohol, or drugs with high volatility, are excreted via the lungs into expired air.

← هاد الاشئ نبلاحظه لو ناكل شوم أو بجل بتكون عملية ال excretion ظاهرة .

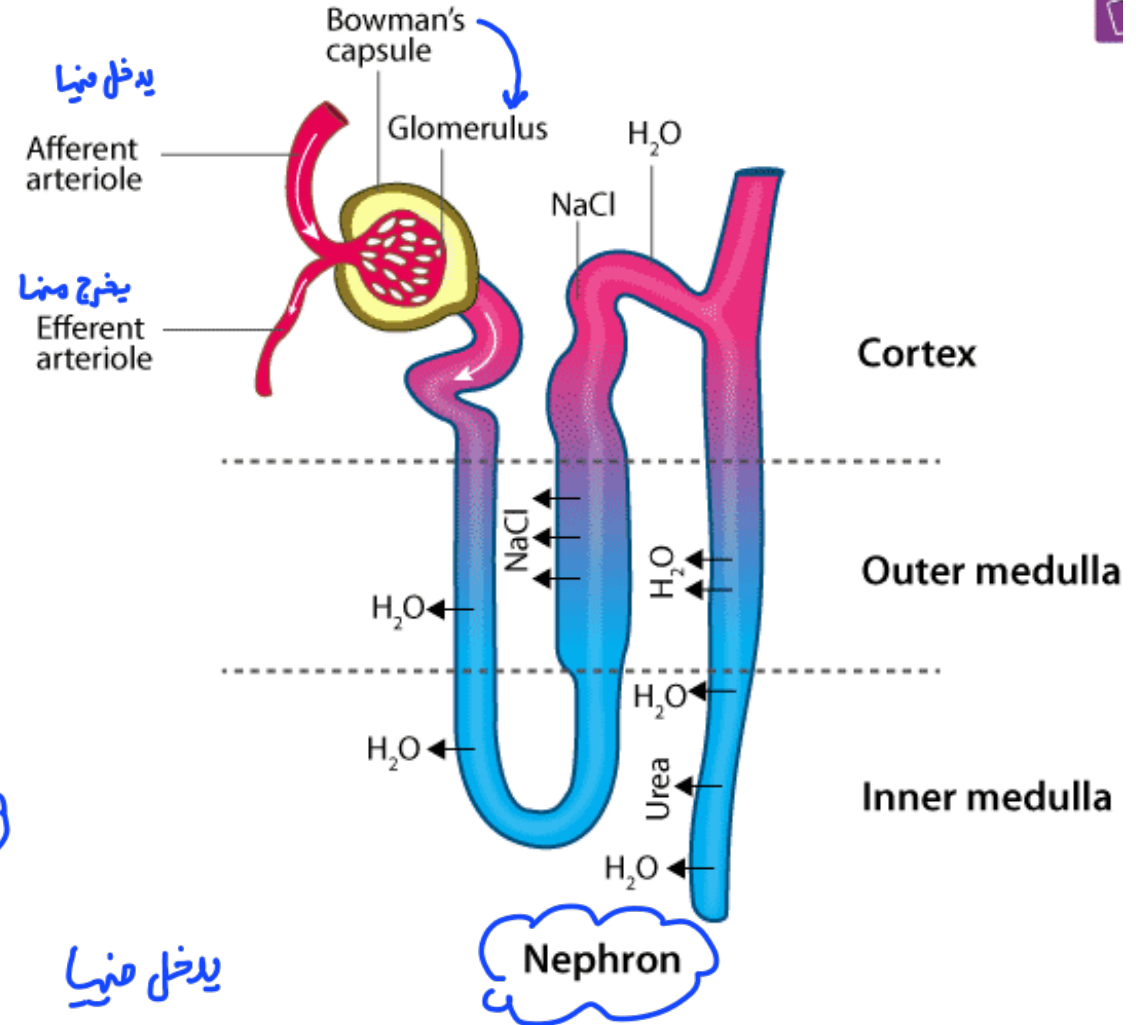
معلومة :

في بعض الأدوية يتدخل الحليب ويمكن تشكل خطورة على الطفل الذي يرضع .

# Drug excretion

## 1. Renal excretion:

- The major organ for the excretion of drugs is the KIDNEY. The functional unit of the kidney is the nephron in which there are three major processes to consider:-



النephron مكون من الـ

① Glomerulus الذي داخل Bowman's Capsul

يدخل من هنا Afferent arteriole ويخرج من هنا efferent arteriole وتفرج هنا لوب

وخلاله عندي ٣ عمليات رئيسية

# Drug excretion

## 1) Passive glomerular

**filtration:** Free drug  $<20$  kDa

## 2) Active tubular secretion:

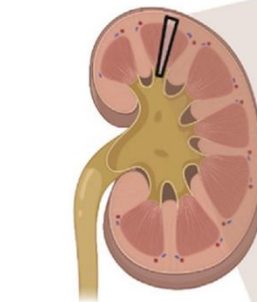
separate transport system for weak acids and bases

## 3) Passive tubular re-

**absorption** : occurs after the drug is filtered through the glomerulus and can be an active or a passive process involving transporting back into the plasma.

