

Dr. Rahef Zayed

sterilization method

اول 20 سلايد ما كان
الهم شرح عشان
كنت تعاريف ميركل
عشان تقدر تدرسهم
وبصدم بلش التفريغ

A hospital- or laboratory-scale steam sterilizer (autoclave)

انا كصيدلاني بدني احافظ / اخلي الابره sterile في طريقتين

Terminal (kill all the
M.O by the final stage of
sterilization) اغلفه اعمله

Aseptic
كل شيء يكون معقد بكل خطوه
وتحت aseptic condition من الصفر
يكون معقم حتى الهواء لازم يكون sterile



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Choice of method for manufacturing a sterile product

▶ **Two strategies** are available for manufacturing sterile products:

- ★ terminal sterilization, in which the product is made, packed in its final container, then sterilized;
- ★ or aseptic manufacture where the product is made from individual sterile ingredients using aseptic techniques.

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Sterilization

- ▶ **Sterilization** is the **complete destruction or removal of all forms of microbial life**, including:
 - ▶ **Bacteria**
 - ▶ **Viruses**
 - ▶ **Fungi**
 - ▶ **Spores** (the most resistant forms)

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موجود قوت

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Choice of method for manufacturing a sterile product

- ▶ The terminal sterilization methods available include:
 - the use of heat (either as steam or hot air),
 - radiation
 - and microbiocidal gases,

Terminal → heat (autoclave) steam, hot air
.radiation, microbiocidal gas (formaldehyde)

None of them is universally applicable to all types of product, nor does any single technique fulfil all the desirable properties of a sterilization method

ما في طريقه مثاليه كل وحده الها ايجابيات وسلبيات

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Desirable properties of a sterilization method

بدي هاي تكون reliable يعني يعتمد عليها لتحقيق المطلوب في التعقيم لحتى اوصل ل 10^{-6} exponent steril assurance level →

- ▶ reliable in terms of achieving the required sterility assurance level of 10^{-6} ;
- ▶ safe for the operators;
- ▶ safe in terms of inducing no damage to the product or its container, or inducing the formation of toxic residue
- ▶ an easily understood process that can readily be controlled and monitored by physical instruments;
- ▶ short exposure time;
- ▶ low cost

يجب ان تكون امنه يعني هاي الحراره ما تسبب خراب للمركب (لمكوناته او package) او نواتج تحلله تكون toxic

مش معقد يعني بسهولة اتحكم ب parameter كل ما حصلت sterile بقصر وقت يكون امن لل product و اقل مصاري (اخر 3 نقاط)

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Choice of method for manufacturing a sterile product

- ▶ Heating methods are preferred by the World Health Organization and the pharmacopoeias,
- ▶ but many products, particularly medical devices containing plastics, cannot be heated, so radiation and ethylene oxide gas are used as alternatives

إذا ما ينفع heat للمستحضر مثل المستلزمات الطبيه (مثل الادوات تبعت القسطره بتكون بلاستيك او بروتين هون استخدم radiation or gas

- ▶ Sterile filtration is a possible approach for heat-sensitive water-soluble drugs,

إذا ما ينفع .gas. radiation. heat هون استخدم)fillration وما بقدر احكي انو terminal لانو بس عملت steril solution الي ذائب فيه الدواء

- ▶ for sterile medicines that cannot be filtered, such as ophthalmic creams, aseptic manufacture may be the best option,

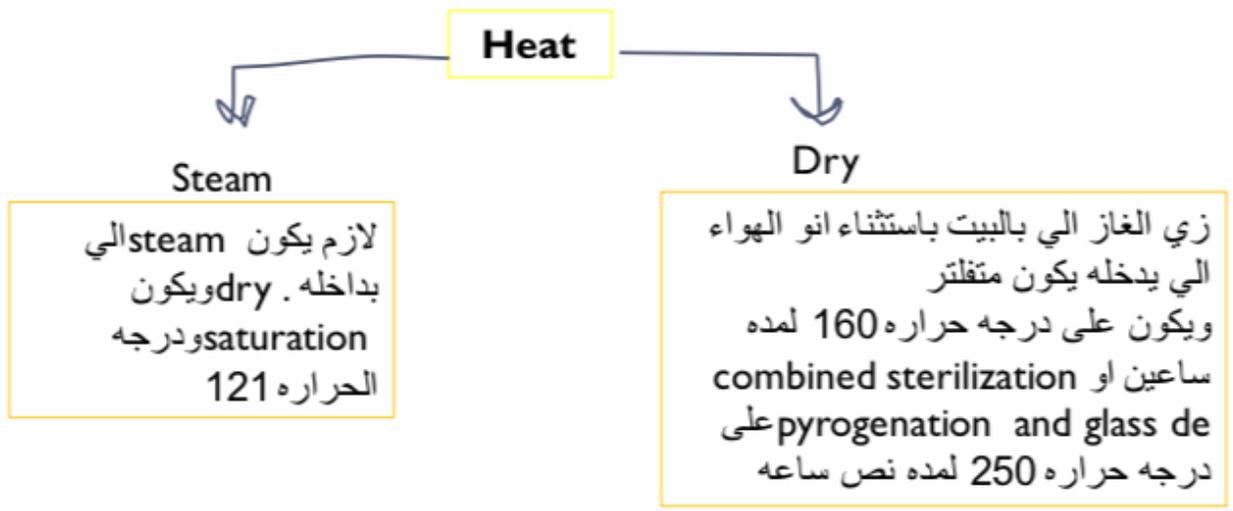
إذا ما زبط لا heat او filtration هون ابلش استخدم aseptic

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Typical operating conditions and applications for common sterilization methods.

| Method | Typical ^a conditions | Common applications |
|---------------------------------|---|---|
| Steam (heating in an autoclave) | Dry, saturated steam at 121°C for 15 minutes | <ul style="list-style-type: none"> • Aqueous solutions in sealed containers (bottled fluids) • Surgical and dental instruments • Dressings (porous loads) • Decontamination of infected materials or laboratory waste |
| Dry heat (hot air oven) | 160°C for two hours, or, in a combined sterilization and glass depyrogenation cycle, 250°C for 30 minutes | <ul style="list-style-type: none"> • Glassware • Oils, fats and waxes, and oily injections |
| Ionizing radiation | An absorbed dose of 25 kGy | <ul style="list-style-type: none"> • Heat sensitive (thermolabile) raw materials • Medical devices |
| Ethylene oxide | 400–1000 mg/l of ethylene oxide, at 45–65°C and 40–80% relative humidity for 0.5–10 h | <ul style="list-style-type: none"> • Medical devices |
| Filtration | Passage of liquid through a bacteria-retentive membrane with a pore size of 0.22 µm or less | <ul style="list-style-type: none"> • Solutions of heat-sensitive, water-soluble and oil-soluble materials |

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Dry على درجات حراره عاليه ووقت اطول

استخدمه لقتل بقايا M.O

Steam درجات حراره اقل ووقت اقل

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Steam Sterilization:

- ▶ The autoclaves used for steam sterilization vary in size from benchtop models of the type commonly found in dental surgeries to large floor-standing industrial machines that are loaded with forklift trucks.

