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Editorial

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Mini review section – Microorganisms are everywhere — in the air and water, on skin and other surfaces. When microbiological contamination occurs in manufacturing, raw materials, product batches are wasted, risking potential recalls and plant shutdowns. Results include lost time and money for manufacturers, product delays and shortages, and related loss of public confidence and consequences leading to potential fines. **Environmental Monitoring (EM)** is a program designed to demonstrate the control of viable (living microorganisms) and non-viable particles in critical areas.

Current Trends section - The word "Surfactant" is a contraction of the three words "Surface Active Agents." Surfactants are materials that lower the surface tension (or interfacial tension) between two liquids or between a liquid and a solid. Surface active agents play an important role as cleaning, wetting, dispersing, emulsifying, foaming and anti-foaming agents in many practical applications and products, including: paints, emulsions adhesives, inks, biocides (sanitizers), shampoos, toothpastes, firefighting (foams), detergents, insecticides, deinking of recycled papers, ski waxes, spermicides (nonoxynol-9).

In Profile Scientist – **Selman Abraham Waksman** (July 22, 1888 – August 16, 1973) was a Ukrainian-born, Jewish-American inventor, biochemist and microbiologist whose research into organic substances—largely into organisms that live in soil—and their decomposition promoted the discovery of streptomycin and several other antibiotics. A professor of biochemistry and microbiology at Rutgers University for four decades, he discovered over twenty antibiotics (a word he coined) and introduced procedures that have led to the development of many others.

Bug of the month - Bifidobacteria are a group of bacteria that normally live in the intestines. They can be grown outside the body and then taken by mouth as medicine. Bifidobacteria are commonly used for diarrhea, constipation, an intestinal disorder called irritable bowel syndrome, for preventing the common cold or flu, and lots of other conditions, but there is no good scientific evidence to support many of these uses.

Did You Know? Impetigo is a bacterial infection that involves the superficial skin. The most common presentation is yellowish crusts on the face, arms, or legs.Less commonly there may be large blisters which affect the groin or armpits. The lesions may be painful or itchy.Fever is uncommon. It is typically due to either Staphylococcus aureus or Streptococcus pyogenes.

Best Practices - Wound dressings represent a part of the management of diabetic foot ulceration. Ideally, dressings should alleviate symptoms, provide wound protection, and encourage healing. No single dressing fulfills all the requirements of a diabetic patient with an infected foot ulcer. Dressing research in this area is generally poor. However, each category of dressings has particular characteristics that aid selection.

"Laughter is the music of the soul" so ease your mind with some humour in our Relax Mood section.

So go on, enjoy reading & don't forget to give us your valuable inputs & feedback.

ENVIRONMENTAL MONITORING: Sampling techniques and its Applications

Microorganisms are everywhere — in the air and water, on skin and other surfaces. When microbiological contamination occurs in manufacturing, raw materials, product batches are wasted, risking potential recalls and plant shutdowns. Results include lost time and money for manufacturers, product delays and shortages, and related loss of public confidence and consequences leading to potential fines.

In recent times, many industries from pharmaceutical, biotechnology, medical device, hospital pharmacies and medical disposables have *clean room* operations of differing sizes and complexities. Clients in these industries have recognized that there is a regulatory compliance to demonstrate clean room performance and controlled product bioburden with monitoring the environmental conditions in their aseptic manufacturing areas.

Cleanrooms are defined as a room, or suite of rooms, in which the concentration of airborne particles is maintained within established parameters; and where other factors are controlled to within specified limits. These rooms are designed to provide control of various environmental factors including some or all of the following:

- Viable and non-viable airborne particles
- Air flow patterns
- Temperature and humidity
- Air pressure
- Containment of hazardous aerosols
- Operating procedures

Environmental Monitoring - Maintaining a Clean Room

In pharmaceuticals, the microbiological quality of drugs and biologics is necessary for their efficacy and patient safety, because microbial contamination of drugs causes immediate adverse effects on patient health in terms of morbidity and mortality, as well as long-term adverse effects, such as cancer, autoimmune, and other diseases. Additionally, microbes can alter the chemistry and pharmacology of drugs, with a potential adverse impact on their effectiveness due to the breakdown of the active ingredients as well as on their safety due to the toxicity of potential degradant products. Therefore, control of microbes in drugs is essential, either by assuring absence of microbes in sterile drugs that are administered parenterally and applied to sensitive tissues or by controlling microbial bioburden to appropriate levels for non-sterile drugs that are administered to regions rich in microbial flora with physical or immunological barriers to infections. Assurance of the absence of bacterial, yeast, and fungal contaminants is provided by the sterility test for sterile drugs.