ليكن Passive Low! 2A

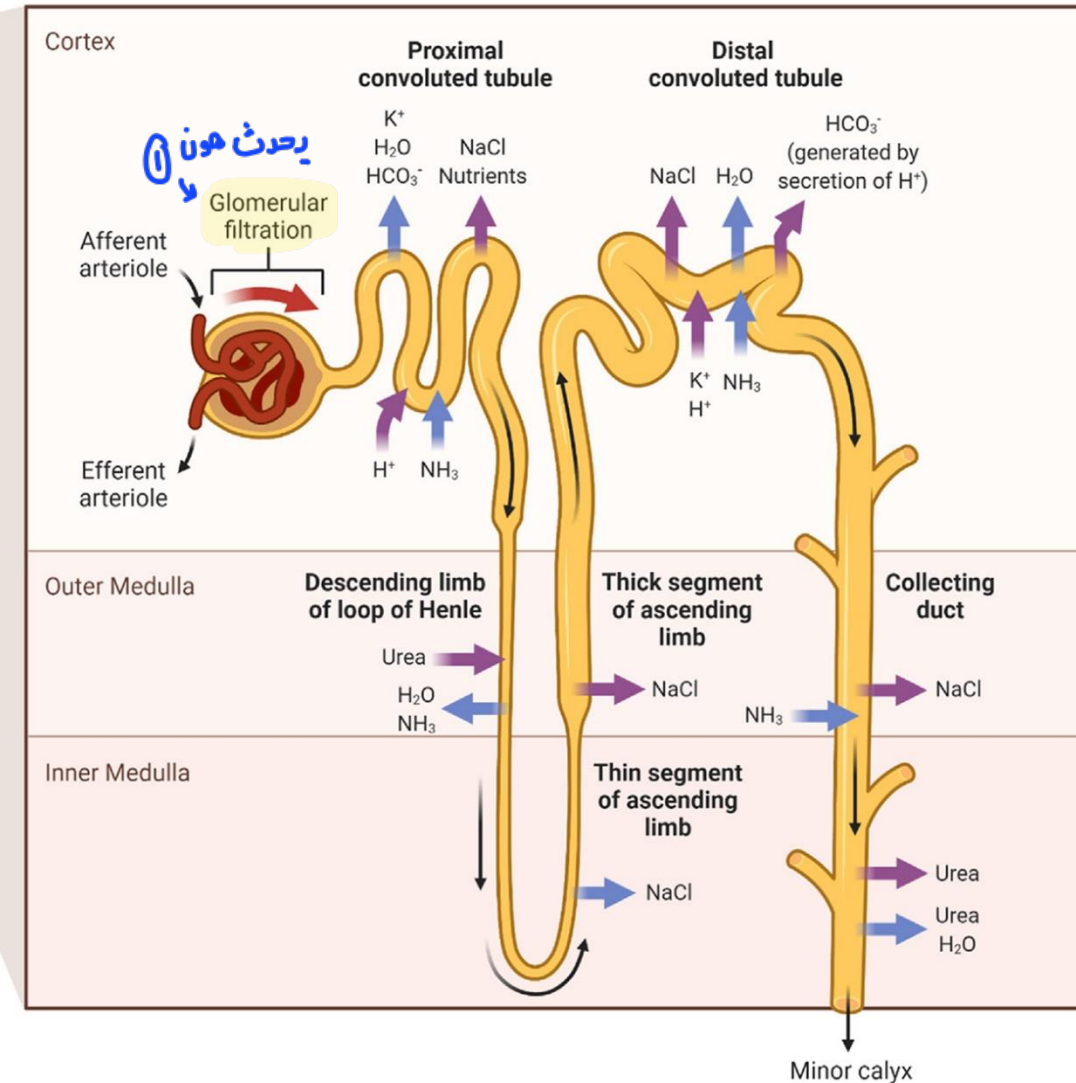
Can be active or Passive



**Reabsorption and secretion**

Active transport →

Passive transport →



## ① Passive glomerular filtration :

يحدث في منطقة الـ Glomerular ، لحجم أقل من 20 kDa يعني ما عندها مشكلة بالـ Small molecules .  
لكن راجع يواجه مشكلة في ما كان Large أو الـ molecule مع بروتين .

20 kDa = 20,000 molecular weight .

