ASEPSIS & ANTI-SEPTICS INTRODUCTION

ASEPSIS is the state of being free from disease-causing contaminants (such as bacteria, viruses, fungi, and parasites) or, preventing contact with microorganisms. The term asepsis often refers to those practices used to promote or induce asepsis in an operative field in surgery or medicine to prevent infection. Ideally, a surgical field is «sterile», meaning it is free of all biological contaminants, not just those that can cause disease, putrefaction, or fermentation, but that is a situation that is difficult to attain, especially given the patient is often a source of infectious agents. Therefore, there is no current method to safely eliminate all of the patients’ contaminants without causing significant tissue damage. However, elimination of infection is the goal of asepsis, not sterility. Today's techniques include a series of steps that complement each other. Foremost remains good hygienic practice. The procedure room is laid out according to specific guidelines, subject to regulations concerning filtering and airflow, and kept clean between surgical cases. A patient who is brought for the procedure is washed and wears a clean gown. The surgical site is washed, possibly shaved, and skin is exposed to a germicide (e.g., an iodine solution such as betadine). In turn, members of the surgical team wash hands and arms with germicidal solution. Operating surgeons and nurses wear sterile gowns and gloves. Hair is covered and a surgical mask is worn. Instruments are sterilized through autoclaving, or, if disposable, are used once. Irrigation is used in the surgical site. Suture material or xenografts have been sterilized beforehand. Dressing material is sterile. Antibiotics are often not necessary in a "clean" case, that is, a surgical procedure where no infection is apparent; however, when a case is considered "contaminated," they are usually indicated.

ANTI-SEPTICS (from Greek ἀντι: anti, "against" + σηπτικός: sēptikos, "putrefactive") are antimicrobial substances that are applied to living tissue/skin to reduce the possibility of infection, sepsis, or putrefaction. Antiseptics are generally distinguished from antibiotics by the latter's ability to be transported through the lymphatic system to destroy bacteria within the body, and from disinfectants, which destroy microorganisms found on non-living objects.
HISTORY
The modern concept of asepsis evolved in the 19th century. Ignaz Semmelweis showed that washing the hands prior to delivery reduced puerperal fever. After the suggestion by Louis Pasteur, Joseph Lister, 1st Baron Lister introduced the use of carbolic acid as an antiseptic and reduced surgical infections rate. Lawson Taft went from antisepsis to asepsis, introducing principles and practices that have remained valid to this day. Ernst von Bergmann introduced the autoclave, a device used for the practice of the sterilization of surgical instruments.

Ignaz Semmelweis
Ernst von Bergmann
Joseph Lister
Louis Pasteur
AIR INFECTION

Microbes in the air so not much chance of air contamination is not great. Dust increases the risk of contamination from the air. In general, efforts to control airborne infection are reduced to dust control and include aeration and ultraviolet irradiation. For dust control applied cleaning. There are 3 types of cleaning:

- **preliminary is that in the morning**, before the start of the trading day, all horizontal surfaces shall be cleaned with a cloth moistened with 0.5% solution of bleach;

- **current cleaned during operation** and is everything that falls to the floor immediately removed.

- **Final cleaning is carried out after the trading day** and consists of cleaning floors and all equipment of 0.5% solution of bleach and include ultraviolet lamps. Sterilize the air with such lamps is impossible, and they are used in place of the greatest sources of infection;

- **ventilation** - very effective method, followed by microbial contamination decreases by 70-80%.

A long time it was thought that the air is not dangerous infection during operations, but with the development of transplantation with the use of immunosuppressive drugs were operating divided into 3 classes:

- **First class** - no more than 300 microbial cells in 1 cubic meter of air;

- **The second class** - up to 120 bacterial cells - this class is designed for cardiovascular operations.

- **third class** - the class of absolute asepsis - less than 5 bacterial cells per cubic meter of air. This can be achieved in a sealed operating room, with ventilation and air sterilization, with the creation within the operating area of high pressure (the air of the operating sought out). And also, in these operating special doors installed gateways.
DROPLET & DIRECT INFECTION

These are bacteria that can be released into the air from the respiratory tract with water vapor, water vapor condenses and drops with these microbes can get into the wound. To reduce the risk of spread of droplet infection in the operating room should not be unnecessary conversations. Surgeons should use the 4-layer masks, which reduce the chance of infection droplet infection by 95%.

All microbes that are able to penetrate into the wound with any tool, with everything that comes in contact with the wound. Dressings: gauze, cotton wool, thread - takes the heat, so the temperature of sterilization should not be less than 120 degrees,
Contemporary operating rooms are devoid of a theater setting (though some in teaching hospitals may have small galleries), making the term "operating theater" a misnomer for the cally with overhead surgical lights, and may have feature controlled temperature and humidity. Sp- support has backup systems in case of a black- ic gases. Key equipment consists of the operating There is storage space for common surgical sup- dedicated scrubbing area that is used es prior to surgery. An operating room will have a to the desired layout during cleaning.

Several operating rooms are part of the operating ating rooms and their wash rooms, it contains (s), storage and cleaning facilities, offices, dedicat- ing suite is climate- and air-controlled, and sepa-

Operating room equipment

The operating table in the center of the room can be raised, lowered, and tilted in any direction.

The operating room lights are over the table to provide bright light, without shadows, during surgery.

The anesthesia machine is at the head of the operating table. This machine has tubes that connect to the patient to assist him or her in
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The anesthesia cart is next to the anesthesia machine. It contains the medications, equipment, and other supplies that the anesthesiologist may need.

Sterile instruments to be used during surgery are arranged on a stainless steel table.

An electronic monitor (which records the heart rate and respiratory rate by adhesive patches) is placed on patient's chest.

The pulse oximeter machine attaches to the patient's finger with an elastic band aid. It measures the amount of oxygen contained in the blood.

Automated blood pressure measuring machine that automatically inflates the blood pressure cuff on patient's arm.

An electrocautery machine uses high frequency electrical signals to cauterize or seal off blood vessels and may also be used to cut through tissue with a minimal amount of bleeding.

If surgery requires, a Heart-lung machine, or other specialized equipment, may be brought into the room.

OPERATING ROOM EQUIPMENT
An operating theater (or theatre) was a non-sterile, tiered theater or amphitheater in which students and other spectators could watch surgeons perform surgery. Within the Commonwealth nations, the term is used synonymously with operating room (OR) or operating suite, the modern facility within a hospital where surgical operations are carried out in a sterile environment. Operatible or chair of some sort at the center for performing operations, and were surrounded by several rows of seats (operating theatres could be cramped or spacious) so students and other spectators could observe the case in progress. The operating theatre was a non-sterile, tiered theater or amphitheater in which students and other spectators could watch surgeons perform surgery. Within the Commonwealth nations, the term is used synonymously with operating room (OR) or operating suite, the modern facility within a hospital where surgical operations are carried out in a sterile environment. Operatible or chair of some sort at the center for performing operations, and were surrounded by several rows of seats (operating theatres could be cramped or spacious) so students and other spectators could observe the case in progress.

The surgeons wore street clothes with an apron to protect them from blood stains, and they operated bare-handed with unsterilized instruments (gut and silk sutures were sold as open strands with reusable, hand-threaded needles; packing gauze was made of sweepings from the floors of cotton mills. In contrast to today’s concept of surgery as a profession that emphasizes cleanliness and conscientiousness, at the beginning of the 20th century the mark of a busy and successful surgeon was the profusion of blood and fluids on his clothes.

In 1884 German surgeon Gustav Neuber implemented a comprehensive set of restrictions to ensure sterilization and aseptic operating conditions through the use of gowns, caps, and shoe covers, all of which were cleansed in his newly-invented autoclave. In 1885 he designed and built a private hospital in the woods where the walls, floors and hands, arms and faces of staff were washed with mercuric chloride, instruments were made with flat surfaces and the shelving was easy-to-clean glass. Neuber also introduced separate operating theaters for infected and uninfected patients and the use of heated and filtered air in the theater to eliminate germs.

In 1890 surgical gloves were introduced to the practice of medicine by William Halsted.
People in the operating room wear surgical clothes to help prevent germs from infecting the surgical incision. The surgical clothing includes the following:

- a protective cap covering their hair
- masks over their lower face, covering their mouths and noses
- shades or glasses over their eyes
- vinyl gloves on their hands
- long gowns
- protective covers on their shoes

The surgeon may also wear special glasses that help him/her to see more clearly.

While operating theaters are no longer used for surgery, some still exist. One of the oldest surviving operating theaters is the Old Operating Theatre in London. Built in 1822, it is now a museum of surgical history. Another theater still exists at the University of Padua, in Italy, inside Palazzo Bo. It was commissioned by the anatomist Girolamo Fabrizio d'Acquapendente in 1594. Another famous operating theater is the Ether Dome in Boston. Built in 1824, it is now a conference room and tourist attraction. In aseptic method of treating wounds are extremely by boiling water, all dressings and instruments also flowing steam or boiling. Asepsis applied before and during surgery on healthy tissues, but does not apply where one can assume the presence of inflammatory agents in the wound.