Environmental Monitoring (EM) is a program designed to demonstrate the control of viable (living microorganisms) and non-viable particles in critical areas. These areas include clean-rooms for drug fill/finish, formulation tank rooms, laminar flow hoods, biological safety hoods and isolators, glove boxes, molding machines, kit assembly lines, Intravenous (IV) compounding areas and sterile packaging. This article section will discuss environmental monitoring from a viable particles perspective. *Viable monitoring* refers to testing for the detection and enumeration of bacteria, yeast and mold. It includes the monitoring of personnel, air and area surfaces for microbial contamination. And differs from non-viable environmental monitoring which is a reference for particle counts measured by a laser counter. Viable counts provide metrics on the potential for contamination of a company's products as well as demonstrating the reliability that a clean room is functioning as designed and being properly maintained.

In pharmaceuticals, microbiological quality needs to be built into the drugs by understanding the sources of contamination, environmental conditions and product attributes that support growth of microbes. Microbiological quality for sterile drugs is assured by employing a robust environmental monitoring (EM) program, appropriate microbiological testing at various stages or intermediate products during manufacture, including the final drug product (DP) and using validated manufacturing processes eg, aseptic manufacturing processes, container closure studies, media fill studies, etc. During routine manufacture of sterile drugs employing aseptic manufacturing processes, EM is an essential and critical component to demonstrate the state of control of the facility, providing information on the microbial quality of manufacturing and testing environments. This is an important element for sterility assurance of sterile drugs. There are a number of guidance documents and regulations on the EM aspects of manufacture of sterile drugs. Microbiological quality of nonsterile drugs is important, too, and can be assured through selection of appropriate controls through a risk analysis process.

United States Pharmacopoeia (USP) drafted guidelines to monitor the environment for manufacture of such drugs. These guidelines describe a risk-based approach to control microbes for manufacture of sterile as well as the non-sterile drugs.

Surface and air monitoring exhibit the asepsis of the product manufacturing operation. Companies who have their clean room facilities monitored do so to ensure their desired/ required quality standards are met as per the Quality certification criteria.

Personnel: Sterile gowning

The areas that are sampled in a manufacturer's clean room include:

1. Personnel – Personnel are the biggest source of contamination in clean areas. Personnel harbor millions of bacteria, carrying them with them everywhere they go. Gowning is the most effective way to protect the cleanroom environment from ourselves. To assess the effectiveness of the gowning program personnel may be monitored on a regular basis for viable counts. Personnel monitoring employs contact plates to assess microbial contamination of clean room personnel.

2. Air - the air in a clean room is controlled and monitored on a regular basis (e.g., daily, weekly, quarterly) for particle counts, viable counts, temperature and humidity. High efficiency particulate air (HEPA) filters are used to control the viable and non-viable particulate counts within the air. HEPA filters have the capability to filter out particulates down to 0.2 µm in size. These filters usually run continuously at a calibrated flow rate in order to maintain the required air quality within the room. Humidity is usually kept at a low level in order to help prevent the proliferation of microbes within the room such as bacteria and mold, which tend to prefer damp conditions in order to replicate.

3. Surfaces (including floors, walls, equipment, etc.) are cleaned and monitored on a regular basis for viable counts by using specially designed contact plates that contain a growth medium, Trypticase Soy Agar (TSA) and Sabouraud Dextrose Agar (SDA). The TSA is a growth medium designed for bacteria and the SDA and a growth medium designed for mold and yeast. TSA and SDA are typically incubated at different temperatures, TSA at 30-35°C which is mainly the optimal growing temperature for most environmental bacteria, and 20-25°C which is the optimal growing temperature for most mold and yeast species.

Two methods of Air sampling in a Clean Room

a. Air Samplers (active air sampling) – Air samplers draw in predetermined volumes of air. The air is drawn over a sterile media plate (SCDA, Soyabean Casein Digest Agar), which is later incubated to reveal the number of viable organisms per cubic feet or liter. Currently agar impaction is the method of choice throughout the industries using a specially designed and calibrated piece of equipment such as the biological air sampler, AccuBas AX1™ – Microxpress, which holds the media plate under a perforated lid and draws in a known amount of air one can accurately measure the amount of viable bacteria within the air.

AccuBas AX1™

b. Settling plates (passive air sampling) – Petri dishes, containing sterile growth media (SCDA) are exposed to the environment for a specific period of time, usually between 30-60 minutes but can be exposed up to four hours before compromising the integrity of the media itself. Viable microorganisms which settle onto the media surface will grow after the plates are incubated. However, passive air sampling is tending to be phased out because it does not reflect microbial contamination with an accurately measured volume of air.

Two methods for surface monitoring in a Clean Room

i. Contact Plates – as mentioned above are special Petri dishes, Kontact™ plates, 55 mm – Microxpress which contain sterile growth medium (SCDA) prepared in a manner so the surface of the media protrudes above the rim of the plate. The contact plate is pressed against any flat surface the needs to be sampled. Any viable microorganisms on the surface will stick to the agar surface and will grow upon proper incubation. This technique reveals the number of viable microorganisms on a surface.

Kontact™ plates, 55 mm

ii. Sterile Swabs – are sterile and stored in a suitable sterile liquid. Different types of Sterile Swabs are SteriStik™ – Microxpress, gamma irradiated sterile cotton swab with polypropylene stick, SteriTrans™ – Microxpress, gamma irradiated sterile transport tube with a cotton swab with polypropylene stick and EMswab™ – Microxpress, gamma irradiated sterile transport tube with a cotton swab and polypropylene stick along with sterile normal saline. These are used to rub over the test surface. The microbiologist can determine the type of microorganisms on the swab by sub-culturing it to media. Swabs are used for surfaces that are not flat, and can be used to sample hard to reach areas of machinery that could not be sampled with a contact plate. Swabbing is more qualitative than quantitative.

SteriStik™

SteriTrans™

EMswab™

Mean values for the number of colonies (cfu) for testing of surfaces

	Acceptable	Unacceptable
Total viable counts	0 – 10/cm^2	>10/cm^2
Enterobacteriaceae	0 – 1/cm^2	>1/cm^2

Many surface sampling methods are recognized by ISO 18593. However, not all methods are suitable in all situations. Contact plates are suitable for semi-quantitative sampling but not for specific pathogen detection in environmental samples. Swab sticks are suitable for semi-quantitative sampling and for the detection (presence or absence tests) of specific pathogens but not for foodborne illness investigations where more powerful detection methods are required.

How Personnel are monitored in a Clean Room

Personnel in critical areas may be monitored for microbial contamination utilizing the *contact plates*. The contact plates

monitor areas of the body that may interact with the sterile field or product exposure areas. These may include gloved hands, forearms, or other areas. Personnel monitoring is a good indication of how well personnel are gowning when they enter the clean room. Many companies utilize this testing for proficiency based training programs for clean room personnel.

How Clean Room are monitored

Environmental organisms recovered from manufacturing areas should be identified to show what organisms are present, and what may be contaminating the product. Knowing these facts will provide the company with important information in monitoring and preventing potential future contamination drawbacks.

Microbial identification is another service which E/M associates incorporated company offers. It is important that proper disinfectants are used on a routine basis to keep the level of house organisms in check. A disinfectant study should be implemented to demonstrate the effectiveness of the sanitizers used against "house organisms". This effectiveness study exhibits to regulatory agencies that the company is using the correct sanitizer at appropriate dilutions and contact times to combat potential contamination.

There are many factors one should consider when determining what locations in a clean room to sample. These factors include potential product exposure areas, processing parameters, equipment design, HEPA locations, and validation criteria. Frequency of monitoring depends on product and quality requirements. Sampling frequency may be subject to change depending on trending analysis and changes in equipment, processing or number of personnel. A sampling plan describing procedures and identifying sample sites, sampling numbers and sample frequency should be developed and properly documented in order to demonstrate that there is a constant level of control over the environment within the clean room facilities.

Alert and Action levels should be implemented based on your products, the intended use of the clean room and the classification of the clean room. There are three classifications for clean room facilities and each has its own Alert and action levels. The three classifications are ISO 5 (Grade A), ISO 7 (Grade C) and ISO 8 (Grade D). ISO 5, having the lowest Alert and Action levels of environmental contaminants and ISO 8 having the highest.

An Alert is an indication that the level of microbial growth may me reaching an undesirable level. If an Action Level occurs, sanitation of the area should begin immediately as well as an assessment of what caused the Action level to be reached. Monitoring should be increased until microbial counts return to a desired level.