اشي ينحط على الطاولة عند دكتور الاسنان
واشي كبير يتثبت بالارض ويتم نقله بشاحنات

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A small top-loading laboratory autoclave.



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A front-loading laboratory autoclave having approximately four times the capacity of that in Previous figure.

هاد يفتح من قدام زي الثلاجه

Note the thermocouple leads inside to record the temperature at different locations in the load

يتم توزيعهم داخل مختلف المناطق داخل autoclave



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Steam Sterilization:

▶ Autoclaves can have:

- ★ circular or rectangular chambers,
- ★ be top-loading or front-loading
- ★ and have doors at one end or, less frequently, at both ends of the chamber (to permit transfer of materials from a nonsterile to a sterile area for example).

الاشياء الي بعملهم تعقيم ما بحطهم بنفس المكان الي ما تم تعقيمهم

Steam Sterilization

- ▶ The doors of modern autoclaves are fitted with thermal locks which prevent the door being opened until the chamber contents are below a preset temperature → for operator safety

درجة حراره الجهاز بتكون 120 ف اذا بفتح الباب
دغري رح يوصل البخار الحامي لوجهي ويعمل
تشوهات لذلك يكون تصميم autoclave للحفاظ على
الامان انو ما يفتح غير لما يوصل لدرجة حراره امنه

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NOTES

Steam Sterilization

Latent heat is energy released or absorbed, by a body or a **thermodynamic system**, during a constant-temperature process that is specified in some way

- ▶ Steam is very much better as a sterilizing agent than water at the same temperature,

Steam more efficient than dry

لو حطيت معلقه بماء مغلي على درجة حراره 100 واستخدمت steam على درجة حراره 100 هون
رح يكون البخار افضل بالتعقيم من الماء

- ▶ because steam has a high latent heat content which is transferred to the objects being sterilized when the steam condenses on them.
- ▶ Steam kills microorganisms by coagulating and denaturing the cell protein.

- ▶ Consequently, **steam quality is particularly important:**

1. it should be dry (containing no liquid water droplets)
2. and saturated (containing the maximum amount of water vapour possible for the given temperature).

يكون كل القطرات على
شكل غاز مش سائل

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Steam Sterilization

ما بدي يكون فيه هواء لانه الهواء يمنع saturation
ويمنع وصوله لدرجة الحرارة المناسبه ويكون تصميمه
انو يطلع كل الهواء الموجد في الاوتو كليف

- ▶ It is essential that **air is removed** from the autoclave chamber and completely replaced by steam during the operating cycle. Failure to remove all the air results in the temperature being lower than that for pure steam at the same pressure (lower than it should be), so there would be a risk of sterilization failure.

notes

The relevant SI unit of pressure is the kilopascal (kPa), although even modern autoclaves do not necessarily use this scale. Instead, the gauge might display pressure in the units of pounds per square inch (psi) or bar (a unit of pressure equal to 100 kPa)

- ▶ Pure steam at 15 psi (105 kPa) has a temperature of 121°C, and any residual air in the chamber will result in a temperature lower than this (pound per square inch) (psi)

Steam Sterilization

في قطرات ماء وهاد ما
بدنا اياه لانو لازم يكون
داخل autoclave dry
saturated



Saturated Water (0% Dryness)
Temperature: 100 °C [212 °F]



Wet Steam (x% Dryness)
Temperature: 100 °C [212 °F]



Saturated Steam (100% Dryness)
Temperature: 100 °C [212 °F]

تم وضع اكبر
كميه ممكنه داخل
هاد فش ولا قطره
ماء

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TYPES OF STEAM

WET STEAM

- Wet steam applies to steam when a portion of its water molecules have given up their energy (latent heat) and condense to form tiny water droplets
- Also known as saturated steam
- Mixture of water in the liquid state (tiny droplets) and gaseous state (steam)



بالوضع الطبيعي انا ما بقدر اشوف الغاز ولكم هون
كل ما بعد عم مصدر الحراره رح يتكاثف ويشكل
قطرات ماء وهاد الي يصير عشان هيك اشوف
يطلع من ابريق الشاي بخار

Wet
Steam

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how air is removed?

- Steam is lighter than air so it rises to the top of the autoclave chamber, and as it accumulates the air is gradually pushed down and out through the valve; autoclaves that remove air in this way are referred to as gravity-displacement or downward-displacement autoclaves.

Slide note:

Larger autoclaves may have vacuum pumps to remove the air, but many smaller ones allow the air to escape through a vent valve

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How air is removed?

- **Vacuum-assisted autoclaves** are required for the removal of air from dressings or from surgical and laboratory equipment in order for steam to penetrate to all parts of the **load**. **ال load هو ال our package**
- A further benefit of a vacuum pump is that it can be used to dry the load at the end of the cycle – particularly useful in the case of dressings.

ال Gauze اللي هو الشاش ، احد طرق تعقيمه هو ال steam sterilizer

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فكرة السلايد انه كيف رح نشيل الهوا؟؟

1) Gravity-displacement (downward-displacement autoclaves)

ال Steam يكون اخف من الهوا فبالتالي يكون فوق والهوا تحت فال steam رح يضغط عليه و يكون في مكان يسحب الهوا بالتالي رح يطلع من المكان بسبب ضغط ال steam

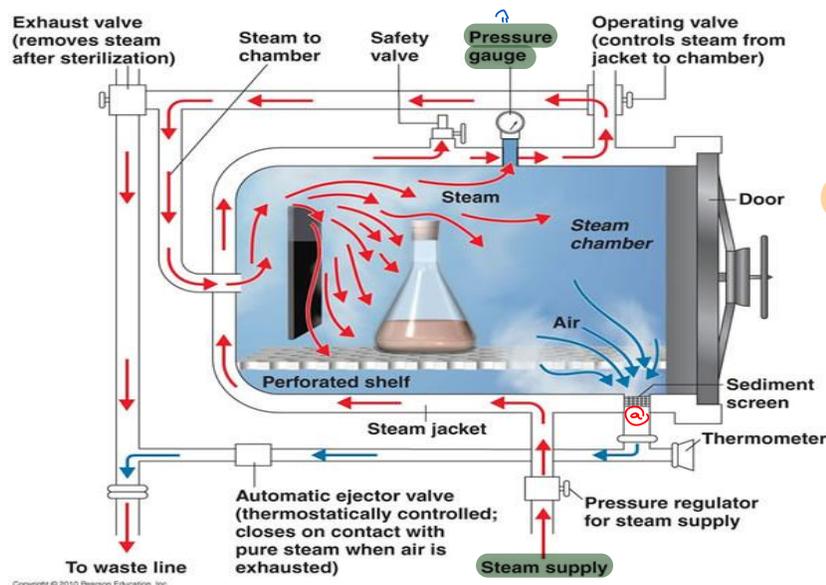
2) Vacuum-assisted autoclaves

هون يكون في vacuum وهاد عبارة عن شفط يشفط الهوا و بفرغه و بنشفه و بزيله من جوا ال autoclave وهاد النوع هو نفسه ال Dynamic autoclave

How air is removed?

- ▶ Vacuum-assisted autoclaves are required for the removal of air from dressings or from surgical and laboratory equipment in order for steam to penetrate to all parts of the load.
- ▶ A further benefit of a vacuum pump is that it can be used to dry the load at the end of the cycle – particularly useful in the case of dressings.

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في الا steam اول ما يدخل رح يكون
اخف من الهواء فيكون فوقه الهواء
ديبلت يضغط على الهواء عشان يطلع
منه جايه (a)
عشان صلبه يسبه gravity displacement autoclave

موتن رح يدخل الا steam

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لازم احافظ على
Pressure
موتن للا steam عشان
اقدر احصل على Temp
الظويه

Steam sterilization: Autoclaves

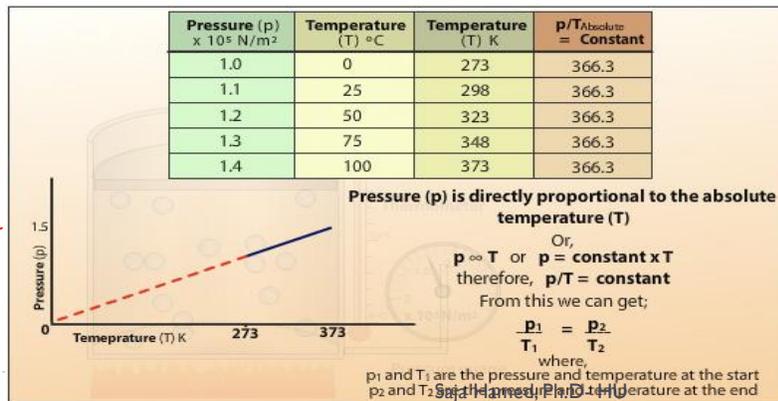
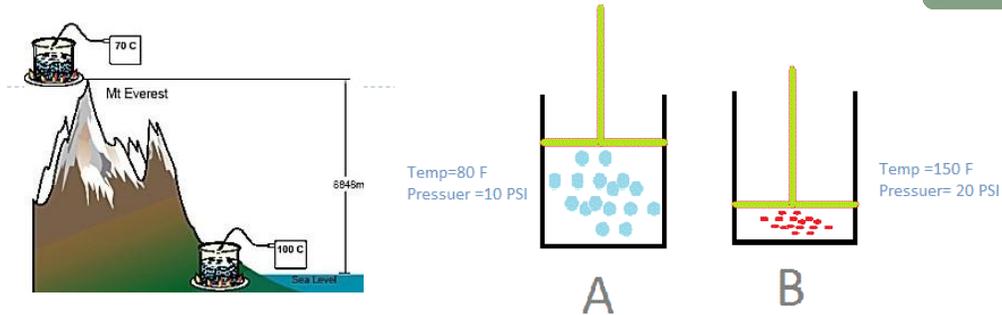
Operation Principle

- When water is heated in a closed container, saturated steam is produced under pressure. *هذا الضغط ضروري عنك لرفع ال temp المطلوبه*
- According to Boyle's Law, when volume of the steam, is kept constant, the temperature is directly proportional to pressure.
- If the pressure is reduced it boils at a lower temperature. If the pressure rises, it boils at a greater temperature.
- At 15 lbs pressure 121° C temperature can be obtained.
- Moist heat coagulates cell proteins of the microorganisms and thus kills all the living entities (including spores) in 15 to 20 minutes.
- Hot saturated steam is efficient means of destroying microorganisms, since it penetrates rapidly and gives up its latent heat as it condenses on the cooler objects.

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Autoclave داخل ال pressure ال
 ال صناد atm pressure
 عناء هوك قدر احتقك درجة تليون
 ال ص 15
 ↑ Pressur ← ↑ temp
 فحاليته باد Killing ال MO بسبب
 وجود ال Latent

atm Pressur = 14.7
 100c = temp ال



كل ما زاد ال Pressur ال ت ال temp

اصالة استخدامات ال autoclave

sterilization (auto claving) بالادوات الي تستخدمها بالمستشفى



sterilization for bottle liquid

الموجود بال lab

بحيث انه هذا ال media يستخدمه مثلا للا culture البكتريا



auto claving للملابس الي تستخدمها بالمستشفى
ملاحظة انه بعد تنظيفها مع اقلها وبعد بيت احطها بال autoclave

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auto claving ← صابون



هذا لاصق خاص كمان اميز منه صابون ال sterilization بحيث انه بعد ما احطه بال autoclave رح يغير عليه خطوط سوداء



لنسا ما صابون! ال sterilization الخطوط لونها ابيض

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كيدومات اذا بجنبوا تحفروهم
عن ال Autoclave
بدمتوره سخن بالفيديو صكت داخلية

▶ Steam Sterilization Essentials

https://www.youtube.com/watch?v=_lWh9a5RAfg

▶ Preparation and packaging and surgical instruments

<https://www.youtube.com/watch?v=LLXPX4oz6es>

▶ Understanding Steam Sterilization

<https://www.youtube.com/watch?v=FUJriqVWs2N0>

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▶ Dry Heat Sterilization → زياد oven (الفرن) ← لده وقت اكثر ودرجة حرارة اعلی

▶ This method simply involves **heating** the item to be sterilized in **a hot air oven**, typically for **2 hours at 160°C**

▶ Alternative combinations are available, for example 1 hour at 170°C or 30 minutes at 180°C.

▶ The temperatures and times required are longer than those for steam:

(i) because dry heat kills microorganisms by oxidative processes which are less efficient than the hydrolytic mechanisms of steam and *Coagulation of protein*

(ii) because dry air does not possess latent heat.

⇒ صلي شرط ساعتين
كل درجة حرارة 160
- ممكن ساعه كل حرارة 170
- ممكن نصف ساعة كل حرارة 180

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Dry Heat Sterilization

Items that can be successfully sterilized by dry heat are:

① those that do not contain water, such as metal instruments, glassware, oils, fats and waxes

الذي لا يحتوي على الماء
مثل Steam لأنه لا يوجد فيه
مياه في درجة الحرارة العالية

② or any heat-stable nonaqueous product like oily injections, ointments or powders.

والذي يمكن استخدامه
مثل Powder برفه ما
يمكن استخدامه مع steam

The method is also used for the depyrogenation of glassware required for the preparation or packaging of injections; 250°C for 30 minutes is common

عملية التخلص من
الpyrogen الموجود
في glassware لكي يبدى
استخدامها لا
injection

الpyrogen عبارة عن
أجزاء صغيرة من
لحم الإنسان
لازم التخلص منها
عند استخدامه
عند استخدامه
عند استخدامه

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Dry Heat Sterilization

Ovens used for laboratory-scale dry heat sterilization are superficially similar to fan-assisted domestic kitchen ovens though usually with 2-3 times the capacity,

الذي ليس التخلص
الذي ليس التخلص
الذي ليس التخلص

but they differ by having:

- ① temperature recorders, عشان أنتو تفهم الtemp وصلت الtemp المطلوبه داخل الoven
- ② thermocouple inlets
- ③ thermal locking doors with non-interruptible operating cycles → الباب مازح يفتح قبل ما تخلص العنبر
- ④ and the facility to filter the air that is drawn into the oven as it cools. → لما تخلص العنبر تخلص يكون بحاجة عشان ابرد الitem بعد دخل الهواء عن طريق الfilter و هيك مازح يسمح بمرور الMO

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A laboratory scale hot air sterilizer



Radiation Sterilization

ليست يستخدم مياه
الطريقة
a, b, c

▶ **Gamma-rays or high-energy electrons are used to sterilize heat-sensitive materials and products:**

(a) **like medical devices** (for example, **prostheses**, **intravenous giving sets**, **syringes and sutures**) **in the case of medical devices, damage to plastics in terms of discoloration and brittleness is a potential problem.**

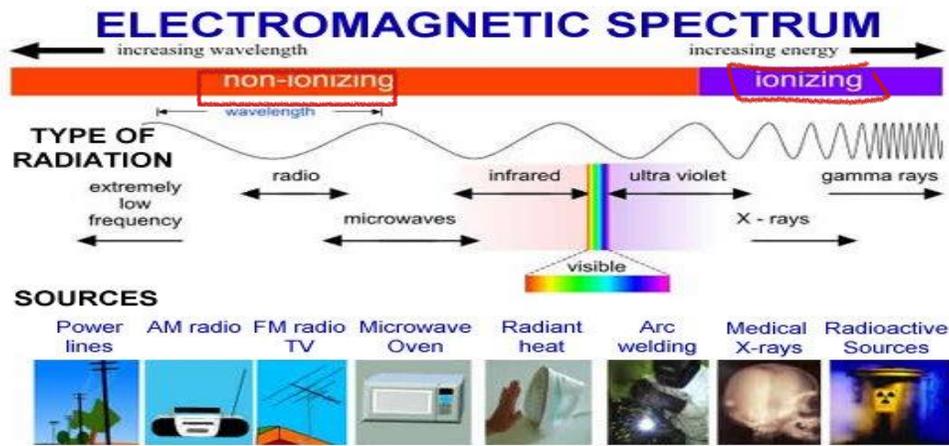
اعضاء مناعية

(b) **surgical instruments,**

(c) **anhydrous medicines** (such as ointments) and **powders**

بمفرده اذا كان ما يخسر بالحرارة بعد استخدام
dly-hamed

Radiation Sterilization



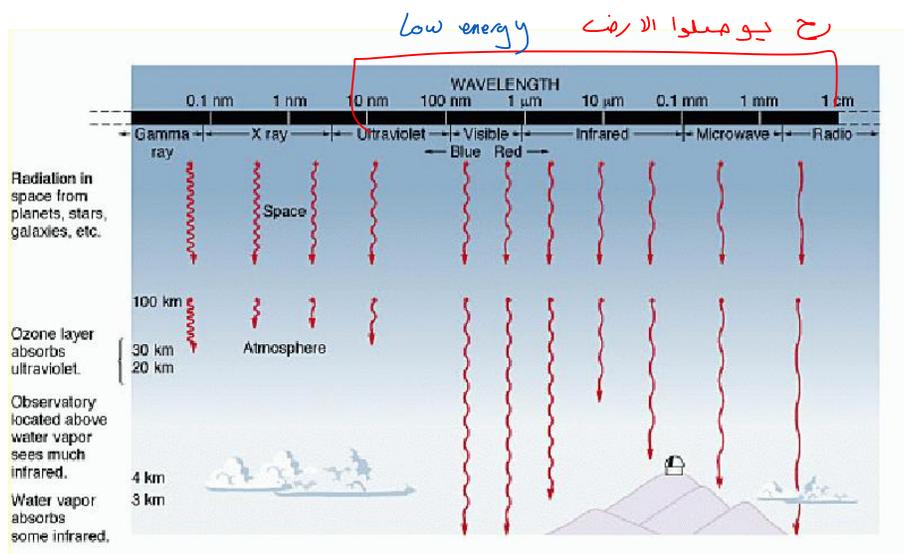
كل صافته اذ اذت اذ energy

X-ray and gamma
 لى صا ر يوصلوا الارض
 بسبب طبقة الازون
 و هبة خطيرات كثير

بيو نستخدمهم بس بطرف
 خاصه و اجزاه خامه عشان
 الحمايه

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Radiation Sterilization



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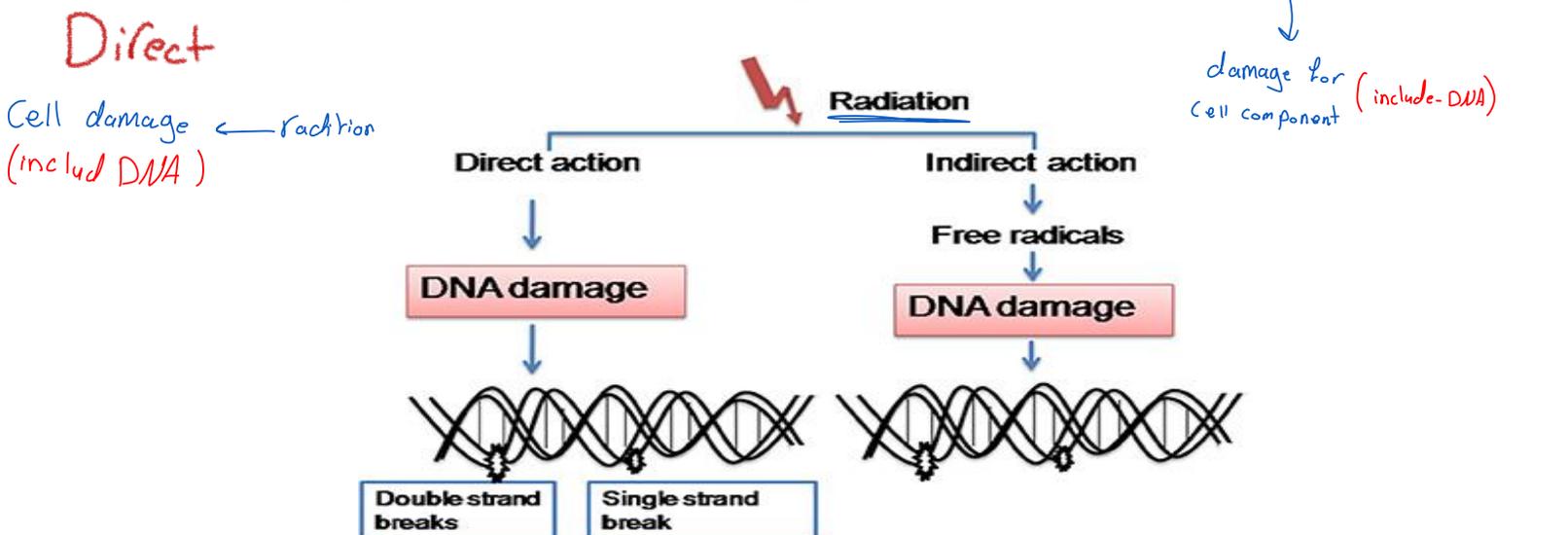
Radiation Sterilization

- ▶ The unit for absorbed radiation dose is the gray (Gy) which has replaced the older unit of the rad. → *ماي الوحدة القبلية*
- ▶ The standard radiation dose recommended for sterilization of pharmaceutical products is 25 kGy

الوحدة التي يستخدمها
 لقياس ال radiation dose هي Gy

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The mechanism by which radiation kills cells is that of ionization causing free radical production and damage to the DNA



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Radiation Sterilization → مكلفه جدا

- ▶ Radiation sterilization facilities are expensive to construct and to operate, so companies manufacturing products to be sterilized in this way normally send them to one of a small number of specialist contractors.

الشركات لما يكون عندها مادة بها radiation sterilization بتجيبها للجهاز
المصنعه لانها مكلفه وصارح بتكون تا واديه
operate + construct (النباذ والتشغيل)

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Radiation Sterilization

- ▶ Gamma radiation is rarely used for water-containing products, why?

because the products of radiolysis of water usually cause too much damage to the drug



ح يخرّبوا drug

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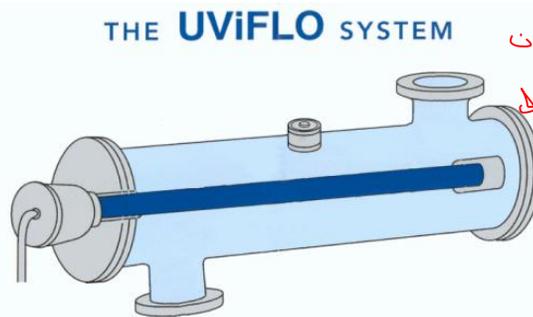
Radiation Sterilization

- ▶ **Ultraviolet light is a nonionizing form of electromagnetic radiation that has poorer penetrating power.** ما بقدر يخترق الاجسام فما بقدر استخدمه على اعمق اشياء من الداخل باستخدام surfaces لا
- ▶ It is commonly used for the disinfection of surfaces in aseptic work areas, air (as in microbiological safety cabinets and operating theatres for example) and for decontamination of water to be used both as an ingredient of medicines and for cleaning purposes. ^{تربط الحمامات}
- ▶ UV treatment could not be used to produce endotoxin-free water for injection. لا UV ما بقدر استخدمه depyrogenation لا

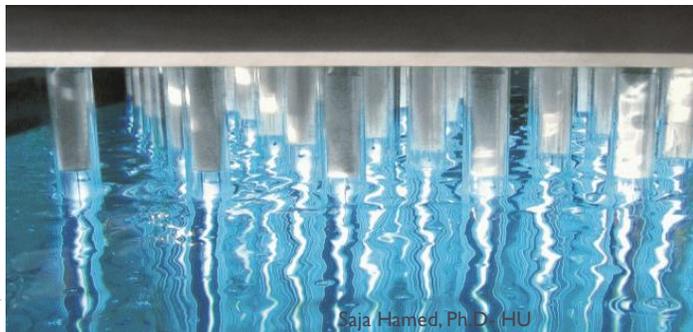
Pyrogen

هي د

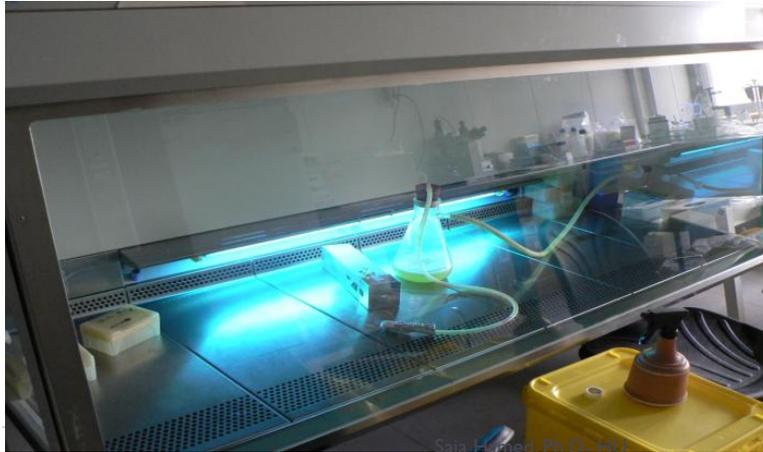
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او UV بالداخل
وال water حواليه على
اضمنه يغير تعقيم لطيف
او water



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Gaseous Sterilization → غير محببة و اقل فعالية

▶ Several microbiocidal gases have been used for sterilization including:

- ① ethylene oxide, [EtOx]
- ② formaldehyde,
- ③ hydrogen peroxide
- ④ and peracetic acid

Ethylene oxide (sometimes referred to as EtOx) is by far the most common and will be the only one considered here

Gaseous Sterilization

صحيح ان دى يكون
ليسبب Cancer وده
يكون مؤذي للجسم

- ▶ It is not a favored method because:
 - it is less reliable than heat and radiation → it needs rigorous in-process monitoring to confirm that sterilizing conditions have been achieved →
 - it is also slow
 - and there are several safety issues concerning its use,

يحتاجه كمان اننا كده
ال دى قبل بنفسي التركيب و
ال Pressure وعشان ارفع
المدى لعمليه ال Sterilization
وانه ال دى قد يوصل
لكل ال Product الموجود

So it is only employed when there is no alternative.

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Gaseous Sterilization

- ▶ Ethylene oxide is suitable for sterilizing materials that are both heat and radiation sensitive:
 - so it is used primarily for disposable medical devices.
 - It is also infrequently used in hospitals for surgical instruments
 - and the sterilization of isolators and chambers, although hydrogen peroxide is now preferred.
- ▶ Ethylene oxide diffuses easily into paper, rubber and many plastics, but it cannot easily penetrate into crystalline materials and its activity is significantly reduced by the presence of organic material (blood, pus or feces) so it cannot be used to sterilize crystalline raw materials or unwashed surgical instruments.

ال object ال بي اعمل دله
Etox sterilization
لازم اننا كده نضيف
قليل من الـ

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هاي اد champer خاصة بخط
اد اجزاه ريسر عليها ولما يخلط

Gaseous Sterilization

لازم يهين Washout للغاز

- ▶ Hospital ethylene oxide sterilizers are similar to conventional autoclaves, being steel chambers of varying capacities from about 65 liters upwards, whilst industrial-scale sterilizers are very much larger



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ال E_6O_x اذا اخلط مع هوا
بنسبة 3.6% ممكن يكون قابل
للانفجار

Gaseous Sterilization

الركتوره هكت بالفيدوا
لا تدرسوا ال *deities*
لبن يمكن د. آلاء تجيب
صعهم

- ▶ Ethylene oxide is a colorless gas that is explosive when mixed with air in proportions greater than 3.6% by volume, so it is normally used as a mixture with carbon dioxide (8.5–80% of ethylene oxide), nitrogen or dichlorodifluoromethane (12% ethylene oxide) to minimize the risk.

الطريقة الاولى
عشان اقلل (*explosive*)

- ▶ Alternatively it is introduced into an evacuated sterilization chamber as the pure gas at subatmospheric pressure.

الطريقة الثانية

1) موش مختلط بالهين (E_6O_x)
2) ال *champer* لازم يكون
اقل من ال *atm pressure*

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Gaseous Sterilization

▶ Ethylene oxide is thought to kill microorganisms by alkylating essential proteins and nucleic acids in the cell

الـ EtOx يح تفسيف باطوب (alkyl) nucleic acid
 الـ Alkylation وهيك ح يخرن الـ Protein
 عتات هيك يخرن Carinogenic (يسبب Cancer)
 Mutagenic

▶ this mechanism of action means that the gas is both mutagenic and carcinogenic.

▶ It also causes acute eye, skin and bronchial irritation at concentrations above 200 parts per million (ppm) but, crucially, many people are unable to detect it by smell until the concentration is about three times that value, or more.

الـ Irritation يبلش كل مستوح
 اقل بكثير من المرحلة اى بهي
 انشمه فيه

▶ Health and safety aspects of ethylene oxide sterilization are therefore a major consideration.

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Filtration sterilization and aseptic manufacture

▶ Many drugs and pharmaceutical materials are damaged both by heat and radiation and are not suitable for gaseous sterilization either

▶ drugs containing proteins (for example, monoclonal antibodies, interferons) and other biological polymers (such as polysaccharide- or DNA-vaccines) → the only sterilization option is to use filtration to physically remove the contaminating microorganisms and then manufacture the product aseptically using sterile ingredients

damage by radiation, heat, gas

عشان هيك الطريقة الوحيدة اى نهدر استخدمها اى الـ المواد هي الـ Filtration + استخدم مطرفات Steril

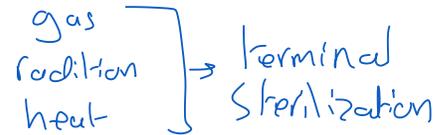
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Filtration sterilization and aseptic manufacture

- ▶ filters are available for the removal of: → *طبعاً حسب حجم الـ Pore*
 - bacteria
 - yeasts and mould spores
 - viruses
 - and they can even remove pyrogens (endotoxins),
- ▶ An advantage afforded by filtration is that the method physically removes both living and dead cells from solution and in this respect it differs from heat and radiation methods where the dead cells remain in the product and possibly contribute to the pyrogen load.
 - Living* ←
 - non-living* ←
 - MO* ← *روح يمشيها كل الـ surface الـ Filter*
- ▶ so filtration is a common means of sterilizing injections and eye drops as well as air and other gases.