Asepsis has a definite advantage in terms of antiseptics outcome, and also because of aseptic method of treating wounds is no poisoning, which are possible in the application of some antiseptics.
SCRUBBING AND GOWNING

Before each operation, all members of the surgical team — that is, those who will touch the sterile surgical field, surgical instruments or the wound — should scrub their hands and arms to the elbows. Scrubbing cannot completely sterilize the skin, but will decrease the bacterial load and risk of wound contamination from the hands.

Every hospital should develop a written procedure for scrubbing that specifies the length and type of scrub to be undertaken. It is usual that the first scrub of the day is longer (minimum 5 minutes) than any subsequent scrubs between consecutive clean operations (minimum 3 minutes).

When scrubbing:

• Remove all jewellery and trim the nails
• Use soap, a brush (on the nails and finger tips) and running water to clean thoroughly around and underneath the nails
• Scrub your hands and arms up to the elbows
• After scrubbing, hold up your arms to allow water to drip off your elbows
• Turn off the tap with your elbow.

After scrubbing your hands:

• Dry them with a sterile towel and make sure the towel does not become contaminated
After scrubbing your hands:

- Dry them with a sterile towel and make sure the towel does not become contaminated your body and higher than your elbows until you put on a sterile gown and sterile gloves.

Surgical gloves prevent transmission of HIV through contact with blood, but there is always the possibility of accidental injury and glove punctured during an operation and rinse your hand with antiseptic or re- is of primary concern; do not compromise it. Change your gloves only when it is safe for the patient.

SKIN PREPARATION

The patient should bathe the night before an elective operation. Hair in the operative site should not be removed unless it will in- terfere with the surgical procedure. Shaving can damage the skin so clipping is better if hair removal is required; it should be done in the operating room.

Just before the operation, wash the operation site and the area surrounding it with soap and water. Prepare the skin with anti- septic solution, starting in the centre and moving out to the periphery entire incision and an adjacent working area, so that you can ma- (Figure 2.7). This area should be large enough to include the Chlorhexidine gluconate and iodine are preferable to alcohol and are noevure during the operation without touching unprepared skin, less irritating to the skin. The solution should remain wet on the skin for at least two minutes.
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Figure 2.7
DRAPING
Scrub, gown and glove before covering the patient with sterile drapes. Leave uncovered only the operative field and those areas necessary for the maintenance of anaesthesia. Secure the drapes with towel clips at each corner (Figure 2.8).

Figure 2.8
2-10
The surgical domain
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DRAPING

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Draping exposes the area of the operative field and provides a sterile field for the operative staff to work. This is designed to maximize surgical exposure and limit potential for contamination. There are many approaches to draping, some of which depend on the kind of drapes being used. Do not place drapes until you are gowned and gloved, so as to maintain the sterility of the drapes. It is important to secure good exposure and a large sterile area. When laying out the drapes, the edges and folds (which hang below the operating table) are considered to be non-sterile.
Asepsis - method of preventing wound infection. Preventive destruction of microbes, preventing them from falling into the wound. Compliance sterility during surgery, sterilization equipment and instruments.

The basis is the aseptic sterilization.

**METHODS OF STERILIZATION:**

- steam under pressure (linen);
- boiling (metal instruments besides cutting);
- dry-air cabinets (you can burn tool over the flame);
- cold sterilization (waterproof rubber gloves to chloramine);
- 96% alcohol (30 min.).

**HARDWARE:** autoclave, boiler, dry-air enclosure. The autoclave has several modes:

- gentle - a temperature of 120 °C and pressure of 1.1 atmosphere;
- working - with a 132 °C and pressure of 2.2 atmosphere;
- a temperature of 160 °C and pressure of 3.3 (3.2) of the atmosphere.

Aseptic and antiseptic is the complex of measures, they cannot be separated. According to the source of infection is divided into exogenous and endogenous. Pathways of endogenous infection: lymphogenous, hematogenous, in intercellular spaces, especially the loose tissue, contact (e.g., a surgical instrument). Special problem for surgeon’s endogenous infection is not, in contrast to exogenous. Depending on the penetration of exogenous infection is divided into air droplet, contact and implantation.
STERILIZATION

Sterilization is a term referring to any process that eliminates (removes) or kills all forms of microbial life, including transmissible agents (such as fungi, bacteria, viruses, spore forms, etc.) present on a surface, contained in a fluid, in medication, or in a compound such as biological culture media. Sterilization can be achieved by applying the proper combinations of heat, chemicals, irradiation, high pressure, and filtration.

In general, surgical instruments and medications that enter an already aseptic part of the body (such as the bloodstream, or penetrating the skin) must be sterilized to a high sterility assurance level, or SAL. Examples of such instruments include scalpels, hypodermic needles and artificial pacemakers. This is also essential in the manufacture of parenteral pharmaceuticals.

Heat (flame) sterilization of medical instruments is known to have been used in Ancient Rome, but it mostly disappeared throughout the Middle Ages resulting in significant increases in disability and death following surgical procedures.

Preparation of injectable medications and intravenous solutions for fluid replacement therapy requires not only a high sterility assurance level, but also well-designed containers to prevent entry of adventitious agents after initial product sterilization.

Sterilization as a definition terminates all life; whereas sanitization and disinfection terminates selectively and partially. Both sanitization and disinfection reduce the number of targeted pathogenic organisms to what are considered "acceptable" levels - levels that a reasonably healthy, intact, body can deal with. An example of this class of process is Pasteurization. A widely-used method for heat sterilization is the autoclave, sometimes called a converter. Autoclaves commonly use steam heated to 121–134 °C (250–273 °F). To achieve sterility, a holding time of at least 15 minutes at 121 °C (250 °F) or 3 minutes at 134 °C (273 °F) is required. Additional sterilizing time is usually required for liquids and instruments packed in layers of cloth, as they may take longer to reach the required temperature (unnecessary in machines that grind the contents prior to sterilization). Following sterilization, liquids in a pressurized autoclave must be cooled slowly to avoid boiling over when the pressure is released. Modern converters operate around this problem by gradual-
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Proper autoclave treatment will inactivate all fungi, bacteria, viruses and also bacterial spores, which can be quite resistant. It will not necessarily eliminate all prions.

For prion elimination, various recommendations state 121–132 °C (250–270 °F) for 60 minutes or 134 °C (273 °F) for at least 18 minutes. The prion that causes the disease scrapie (strain 263K) is inactivated relatively quickly by such sterilization procedures; however, other strains of scrapie, as well as strains of CJD and BSE are more resistant. Using mice as test animals, one experiment showed that heating BSE positive brain tissue at 134–138 °C (273–280 °F) for 18 minutes resulted in only a 2.5 log decrease in prion infectivity. (The initial BSE concentration in the tissue was relatively low). For a significant margin of safety, cleaning should reduce infectivity by 4 logs, and the sterilization method should reduce it a further 5 logs.

To ensure the autoclaving process was able to cause sterilization, most autoclaves have meters and chart that record or display pertinent information such as temperature and pressure as a function of time. Indicator tape is often placed on packages of products prior to autoclaving. A chemical in the tape will change color when the appropriate conditions have been met. Some types of packaging have built-in indicators on them.

Biological indicators (“bioindicators”) can also be used to independently confirm autoclave performance. Simple bioindicator devices are commercially available based on microbial spores. Most contain spores of the heat resistant microbe Geobacillus stearothermophilus (formerly Bacillus stearothermophilus), among the toughest organisms for an autoclave to destroy. Typically these devices have a
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For effective sterilization, steam needs to penetrate the autoclave load uniformly, so an autoclave must not be overcrowded, and the lids of bottles and containers must be left ajar. Alternatively steam penetration can be achieved by shredding the waste in some Autoclave models that also render the end product unrecognizable. During the initial heating of the chamber, residual air must be removed. Indicators should be placed in the most difficult places for the steam to reach to ensure that steam actually penetrates there.
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For autoclaving, as for all disinfection or sterilization methods, cleaning is critical. Extraneous biological matter or grime may shield organisms from the property intended to kill them, whether it physical or chemical. Cleaning can also remove a large number of organisms. Proper cleaning can be achieved by physical scrubbing. This should be done with detergent and warm water to get the best results. Cleaning instruments or utensils with organic matter, cool water must be used because warm or hot water may cause organic debris to coagulate. Treatment with ultrasound or pulsed air can also be used to remove debris.
OTHER HEAT STERILIZATION METHODS

Other heat methods include flaming, incineration, boiling, tindalization, and using dry heat.

Flaming is done to loops and straight-wires in microbiology labs. Leaving the loop in the flame of a Bunsen burner or alcohol lamp until it glows red ensures that any infectious agent gets inactivated. This is commonly used for small metal or glass objects, but not for large objects (see Incineration below). However, during the initial heating infectious material may be "sprayed" from the wire surface before it is killed, contaminating nearby surfaces and objects. Therefore, special heaters have been developed that surround the inoculating loop with a heated cage, ensuring that such sprayed material does not further contaminate the area. Another problem is that gas flames may leave residues on the object, e.g. carbon, if the object is not heated enough.

A variation on flaming is to dip the object in 70% ethanol (or a higher concentration) and merely touch the object briefly to the Bunsen burner flame, but not hold it in the gas flame. The ethanol will ignite and burn off in a few seconds. 70% ethanol kills many, but not all, bacteria and viruses, and has the advantage that it leaves less residue than a gas flame. This method works well for the glass "hockey stick"-shaped bacteria spreaders.

Incineration will also burn any organism to ash. It is used to sanitize medical and other biohazardous waste before it is discarded with non-hazardous waste.

Boiling in water for fifteen minutes will kill most vegetative bacteria and inactivate viruses, but boiling is ineffective against prions and many bacterial and fungal spores; therefore boiling is unsuitable for sterilization. However, since boiling does kill most vegetative microbes and viruses, it is useful for reducing viable levels if no better method is available. Boiling is a simple process, and is an option available to most people, requiring only water, enough heat, and a container that can withstand the heat; however, boiling can be hazardous and cumbersome.
DRY HEAT STERILIZER

Dry heat can be used to sterilize items, but as the heat takes much longer to be transferred to the organism, both the time and the temperature must usually be increased, unless forced ventilation of the hot air is used. The standard setting for a hot air oven is at least two hours at 160 °C (320 °F). A rapid method heats air to 190 °C (374 °F) for 6 minutes for unwrapped objects and 12 minutes for wrapped objects. Dry heat has the advantage that it can be used on powders and other heat-stable items that are adversely affected by steam (for instance, it does not cause rusting of steel objects).

Prions can be inactivated by immersion in sodium hydroxide (NaOH 0.09N) for two hours plus one hour autoclaving (121 °C/250 °F). Several investigators have shown complete (>7.4 logs) inactivation with this combined treatment. However, sodium hydroxide may corrode surgical instruments, especially at the elevated temperatures of the autoclave.

Glass bead sterilizer, once a common sterilization method employed in dental offices as well as biologic laboratories, is not approved by the U.S. Food and Drug Administration (FDA) and Centers for Disease Control and Prevention (CDC) to be used as inter-patients sterilizer since 1997. Still it is popular in European as well as Israeli dental practice although there are no current evidence-based guidelines for using this sterilizer.

DRY STERILIZATION PROCESS

Dry sterilization process (DSP) uses hydrogen peroxide at a concentration of 30-35% under low pressure conditions. This process achieves bacterial reduction of 10–6...10–8. The complete process cycle time is just 6 seconds, and the surface temperature is increased only 10-15 °C (18 to 27 °F). Originally designed for the sterilization of plastic bottles in the beverage industry, because of the high germ reduction and the slight temperature increase the dry sterilization process is also useful for medical and pharmaceutical applications.
Chemicals are also used for sterilization. Although heating provides the most reliable way to rid objects of all transmissible agents, it is not always appropriate, because it will damage heat-sensitive materials such as biological materials, fiber optics, electronics, and many plastics. Low temperature gas sterilizers function by exposing the articles to be sterilized to high concentrations (typically 5 - 10% v/v) of very reactive gases (alkylating agents such as ethylene oxide, and oxidizing agents such as hydrogen peroxide and ozone). Liquid sterilants and high disinfectants typically include oxidizing agents such as hydrogen peroxide and peracetic acid and aldehydes such as glutaraldehyde and more recently ophthalaldehyde. While the use of gas and liquid chemical sterilants/high level disinfectants avoids the problem of heat damage, users must ensure that article to be sterilized is chemically compatible with the sterilant being used. The manufacturer of the article can provide specific information regarding compatible sterilants. In addition, the use of chemical sterilants poses new challenges for workplace safety. The chemicals used as sterilants are designed to destroy a wide range of pathogens and typically the same properties that make them good sterilants makes them harmful to humans. Employers have a duty to ensure a safe work environment and work practices, engineering controls and monitoring should be employed appropriately.
ETHYLENE OXIDE

Ethylene oxide (EO or EtO) gas is commonly used to sterilize objects sensitive to temperatures greater than 60 °C and / or radiation such as plastics, optics and electrics. Ethylene oxide treatment is generally carried out between 30 °C and 60 °C with relative humidity above 30% and a gas concentration between 200 and 800 mg/l, and typically lasts for at least three hours. Ethylene oxide penetrates well, moving through paper, cloth, and some plastic films and is highly effective. EtO can kill all known viruses, bacteria and fungi, including bacterial spores and is compatible with most materials (e.g. of medical devices), even when repeatedly applied. However, it is highly flammable, toxic and carcinogenic.

A typical process consists of a preconditioning phase, the actual sterilization run and a period of post-sterilization aeration to remove toxic residues, such as ethylene oxide residues and by-products such as ethylene glycol (formed out of EtO and ambient humidity) and ethylene chlorohydrine (formed out of EtO and materials containing chlorine, such as PVC). Besides moist heat and irradiation, ethylene oxide is the most common sterilization method, used for over 70% of total sterilizations, and for 50% of all disposable medical devices.

The two most important ethylene oxide sterilization methods are: (1) the gas chamber method and (2) the micro-dose method. To benefit from economies of scale, EtO has traditionally been delivered by flooding a large chamber with a combination of EtO and other gases used as dilutants (usually CFCs or carbon dioxide). This method has drawbacks inherent to the use of large amounts of sterilant being released into a large space, including air contamination produced by CFCs and/or large amounts of EtO residuals, flammability and storage issues calling for special handling and storage, operator exposure risk and training costs.

Ethylene oxide is still widely used by medical device manufacturers for larger scale sterilization (e.g. by the pallet), but while still used, EtO is becoming less popular in hospitals. Since EtO is explosive from its lower explosive limit of 3% all the way to 100%, EtO was traditionally supplied with an inert carrier gas such as a CFC or halogenated hydrocarbon. The use of CFCs as the carrier gas was
banned because of concerns of ozone depletion and halogenated hydrocarbons are being replaced by so-called 100% EtO systems because of the much greater cost of the blends. In hospitals, most EtO sterilizers use single use cartridges (e.g. 3M's Steri-Vac line, or Steris Corporation's Stericert sterilizers because of the convenience and ease of use compared to the former plumbed gas cylinders of EtO blends. Another 100% method is the so-called micro-dose sterilization method, developed in the late 1950s, using a specially designed bag to eliminate the need to flood a larger chamber with EtO. This method is also known as gas diffusion sterilization, or bag sterilization. This method minimizes the use of gas.

Another reason for the decrease in use of EtO are the well known health effects. In addition to being a primary irritant, EtO is now classified by the IARC as a known human carcinogen. The US OSHA has set the permissible exposure limit (PEL) at 1 ppm calculated as an eight hour time weighted average (TWA) [29 CFR 1910.1047] and 5 ppm as a 15 minute TWA. The NIOSH Immediately dangerous to life and health limit for EtO is 800 ppm. The odor threshold is around 500 ppm and so EtO is imperceptible until concentrations well above the OSHA PEL. Therefore, OSHA recommends that some kind of continuous gas monitoring system be used to protect workers using EtO for sterilization. While the hazards of EtO are generally well known, it should be noted that all chemical sterilants are designed to kill a broad spectrum of organisms, by exposing them to high concentrations of reactive chemicals. Therefore, it is no surprise that all the common chemical gas sterilants are toxic and adequate protective measures must be taken to protect workers using these materials.
OZONE

Ozone is used in industrial settings to sterilize water and air, as well as a disinfectant for surfaces. It has the benefit of being able to oxidize most organic matter. On the other hand, it is a toxic and unstable gas that must be produced on-site, so it is not practical to use in many settings.

Ozone offers many advantages as a sterilant gas; ozone is a very efficient sterilant because of its strong oxidizing properties (E = 2.076 vs SHE, CRC Handbook of Chemistry and Physics, 76th Ed, 1995–1996) capable of destroying a wide range of pathogens, including prions without the need for handling hazardous chemicals since the ozone is generated within the sterilizer from medical grade oxygen. In 2005 a Canadian company called TSO3 Inc received FDA clearance to sell an ozone sterilizer for use in healthcare. The high reactivity of ozone means that waste ozone can be destroyed by passing over a simple catalyst that reverts it back to oxygen and also means that the cycle time is relatively short (about 4.5 hours for TSO3's model 125L). The downside of using ozone is that the gas is very reactive and very hazardous. The NIOSH immediately dangerous to life and health limit for ozone is 5 ppm, 160 times smaller than the 800 ppm IDLH for ethylene oxide. Documentation for Immediately Dangerous to Life or Health Concentrations (IDLH): NIOSH Chemical Listing and Documentation of Revised IDLH Values (as of 3/1/95) and OSHA has set the PEL for ozone at 0.1 ppm calculated as an eight hour time weighted average (29 CFR 1910.1000, Table Z-1). The Canadian Center for Occupation Health and Safety provides an excellent summary of the health effects of exposure to ozone. The sterilant gas manufacturers include many safety features in their products but prudent practice is to provide continuous monitoring to below the OSHA PEL to provide a rapid warning in the event of a leak and monitors for determining workplace exposure to ozone are commercially available.
BLEACH

Chlorine bleach is another accepted liquid sterilizing agent. Household bleach consists of 6.25% sodium hypochlorite. It is usually diluted to 1/10 immediately before use; however to kill Mycobacterium tuberculosis it should be diluted only 1/5, and 1/2.5 (1 part bleach and 1.5 parts water) to inactivate prions. The dilution factor must take into account the volume of any liquid waste that it is being used to sterilize. Bleach will kill many organisms immediately, but for full sterilization it should be allowed to react for 20 minutes. Bleach will kill many, but not all spores. It is also highly corrosive.

Bleach decomposes over time when exposed to air, so fresh solutions should be made daily.

GLUTARALDEHYDE AND FORMALDEHYDE

Glutaraldehyde and formaldehyde solutions (also used as fixatives) are accepted liquid sterilizing agents, provided that the immersion time is sufficiently long. To kill all spores in a clear liquid can take up to 22 hours with glutaraldehyde and even longer with formaldehyde. The presence of solid particles may lengthen the required period or render the treatment ineffective. Sterilization of blocks of tissue can take much longer, due to the time required for the fixative to penetrate. Glutaraldehyde and formaldehyde are volatile, and toxic by both skin contact and inhalation. Glutaraldehyde has a short shelf life (<2 weeks), and is expensive. Formaldehyde is less expensive and has a much longer shelf life if some methanol is added to inhibit polymerization to paraformaldehyde, but is much more volatile. Formaldehyde is also used as a gaseous sterilizing agent; in this case, it is prepared on-site by depolymerization of solid paraformaldehyde. Many vaccines, such as the original Salk polio vaccine, are sterilized with formaldehyde.

PHTHALALDEHYDE

Ortho-phthalaldehyde (OPA) is a chemical sterilizing agent that received Food and Drug Administration (FDA) clearance in late 1999. Typically used in a 0.55% solution, OPA shows better myco-bactericidal activity than glutaraldehyde. It also is effective against glutar-
aldehyde-resistant spores. OPA has superior stability, is less volatile, and does not irritate skin or eyes, and it acts more quickly than glutaraldehyde. On the other hand, it is more expensive, and will stain proteins (including skin) gray in color. Some side effects from equipment sterilized using this reagent have been reported.

**HYDROGEN PEROXIDE**

Hydrogen peroxide is another chemical sterilizing agent. It is relatively non-toxic when diluted to low concentrations, such as the familiar 3% retail solutions although hydrogen peroxide is a dangerous oxidizer at high concentrations (> 10% w/w). Hydrogen peroxide is strong oxidant and these oxidizing properties allow it to destroy a wide range of pathogens and it is used to sterilize heat or temperature sensitive articles such as rigid endoscopes. In medical sterilization hydrogen peroxide is used at higher concentrations, ranging from around 35% up to 90%. The biggest advantage of hydrogen peroxide as a sterilant is the short cycle time. Whereas the cycle time for ethylene oxide (discussed above) may be 10 to 15 hours, the use of very high concentrations of hydrogen peroxide allows much shorter cycle times. Some hydrogen peroxide modern sterilizers, such as the Sterrad NX have a cycle time as short as 28 minutes.

Hydrogen peroxide sterilizers have their drawbacks. Since hydrogen peroxide is a strong oxidant, there are material compatibility issues and users should consult the manufacturer of the article to be sterilized to ensure that it is compatible with this method of sterilization. Paper products cannot be sterilized in the Sterrad system because of a process called cellulostics, in which the hydrogen peroxide would be completely absorbed by the paper product. The penetrating ability of hydrogen peroxide is not as good as ethylene oxide and so there are limitations on the length and diameter of lumens that can be effectively sterilized and guidance is available from the sterilizer manufacturers.

While hydrogen peroxide offers significant advantages in terms of throughput, as with all sterilant gases, sterility is achieved through the use of high concentrations of reactive gases. Hydrogen peroxide is primary irritant and the contact of the liquid solution with skin
will cause bleaching or ulceration depending on the concentration and contact time. The vapor is also hazardous with the target organs being the eyes and respiratory system. Even short term exposures can be hazardous and NIOSH has set the Immediately Dangerous to Life and Health Level (IDLH) at 75 ppm, less than one tenth the IDLH for ethylene oxide (800 ppm). Prolonged exposure to even low ppm concentrations can cause permanent lung damage and consequently OSHA has set the permissible exposure limit to 1.0 ppm, calculated as an 8 hour time weighted average (29 CFR 1910.1000 Table Z-1). Employers thus have a legal duty to ensure that their personnel are not exposed to concentrations exceeding this PEL. Even though the sterilizer manufacturers go to great lengths to make their products safe through careful design and incorporation of many safety features, workplace exposures of hydrogen peroxide from gas sterilizers are documented in the FDA MAUDE database. When using any type of gas sterilizer, prudent work practices will include good ventilation (10 air exchanges per hour), a continuous gas monitor for hydrogen peroxide as well as good work practices and training. Further information about the health effects of hydrogen peroxide and good work practices is available from OSHA and the ATSDR.

Hydrogen peroxide can also be mixed with formic acid as needed in the Endoclens device for sterilization of endoscopes. This device has two independent asynchronous bays, and cleans (in warm detergent with pulsed air), sterilizes and dries endoscopes automatically in 30 minutes. Studies with synthetic soil with bacterial spores showed the effectiveness of this device.

Vaporized hydrogen peroxide (VHP) is used to sterilize large enclosed and sealed areas such as entire rooms and aircraft interiors.
PERACETIC ACID

Peracetic acid (0.2%) is used to sterilize instruments in some STERIS Corporation systems.

SILVER

Silver ions and silver compounds show a toxic effect on some bacteria, viruses, algae and fungi, typical of heavy metals like lead or mercury, but without the high toxicity to humans that is normally associated with these other metals. Its germicidal effects kill many microbial organisms in vitro, but testing and standardization of silver products is yet difficult.

Hippocrates, the father of modern medicine, wrote that silver had beneficial healing and anti-disease properties, and the Phoenicians used to store water, wine, and vinegar in silver bottles to prevent spoiling. In the early 1900s people would put silver dollars in milk bottles to prolong the milk's freshness. The exact process of silver's germicidal effect is still not well understood. One of the explanations is the oligodynamic effect, which accounts for the effect on microorganisms but not on viruses.

Silver compounds were used to prevent infection in World War I before the advent of antibiotics. Silver nitrate solution was a standard of care but was largely replaced by silver sulfadiazine cream (SSD Cream), which was generally the "standard of care" for the antibacterial and antibiotic treatment of serious burns until the late 1990s. Now, other options, such as silver-coated dressings (activated silver dressings), are used in addition to SSD cream. However, the evidence for the use of such silver-treated dressings is mixed and although the evidence on if they are effective is promising; it is marred by the poor quality of the trials used to assess these products. Consequently a major systematic review by the Cochrane Collaboration found insufficient evidence to recommend the use of silver-treated dressings to treat infected wounds.

The widespread use of silver went out of fashion with the development of antibiotics. However, recently there has been renewed interest in silver as a broad-spectrum antimicrobial. In particular, silver is being used with alginate, a naturally occurring biopolymer derived...
from seaweed, in a range of products designed to prevent infections as part of wound management procedures, particularly applicable to burn victims. In 2007, AGC Flat Glass Europe introduced the first antibacterial glass to fight hospital-caught infection: it is covered with a thin layer of silver. In addition, Samsung has introduced washing machines with a final rinse containing silver ions to provide several days of antibacterial protection in the clothes. Kohler has introduced a line of toilet seats that have silver ions embedded to kill germs. A company called Thomson Research Associates has begun treating products with Ultra Fresh, an anti-microbial technology involving "proprietary nano-technology to produce the ultra-fine silver particles essential to ease of application and long-term protection." The U.S. Food and Drug Administration (FDA) has recently approved an endotracheal breathing tube with a fine coat of silver for use in mechanical ventilation, after studies found it reduced the risk of ventilator-associated pneumonia.

It has long been known that antibacterial action of silver is enhanced by the presence of an electric field. Applying a few volts of electricity across silver electrodes drastically enhances the rate that bacteria in solution are killed. It was found recently that the antibacterial action of silver electrodes is greatly improved if the electrodes are covered with silver nanorods. Note that an enhanced antibacterial property of nanoparticles compared to bulk material is not limited to silver, but has also been demonstrated on other materials such as ZnO.

POTENTIAL FOR CHEMICAL STERILIZATION OF PRIONS

Prions are highly resistant to chemical sterilization. Treatment with aldehydes (e.g., formaldehyde) have actually been shown to increase prion resistance. Hydrogen peroxide (3%) for one hour was shown to be ineffective, providing less than 3 logs (10⁻³) reduction in contamination. Iodine, formaldehyde, glutaraldehyde and peracetic acid also fail this test (one hour treatment). Only chlorine, phenolic compounds, guanidinium thiocyanate, and sodium hydroxide (NaOH) reduce prion levels by more than 4 logs. Chlorine and NaOH are the most consistent agents for prions. Chlorine is too corrosive to use on certain objects. Sodium hydroxide has had many studies showing its effectiveness.
RADIATION STERILIZATION

Methods of sterilization exist using radiation such as electron beams, X-rays, gamma rays, or subatomic particles.

Non Ionizing Radiation Sterilization

Ultraviolet light irradiation (UV, from a germicidal lamp) is useful only for sterilization of surfaces and some transparent objects. Many objects that are transparent to visible light absorb UV, glass for example completely absorbs all UV light. UV irradiation is routinely used to sterilize the interiors of biological safety cabinets between uses, but is ineffective in shaded areas, including areas under dirt (which may become polymerized after prolonged irradiation, so that it is very difficult to remove). It also damages some plastics, such as polystyrene foam if exposed for prolonged periods of time.

IONIZING RADIATION STERILIZATION

The safety of irradiation facilities is regulated by the United Nations International Atomic Energy Agency and monitored by the different national Nuclear Regulatory Commissions. The incidents that have occurred in the past are documented by the agency and thoroughly analyzed to determine root cause and improvement potential. Such improvements are then mandated to retrofit existing facilities and future design.

Gamma rays are very penetrating and are commonly used for sterilization of disposable medical equipment, such as syringes, needles, cannulas and IV sets, and food. The gamma radiation is emitted from a radioisotope (usually Cobalt-60 or caesium-137). Caesium-137 is used in small hospital units to treat blood before transfusion to prevent Graft-versus-host disease. Use of a radioisotope requires shielding for the safety of the operators while in use and in storage as these radioisotopes continuously emits gamma rays (cannot be turned off). With most designs the radioisotope is lowered into a water-filled source storage pool (the water in the pool absorbs the radiation) to allow maintenance personnel to enter the radiation shield. One variant of gamma irradiators keeps the radioiso-
tope under water at all times and lowers the product to be irradiated under water in hermetic bells. No further shielding is required for such designs. Other uncommonly used designs feature dry storage by providing movable shields that reduce radiation levels in areas of the irradiation chamber. An incident in Decatur, Georgia where water soluble caesium-137 leaked into the source storage pool requiring NRC intervention has led to near elimination of this radioisotope; it has been replaced by the more costly, non-water soluble cobalt-60.

Electron beam processing is also commonly used for sterilization. Electron beams use an on-off technology and provide a much higher dosing rate than gamma or x-rays. Due to the higher dose rate, less exposure time is needed and thereby any potential degradation to polymers is reduced. A limitation is that electron beams are less penetrating than either gamma or x-rays. Facilities rely on substantial concrete shields to protect workers and the environment from radiation exposure.

X-rays, High-energy X-rays (bremsstrahlung) are a form of ionizing energy allowing irradiating large packages and pallet loads of medical devices. Their penetration is sufficient to treat multiple pallet loads of low-density packages with very good dose uniformity ratios. X-ray sterilization is an electricity based process not requiring chemical nor radio-active material. High energy and high power X-rays are generated by an X-ray machine that can be turned off for when not in use, and therefore does not require any shielding when in storage. X-rays are generated by colliding accelerated electrons with a dense material (target) such as tantalum or tungsten in a process known as bremsstrahlung-conversion. These systems generally have low energetic efficiency during the conversion of electron energy to photon radiation requiring much more electrical energy than other systems.

Subatomic particles may be more or less penetrating, and may be generated by a radioisotope or a device, depending upon the type of particle.

Irradiation with X-rays or gamma rays does not make materials radioactive. Irradiation with particles may make materials radioactive, depending upon the type of particles and their energy, and the type of target material: neutrons and very high-energy particles can
make materials radioactive, but have good penetration, whereas lower energy particles (other than neutrons) cannot make materials radioactive, but have poorer penetration.

Sterilization by irradiation with gamma rays may however in some cases affect material properties.

Irradiation is used by the United States Postal Service to sterilize mail in the Washington, DC area. Some foods (e.g. spices, ground meats) are irradiated for sterilization (see food irradiation).

Cleaning methods that do not achieve sterilization

This is a brief list of cleaning methods that may be thought to "kill germs" but do not achieve sterilization.

Washing in a dishwasher: Dishwashers often only use hot tap water or heat the water to between 49 and 60 °C (120 and 140 °F), which is not hot enough to kill some bacteria on cooking or eating utensils.

Bathing cannot sterilize skin, even using antibacterial soap.

Disinfectants (for non-living objects) or antiseptics (for living objects such as skin) can kill or remove bacteria and viruses, but not all.

Pasteurization of food also kills some bacteria and viruses, but not all.
CONTROL OF STERILITY

There are 3 methods of control:

- **PHYSICAL.** Take the tube, which is placed a substance melts at a temperature of about 120 degrees, for example, sulfur, benzoic acid. The tubes were placed with sterilizable objects. The disadvantage of this method of control is that we see that the powder is melted and then the required temperature has been reached, but we cannot be sure that it was so for the duration of exposure;

- **CHEMICAL CONTROL.** Take the filter paper, put it in a starch solution, and then dipped into a solution of Lugol. It gets dark-brown color. After exposure, the starch in the autoclave at a temperature above 120 degrees is destroyed, the paper discolored. The method has the same disadvantage as the physical.

- **BIOLOGICAL CONTROL.** This method is the most reliable. Take samples of sterilized materials and spread on nutrient medium. If you did not find germs - it's okay. Found microbes - so it is necessary to sterilize again. The disadvantage is that the answer we get only 48 hours, and the material is considered to be sterile after autoclaving Bikse within 48 hours. Hence, the material used before receiving a response from the bacteriological laboratory.

The most dangerous source of infection contact - hand surgeon. To sterilize the skin apply physical methods, in addition, more complexity is the fact that after the treatment of hands again they are contaminated by sebum, sweat glands. Therefore apply tanning the skin with alcohol, tannin, with a sharp spasm of sweat ducts, sebaceous glands and infection that is there, unable to get out.

In recent years, mainly used in chemical processing techniques of hands: common scrubbing pervomur. This method is very reliable: the glove juice formed within 12 hours after wearing gloves (in the experiment) remained sterile.
ANTISEPTIC

Antiseptics (from Greek ἀντι: anti, "against" + σηπτικός: sēptikos, "putrefactive") are antimicrobial substances that are applied to living tissue/skin to reduce the possibility of infection, sepsis, or putrefaction. Antiseptics are generally distinguished from antibiotics by the latter’s ability to be transported through the lymphatic system to destroy bacteria within the body, and from disinfectants, which destroy microorganisms found on non-living objects.

Some antiseptics are true germicides, capable of destroying microbes (bacteriocidal), while others are bacteriostatic and only prevent or inhibit their growth.

Antibacterials are antiseptics that have the proven ability to act against bacteria. Microbicides which destroy virus particles are called viricides or antivirals.

Joseph Lister

The widespread introduction of antiseptic surgical methods followed the publishing of the paper Antiseptic Principle of the Practice of Surgery in 1867 by Joseph Lister, inspired by Louis Pasteur’s germ theory of putrefaction. In this paper, Lister advocated the use of carbolic acid (phenol) as a method of ensuring that any germs present were killed. Some of this work was anticipated by:

Oliver Wendell Holmes, Sr., who published The Contagiousness of Puerperal Fever in 1843.

Ignaz Semmelweis, who published his work The Cause, Concept and Prophylaxis of Childbed Fever in 1861, summarizing experiments and observations since 1847.

Florence Nightingale, who contributed substantially to the report on the Royal Commission on the Health of the Army (1856–1857), based on her earlier work.

George H. Tichenor, who experimented with the use of alcohol on wounds c. 1861–1863 during the American Civil War.
DEBRIDEMENT

Necrotic tissue from the left leg is being surgically debrided in a patient with necrotizing fasciitis.

Debridement (/dɪˈbrɪdment/) is the medical removal of dead, damaged, or infected tissue to improve the healing potential of the remaining healthy tissue. Removal may be surgical, mechanical, chemical, autolytic (self-digestion), and by maggot therapy, where certain species of live maggots selectively eat only necrotic tissue.

In oral hygiene and dentistry, debridement refers to the removal of plaque and calculus that have accumulated on the teeth. Debridement in this case may be performed using ultrasonic instruments, which fracture the calculus, thereby facilitating its removal, as well as hand tools, including periodontal scaler and curettes, or through the use of chemicals such as hydrogen peroxide.

In podiatry practitioners such as chiropodists, podiatrists and foot health practitioners remove callus, corns, verruca’s etc.

Debridement is an important part of the healing process for burns and other serious wounds; it is also used for treating some kinds of snake and spider bites.

Sometimes the boundaries of the problem tissue may not be clearly defined. For example, when excising a tumor, there may be micrometastases along the edges of the tumor that are too small to be detected, and if not removed, could cause a relapse. In such circumstances, a surgeon may opt to debride a portion of the surrounding healthy tissue — as little as possible — to ensure that the tumor is completely removed.

AUTOLYTIC DEBRIDEMENT

Autolysis uses the body’s own enzymes and moisture to re-hydrate, soften and finally liquefy hard eschar and slough. Autolytic debridement is selective; only necrotic tissue is liquefied. It is also virtually painless for the patient. Autolytic debridement can be achieved with the use of occlusive or semi-occlusive dressings which maintain wound fluid in contact with the necrotic tissue. Autolytic debride-
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ENZYMATIC DEBRIDEMENT

Chemical enzymes are fast acting products that produce slough of necrotic tissue. Some enzymatic debrides are selective, while some are not. This method works best on any wound with a large amount of necrotic debris, or with eschar formation.

MECHANICAL DEBRIDEMENT

This technique has been used for decades in wound care. Allowing a dressing to proceed from moist to dry, then manually removing the dressing causes a form of non-selective debridement. This method works best on wounds with moderate amounts of necrotic debris.

SURGICAL DEBRIDEMENT

Sharp surgical debridement and laser debridement under anesthesia are the fastest methods of debridement. They are very selective, meaning that the person performing the debridement has complete control over which tissue is removed and which is left behind. Surgical debridement can be performed in the operating room or at bedside, depending on the extent of the necrotic material. This method works best on wounds with a large amount of necrotic tissue in conjunction with infected tissue.
SOME COMMON ANTISEPTICS

Alcohols. Most commonly used are ethanol (60–90%), 1-propanol (60–70%) and 2-propanol/isopropanol (70–80%) or mixtures of these alcohols. They are commonly referred to as "surgical alcohol". Used to disinfect the skin before injections along with iodine (tincture of iodine) or some cationic surfactants (benzalkonium chloride 0.05–0.5%, chlorhexidine 0.2–4.0% or octenidine dihydrochloride 0.1–2.0%).

Quaternary ammonium compounds. Also known as Quats or QAC's, include the chemicals benzalkonium chloro-trimethylammonium bromide (CTMB), cetylpyridinium chloride (Cetrim, CPC) and benzethonium chloride (BZT). Benzalkonium chloride is used in some pre-operative skin disinfectants (conc. 0.05–0.5%) and antiseptic towels. The antimicrobial activity of Quats is inactivated by anionic surfactants, such as soaps. Related disinfectants include chlorhexidine and octenidine.

Boric acid. Used in suppositories to treat yeast infections of the vagina, in eyewashes, and as an antiviral to shorten the duration of cold sore attacks. Put into creams for burns. Also common in trace amounts in eye contact solution.

Brilliant Green. A triarylmethane dye still widely used as 1% ethanol solution in Eastern Europe and ex-USSR countries for treatment of small wounds and abscesses. Efficient against gram-positive bacteria.

Chlorhexidine Gluconate. A biguanidine derivative, used in concentrations of 0.5–4.0% alone or in lower concentrations in combination with other compounds, such as alcohols. Used as a skin antiseptic and to treat inflammation of the gums (gingivitis). The microbi-cidal action is somewhat slow, but remanent. It is a cationic surfactant, similar to Quats.

Hydrogen peroxide. Used as a 6% (20 Vols) solution to clean and deodorize wounds and ulcers. More common 3% solutions of hydroperoxide (BAC), cetyl benzalkonium chloride are given, often along with iodine (tincture of iodine) or some cationic surfactants.
drogen peroxide have been used in household first aid for scrapes, etc. However, even this less potent form is no longer recommend-
ed for typical wound care as the strong oxidization causes scar formation and increases healing time. Gentle washing with mild soap and water or rinsing a scrape with sterile saline is a better practice.

**Iodine.** Usually used in an alcoholic solution (called tincture of iodine) or as Lugol's iodine solution as a pre- and post-operative anti-
septic. No longer recommended to disinfect minor wounds because it induces scar tissue formation and increases healing time. Gentle washing with mild soap and water or rinsing a scrape with sterile saline is a comparatively better practice. Novel iodine antiseptics contain-
ing povidone-iodine (an iodophor, complex of povidone, a water-soluble polymer, with triiodide anions I3-, containing about 10% of active iodine) are far better tolerated, don't negatively affect wound healing, and leave a deposit of active iodine, thereby creating the so-called "remnant," or persistent, effect. The great advantage of iodine antiseptics is their wide scope of antimicrobial activity, killing all principal pathogens and, given enough time, even spores, which are considered to be the most difficult form of microorganisms to be inactivated by disinfectants and antiseptics.

**Mercurochrome.** Not recognized as safe and effective by the U.S. Food and Drug Administration (FDA) due to concerns about its mercury content. Other obsolete organomercury antiseptics include bis-(phenylmercuric) monohydrogenborate (Famosept).

**Manuka Honey.** Recognized by the U.S. Food and Drug Administration (FDA) as a medical device for use in wounds and burns. Active +15 is equal to a 15% solution of phenol.

**Octenidine dihydrochloride.** A cationic surfactant and bis-(dihydropyridinyl)-decane derivative, used in concentrations of 0.1–2.0%. It is similar in its action to the Quats, but is of somewhat broader spectrum of activity. Octenidine is currently increasingly used in continental Europe as a QAC's and chlorhexidine (with respect to its slow action and concerns about the carcinogenic impurity 4-
chlooroaniline) substitute in water- or alcohol-based skin, mucosa and wound antiseptic. In aqueous formulations, it is often potentiated with addition of 2-phenoxyethanol.
Phenol (carbolic acid) compounds. Phenol is germicidal in strong solution, inhibitory in weaker ones. Used as a "scrub" for pre-operative hand cleansing. Used in the form of a powder as an antiseptic baby powder, where it is dusted onto the navel as it heals. Also used in mouthwashes and throat lozenges, where it has a painkilling effect as well as an antiseptic one. Example: TCP. Other phenolic antiseptics include historically important, but today rarely used (sometimes in dental surgery) thymol, today obsolete hexachlorophene, still used triclosan and sodium 3,5-dibromo-4-hydroxybenzenesulfonate (Dibromol).

Polyhexanide (polyhexamethylene biguanide, PHMB). Antimicrobial compound suitable for clinical use in critically colonized or infected acute and chronic wounds. The physicochemical action on the bacterial envelope prevents or impedes the development of resistant bacterial strains.

Sodium chloride. Used as a general cleanser. Also used as an antiseptic mouthwash. Only a weak antiseptic effect, due to hyperosmolality of the solution above 0.9%.

Sodium hypochlorite. Used in the past, diluted, neutralized and combined with boric acid in Dakin's solution.

Calcium hypochlorite. Used by Semmelweis, as "chlorinated lime", in his revolutionary efforts against childbed fever.

Sodium bicarbonate (NaHCO₃) has antiseptic and disinfectant properties.
ANTIBACTERIAL

An antibacterial is an agent that inhibits bacterial growth or kills bacteria. The term is often used synonymously with the term antibiotic(s); today, however, with increased knowledge of the causative agents of various infectious diseases, antibiotic(s) has come to denote a broader range of antimicrobial compounds, including anti-fungal and other compounds.

The term antibiotic was first used in 1942 by Selman Waksman and his collaborators in journal articles to describe any substance produced by a microorganism that is antagonistic to the growth of other microorganisms in high dilution. This definition excluded substances that kill bacteria, but are not produced by microorganisms (such as gastric juices and hydrogen peroxide). It also excluded synthetic antibacterial compounds such as the sulfonamides. Many antibacterial compounds are relatively small molecules with a molecular weight of less than 2000 atomic mass units.

With advances in medicinal chemistry, most of today’s antibacterial chemically are semisynthetic modifications of various natural compounds. These include, for example, the beta-lactam antibacterials, which include the penicillins (produced by fungi in the genus Penicillium), the cephalosporins, and the carbapenems. Compounds that are still isolated from living organisms are the aminoglycosides, whereas other antibacterials—for example, the sulfonamides, the quinolones, and the oxazolidinones—are produced solely by chemical synthesis. In accordance with this, many antibacterial compounds are classified on the basis of chemical/biosynthetic origin into natural, semisynthetic, and synthetic. Another classification system is based on biological activity; in this classification, antibacterials are divided into two broad groups according to their biological effect on microorganisms: bactericidal agents kill bacteria, and bacteriostatic agents slow down or stall bacterial growth.

HISTORY

Selman Waksman
Penicillin, the first natural antibiotic discovered by Alexander Fleming in 1928

Before the early 20th century, treatments for infections were based primarily on medicinal folklore. Mixtures with antimicrobial properties that were used in treatments of infections were described over 2000 years ago. Many ancient cultures, including the ancient Egyptians and ancient Greeks, used specially selected mold and plant materials and extracts to treat infections. More recent observations made in the laboratory of antibiosis between micro-organisms led to the discovery of natural antibacterials produced by microorganisms.

Louis Pasteur observed, "if we could intervene in the antagonism observed between some bacteria, it would offer perhaps the greatest hopes for therapeutics". The term 'antibiosis', meaning "against life," was introduced by the French bacteriologist Vuillemin as a descriptive name of the phenomenon exhibited by these early antibacterial drugs. Antibiosis was first described in 1877 in bacteria when Louis Pasteur and Robert Koch observed that an airborne bacillus could inhibit the growth of Bacillus anthracis. These drugs were later renamed antibiotics by Selman Waksman, an American microbiologist, in 1942. John Tyndall first described antagonistic activities by fungi against bacteria in England in 1875. Synthetic antibiotic chemotherapy as a science and development of antibacterials began in Germany with Paul Ehrlich in the late 1880s. Ehrlich noted certain dyes would color human, animal, or bacterial cells, while others did not. He then proposed the idea that it might be possible to create chemicals that would act as a selective drug that would bind to and kill bacteria without harming the human host. After screening hundreds of dyes against various organisms, he discovered a medicinally useful drug, the synthetic antibacterial Salvarsan now called arsphenamine.

In 1895, Vincenzo Tiberio, physician of the University of Naples discovered that a mold (Penicillium) in a water well has an antibacterial action. After this initial chemotherapeutic compound proved effective, others pursued similar lines of inquiry, but it was not until in 1928 that Alexander Fleming observed antibiosis against bacteria by a fungus of the genus Penicillium. Fleming postulated the effect...
al action. After this initial chemotherapeutic compound proved effective, others pursued similar lines of inquiry, but it was not until in 1928 that Alexander Fleming observed antibiosis against bacteria by a fungus of the genus Penicillium. Fleming postulated the effect was mediated by an antibacterial compound named penicillin, and that its antibacterial properties could be exploited for chemotherapy. He initially characterized some of its biological properties, but he did not pursue its further development.

The first sulfonamide and first commercially available antibacterial antibiotic, Prontosil, was developed by a research team led by Gerhard Domagk in 1932 at the Bayer Laboratories of the IG Farben conglomerate in Germany. Domagk received the 1939 Nobel Prize for Medicine for his efforts. Prontosil had a relatively broad effect against Gram-positive cocci, but not against enterobacteria. Research was stimulated apace by its success. The discovery and development of this sulfonamide drug opened the era of antibacterial antibiotics. In 1939, coinciding with the start of World War II, Rene Dubos reported the discovery of the first naturally derived antibiotic, gramicidin from B. brevis. It was one of the first commercially manufactured antibiotics universally and very effectively used to treat wounds and ulcers during World War II. Research results obtained during that period were not shared between the Axis and the Allied powers during the war. Florey and Chain succeeded in purifying the first penicillin, penicillin G procaine in 1942, but it did not become widely available outside Allied military before 1945. The chemical structure of penicillin was determined by Dorothy Crowfoot Hodgkin in 1945. Purified penicillin displayed potent antibacterial activity against a wide range of bacteria and had low toxicity in humans. Furthermore, its activity was not inhibited by biological constituents such as pus, unlike the synthetic sulfonamides. The discovery of such a powerful antibiotic was unprecedented, and the development of penicillin led to renewed interest in the search for antibacterial compounds with similar efficacy and safety. For their discovery and development of penicillin as a therapeutic drug, Ernst Chain, Howard Florey, and Alexander Fleming shared the 1945 Nobel Prize in Medicine. Florey credited Dubos with pioneering the approach of deliberately and systematically searching for antibacterial compounds, which had led to the discovery of gramicidin and had revived Florey's research in penicillin.
Antibacterial antibiotics are commonly classified based on their mechanism of action, chemical structure, or spectrum of activity. Most target bacterial functions or growth processes. Those that target the bacterial cell wall (penicillins and cephalosporins) or the cell membrane (polymixins, Polysporin, Neosporin, Polymyxin B, Polymyxin E), or interfere with essential bacterial enzymes (rifamycins, Rifampicin or Rifampin, Rifabutin, Rifapentine, Rifaximin, lipiarmycins, quinolones, and sulfonamides) have bactericidal activities.

Exception: 5th generation Cephalosporins are effective against MRSA

- Cefacectile (cephacetrile),
- Cefadroxil (cefadroxyl; Duricef),
- Cephalexin (cephalexin; Keflex),
- Cefaloglycin (cephaloglycin),
- Cefalonium (cephalonium),
- Cefapirin (cephapirin; Cefadryl),
- Cefatrizine,
- Cefazaflur,
- Cefazedone,
- Cefazolin cephalozin;

Ernst Boris Chain (1945)

Cefaloridine (cephaloradine),
Cefalotin (cephalothin; Keflin),

Howard Florey

Cefapirin (cephapirin; Cefadyl),
Cefatrizine,
Ceftrizine,
Cefazaflur,
Cefazedone,
Cefazolin cephalozolin;
Ancef,
Kefzol,
Cefradine (cephradine; Velosef),
Cefroxadine,
Ceftezole.

Gram-positive:
Activity against penicillinase-producing, methicillin-susceptible staphylococci and streptococci (though they are not the drugs of choice for such infections). No activity against methicillin-resistant staphylococci or enterococci.

Gram-negative: Activity against Proteus mirabilis, some Escherichia coli, and Klebsiella pneumoniae ("PEcK"), but have no activity against Bacteroides fragilis, Pseudomonas, Acinetobacter, Enterobacter, indole-positive Proteus, or Serratia.

Cefaclor (Ceclor, Distaclor, Keflor, Raniclor),
Cefonicid (Monocid),
Cefprozil (cefoxitin; Cefzil),
Cefuroxime (Zefu, Zinnat, Zinacef, Ceftin, Biofuroksym, Xorimax),
Cefuzonam. Second generation cephalosporins with antianaerobe activity:
Cefmetazole,
Cefotetan,
Cefoxitin.
The following cephems are also sometimes grouped with second-generation cephalosporins:
Carbacephems: loracarbef (Lorabid);
Cephamycins: cefbuperazone, cefmetazole (Zefazone), cefminox, cefotetan
(Cefotan), cefoxitin (Mefoxin), Cefotiam.
Gram-positive: Less than first-generation.
Gram-negative: Greater than first-generation: HEN (Haemophilus influenzae, Enterobacter aerogenes and some Neisseria + the PEcK described above.
Cefcapene,
Cefdaloxime,
Cefdinir (Zinir, Omnicef, Kefnir),
Cefditoren,
Cefetamet,
Cefixime (Zifi, uprax),
Cefmenoxime,
Cefodizime,
Cefotaxime (Claforan),
Cefovecin (Convenia),
Cefpimizole,
Cefpodoxime (Vantin, PECEF),
Cefteram,
Ceftibuten (Cedax),
Ceftiofur,
Ceftiolene,
Ceftizoxime (Cefizox),
Ceftriaxone (Rocephin).

Third-generation cephalosporins with antipseudomonal activity:
Cefoperazone (Cefobid),
Ceftazidime (Fortum, Fortaz).
The following cephems are also sometimes grouped with third-generation cephalosporins:
Oxacephems: latamoxef (moxalactam).

Gram-positive: Some members of this group (in particular, those available in an oral formulation, and those with anti-pseudomonal activity) have decreased activity against Gram-positive organisms.

Gram-negative: Third-generation cephalosporins have a broad spectrum of activity and further increased activity against Gram-negative organisms. They may be particularly useful in treating hospital, although increasing levels of extended-spectrum beta-lactamases are reducing the clinical utility of this class of antibiotics. They are also able to penetrate the CNS, making them useful against meningitis caused by pneumococci, meningococci, H. influenzae, and susceptible E. coli, Klebsiella, and penicillin-resistant N. gonorrhoeae. Since 2007, third-generation cephalosporins (ceftriaxone or cefixime) have been the only recommended treatment for gonorrhea in the United States.

Cefclidine,
Cefepime (Maxipime),
Cefluprenam,
Cefoselis,
Cefozopran,
Cefpirome (Cefrom),
Cefquinome.

The following cephems are also sometimes grouped with fourth-generation cephalosporins:
Oxacephems: flomoxef
Gram-positive: They are extended-spectrum agents with similar activity against Gram-positive organisms as first-generation cephalosporins.

Gram-negative: Fourth-generation cephalosporins are zwitterions that can penetrate the outer membrane of Gram-negative bacteria. They also have a greater resistance to beta-lactamases than the third-generation cephalosporins. Many can cross the blood–brain barrier and are effective in meningitis. They are also used against Pseudomonas aeruginosa.

Ceftobiprole,

Ceftaroline

Ceftobiprole has been described as "fifth-generation" cephalosporin, though acceptance for this terminology is not universal. Ceftobiprole (and the soluble prodrug medocaril) are on the FDA fast-track.

Ceftobiprole has powerful antipseudomonal characteristics and appears to be less susceptible to development of resistance. Ceftaroline has also been described as "fifth-generation" cephalosporin, but does not have the anti-pseudomonal or VRE coverage of ceftobiprole.

Those that target protein synthesis (aminoglycosides, macrolides, and tetracyclines) are usually bacteriostatic. Further categorization is based on their target specificity. "Narrow-spectrum" antibacterial antibiotics target specific types of bacteria, such as Gram-negative or Gram-positive bacteria, whereas broad-spectrum antibiotics affect a wide range of bacteria. Following a 40-year hiatus in discovering new classes of antibacterial compounds, four new classes of antibacterial antibiotics have been brought into clinical use: cycliclipopeptides (such as daptomycin), glycyclyclines (such as tigecycline), oxazolidinones (such as linezolid) and lipiarmycins (such as as fidaxomicin).
ADMINISTRATION

Oral antibacterials are orally ingested, whereas intravenous administration may be used in more serious cases, such as deep-seated systemic infections. Antibiotics may also sometimes be administered topically, as with eye drops or ointments.

SIDE-EFFECTS

Antibacterials are screened for any negative effects on humans or other mammals before approval for clinical use, and are usually considered safe and most are well tolerated. However, some antibacterials have been associated with a range of adverse effects. Side-effects range from mild to very serious depending on the antibiotics used, the microbial organisms targeted, and the individual patient. Safety profiles of newer drugs are often not as well established as for those that have a long history of use. Adverse effects range from fever and nausea to major allergic reactions, including photodermatitis and anaphylaxis. Common side-effects include diarrhea, resulting from disruption of the species composition in the intestinal flora, resulting, for example, in overgrowth of pathogenic bacteria, such as Clostridium difficile. Antibacterials can also affect the vaginal flora, and may lead to overgrowth of yeast species of the genus Candida in the vulvo-vaginal area. Additional side-effects can result from interaction with other drugs, such as elevated risk of tendon damage from administration of a quinolone antibiotic with a systemic corticosteroid.

ANTIBIOTIC RESISTANCE

The emergence of resistance of bacteria to antibacterial drugs is a common phenomenon. Emergence of resistance often reflects evolutionary processes that take place during antibacterial drug therapy. The antibacterial treatment may select for bacterial strains with physiologically or genetically enhanced capacity to survive high doses of antibacterials. Under certain conditions, it may result in preferential growth of resistant bacteria, while growth of susceptible bacteria is inhibited by the drug. For example, antibacterial selection within whole bacterial populations for strains having previously acquired antibacterial-resistance genes was demonstrated in 1943 by the Luria–Delbrück experiment. Survival of bacteria often results from an inheritable resistance. Resistance to antibacterials also oc-
within whole bacterial populations for strains having previously acquired antibacterial-resistance genes was demonstrated in 1943 by the Luria–Delbrück experiment. Survival of bacteria often results from an inheritable resistance. Resistance to antibacterials also occurs through horizontal gene transfer. Horizontal transfer is more likely to happen in locations of frequent antibiotic use. Antibacterials such as penicillin and erythromycin, which used to have high efficacy against many bacterial species and strains, have become less effective, because of increased resistance of many bacterial strains. Antibacterial resistance may impose a biological cost, thereby reducing fitness of resistant strains, which can limit the spread of antibacterial-resistant bacteria, for example, in the absence of antibacterial compounds. Additional mutations, however, may compensate for this fitness cost and can aid the survival of these bacteria.

Antibacterial-resistant strains and species, sometimes referred to as "superbugs", now contribute to the emergence of diseases that were for a while well controlled. For example, emergent bacterial strains causing tuberculosis (TB) that are resistant to previously effective antibacterial treatments pose many therapeutic challenges. Every year, nearly half a million new cases of multidrug-resistant tuberculosis (MDR-TB) are estimated to occur worldwide. For example, NDM-1 is a newly identified enzyme conveying bacterial resistance to a broad range of beta-lactam antibacterials. United Kingdom Health Protection Agency has stated that "most isolates with NDM-1 enzyme are resistant to all standard intravenous antibiotics for treatment of severe infections."

**MISUSE**

This poster from the U.S. Centers for Disease Control and Prevention "Get Smart" campaign, intended for use in doctors' offices and other healthcare facilities, warns that antibiotics do not work for viral illnesses such as the common cold.

**ANTIBIOTIC MISUSE**
ANTIBIOTIC MISUSE

Inappropriate antibacterial treatment and overuse of antibiotics have contributed to the emergence of antibacterial-resistant bacteria. Self prescription of antibacterials is an example of misuse. Many antibacterials are frequently prescribed to treat symptoms or diseases that do not respond to antibacterial therapy or are likely to resolve without treatment, or incorrect or suboptimal antibacterials are prescribed for certain bacterial infections. The overuse of antibacterials, like penicillin and erythromycin, have been associated with emerging antibacterial resistance since the 1950s. Widespread usage of antibacterial drugs in hospitals has also been associated with increases in bacterial strains and species that no longer respond to treatment with the most common antibacterials.

Common forms of antibacterial misuse include excessive use of prophylactic antibiotics in travelers and failure of medical professionals to prescribe the correct dosage of antibacterials on the basis of the patient's weight and history of prior use. Other forms of misuse include failure to take the entire prescribed course of the antibacterial, incorrect dosage and administration, or failure to rest for sufficient recovery. Inappropriate antibacterial treatment, for example, is the prescription of antibacterials to treat viral infections such as the common cold. One study on respiratory tract infections found "physicians were more likely to prescribe antibiotics to patients who appeared to expect them". Multifactorial interventions aimed at both physicians and patients can reduce inappropriate prescription of antibiotics.

A **vaccine** is a biological preparation that improves immunity to a particular disease. A vaccine typically contains an agent that resembles a disease-causing microorganism, and is often made from weakened or killed forms of the microbe, its toxins or one of its surface proteins. The agent stimulates the body's immune system to recognize the agent as foreign, destroy it, and "remember" it, so that the immune system can more easily recognize and destroy any of these microorganisms that it later encounters.

Vaccines can be prophylactic (example: to prevent or ameliorate the effects of a future infection by any natural or "wild" pathogen), or therapeutic (e.g. vaccines against cancer are also being investigated; see cancer vaccine).
The term vaccine derives from Edward Jenner's 1796 use of cow pox (Latin variola vaccinia, adapted from the Latin vaccīn-us, from vacca, cow), to inoculate humans, providing them protection against smallpox.

**PLASMIDS**

The use of plasmids has been validated in preclinical studies as a protective vaccine strategy for cancer and infectious diseases. However, in human studies this approach has failed to provide clinically relevant benefit. The overall efficacy of plasmid DNA immunization depends on increasing the plasmid’s immunogenicity while also correcting for factors involved in the specific activation of immune effector cells.

**BACTERIOPHAGE**

A bacteriophage (from 'bacteria' and Greek φαγεῖν phagein "to devour") is any one of a number of viruses that infect bacteria. They do this by injecting genetic material, which they carry enclosed in an outer protein capsid. The genetic material can be ssRNA, dsRNA, ssDNA, or dsDNA ("ss-" or "ds-" prefix denotes single-strand or double-strand) along with either circular or linear arrangement. Phages are widely distributed in locations populated by bacterial hosts, such as soil or the intestines of animals. One of the densest natural sources for phages and other viruses is sea water, where up to 9×108 virions per milliliter have been found in microbial mats at the surface, and up to 70% of marine bacteria may be infected by phages. They have been used for over 90 years as an alternative to antibiotics in the former Soviet Union and Eastern Europe, as well as in France. They are seen as a possible therapy against multi-drug-resistant strains of many bacteria.

James Gillray, The Cow-Pock—or—the Wonderful Effects of the New Inoculation!(1802)
Bacteriophages are among the most common and diverse entities in the biosphere. The term is commonly used in its shortened form, phage.

Phages are widely distributed in locations populated by bacterial hosts, such as soil or the intestines of animals. One of the densest natural sources for phages and other viruses is sea water, where up to 9×10^8 virions per milliliter have been found in microbial mats at the surface, and up to 70% of marine bacteria may be infected by phages. They have been used for over 90 years as an alternative to antibiotics in the former Soviet Union and Eastern Europe, as well as in France. They are seen as a possible therapy against multidrug-resistant strains of many bacteria.

**INTRAVENOUS IMMUNOGLOBULIN**

Intravenous immunoglobulin (IVIG) is a blood product administered intravenously. It contains the pooled, polyvalent, IgG (immunoglobulin (antibody) G) extracted from the plasma of over one thousand blood donors. IVIG's effects last between 2 weeks and 3 months. It is mainly used as treatment in three major categories:

- Immune deficiencies such as X-linked agammaglobulinemia, hypogammaglobulinemia (primary immune deficiencies), and acquired compromised immunity conditions (secondary immune deficiencies) featuring low antibody levels.
- Autoimmune diseases, e.g. Immune thrombocytopenia ITP, and Inflammatory diseases, e.g. Kawasaki disease.
- Acute infections.

Researchers are currently investigating the use of IVIG in early Alzheimer's disease, with encouraging results. IVIG is given as a plasma protein replacement therapy (IgG) for immune deficient patients who have decreased or abol-
Although routine use of IVIG is common practice, sometimes for long term treatments, and is considered safe, complications of IVIG therapy are known and include:

- **Headache**
- **Dermatitis** - usually peeling of the skin of the palms and soles.
- **Infection** (such as HIV or viral hepatitis) by contaminated blood product; there is also an as of yet unknown risk of contracting variant CJD (vCJD) however the process whereby the product is extracted shows that the contaminants are usually not present in the product.
- **Pulmonary edema** from fluid overload, due to the high colloid oncotic pressure of IVIG.
- **Allergic/anaphylactic reactions**; for example, anaphylactic shock, especially in IgA deficient patients, who by definition can still produce IgG antibodies (IgA deficient patients are more likely to produce IgG against the IVIG administration than normal patients).
- **Damage** such as hepatitis caused directly by antibodies contained in the pooled IVIG.
- **Acute kidney injury**
- **Venous thrombosis**
- **Aseptic meningitis**