A well-developed Environmental Monitoring Program is a proactive way to assure the cleanliness of the manufacturing facility is maintained.

Current Guidelines for Viable and Non-Viable Specifications within Clean Rooms

There are differences across the major guidance documents regarding the limits for both viable and non-viable particulates. The ISO 14644-1 deals entirely with non-viable particulate sizes for various clean-room classifications. The European Commission Annex one and the United States Pharmacopeia <1116> focus on both viable and non-viable particulates within grades A (class 100), B (class 1000), C (class 10,000), and D (class 100,000).

ISO 14644-1 Cleanroom Classifications

Generally a "clean room" is an enclosed room that has equipment which controls the amount of particulate matter in the air by using air pressure and filters. To meet requirements of a "clean room" as defined by Federal Standard 209E and newer ISO Standards, all clean rooms must not exceed a particulate count as specified in the air cleanliness class.

As of November 29th 2001, the Federal Standard 209E has been replaced with ISO 14644-1. This method is simple; the number assigned to the class is the classification that the room must be designed to. In the Federal Standard 209E, Class 1 was the cleanest with zero bioburden in the clean room, however, in the new ISO 14644-1 Standard, Class 3 is the cleanest. This difference is because the federal standards were measured in cubic feet and the ISO standards are measured in cubic meters.

CLEAN ROOM FACTS

What is measured in the air?

Class 3, 4, and 5 are based on the maximum number of 0.1 and 0.5 micron particles that are permitted in a cubic foot of air approaching any work operation within the room. Class 6, 7 and 8 are based on the number 0.5 micron particles.

What is a micron?

To give you an idea of what is being measured; one micron is one-hundredth the width of a human hair. The smallest particle seen with the naked eye is a 10 micron particle.

Clean rooms can control 0.01 and 0.05 micron particles!

Where do these particles come from?

The clean room is under positive pressure, keeping out new particles from coming in. So where do they come from? Micro-organisms come from people in the room and other particulates from the processes in the room. Microbes come from skin cells of humans. We shed our outermost layer of skin every 24 hours that is 1 billion flakes every 24 hours! One flake is about 35 microns.

What are the clean room classifications?

The ISO 14644-1 has changed these numbers to simple classes:

ISO 14644-1 Cleanroom Standards							
Classification	Maximum Particles/m^3						FED STD 209E Equivalent
	≥0.1µm	≥0.2µm	≥0.3µm	≥0.5µm	≥1µm	≥5µm	
ISO 1	10	2.37	1.02	0.35	0.083	0.0029	
ISO 2	100	23.7	10.2	3.5	0.83	0.029	
ISO 3	1,000	237	102	35	8.3	0.029	Class 1
ISO 4	10,000	2,370	1,020	352	83	2.9	Class 10
ISO 5	100,000	23,700	10,200	3,520	832	29	Class 100
ISO 6	1.0×10^6	237,000	102,000	35,200	8,320	293	Class 1,000
ISO 7	1.0×10^7	2.37×10^6	1,020,000	352,000	83,200	2,930	Class 10,000
ISO 8	1.0×10^8	2.37×10^7	1.02×10^7	3,520,000	832,000	29,300	Class 100,000
ISO 9	1.0×10^9	2.37×10^8	1.02×10^8	35,200,000	8,320,000	293,000	Room Air

The now defunct Federal Standard 209E classifications are as follows:

US FED Standard 209E Cleanroom Standards						
Classification	Maximum Particles/ft^3					ISO 14644-1 Equivalent
	≥0.1µm	≥0.2µm	≥0.3µm	≥0.5µm	≥5µm	
1	35	7.5	3	1	0.007	ISO 3
10	350	75	30	10	0.07	ISO 4
100	3,500	750	300	100	0.7	ISO 5
1,000	35,000	7,500	3,000	1,000	7	ISO 6
10,000	350,000	75,000	30,000	10,000	70	ISO 7
100,000	3.5×10^5	750,000	300,000	100,000	700	ISO 8
US Fed. Standard 209E was officially cancelled by the General Services Administration of the US Dept. of Commerce November 29, 2001, but is still widely used.						

The British Standard BS5295 Classifications are:

BS 5295 Cleanroom Standards					
Classification	≥0.5µm	≥1µm	≥5µm	≥10µm	≥25µm
Class 1	3,000		0	0	0
Class 2	300,000		2,000	30	
Class 3		1,000,000	20,000	4,000	300
Class 4			200,000	40,000	4,000
BS 5295 *Class 1* also requires that the greatest particle present in any sample does not exceed 5µm.					

The GMP EU Classifications are:

GMP EU Classification				
Classification	Maximum Particles/m^3			
	At Rest		In Operation	
	0.5µm	5µm	0.5µm	5µm
Class A	3,520	20	3,500	20
Class B	3,520	29	352,000	2,900
Class C	352,000	2,900	3,520,000	29,000
Class D	3,520,000	29,000		

Parameters for maintaining classified areas and application of Environmental Monitoring:

Air Quality: A properly designed clean room must have a high rate of air changes to scrub the room of particulates. A Class 5 room can have an air change rate of 400 to 600 times per hour while a class 7 room can change at 50 to 60 changes per hour.

Airflows: Only HEPA-filtered air should enter the cleanroom and ante-room from HEPA filters installed at the 'terminal 'point, i.e. in ceilings. HEPA filters should be proprietary cleanroom modules in purpose-designed ceiling frames. These modules are available in fan-assisted configuration with fan-speed control, or non-fan-assisted; and should operate at a velocity of > 0.4 m/s and < 0.6 m/s. The location of HEPA filters and return air grilles should create air movement from the designated 'clean' zone of the room to the 'less-clean' zone. Return air grilles should be at low level.

Room air-change rate: Air supply to the cleanroom should provide a room air-change rate of > twenty (20) per hour. Air cleanliness will be enhanced by higher air-change rates, e.g. > 30/h typically, heat load calculations result in such a rate. When the doors are open, the supply-air volume should maintain an outward flow of air.

Room pressures: Cleanroom air pressure should be higher than that of the ante-room (waiting or changing room) and the surrounding uncontrolled area. The pressure gradient between these zones should be ≥ 15 Pa. Typical values are:

Cleanroom: 30 Pa positive pressure

Ante-room: 15 Pa positive pressure

Suitable manometers should be installed outside the ante-room to indicate room pressures of the facility.

Testing and Certification: Once the room is completed, most specifications call for testing and certification. Some requirements state that the room should be tested annually also. Testing is usually conducted by an independent testing agency using the ISO Standards. It is also imperative for the owner to purchase a clean room monitor in order to determine the daily status of the room.

Data collection and review: Each month, the site list and results should be reviewed by lab management to ensure sampling is conducted as per the SOP, that out-of-specification results have been addressed, and that corrective actions were effective and verified. This review also allows identification of developing trends. All data should be reviewed in a historical context and relevant corrective/preventive actions should be included in the monthly review.

Environmental Monitoring - Applications

Applications include the manufacture of bio-pharma products, sterile pharmaceuticals, clinical and health-care systems, research institutes, food industries, cosmetics industry, electronics components, medical devices and implants and the maintenance of sensitive or critical systems. GMP codes and specifications for many applications require that the critical process be performed in a Class 5 laminar flow cabinet installed in a Class 7 cleanroom.

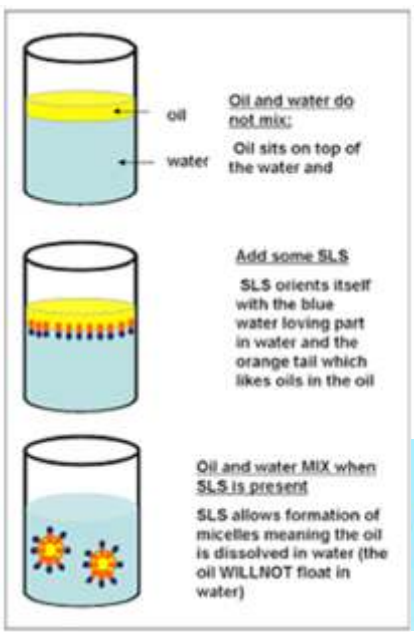
Environmental monitoring and microbiological testing play a critical role in ensuring the safety of products and the efficacy of drugs and biologics by preventing their contamination with microbes. Microbiological testing alone does not provide complete or absolute assurance of absence of microbial contamination. However, such testing combined with a robust environmental monitoring program and the use of validated manufacturing processes provides a high degree of assurance of the microbial safety of products. To build microbiological quality, it is important to understand the ways to prevent contamination and risks of microbial growth in intermediate products, components, active biological ingredients, final product. Manufacturing processes (sterile or non-sterile) should be based on factors such as risk analysis, target population for the product, and the route of instillation.

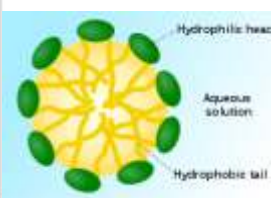
An effective laboratory EMP will help verify cleaning and sanitation effectiveness, employee practices, and air quality in the laboratory. The Environmental monitoring program also incorporates direction when there is an out-of-specification result and the appropriate investigative process. These practices ensure accountability and quality results that clientele can depend on.

Surfactant-types

The word "Surfactant" is a contraction of the three words "Surface Active Agents." What is a surfactant? Surfactants are materials that lower the surface tension (or interfacial tension) between two liquids or between a liquid and a solid. In the general sense, any material that affects the interfacial surface tension, can be considered a surfactant, but in the practical sense, surfactants may act as wetting agents, emulsifiers, foaming agents, and dispersants, antiseptics, and disinfectants. As antimicrobials, they alter the energy relationship at interfaces.

Surface active agents play an important role as cleaning, wetting, dispersing, emulsifying, foaming and anti-foaming agents in many practical applications and products, including: paints, emulsions adhesives, inks, biocides (sanitizers), shampoos, toothpastes, firefighting (foams), detergents, insecticides, deinking of recycled papers, ski waxes, spermicides (nonoxynol-9).





In the bulk aqueous phase, surfactants form masses, such as micelles, where the hydrophobic tails form the core and the hydrophilic heads are immersed in the surrounding liquid. Other types of structures can also be formed, such as spherical micelles or lipid bilayers. The shape of the molecules depends on the balance in size between hydrophilic head and hydrophobic tail. A measure of this is the HLB, Hydrophilic-lipophilic balance. Higher HLB surfactants (>10) are hydrophilic ("water loving") and form O/W (Oil-in-water) emulsions. Lipophilic surfactants possess low HLB values (1-10) and form W/O (water-in-oil) emulsions. Dish detergents, surfactants for emulsion polymerization, and the following example (SLS = Sodium Lauryl Sulfate) are high HLB surfactants.

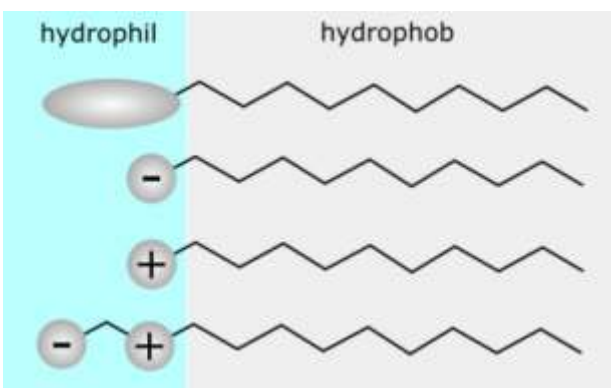
The dynamics of surface active agent adsorption is of great importance for practical applications such as in emulsifying or coating processes as well as foaming, where bubbles or drops are rapidly generated and need to be stabilized.

As the interface is created, the adsorption is limited by the diffusion of the surfactant to the interface, which can result in the kinetics being limited. These energy barriers can be due to steric or electrostatic repulsions; steric repulsions form the basis of how dispersants function. Surface rheology of surfactant layers, are important to the stability of foams and emulsions.

Most surfactants' "tails" are fairly similar, consisting of a hydrocarbon chain, which can be branched, linear, or aromatic. Fluorosurfactants have fluorocarbon chains. Siloxane surfactants have siloxane chains. Recent advances in surfactant technology has seen the development of mixed chains or/and complex structures.

There are 4 types of surfactants with a brief review of each as follows. These classifications are based upon the composition of the polarity of the head group: nonionic, anionic, cationic, amphoteric.

Surfactant classification according to the composition of their head: nonionic, anionic, cationic, amphoteric.



A non-ionic surfactant has no charge groups in its head. The head of an ionic surfactant carries a net charge. If the charge is negative, the surfactant is more specifically called anionic; if the charge is positive, it is called cationic. If a surfactant contains a head with two oppositely charged groups, it is termed zwitterionic. Commonly encountered surfactants of each type are listed as follows. A complete compendium can be found on ULProspector.com.

Non-ionic surfactant

Many long chain alcohols exhibit some surfactant properties. Some examples of non-ionic surfactants include:

Trade name	Structure/name	Applications
Triton™ X-100	Polyoxyethylene glycol octylphenol ethers: C8H17–(C6H4)–(O-C2H4)1–25–OH	Wetting agent - coatings
Nonoxynol-9	Polyoxyethylene glycol alkylphenol ethers: C9H19–(C6H4)–(O-C2H4)1–25–OH	Spermacide
Polysorbate	Polyoxyethylene glycol sorbitan alkyl esters	Food ingredient
Span®	Sorbitan alkyl esters	Polishes, cleaners, fragrance carriers
Poloxamers, Tergitol™, Antarox®	Block copolymers of polyethylene glycol and polypropylene glycol	Various

Non-ionic surfactants

Nonionic surfactants are also found in many cleaning products, including carpet products. Nonionics have no charge on their

hydrophilic end, which helps make them superior oily soil emulsifiers.

Some nonionics are high foamers (like anionics), while others do not generate much foam. Because of their lower foam profile and strong emulsifying potential, these surfactants are the preferred choice when formulating extraction cleaners and pre sprays.

However, unlike anionic surfactants, nonionics are thick liquids or syrups that are sticky or "gooey" to the touch. When left in the carpet, nonionic surfactants are the primary contributors to rapid resoiling.

Even with that being the case, their importance as cleaners outweighs this negative, and the cleaner or technician must take care to remove as much of the detergent residue as possible from the carpet in order to get the cleaning benefits of nonionics without their negatives.

Nonionic surfactants include:
- Ethoxylates
- Alkoxylates
- Cocamide

Based on the position of the hydrophobic moiety in the molecule, surfactants are classified as anionic or cationic.

An-ionic surfactant

Anionic surfactants contain anionic functional groups at their head, such as sulfonate, phosphate, sulfate and carboxylates. Alkyl sulfates include ammonium lauryl sulfate, sodium lauryl and the related alkyl-ether sulfates sodium laurethsulfate, also known as sodium lauryl ether sulfate (SLES), and sodium myrethsulfate. These are the most common surfactants and comprise the alkyl carboxylates (soaps), such as sodium stearate. The stearates comprise >50% of the global usage of surfactants. Many of these find utilization in emulsion polymerization. Other anionic surfactants include dioctyl sodium sulfosuccinate (DOSS), perfluorooctanesulfonate (PFOS), linear alkylbenzene sulfonates (LABs) and perfluorobutanesulfonate, as well as alkyl-aryl ether phosphates. More specialized species include sodium lauroylsarcosinate and carboxylate-based fluorosurfactants such as perfluorononanoate, perfluorooctanoate (PFOA or PFO).

Trade name	Structure/name	Applications
PENTEX® 99	Dioctyl sodium sulfosuccinate (DOSS)	Wetting agent – coatings, toothpaste
PFOS	Perfluorooctanesulfonate (PFOS)	Scotchguard™, Skydrol™
Calsoft®	Linear alkylbenzene sulfonates	Laundry detergents, dishwasher detergents
Texapon®	Sodium lauryl ether sulfate	Shampoos, bath products
Darvan®	Lignosulfonate	Concrete plasticizer, plasterboard, DMSO
N/A	Sodium stearate	Handsoap, HI&I productsv

Generally, they make a lot of foam when agitated. Also, they tend to be flaky or powdery when dry, not sticky like other surfactants. Soaps are dipolar anionic detergents with the general formula RCOONa/K, which dissociate in water into hydrophilic K+ or Na+ ions and lipophilic fatty acid ions. Because NaOH and KOH are strong bases (whereas most fatty acids are weak acids), most soap solutions are alkaline (pH 8–10) and may irritate sensitive skin and mucous membranes. Soaps emulsify lipoidal secretions of the skin and remove, along with most of the accompanying dirt, desquamated epithelium and bacteria, which are then rinsed away with the lather. The antibacterial potency of soaps is often enhanced by inclusion of certain antiseptics, eg, hexachlorophene, phenols, carbanilides, or potassium iodide. They are incompatible with cationic surfactants.

Cationic surfactant

Cationic surfactants are comprised of a positively charged head. Most of cationic surfactants find use as anti-microbials, anti-fungals, etc. in HI&I (Benzalkonium chloride (BAC), