

# تفريغ تعقيم

محاضرة: PARENTERALS p.1

الصيدلانية: ياسمين خليل



لجان الرفعات



اللهم علمنا ما ينفعنا وانفعنا بما علمتنا وزنا علماً



! بدہ حفظاً کثیر کثیر کثیر

الناس السريعة بالحفظ اللهم بارك مبارك عليهم

# PARENTERALS

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Chapter 15 from Ansel's, 9<sup>th</sup> Ed

بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

# Introduction:

- pharmaceutical dosage forms with the common characteristic of sterility:
 

الأشكال الصيدلانية التي لا يتم تكونها معقمة

  1. Small and large-volume injectable preparations,
  2. irrigation fluids intended to bathe body wounds or surgical openings, and dialysis solutions.

لتقسيم الفتحات في الجسم بعد العمليات الجراحية + غسيل الكلى
  3. Biologic preparations, including vaccines, toxoids, and antitoxins,

(1) (2)
  4. Ophthalmic preparations →
 

تحضيرات العين
- Sterility in these preparations is essential because they are placed in direct contact with the internal body fluids or tissues, where infection can easily arise.

السبب يا، منهم كما نرى  
يكونوا امعتنا ؟

تحفيزات معتمة + خالية من Pyrogen ، ممكن تكون سائلة ،  
 او صلبة من دوائه  
 واحد او اكثر وتفضل على شكل dose واحدة او اكثر

1) parenteral preparations are sterile,  
 2) pyrogen-free <sup>[a]</sup> liquids (solutions, emulsions, or  
<sup>[b]</sup> suspensions) or solid dosage forms containing one  
 or more active ingredients, packaged in either  
single-dose or multi-dose containers.

They are intended for administration by injection,  
infusion, or implantation into the body.  
 Parenteral drugs are [administered directly into  
 veins, muscles or under the skin or more specialized  
tissues such as the spinal cord].

انتاجها  
 صقن ،  
 Sus release  
 ترافعة داخل  
 الجسم

# Injections

- **Injections:**

- are sterile, <sup>100% free من مواد الوائج</sup>
- pyrogen <sup>Pyrogen</sup> limited, that is, bacterial endotoxin units limit, <sup>لأنه تقاس بوحدة (units) حسب حجم الدواء بكمية فيها</sup> preparations <sup>ببساطة اعوا فقط</sup>
- intended to be administered parenterally
- The term **parenteral** refers to the injectable routes of administration: <sup>↳ out side GIT</sup>
- It derives from the Greek words **para** (outside) and **enteron** (intestine) and denotes routes of administration other than the oral route.

ويمكن تقدير inhalation doses

Parenteral <sup>حقن</sup>  
 injection only <sup>وكمية الحقن</sup>

# Injections

اللهم ارحم ايتهم اغفر له

واغفر عنه وادخله وارمله

الجنة بغير حساب وعذاب

- The parenteral routes are used when:
  - rapid drug action is desired, as in emergencies
  - when the patient is uncooperative,
  - Unconscious
  - or unable to accept or tolerate oral medication
  - or when the drug itself is ineffective by other routes.

نرى الطوارئ  
ببساطة سريعة

في حالة عدم وعي  
المرضى بنفسي صفت

لو المرء من صا  
محدودة قدرة بلع  
بمكاتب هبلية في الحقن غير مناسب

as insulin

صين بيطي القند ؟

- most injections are administered by the physician, physician's assistant, or nurse in the course of medical treatment (With the exception of insulin injections, which are commonly self- administered by diabetics)

النسو بين الحقن  
بأخذها لحاله

تاريخ الحقن

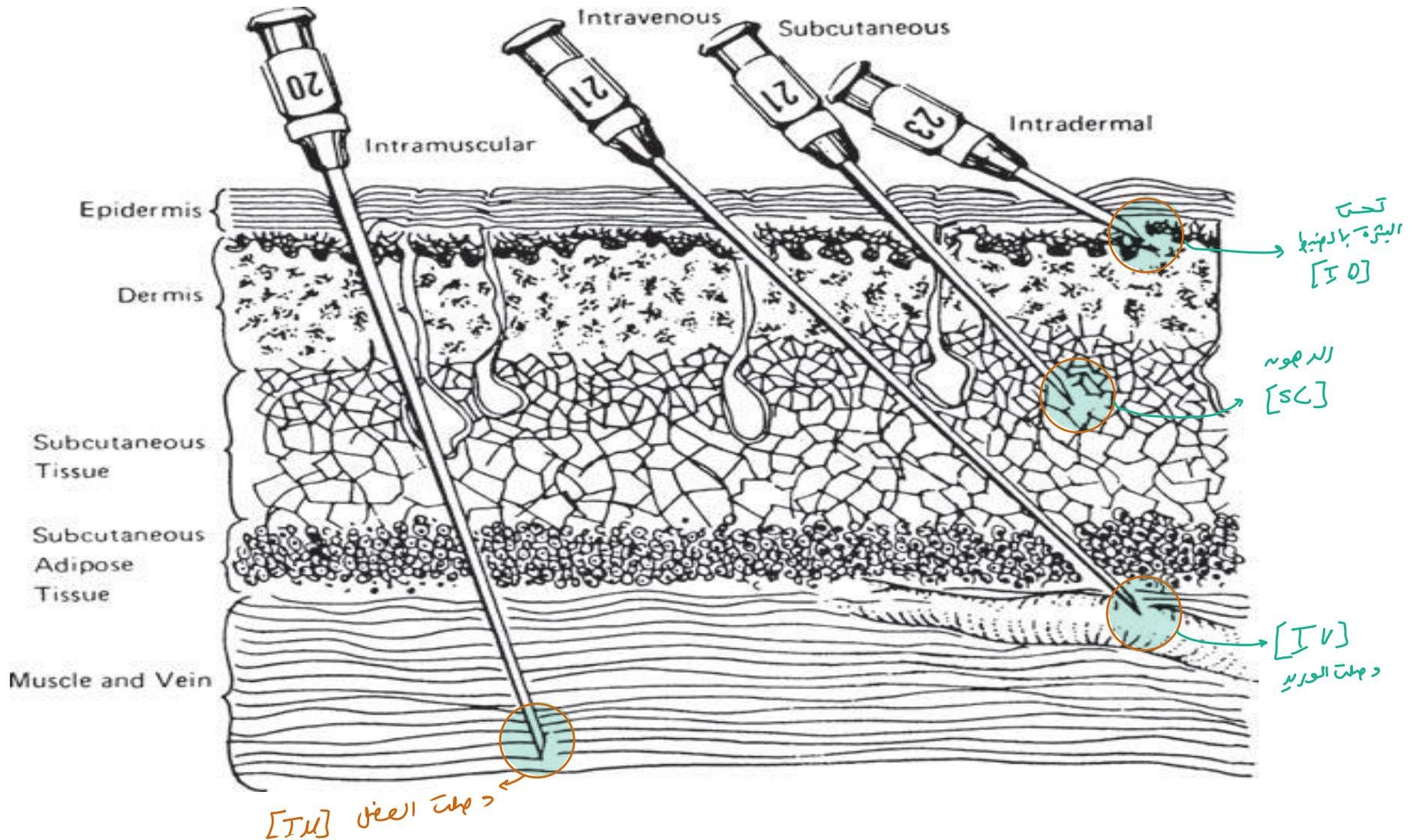
- The earliest injectable drug to receive official recognition was the hypodermic morphine solution, which appeared first in the 1874



جداً  
كبيرة  
واحدة  
تتألم كثير كانه ضل  
تحت جلده من دجها  
مقارنة  
مع ذابرا اليوم المحدث

# PARENTERAL ROUTES OF ADMINISTRATION

- Drugs may be injected into almost any organ or area of the body:
  - including the joints (*intraarticular*),
  - joint fluid area (*intrasynovial*),
  - spinal column (*intraspinal*),
  - spinal fluid (*intrathecal*),
  - arteries (*intra-arterial*),
  - and in an emergency, even the heart (*intracardiac*).
- However, most injections go into a vein (*intravenous, IV*), into a muscle (*intramuscular, IM*), into the skin (*intradermal, ID; intracutaneous*), or under the skin (*subcutaneous, SC; sub-Q, SQ; hypodermic, hypo*)



**FIGURE 15.1** Routes of parenteral administration. Numbers on needles indicate gauge of the needles (outside diameter of shaft).

# □ Intravenous Route

- IV injection of drugs had its scientific origin in 1656 in the experiments of Sir Christopher Wren, architect of St Paul's Cathedral and Using a bladder and quill for a syringe and needle, he injected wine, ale, opium, and other substances into the veins of dogs and studied their effects.



## Pig bladders and feather quills: a history of vascular access devices.

**Source:** British Journal of Nursing . 2014 IV Therapy Supplement, Vol. 23, pS21-S25. 5p. 3 Black and White Photographs.

**Author(s):** Kelly, Linda J.

### Abstract:

Vascular access is a requirement for many hospitalised patients. Over the years there have been many technological refinements and advances in the Renaissance period, the discovery of the circulatory system in the 15th century, to the present day, and will give the reader a notion of the origins and :

# Intravenous Route

## IV drugs provide:

أدوية سريعة

- **rapid action** compared with other routes of administration

← صا  
- **Drug absorption is not a factor**, optimum blood levels may be achieved with accuracy and immediacy

ببعض  
إستراتيجيات  
علاجية  
بمعدل 100%  
صا  
بمعدل 100%  
In emergencies, IV administration of a drug may be lifesaving because of the placement of the drug directly into the circulation

## On the negative side:

سلبيات

- once a drug is administered intravenously, **it cannot be retrieved**.

فجر د فوول الوداد للدم لو كسنت خلطانة في الجرعة فلاه سلا صكح و تعيشوا

- In the case of an adverse reaction to the drug the drug **cannot be easily removed from the circulation**, as it could, by induction of vomiting after oral administration of the same drug.

نفس الوداد  
صنك شخص  
طوعه  
صا  
المادة الضارة إلى أعطينها  
صا بنقد رنخل إلى إنه تعالج Symptoms  
التي ظهرت

- The IV dose may differ greatly from the oral dose. Thus, great care must be taken to prevent overdosing or under-dosing.

جرعة ال IV كسيتي بخودنا ال oral وانكيد أقل صونها كانه صا صا صا في الجرعة ال IV في جرعة ال oral

# Intravenous Route

- Both small and large volumes of drug solutions may be administered intravenously.
- The use of 1,000-mL containers of solutions for IV infusion is common-place in the hospital:
  - solutions, containing such agents as nutrients *large*
  - plasma volume expanders, *large*
  - electrolytes, *large*
  - amino acids, *large*

The infusion or flow rate may be adjusted according to the needs of the patient.

*sustained  
release*

# Intravenous Route

د. سبجي حذفنا الأرقام  
هدول

- flow rates for IV fluids range from 42 to 150 mL per hour.
- Lower rates are used for keep-open (KO, KVO) lines.
- The main hazard of IV infusion:
  - thrombus formation induced by the catheter or needle touching the wall of the vein.

Small blood clot

صا بتتكون  
من مكانها  
وصمكن  
تسخر الوعاء  
الدموي

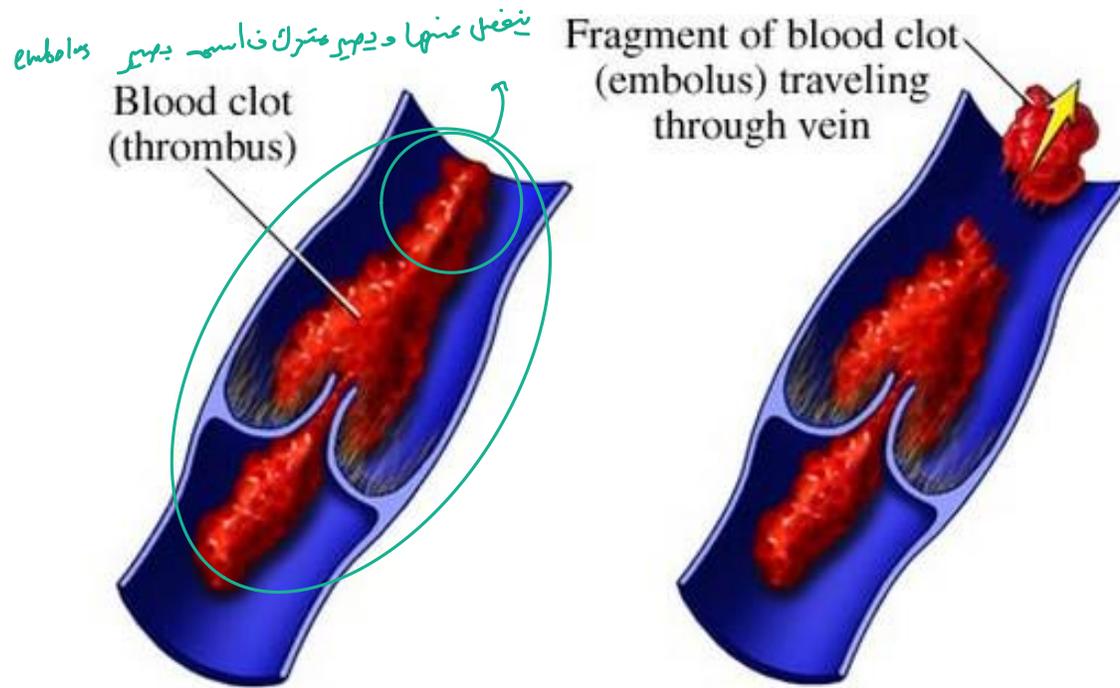
- A **thrombus** is a blood clot formed within the blood vessel (or heart), usually because of slowing of the circulation or an alteration of the blood or vessel wall.

هذه الحالة  
تكون بين حتمت جمع الدم  
دبتمل انشاء اللوواء بهه مكانه  
عبر ابي تكونت فيه

- Once such a clot circulates, it becomes an **embolus**, carried by the blood stream until it lodges in a blood vessel, obstructing it and resulting in a block or occlusion referred to as an **embolism**.

block / occlusion

IV infusion  
هم ابي بتسخر صغوم  
thrombus  
embolus



اللهم اشفي مرضي الحليلين  
وارحم مرضيهم آمين

# Intravenous Route

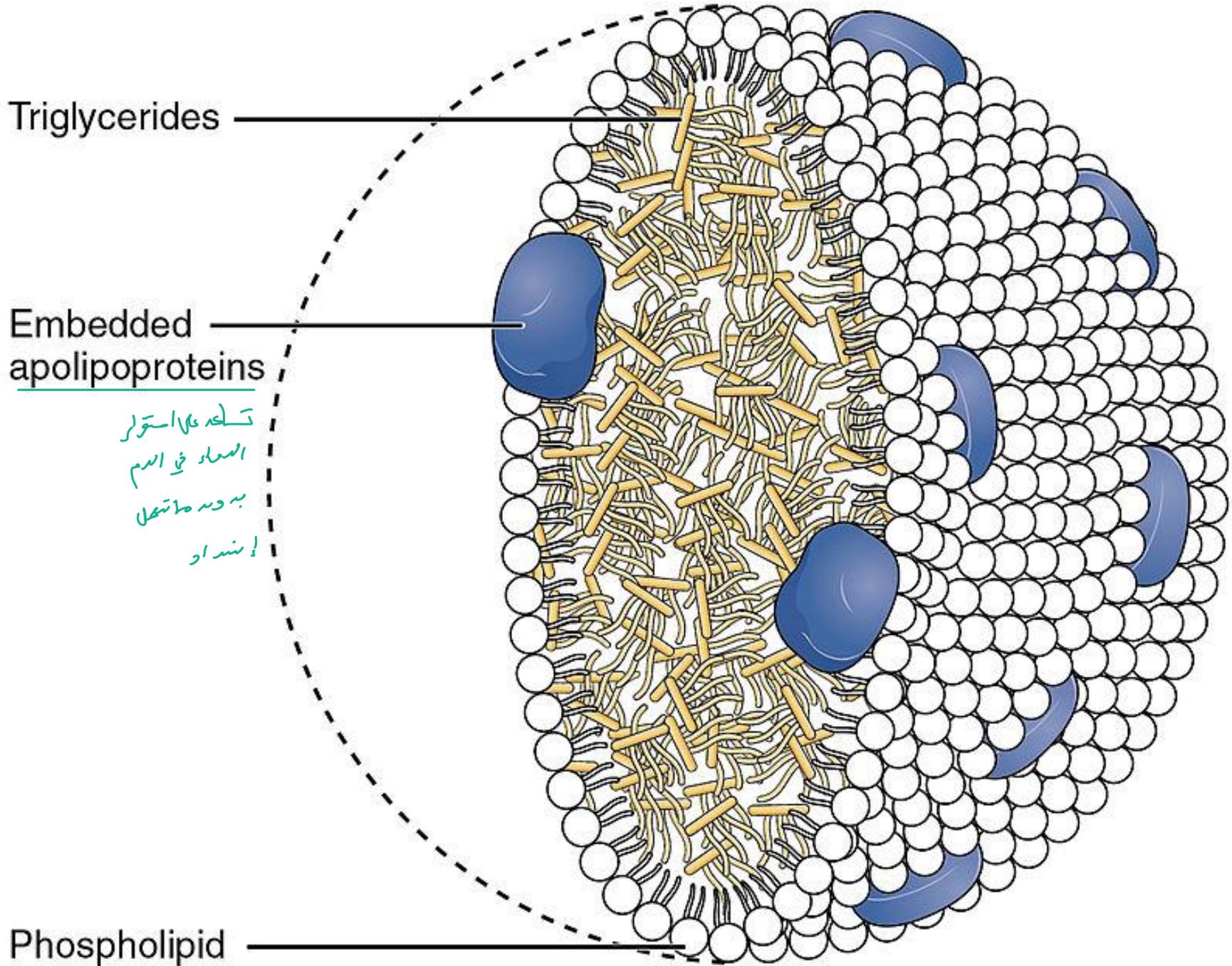
لوجانه oil طرح أميسوله mixing مع الدم

- IV drugs ordinarily must be in aqueous solution:
  - they must mix with the circulating blood
  - and not precipitate from solution → Such an event can lead to pulmonary microcapillary occlusion and blockage of blood flow.
- IV fat emulsions (e.g., [Intralipid, 20%, 30%, Baxter; Liposyn II, 10%, 20%, Hospira; Liposyn III, 10% to 30%, Hospira]) have gained acceptance for use as a source of calories and essential fatty acids for patients requiring parenteral nutrition for extended periods, usually more than 5 days.
- The product contains up to 30% soybean oil emulsified with egg yolk phospholipids in a vehicle of glycerin in water for injection.

لا ينبغي  
يؤدي إلى

للمقدنية

aqueous



Triglycerides

Embedded  
apolipoproteins

تسلسل على استوار  
السما في الدم  
به وده ما تعلق  
! بنسداد

Phospholipid

8 ايه يا انت سبحان  
ياي كنته صا الظالمين

# Intralipid® 20% 10 x 100 ml

Fat emulsion for intravenous use

100 ml contains: Purified soybean oil 20 g  
Excipients: Purified egg phospholipids 1.2 g, Glycerol anhydrous 2.2 g, may contain Sodium hydroxide,  
Water for injection to 100 ml.

مكونات و صنية بلا ايه يذوبين في الدم عادي  
صانه vehicle

Energy content: 0.84 MJ (200 kcal)/100 ml.

The contents of this bag are for a single infusion only. Any remaining emulsion must be discarded.  
Electrolyte solutions should not be added to this bag.  
Read the package leaflet before use.

Store at or below 25°C. Do not freeze.

Fresenius Kabi Limited, Cestrian Court, Eastgate Way  
Manor Park, Runcorn, Cheshire, WA7 1NT, UK

PL 8828/0110  
MA 134-00101

POM

V002/UK

Batch no: 10XX1234  
Expiry date: 01/2012  
X1234567L



123456

400266 / 01  
83 18 00-220



- Automated IV delivery systems for intermittent self administration of analgesics became commercially available.
- Patient-controlled analgesia (PCA)
- PCA devices can be used for IV, SC, or epidural administration.



2

# Intramuscular Route

- IM injections of drugs:

الا استجابة صحتها رزين  
 كريمة IV بسن يتقبل قهوة أفول صفة  
 كينها تبصل كالكه de أكيد

- provide effects that are less rapid but generally longer lasting than those obtained from IV administration <sup>IV كانه قفقا</sup>
- Aqueous or oleaginous solutions or suspensions of drug substances may be administered intramuscularly. <sup>aqueous</sup>
- Depending on the type of preparation, absorption rates vary widely, explain? Soln. vs susp. and aq. vs oil
- What determine the physical type of preparation?
  1. properties of the drug itself ✓
  2. and the therapeutic goals. ✓

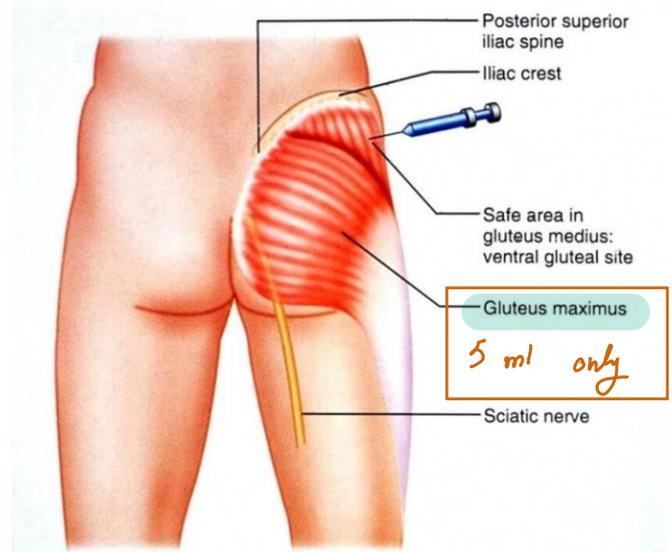
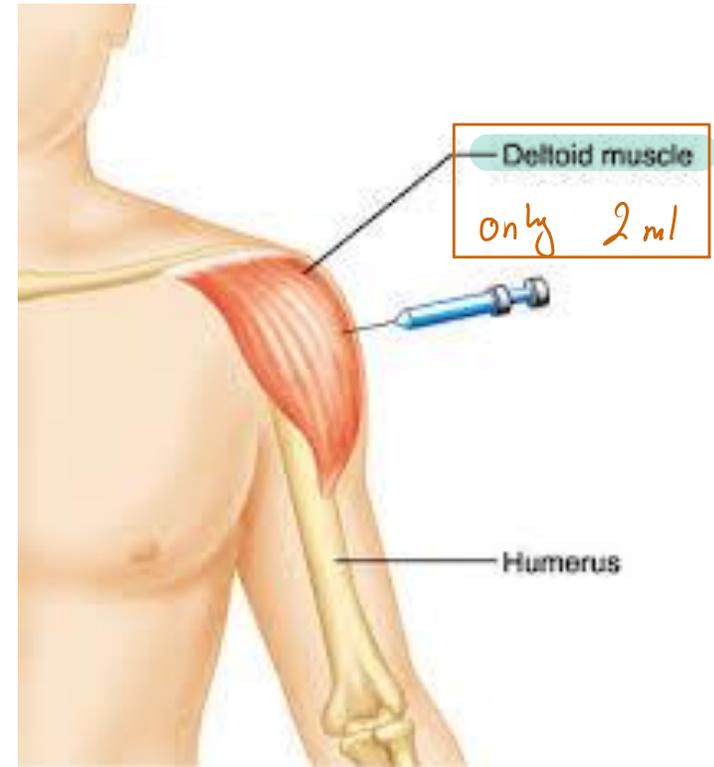
- The point of injection should be as far as possible from major nerves and blood vessels.
- paralysis resulting from neural damage, hematoma, and scarring.
- The volume of medication that may be conveniently administered by the IM route is limited, generally to a maximum of 5 mL in the gluteal region and 2 mL in the deltoid of the arm.

لا، زم ننتبه

نعملي بعيد

كنا الأوعية كما نعمل في الرقبة

عشان ما يهين  
نقل



## 3 Subcutaneous Route

- The SC route may be used for injection of small amounts of medication.
- The site of injection is usually rotated when injections are frequently given → daily insulin injections.  
بنظر نفي المنهكة كل مرة حتى لو بنقنا كمية صغيرة
- The maximum amount of medication that can be comfortably injected subcutaneously is about 1.3 mL, and amounts greater than 2 mL will most likely cause painful pressure.  
بمسبب الألم
- Syringes with up to 3-mL capacities and 24- to 26-gauge needles are used.

# Subcutaneous Route

SC هدر صا بظهور

- Irritating drugs and those in thick suspension may produce induration, sloughing, or abscess and may be painful.
- Such preparations are not suitable for SC injection.

4

## Intradermal Route

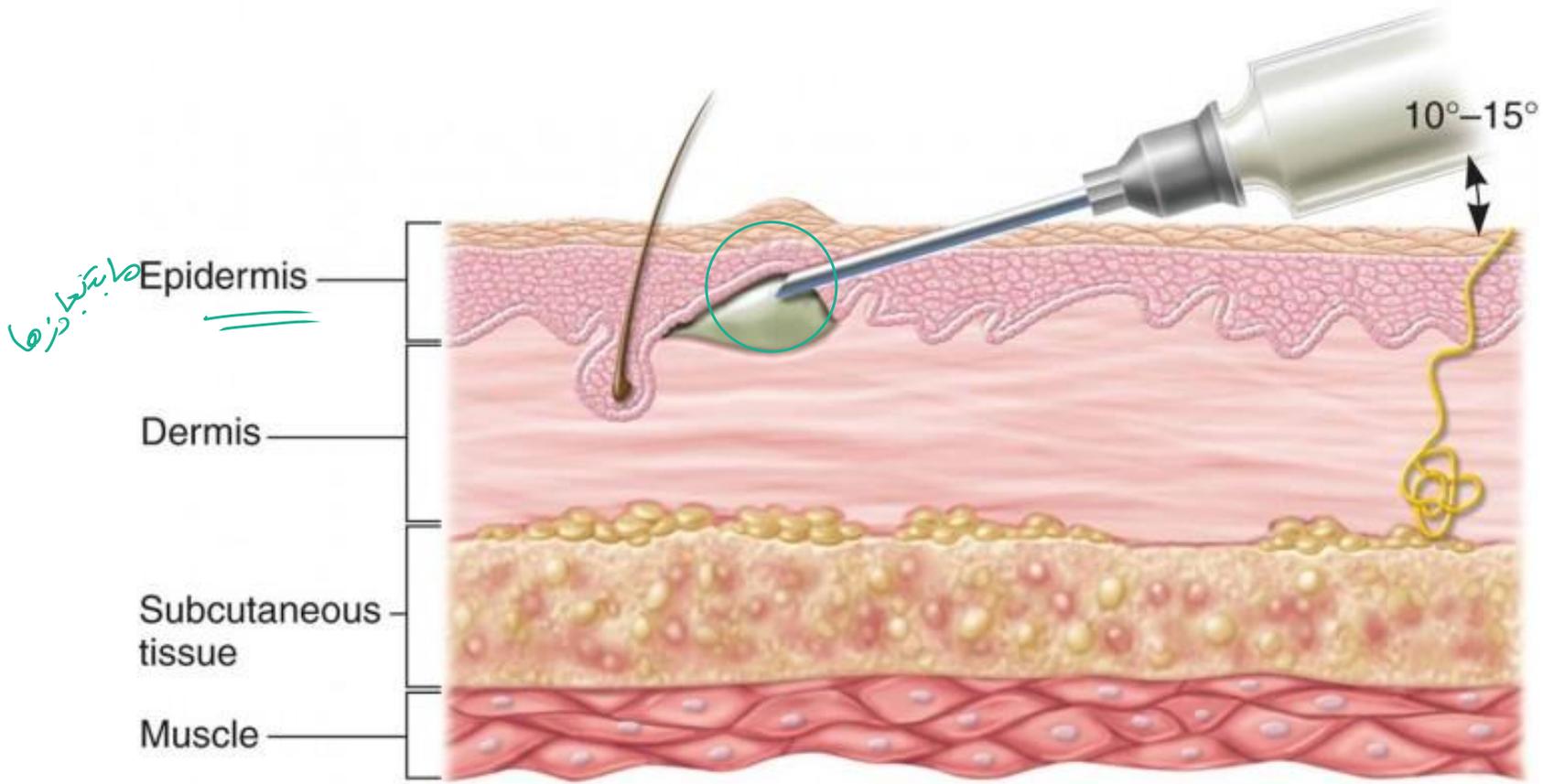
- A number of substances may be effectively injected into the <sup>epi</sup>corium (dermis), the more vascular layer of the skin just beneath the epidermis.
- These substances include various agents for diagnostic determinations, desensitization, or immunization.
- The usual site for ID injection is the anterior forearm.
- A short and narrow needle is usually employed.
- Usually, only about 0.1 mL may be administered in this manner.



## INTRADERMAL TECHNIQUE

- **26 TO 27 GAUGE NEEDLE**
- **SYRINGE: 1 ML (CALIBRATED IN 0.01 ML INCREMENTS)**

دبے انہیں ایسٹیکر  
والحکین



صابتیخارفا

# INTRADERMAL INJECTION

- ▶ **Most commonly used site:** Inner surface of the forearm
- ▶ Subscapular region of the back can be used as well as the deltoid region



# OFFICIAL TYPES OF INJECTIONS:

According to the USP, injectable materials are separated into:

1. **Injection:** Liquid preparations that are drug substances or solutions thereof (e.g., Insulin Injection, USP).  
 liquid, solution
2. **For injection:** Dry solids that, upon addition of suitable vehicles, yield solutions conforming in all respects to the requirements for injections (e.g., Cefuroxime for injection, USP).  
 Dry solid  
 زي  
 للحقن
3. **Injectable emulsion:** Liquid preparation of drug substance dissolved or dispersed in a suitable emulsion medium (e.g., Propofol, USP).
4. **Injectable suspension:** Liquid preparation of solid suspended in a suitable liquid medium (e.g., Methylprednisolone Acetate Suspension, USP).
5. **For injectable suspension:** Dry solid that, upon addition of suitable vehicle, yields preparation conforming in all respects to the requirements for injectable suspensions (e.g., Imipenem and Cilastatin for injectable suspension, USP).  
 زي صبر  
 For injection

بعضیہ شکل Suspension ↗

- if a drug is unstable in solution??
- If the drug is unstable in water [prepare it as suspen, or change water to oil] or as dry powder
- If an aqueous solution is desired???, a water-soluble salt form of the insoluble drug is frequently prepared.

IV ○ Aqueous or blood-miscible solutions may be injected directly into the blood stream. Blood-immiscible liquids, such as oleaginous injections and suspensions, can interrupt the normal flow of blood, and their use is **generally** restricted to other than IV administration.

not- IV }

- The onset and duration of action of a drug may be somewhat controlled:
  1. by its chemical form,
  2. the physical state of the injection (solution or suspension),
  3. and the vehicle.
- Drugs in aqueous suspension are ?????????? rapid acting than drugs in oleaginous suspension.
- If long action is desired to reduce the frequency of injections. These long-acting injections are called repository or depot preparations.

- The solutions and suspensions of drugs intended for injection are prepared taking the following considerations:  
look for pg 437

① Solvents or vehicles must meet special purity and other standards ensuring their safety by injection.

صاحبكوه الاختيار عيشو اي

2. The use of added substances, such as buffers, stabilizers, and antimicrobial preservatives, fall under specific guidelines of use and are restricted in certain parenteral products. The use of coloring agents is strictly prohibited.

كـ الا شياء الي كانت اياها قتها عادي

صحتك تكون ممنوعة في الحقن مثل الالوان  
لبات route of administration

! اذا لقيتوا المادة الي داخل الابهة طونة ن هاد لونه الحوية  
العقار مشا ! ضافة صبي

3. Parenteral products are always sterilized, meet sterility standards, and must be pyrogen limited.

4. Parenteral solutions must meet compendial standards for particulate matter. *undissolved particles*
5. Parenteral products must be prepared **in environmentally controlled areas**, under strict sanitation standards, and by personnel specially trained and clothed to maintain the sanitation standards.  
*Clean Rooms*
6. Parenteral products are packaged in special hermetic containers of specific and high quality. Special quality control procedures are used to ensure hermetic seal and sterile condition.  
*صحيحة الإغلاق*
7. Each container of an injection is filled to a volume in slight excess of the labeled volume to be withdrawn. This overfilling permits ease of withdrawal and administration of the labeled volumes.
8. The volume of injection permitted in **multiple-dose containers** is restricted, as are

the types of containers (single-dose or multiple-dose) that may be used for certain injections.

9. Specific **labeling regulations** apply to injections.
10. **Sterile powders intended for solution or suspension** immediately prior to injection are frequently packaged as lyophilized or freeze-dried powders to permit ease of solution or suspension upon the addition of the solvent or vehicle.

*تحتوي على نبتون*  
*النتيجة يمكن أن تكون سهولة في تحضيرها*

# SOLVENTS AND VEHICLES FOR INJECTIONS

- **The most frequently used solvent for injections is water for injection, USP:**

- This water is purified by **distillation** or by **reverse osmosis** <sup>①</sup>
- and meets the same standards for the presence of total solids as does **Purified Water, USP**—that is, not more than 1 mg/100 mL water for injection, USP <sup>②</sup>
- and may **not contain added** substances. <sup>③</sup>
- **water for injection is not required to be sterile** <sup>④</sup>
- it must be **pyrogen free**. <sup>④</sup>  
*limited*
- The water is intended to be used in the manufacture of injectable products to **be sterilized after preparation**. <sup>⑤</sup>
- Water for injection should be stored in tight containers at temperatures below or above the range in which microbial growth occurs. <sup>⑥</sup>
- Water for injection is intended to be used **within 24 hours** after collection. <sup>⑦</sup>
- the water should be collected in sterile and **pyrogen-free containers**. The containers are **usually glass or glass lined**. <sup>⑧</sup>

*not plastic*

# SOLVENTS AND VEHICLES FOR INJECTIONS

نوع  
مستحضر

have no tonicity to blood as normal saline

## **Sterile water for injection, USP:**

- is packaged in single-dose containers not larger than 1 L.
- it must be pyrogen free
- have an allowable endotoxin level, not more than 0.25 USP endotoxin units per milliliter.
- it may not contain any antimicrobial agent or other added substance..
- This water is intended to be used as a solvent, vehicle, or diluent for already sterilized and packaged injectable medications.
- The 1-L bottles cannot be administered intravenously because they have no tonicity. Thus, they are used for reconstitution of multiple antibiotics.

بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ  
رَبِّنا نبي صفيح

# SOLVENTS AND VEHICLES FOR INJECTIONS

## ← Bacteriostatic water for injection, USP:

- Is sterile water for injection containing one or more suitable antimicrobial agents.
- It is packaged in prefilled syringes or in vials containing not more than 30 mL of the water.
- The water is employed as a sterile vehicle in the preparation of small volumes of injectable preparations.
- the water must be used only in parenterals that are administered in small volumes (toxic amounts of the antimicrobial agents that would be injected along with the medication).  
 لو كانه كمية كبيرة  
 يعني لو كانه في جرعة عالية من مادة داخل الدم
- if more than 5 mL of solvent is required, sterile water for injection rather than bacteriostatic water for injection is preferred.
- chemical compatibility of the bacteriostatic agent or agents with the particular medicinal agent being dissolved or suspended.

يمكن استخدامها أكثر من مرة، لأنه فيها مادة حافظة صالحة قبل

- USP labeling requirements demand that the label state Not for use in neonates



# SOLVENTS AND VEHICLES FOR INJECTIONS

- ④ • **Sodium chloride injection, USP:**
- is a sterile isotonic solution of sodium chloride in water for injection.
  - It contains no antimicrobial agents
  - has approximately 154 mEq each of sodium and chloride ions per liter.
  - It may be used as a sterile vehicle in solutions or suspensions of drugs for parenteral administration.
  - is frequently used as a catheter or IV line flush to maintain patency.

has **no** preservative or antimicrob agents

**SODIUM CHLORIDE**  
INJECTION, USP  
**0.9%**

NDC 0517-2810-25  
25 x 10 mL  
SINGLE DOSE VIALS

**FOR DRUG DILUENT USE**  
**PRESERVATIVE FREE**

**Rx Only**

Each mL contains: Sodium Chloride 9 mg, Water for Injection q.s. pH adjusted with Hydrochloric Acid and/or Sodium Hydroxide.

**0.3 mOsmol/mL**. Sterile, nonpyrogenic.

**WARNING: DISCARD UNUSED PORTION.**

Store at 20°-25°C (68°-77°F); excursions permitted to 15°-30°C (59°-86°F)

(See USP Controlled Room Temperature)

Directions for Use: See Package Insert

AMERICAN REGENT, INC.  
SHIRLEY, NY 11967

Rev. 11/05

Lot / Exp.



# SOLVENTS AND VEHICLES FOR INJECTIONS

## • Bacteriostatic sodium chloride injection, USP:

- is a sterile isotonic solution of sodium chloride in water for injection.
- It contains one or more suitable antimicrobial agents, which must be specified on the labeling.
- Sodium chloride 0.9% renders the solution isotonic.
- This solution may not be packaged in containers larger than 30 mL.
- When this solution is used as a vehicle, care must be exercised to ensure compatibility of the added medicinal agent with the preservative or preservatives and with the sodium chloride
- also used to flush a catheter or IV line to maintain its patency

# SOLVENTS AND VEHICLES FOR INJECTIONS

- bacteriostatic sodium chloride injection also carries the warning Not for use in neonates.

NDC 63323-259-30 205930

**BACTERIOSTATIC  
SODIUM CHLORIDE  
INJECTION, USP**

**0.9%**

**NOT FOR USE  
IN NEWBORNS**

**30 mL** Rx only  
Multiple Dose Vial

**FOR DRUG DILUENT  
USE ONLY**

**NOT FOR INHALATION**

**Sterile, Nonpyrogenic**

Each mL contains: Sodium chloride 9 mg; methylparaben 0.12%; propylparaben 0.012%; Water for Injection q.s. HCl and/or NaOH may have been added for pH adjustment.

Usual Dosage: See insert.

Store at 20° to 25°C (68° to 77°F) [see USP Controlled Room Temperature].

**APP**  
APP Pharmaceuticals, LLC  
Schaumburg, IL 60173

401735D

LOT/EXP



# SOLVENTS AND VEHICLES FOR INJECTIONS

- **Ringer's injection, USP:**  $KCl + NaCl + CaCl$ 
  - is a sterile solution of sodium chloride, potassium chloride, and calcium chloride in water for injection.
  - The three agents are present in concentrations similar to those of physiologic fluids.
  - Ringer's is employed as a vehicle for other drugs or alone as an electrolyte replenisher and plasma volume expander.

← الاستحسان

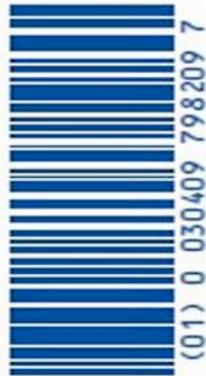
1000 mL

NDC 0409-7982-09

# RINGER'S INJECTION, USP

EACH 100 mL CONTAINS SODIUM CHLORIDE 860 mg; POTASSIUM CHLORIDE 30 mg; CALCIUM CHLORIDE, DIHYDRATE 33 mg IN WATER FOR INJECTION. MAY CONTAIN HCl OR NaOH FOR pH ADJUSTMENT. ELECTROLYTES PER 1000 mL: SODIUM 147 mEq; POTASSIUM 4 mEq; CALCIUM 4 mEq; CHLORIDE 155 mEq.

309 mOsmol/LITER (CALC.). pH 5.4 (5.0 TO 7.5). DO NOT ADMINISTER CALCIUM CONTAINING SOLUTIONS CONCURRENTLY WITH STORED BLOOD. ADDITIVES MAY BE INCOMPATIBLE. CONSULT WITH PHARMACIST, IF AVAILABLE. WHEN INTRODUCING ADDITIVES, USE ASEPTIC TECHNIQUE, MIX THOROUGHLY AND DO NOT STORE. SINGLE-DOSE CONTAINER. FOR INTRAVENOUS OR SUBCUTANEOUS USE. USUAL DOSAGE: SEE INSERT. STERILE, NONPYROGENIC. USE ONLY IF SOLUTION IS CLEAR AND CONTAINER IS UNDAMAGED. MUST NOT BE USED IN SERIES CONNECTIONS.



Rx ONLY



CONTAINS DEHP



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IM-0051 (4/04)

HOSPIRA, INC., LAKE FOREST, IL 60045 USA



دبّ کا تکیلی ہی  
نفسی ہل فہ عین

# SOLVENTS AND VEHICLES FOR INJECTIONS

في مصل الاسترخاء

## 5 • **Lactated Ringer's Injection, USP:** مصل مزيل الحماض

- has different quantities of the three salts in Ringer's injection
- and it contains sodium lactate.
- This injection is a fluid and electrolyte replenisher and a systemic alkalizer.

LOT

EXP

250 mL

6E2322  
NDC 0338-6307-02

# Lactated Ringer's Injection USP

EACH 100 mL CONTAINS 600 mg SODIUM CHLORIDE USP 310 mg SODIUM LACTATE 30 mg POTASSIUM CHLORIDE USP 20 mg CALCIUM CHLORIDE USP pH 6.5 (6.0 to 7.5) mEq/L SODIUM 130 POTASSIUM 4 CALCIUM 2.7 CHLORIDE 109 LACTATE 28 OSMOLARITY 273 mOsmol/L (CALC) STERILE NONPYROGENIC SINGLE DOSE CONTAINER **NOT FOR USE IN THE TREATMENT OF LACTIC ACIDOSIS** ADDITIVES MAY BE INCOMPATIBLE CONSULT WITH PHARMACIST IF AVAILABLE WHEN INTRODUCING ADDITIVES USE ASEPTIC TECHNIQUE MIX THOROUGHLY Do NOT STORE Dosage INTRAVENOUSLY AS DIRECTED BY A PHYSICIAN SEE DIRECTIONS CAUTIONS SQUEEZE AND INSPECT INNER BAG WHICH MAINTAINS PRODUCT STERILITY DISCARD IF LEAKS ARE FOUND MUST NOT BE USED IN SERIES CONNECTIONS Do NOT ADMINISTER SIMULTANEOUSLY WITH BLOOD Do NOT USE UNLESS SOLUTION IS CLEAR **Rx ONLY** STORE AT ROOM TEMPERATURE (25°C/77°F) UNTIL READY TO USE AVOID EXCESSIVE HEAT SEE INSERT

50

100

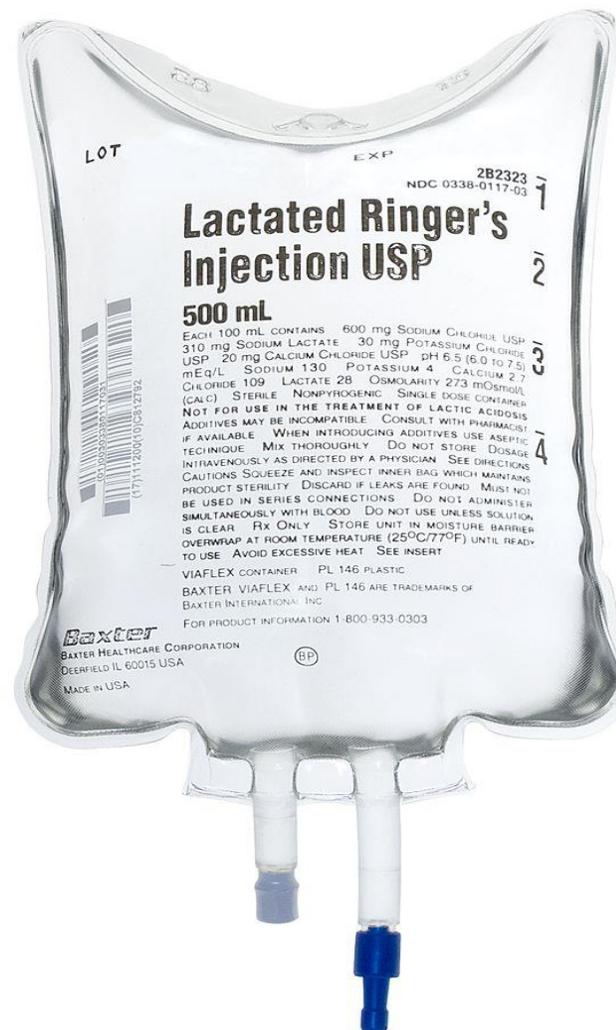
150

200

**Baxter**  
BAXTER HEALTHCARE CORPORATION  
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MADE IN USA

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AVIVA CONTAINER



اللهم انصر  
رجالنا تحت  
الأنفاه

# NONAQUEOUS VEHICLES

not IV  
use  
→ I M use

- restrictions on the fixed vegetable oils in parenteral products:
  - For one thing, they must remain clear when cooled to 10°C (50°F) to ensure the stability and clarity of the injectable product during refrigeration.
  - The oils must not contain mineral oil or paraffin, as these materials are not absorbed by body tissues.
  - Oils to be employed in injections must meet officially stated requirements of iodine number and saponification number.
  - Some patients exhibit allergic reactions to specific oils → label must state the specific oil.
  - The most commonly used fixed oils in injections are corn oil, cottonseed oil, peanut oil, and sesame oil.

الزيت العادي كما يبرد  
مع يبطل clear ولكن  
... non-aqueous  
مع يظل clear متمازج بارد

- oleaginous injections are administered intramuscularly
- Not IV → the oil will occlude the pulmonary microcirculation

← إِنَّ اللَّهَ لَا يُغَيِّرُ مَا بِقَوْمٍ  
حَتَّىٰ يُغَيِّرُوا مَا بِأَنفُسِهِمْ ۗ

# Pyrogens and Pyrogen Testing

- **Pyrogens:** A pyrogen is a substance that induces fever. These can be either internal (endogenous) or external (exogenous) to the body

صحت تكون من داخل الجسم و ترفع fever

أدوية خارجية و ترفع fever

exotoxin متنازي  
gram (-) bacteria  
معلوم موجودة في الهيكل الخارجي لـ

أي هو إفرز من

البكتيريا

وليس من

صنها

• **Endotoxin:** An "endotoxin" is a toxin that is a structural

molecule of the bacteria that is recognized by the immune system. "endotoxin" are, in fact, due to lipopolysaccharide found in the outer membrane of various Gram-negative bacteria → is thermostable and water soluble, it may remain in water even after sterilization by autoclaving or by bacterial filtration.

heat وقياس

filtration وقياس

تنقية

# Pyrogens and Pyrogen Testing

*endo toxin unit*

- USP injection monographs state a bacterial endotoxin unit limit, USP EU. Thus, injections are not pyrogen or endotoxin free but are limited.

ited. The following are examples from the USP 32-NF 27 (12):

Dextrose Injection: Contains not more than 0.5 USP EU per mL for injections containing less than 5% dextrose and not more than 10.0 USP EU per mL for injections containing between 5% and 70% dextrose.

Digoxin Injection: Contains not more than 200.0 USP EU per mg of digoxin.

Gentamicin Injection: Contains not more than 0.71 USP EU per mg of gentamicin.

1 EU =

الكمية من lipopolysacch الموجود في  $10^5$  E. coli

في يتسبب أعراضها إلا حمى والعدوى عند الإبتلاء  
عند تعرضه 5 EU

## Maximum acceptable endotoxin level [\[edit\]](#)

Because endotoxin molecular weight may vary a great deal (10,000 to 1,000,000 Da), endotoxin levels are measured in "endotoxin units" (EU). One EU is approximately equivalent to 100 pg of E. coli lipopolysaccharide—the amount present in around  $10^5$  bacteria. Humans can develop symptoms when exposed to as little as 5 EU/kg body weight. These symptoms include, but are not limited to, fever, blood pressure, increased heart rate, and low urine output; and even small doses of endotoxin in the blood stream are often fatal.

! هزيب دوزي 5 بملغ ثم يتسبب  
Endotoxin داخل جسمك

The FDA has set the following maximum permissible endotoxin levels for drugs distributed in the United States:

- Drug (injectable, intrathecal) - 0.2 EU/kg body weight <sup>المحل الحقني</sup>
- Drug (injectable, non-intrathecal) - 5 EU/kg body weight
- Sterile water - 0.25-0.5 EU/ml (depends on intended use)

← لو الوزن 55 kg ← 5 EU × 55 kg  
= [275]

وبه ها بفس Fever

اللهم اكفني بجلالك عن مراملك  
واعنني بفضلك عن سوال

Pyrogens طيرس زالة

# Pyrogen removal (depyrogenation)

## 1. Ion exchange chromatography:

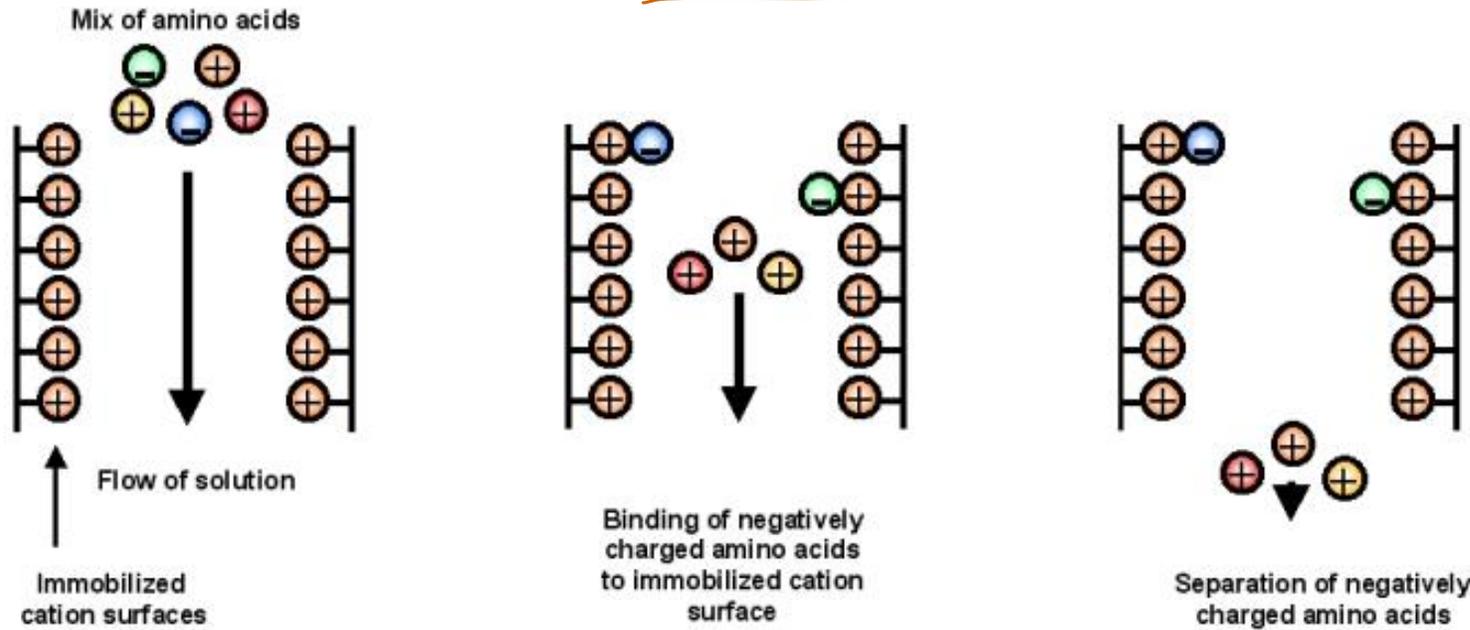
Endotoxins are negatively charged, and will bind to an anion exchanger chromatography column

Endotoxins are (-) charge cause of lipopolysac في لو سرر ن التحميرة ابي فيها endotox على

anion exchanger -

على تحميرة المر صوية في مر تعلق التحميرة من المر به وه endotox يكونه صارتجا ذبه

Ion-exchange chromatography (anion exchange)

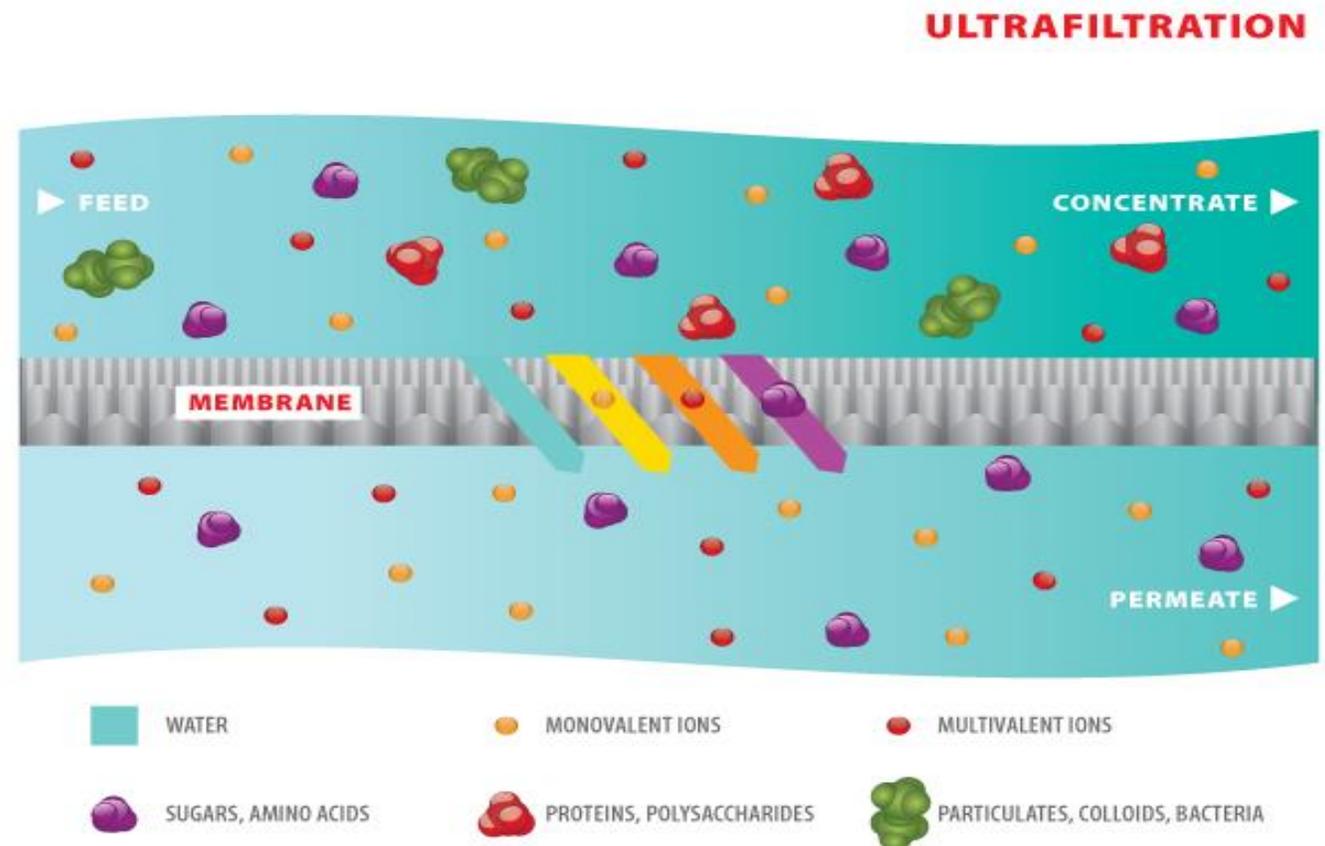


# Pyrogen removal (depyrogenation)

## ② • Ultrafiltration:

ترشيح

- this method is best used only when all endotoxins present are larger than 300,000 Da



3) • **Distillation:** *lipopoly sac*

- The large LPS molecules do not easily vaporize, and are thus left behind in the heating vessel

😊 [كلام داسبي] صحت صفا

		Water Purification Technology					
		Distillation	Reverse Osmosis	Ultrafiltration	Adsorption	Filtration	Deionization
Water Impurities	Pyrogens	👉👉	👉👉	👉👉	👉		
	Bacteria	👉👉	👉👉	👉👉		👉👉	
	Particles	👉👉	👉👉	👉👉		👉👉	
	Inorganic Ions	👉👉	👉				👉👉
	Organics	👉	👉		👉👉		
	Dissolved Gases	👉			👉		👉👉
	Nucleases			👉	👉		
Total Purity Number		10	8	7	5	4	4

EXCELLENT WATER PURIFICATION	👉👉
GOOD WATER PURIFICATION	👉
POOR WATER PURIFICATION	

دب اجعلني صميم المهلة  
وصن ذريتي

# De-pyrogenation

Emphasis is placed on prevention of introduction of pyrogens

Removal

- glassware, metals
  - 250 °C for 45 minutes [Dry heat]
- water

تابعة للمجهر  
القوة التي صفتها

- oxidation to nonvolatile solvents using potassium permanganate, then distill

صلوب صفة

- reverse osmosis

بسه الصفوا  
الي مشوب  
هو

- plastics [heat sensitive so ↓]
- protect against contamination

أعشروا من ذكر الله  
وتلاوة القرآن  
والصيام والتكبير  
في هذه الأيام الفضيلة  
نسألك اللهم العيون