\* الخطوتين الأوليات ← ① + ② ← بصير فيهم إفراز الأدوية وأشياء أخرى من الدم إلى kidney

تسمى لأنهم يروحوا على Urine

\* الخطوة ③ ← Reabsorption لبعض المواد مثل الجلوكوز .

■ الـ major driving force هو hydrostatic Pressure (ضغط الدم الذي جاي على الكلية)

وكمية الدم الذي بتوصل الكلية عالية بتوصل 25% والـ hydrostatic Pressure هو الضغط

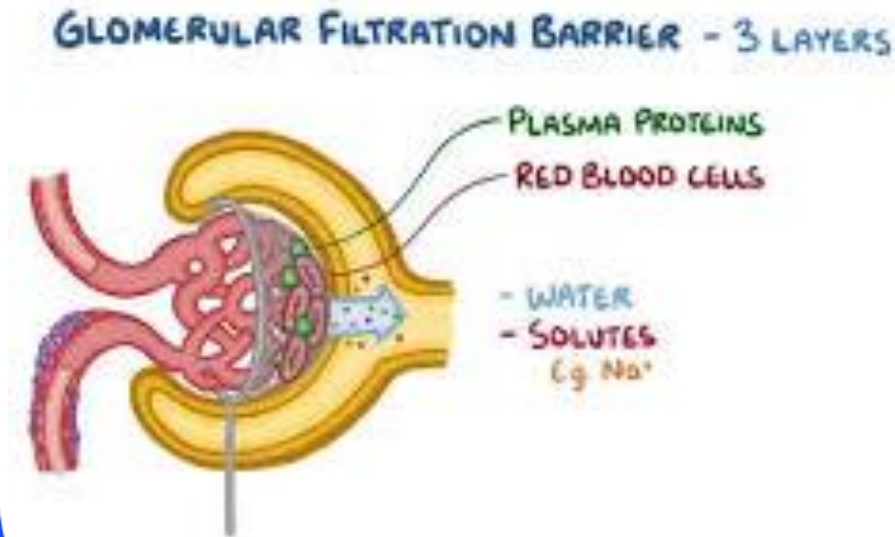
الناج عن الامتلاء فيعمل عملية filtration وبغاي الجزئيات تطلع .

# Drug excretion

## 1) Glomerular filtration

- Glomerular filtration is a unidirectional process.
- It occurs for most small molecules ( $MW < 500$ ), including undissociated (nonionized) and dissociated (ionized) drugs.
- The major driving force for glomerular filtration is the hydrostatic pressure within the glomerular capillaries.
- Kidneys receive a large blood supply (approximately 25% of the cardiac output) via the renal artery, with little decrease in hydrostatic pressure.

في اتجاه واحد



# Drug excretion

• هي أم ح مغيرة لكن لأنها مرتبطة ببروتين ما بحير اليا  
glomerular filtration

## 1) Glomerular filtration

الإدوية المرتبطة ببروتين .

- Protein-bound drugs act as large molecules and do not get filtered at the glomerulus.
- Glomerular filtration of drugs is directly related to the free or nonprotein-bound drug concentration in the plasma.
- As the free drug concentration in the plasma increases, glomerular filtration of the drug increases proportionately, thus increasing renal drug clearance for some drugs.

• كلما كان نسبة إرتباط الدواء بالبروتين عالي معناته نسبة ار  
free (تكون قليلة وار  
glomerular filtration Rate (تكون قليلة .  
عكسي  
[free + glomerular filtration Rate

# Drug excretion

## 1) Glomerular filtration

- Glomerular filtration rate (GFR) is measured using a drug eliminated primarily by filtration only (not reabsorbed or secreted).
- Inulin and creatinine are often used to measure GFR, although creatinine is also secreted.
- Clearance of inulin is approximately equal to the GFR, which can be 120 mL/min.
- GFR correlates fairly well with body surface area.

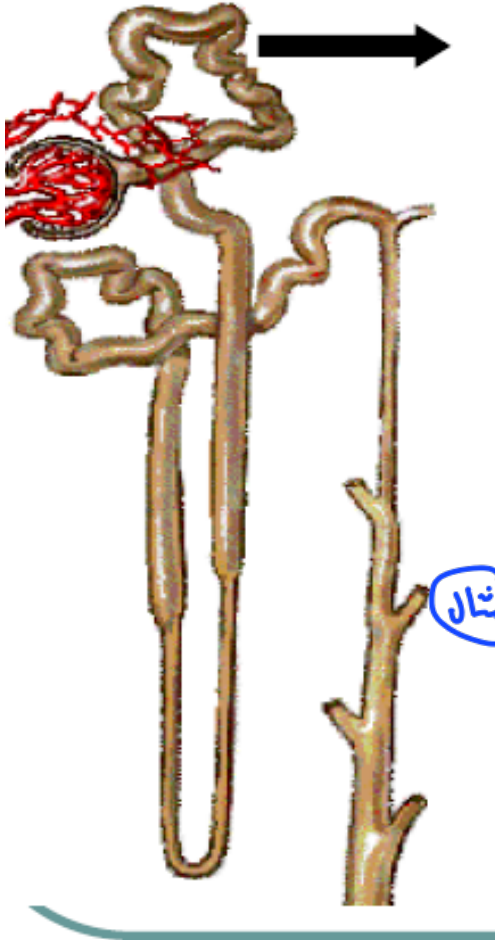
مثال

لا يمتص في الكلى ولا يفرز  
excretion

# Drug excretion

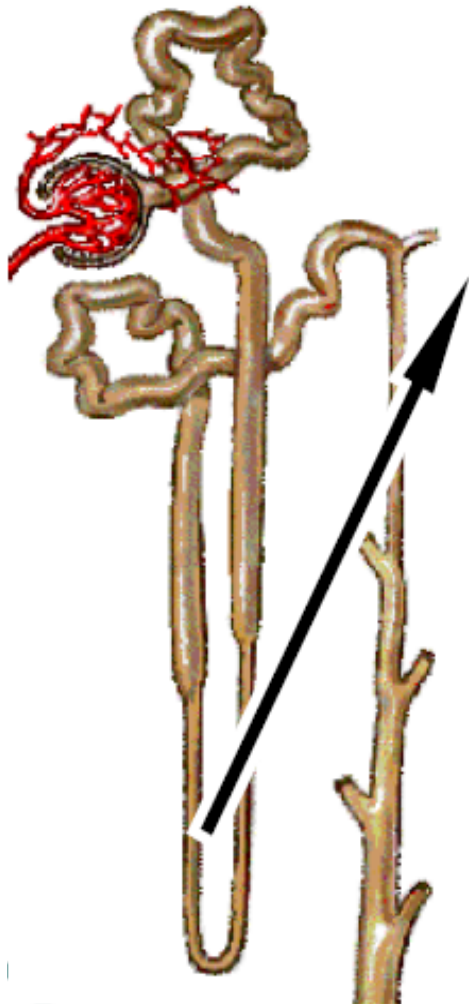
## 2) Tubular secretion

-



- Only less than 20% of renal plasma flow is filtered through the glomerulus, leaving at least 80% to pass on to the peritubular capillaries of the proximal tubule.
- There, drug molecules are transferred to the tubular lumen by two non-selective carriers (one transports acidic drugs, while the other handles organic bases).
- This is active transport and therefore:
- It can secrete all of the drug (even if it is bound to plasma protein) making it the most effective mechanism of renal elimination .
- **Penicillin**, for example being 80% protein-bound is cleared only slowly by filtration, but almost completely removed by proximal tubular secretion
- Competitive inhibition of the secretion of one compound by another may occur (inhibition of penicillin excretion by **probenecid**).

# Drug excretion



مسؤول للحفاظ على الماء و دال Concentration for Urine

- In the **loop of Henle**, 99% of the filtered water is re-absorbed.
- All solutes (including drugs) in the lumen are therefore significantly concentrated.
- When the drugs reach the distal tubule, their high luminal concentration favours their re-absorption

وهاد بخلي سolute  
تركزها عالي

# Drug excretion

بعض الـ  $\text{filtered lipophilic drugs}$  extensive reabsorption يعاد امتصاصها  
بتطلع من الـ Loop باتجاه الأوعية الدموية، فإذا كان الـ drug ← non-ionized  
فيا إحصائية كبيرة إنه يعبر الـ re-absorption.

## 3) Tubular re-absorption



- In the distal tubule there is passive excretion and re-absorption of lipid soluble drugs. Filtered lipophilic drugs are extensively reabsorbed. Thus if a drug is non-ionized or in the unionized form it may be readily reabsorbed.
- Many drugs are either weak bases or acids and therefore the pH of the filtrate can greatly influence the extent of tubular re-absorption for many drugs.
  - When urine is acidic weak acid drugs tend to be reabsorbed.
  - Alternatively when urine is more alkaline, weak bases are more extensively reabsorbed.  
(continued)

Ionization الـ  
لها يعتمد على pH

### 3) Tubular re-absorption



Urine pH varies from 4.5 to 8.0 depending on the diet (e.g. meat can cause a more acidic urine) or drugs (which can increase or decrease urine pH).

In drug overdose it is possible to increase the excretion of some drugs by suitable adjustment of urine pH.

In overdoses with weak acids (pentobarbital, aspirin) injecting sodium bicarbonate increases drug excretion.

In overdoses with weak bases (codeine, amphetamine) ammonium chloride lowers pH and increases ionization of bases