*ميزه خامه فيها
لا يبي قبله روح يقتلوا
الـ MO بين ممكن يضل
الجزء الميت موجود*

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Filtration sterilization and aseptic manufacture

- ▶ Filtration is not a terminal sterilization process,
 - ▶ Solutions that are filter sterilized still have to be dispensed into their containers and the operation being undertaken in a class A atmosphere
 - ▶ Media fill test for the same factory filling line that would be used to fill the product

*Filtration بعد الـ
Container لسايي احطه
وهذا يعني لازم يكون فيه
aseptic condition*

*عشان يتأكدوا انه الـ media الـ بي
احطه الـ filling line ما فيها اي MO
يعني aseptic*

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Filtration sterilization and aseptic manufacture

- ▶ Sterilization-grade filters are made of cellulose derivatives and polymers like PTFE, polycarbonate and polyethersulfone

نح استخدم small Filter
واركها على السرنجة او
ممكن يكون Long Filter



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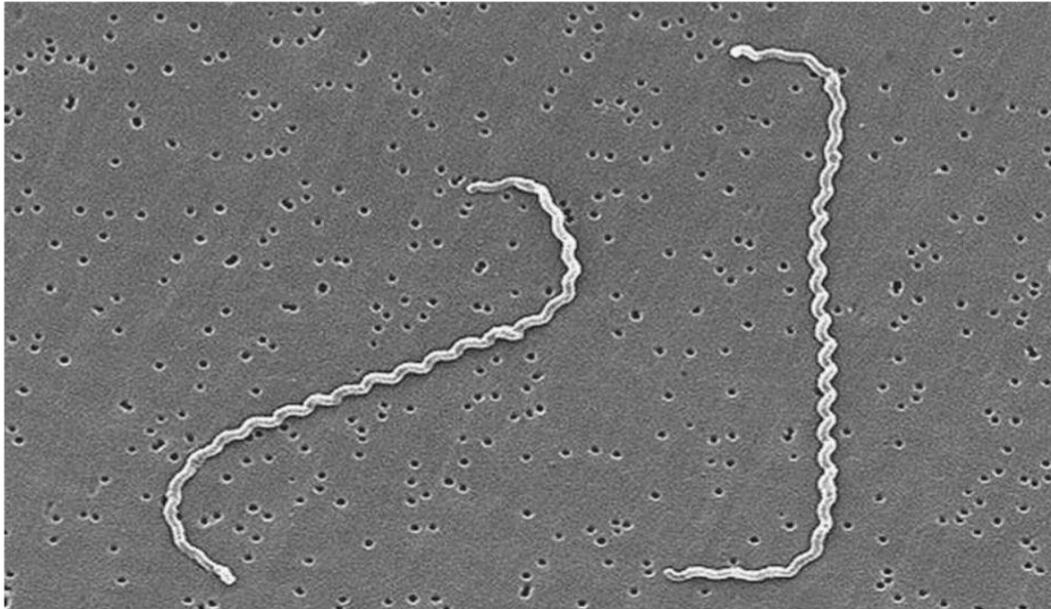
A selection of disposable units that fit onto syringes for sterilizing small volumes of liquid

- ▶ Filters are available having a wide variety of pore sizes, and for sterilizing purposes **0.2 μm** or **0.22 μm** diameter pores are recommended
- ▶ but **0.1 μm** membranes are becoming more popular.



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مسئله قادره تسفل
 باء pore size
Leptospira bacteria attached to the surface of a 0.2 μm pore size filter membrane



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Membrane filters

فيلتر
 خلاصه ال

- ▶ good particle removal (sterilizing efficiency)
- ▶ good mechanical strength
- ▶ they are easily sterilized in situ by steam,
- ▶ of low fluid retention, → روعيت ادر لسه ال يكون سهل
- ▶ low solute absorption, → الدوا لازم ما يهرس اليه لانه ربح تقبل كميته العوا بال solution
- ▶ no grow-through of microorganisms
- ▶ and no shedding of fibers into the filtrate. → ال fiber مصنوعه تسفل على ال solution

absorption

MO ما تعيش
 جواهر

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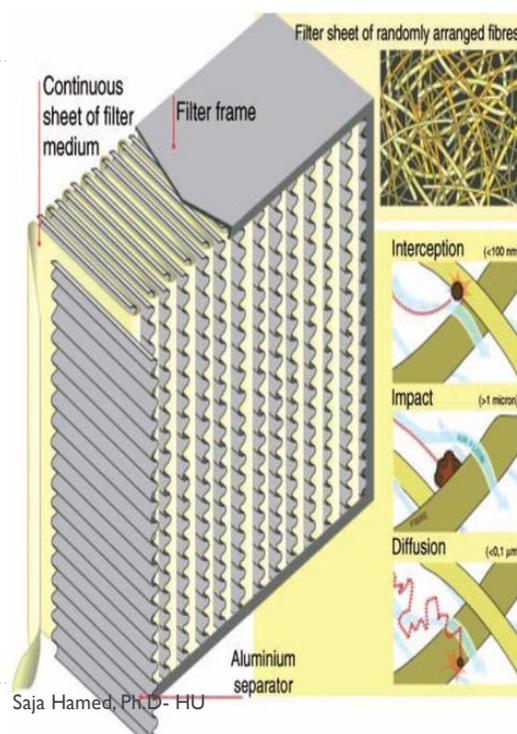
Filtration sterilization and aseptic → *هذه الطريقة هي الحل الأفضل* manufacture

- ▶ Filtration is the most convenient method of sterilizing air and other gases and it is used to supply air to pharmaceutical manufacturing suites ('clean rooms') and isolators, surgery rooms and microbiological safety cabinets

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<http://www.asbestosguru-oberta.com/hepa.htm>

- ▶ Depth filters, typically made of glass microfibres separated by aluminium sheets, are normally used for gas filtration
- ▶ High efficiency particulate air (HEPA) filters typically remove 99.97% of airborne particles of 0.3 μm in diameter, although some with higher specifications exist.



Capture mechanism of HEPA filter

▶ The filter media is made up of densely packed fibers.

▶ Each fiber traps particles in the airstream passing through the filter by the three physical mechanisms. *حسب حجم الـ Particle*

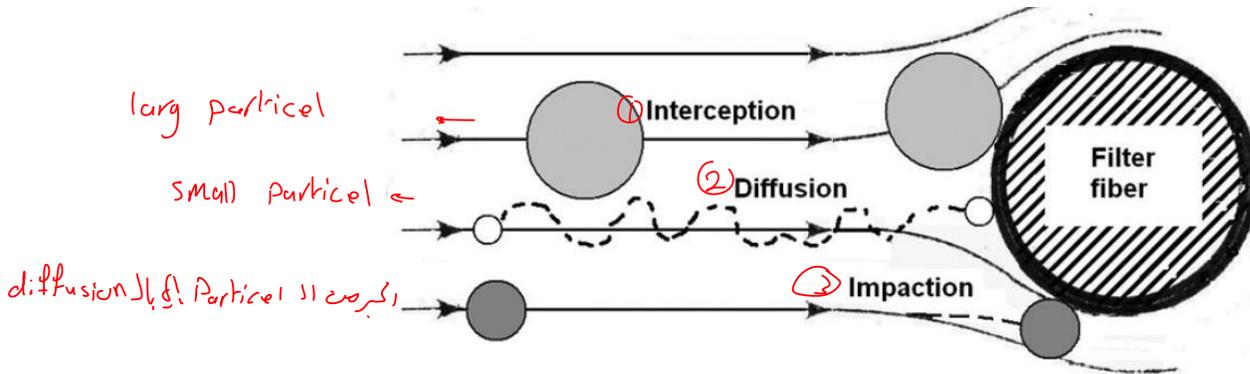


Figure 4. Capture mechanisms for a depth filter

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<http://www.asbestosguru-oberta.com/hepa.htm>

Capture mechanisms of HEPA filter

▶ Watch: **3D filtration principles**

<https://www.youtube.com/watch?v=AuVbcvPcjAw>

large particle

▶ **Interception** – A particle following an imaginary airflow streamline is intercepted by the fiber because the diameter of the particle is more than twice the distance from the fiber surface to the streamline that passes through the center of the particle. *الـ Particle لما تخطى الـ Filter fiber*

▶ **Impaction** – The trajectory of the particle departs from the imaginary airflow streamline due to its inertia, which is a function of the particle's mass and velocity, and the particle impacts the fiber. *تصير بانجاة الـ Filter*

▶ **Diffusion** – The particle's trajectory oscillates about the imaginary airflow streamline in a random manner known as **Brownian motion**, which can cause the particle to impact the fiber. *بادي بس روي غير اختناك الـ Filter fiber ح يوقفها*

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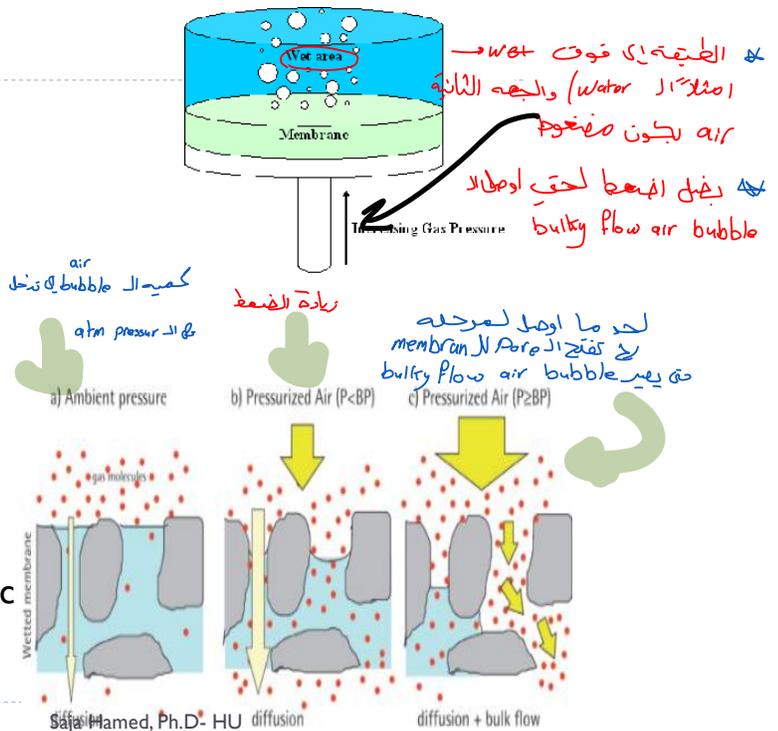
bubble point test - لاقيس

- ▶ **Filter integrity**
- ▶ A procedure which measures the pressure needed to be applied to the upstream side of a filter causing bulk or open pore flow through the largest pores of a wetted filter.

▶ Watch:

Bubble Point Filter Test

<https://www.youtube.com/watch?v=RDjSCb4sC2c&t=24s>



Test for sterility

- ▶ the item to be tested is placed into liquid culture medium and if, after incubation, there are no signs of growth (turbidity) the item is deemed to have passed the test. (sterile)
- ▶ Tests for sterility have been internationally harmonized
- ▶ **False positive result** → many companies, even quite large ones, do not conduct their own sterility testing but engage specialist contract laboratories to undertake it on their behalf.

Sterility tests and endotoxin tests could be considered to be more important than many of the other quality-control tests, Why?

• **Failing and scrapping a batch** that is really sterile costs the money that has been invested in its manufacture, whilst passing a batch that is really contaminated risks initiating infections in patients who receive the medicine.

• Contaminated batches are likely to lead to product recalls, damage to the company reputation, major scrutiny from regulators and possibly even litigation

False positive

False negative

يعني لما المصنع يصنع عينات contaminated رح تدهور سمعة المصنع و يكون في مقاضاة