
Bio Pharma
Lama Nofal

Drug distribution

وجود الدواء داخل الدم وتوزيعه داخل الدم والخلايا
بمعنى اخر توزيع الدواء داخل الدم حتى يوصل
الخلايا

Distribution

the main organ responsible for execration :kidney

لايوجد بالجسم شيء ثابت عشان هيك هيي عملية راجعة والسبب انو الدوا مايضل داخل الخلية فقط برتبط ببروتين معين وبرجع يطلع من الدم للخلايا وبالعكس

Drug distribution: means the reversible transfer of drug from one location to another within the body.

في بعض انواع الادوية لايجوز للمرأة المرضعة ان تأخذها لانه ممكن تسبب سمية للحليب وتأثر على الطفل الرضيع

- The distribution of drugs in the body depends on:

1- their lipophilicity

الدوا لازم يكون lipophilic حتى يصيرلو امتصاص والسبب بهاد انو الغشاء مكون من phospholipid bilayer وعشان يقدر يمر لازم يكون لايبو ونفس الاشي بنطبق على distribution

2- protein binding.

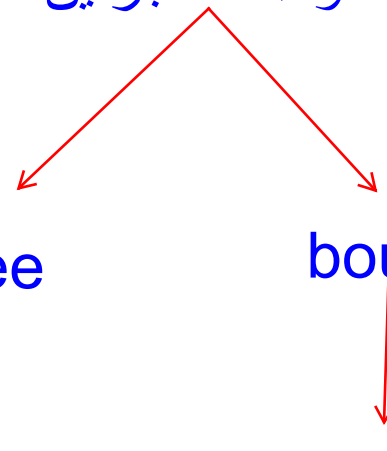
Low plasma binding or high tissue binding or high lipophilicity usually means an extensive tissue distribution.

البروتينات تفرز عن طريق الكبد واشهرها بروتين الالبومين بالتالي وجود البروتينات داخل الدم مهم وبعض البروتينات وجودها يسمح بارتباطها ببعض الادوية ومش شرط يكون البروتين داخل الدم لا ممكن يكون موجود داخل الخلايا

وصول الدواء الى الخلايا الغير مستهدفة يسمى adverse effect

شو بهمني اذا ارتبط الدوا بالبروتين ؟؟؟

في حركية الدواء عنا جزئين



جزء الدوا المرتبط بالبروتين

الجزء الحر من الدوا اللي ما ارتبط بالبروتين وهاد الجزء هو المسؤول عن إعطاء التأثير

الادوية الي الها highly protein bound

مثل warfarin , digoxin بكون الها تقريبا نسبة 80-90%

high protein bound بالتالي رح يكون التاثير بنسبة 10%

فالشخص اللي عندو مشاكل في تصنيع البروتينات بالكبد رح تقل نسبة البروتين ورح تزيد كمية free

نسبة التاثير رح تكون من 10-20 % بالتالي رح تزيد السمية

فيلي عندهم مشاكل بالكبد الجرعة الهم من هاد النوع من الادوية رح يكون اقل

من الدم للخلايا

highly protein bound / highly plasma protein bound >>low volume of distribution

في الخلية

highly protein bound >> high volume of distribution

السبب انها اصلا موجودة داخل الخلايا

Distribution

وهي خاصية للدوا مش للجسم وتعني مقدار توزيع الدوا داخل الجسم

- In pharmacokinetics, the distribution is described by the parameter V, the apparent volume of distribution.

ظاهري وليس حقيقي

- At equilibrium, V will theoretically not be lower than 7 L in a 70-kg person, but it has no upper limit.

lipophilicity ↑

plasma protein binding ↓

tissue protein binding ↑

lower limit اله

upper limit بس ما اله

Drug distribution patterns

العمر النصفي للدوا وهي احد الوسائل التي تحدد الـ elimination or execration

The extent to which a drug distributes affects the half-life of the drug and the fluctuation of the concentration at steady state.

الاضطراب كلما دخل الدوا جوا الخلايا بشكل اكبر كلما قل في الدم

Distribution can be thought of as following one of four types of patterns:

احد الادوية التي تستخدم كمدر بول فهاد النوع من الادوية مابدي ياه يدخل داخل الخلايا بدي التأثير تبعو يكون داخل الدم

1-The drug may remain largely within the vascular system. Mannitol and plasma substitutes such as dextran are examples of this type, but drugs which are strongly bound to plasma protein may also approach this pattern.

high molecular weight
low protein bound inside the tissue
low lipophilicity

نسبة الدوا الحر رح تكون عالية

رح يضل موجود بالدم

Drug distribution patterns

رسمة تبين توزيع
الادوية داخل الجسم

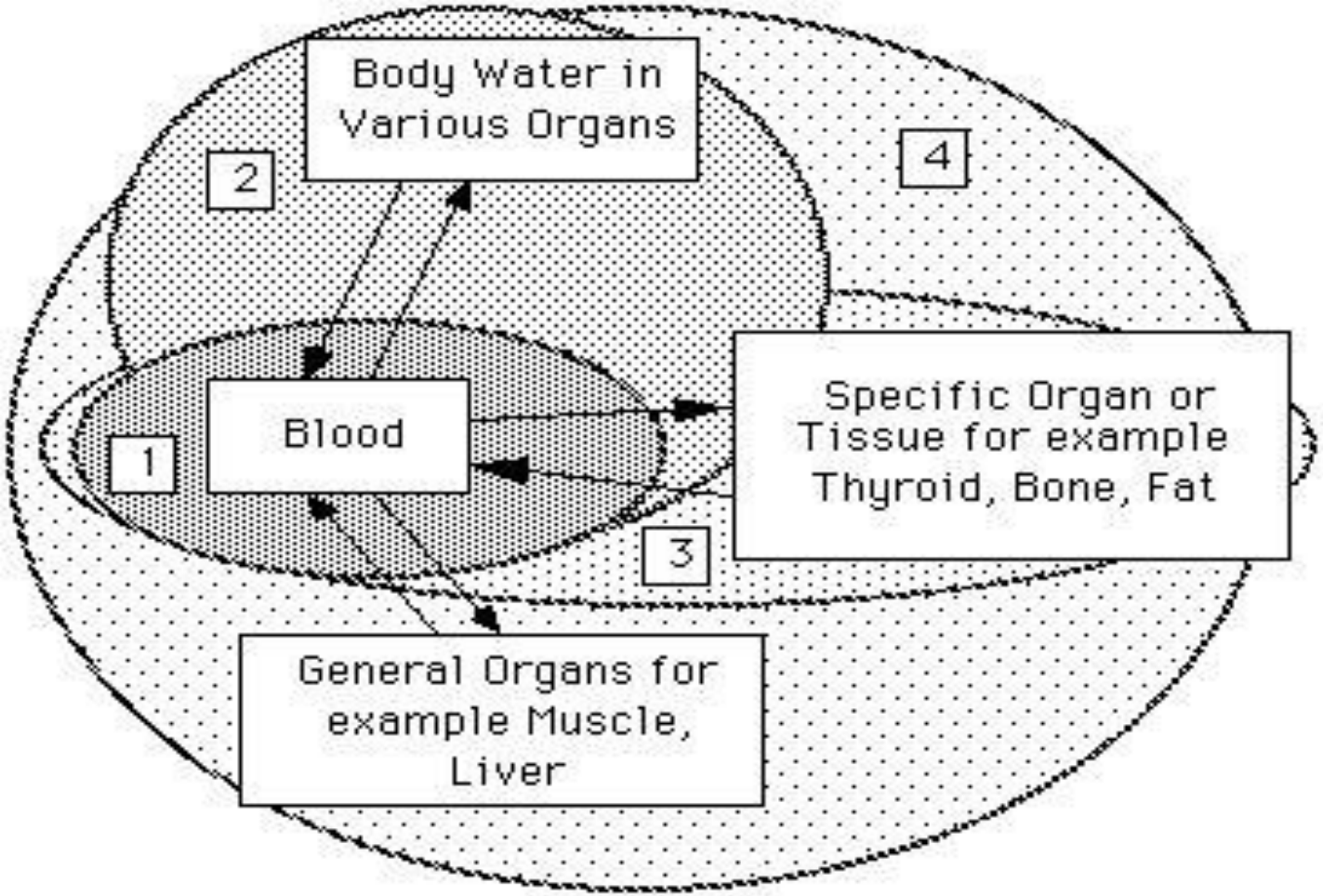


Diagram Representing Various Volumes Distribution Patterns

Drug distribution patterns

2- Some low molecular weight water soluble compounds such as ethanol and a few sulfonamides become uniformly distributed throughout the body water.

شكل توزعها

body water حجمها قليل تتوزع على طول
or
body fluid

Drug distribution patterns

ملاحظة عامة اللي مظلل عليهم بالاصفر هم عبارة عن أسماء ادوية او امثلة

3- A few drugs are concentrated specifically in one or more tissues that may or may not be the site of action.

Iodine is concentrated by the thyroid gland.

The antimalarial drug chloroquine may be present in the liver at concentrations 1000 times those present in plasma.

Drug distribution patterns

مشكلة هاد الدوا انو برتبط على اماكن تواجد الكالسيوم زي العظام والاسنان وطبعا حكينا عنو بالمحاضرات اللي فاتو

Tetracycline is almost irreversibly bound to bone and developing teeth.

Consequently tetracyclines should only be given to young children or infants in extreme conditions as it can cause discoloration and mottling of the developing second set of teeth.

سلبياته
يغير اللون
يؤثر على نمو العظام والاسنان الدائمة

Another type of specific concentration may occur with highly lipid soluble compounds which distribute into fat tissue.

Drug distribution patterns

4- Most drugs exhibit a non-uniform distribution in the body with variations that are largely determined by the ability to pass through membranes and their lipid/water solubility.

The highest concentrations are often present in the kidney, liver, and intestine usually reflecting the amount of drug being excreted.

high lipid solubility

بدخل داخل الخلايا بشكل اكبر

Drug distribution patterns

- Apparent volume of distribution (V) is a useful indicator of the type of pattern that characterizes a particular drug.

نسبة البلازما

تتبع لتايب 1
- A value of V in the region of 3-5 liter (in an adult) would be compatible with pattern 1. This is approximately the volume of plasma.

تتبع لتايب 2
- Pattern two would be expected to produce a V value of 30 to 50 liter, corresponding to total body water.

تايب 3
- Agents or drugs exhibiting pattern 3 would exhibit very large values of V. Chloroquine has a V value of approximately 115 L/ kg .

تايب 4
- Drugs following pattern 4 may have a V value within a wide range of values.

Drug distribution patterns

Volumes of body fluids	
Fluid substances	**Volume (liter)**
Extracellular Fluid	19
Plasma	3
Interstitial fluids	16
Intracellular fluids	23
Total body water	42

تقريبا 28 لتر

Factors affecting drug distribution

Factors Affecting Distribution	
A- Rate of distribution	**B- Extent of Distribution**
1. Membrane permeability 2. Blood perfusion	1. Lipid Solubility 2. pH – pKa 3. Plasma protein binding 4. Tissue drug binding

Factors affecting drug distribution

بهمني يكون الدوا
lipid soluble
عشان يكون الـ
membrane
permeability
عالية

A. Rate of distribution

1. Membrane permeability:

- Capillary walls are quite permeable.
- Lipid soluble drugs pass through very rapidly.
- Water soluble compounds penetrate more slowly at a rate more dependent on their size.
- Low molecular weight drugs pass through by simple diffusion. For compounds with molecular diameter above 100 Å transfer is slow.
- For drugs which can be ionized the drug's pKa and the pH of the blood will have a large effect on the transfer rate across the capillary membrane.

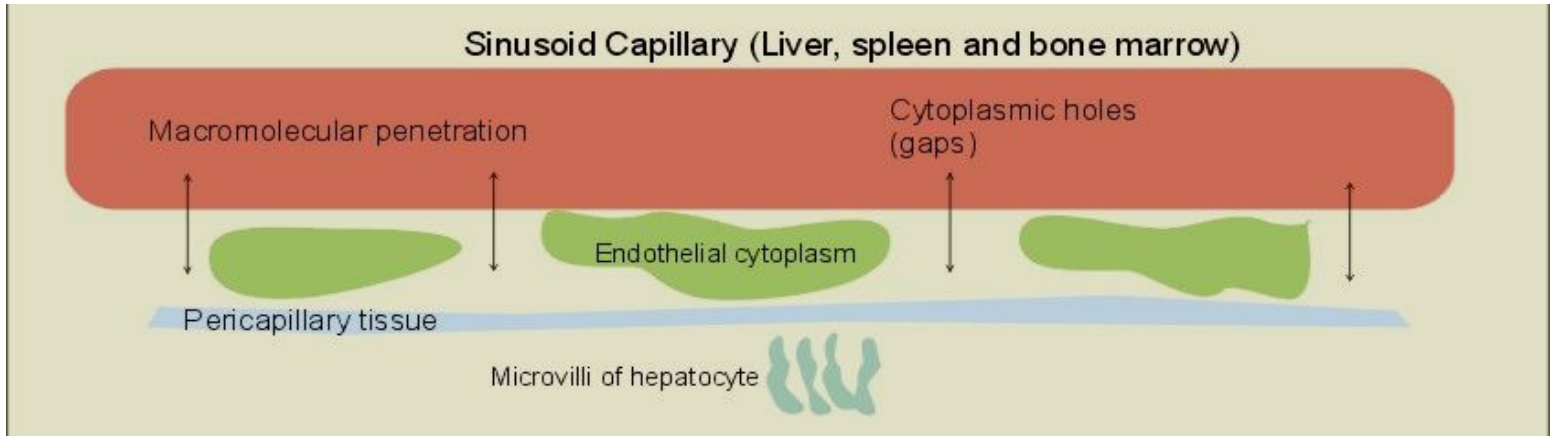
بهمني يكون الدوا
عشان يقدر يدخل داخل الخلايا unionized

Factors affecting drug distribution

- There are two deviations to the typical capillary structure which result in variation from normal drug tissue permeability.

i) Permeability is greatly increased in the renal capillaries by pores in the membrane of the endothelial cells, and in specialized hepatic capillaries, known as sinusoids which may lack a complete lining. This results in more extension distribution of many drugs out of the capillary bed.

مثال عليها محفظة بومان في الكلية

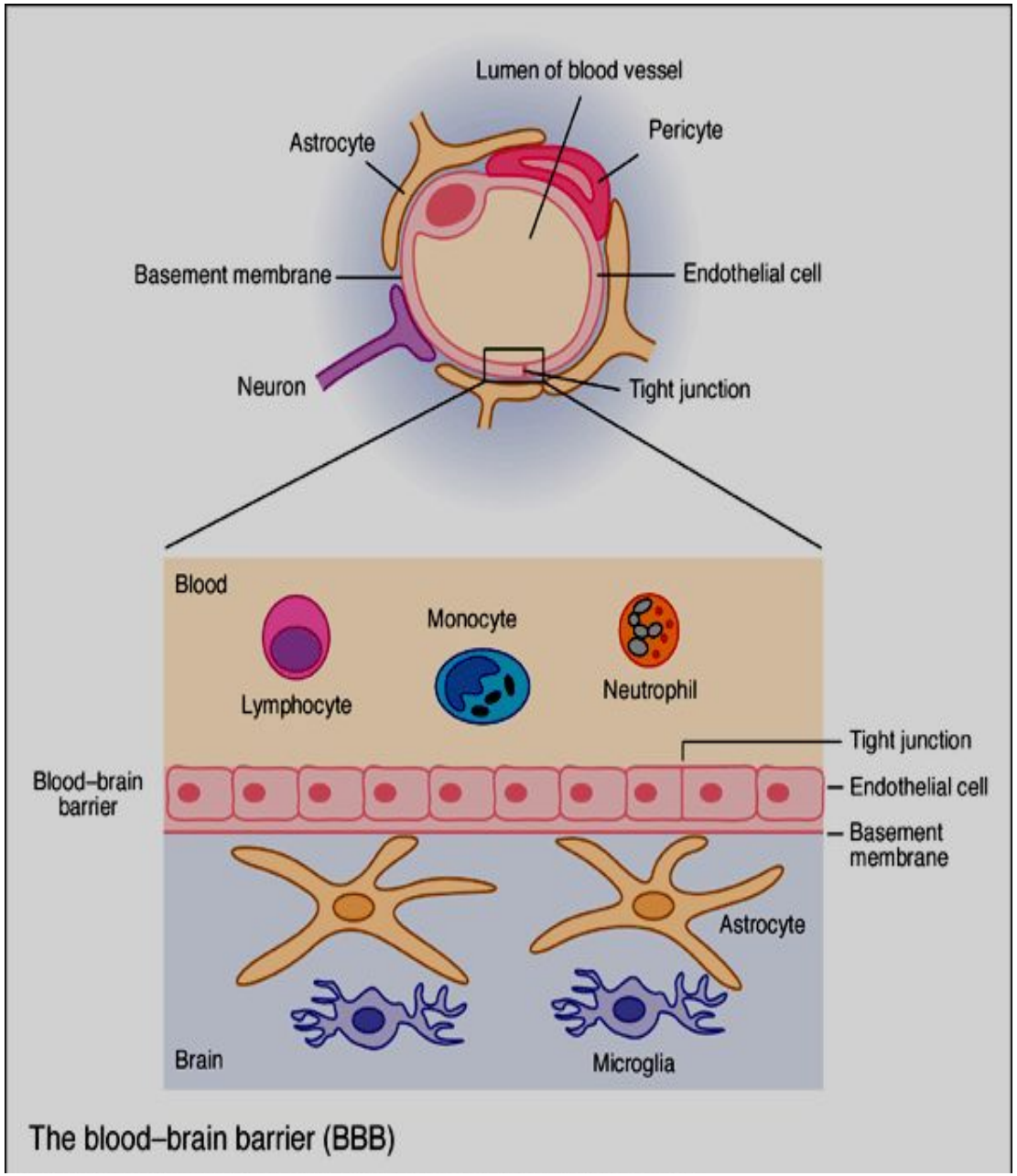


II) On the other hand, brain capillaries seem to have impermeable walls restricting the transfer of molecules from blood to brain tissue.

Lipid soluble compounds can be readily transferred but the transfer of polar substances is severely restricted.

This is the basis of the "blood-brain" barrier.

الادوية اللي بدي ياها توصل للـ CNS
لازم تكوم كاملة lipophilic



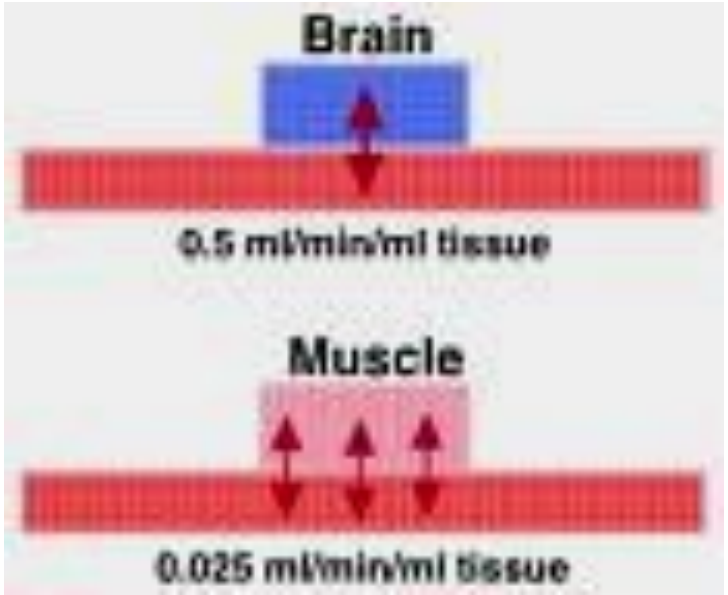
The blood–brain barrier (BBB)

Factors affecting drug distribution

تساعد في وصول اكبر قدر ممكن من الادوية

2. Blood perfusion rate: التروية

- The rate at which blood perfuses to different organs varies widely:



Blood Perfusion Rate		
Organ	**Perfusion Rate (mL/min/mL of tissue)**	**Percent of cardiac output (CO)**
Bone	0.02	5
Brain	0.55 - 0.5	15 - 14
Fat	0.03 - 0.01	4 - 2
Heart	0.7 - 0.6	4
Kidneys	4.5 - 4.0	24 - 22
Liver	0.95 - 0.8	27 - 25
Muscle	0.030 - 0.025	15
Skin	0.05 - 0.04	6 - 5

Factors affecting drug distribution

- The rate at which a drug reaches different organs and tissues will depend on the blood flow to those regions.

- Equilibration is rapidly achieved with heart, lungs, liver, kidneys and brain where blood flow is high.

- Skin, bone, and depot fat equilibrate much more slowly.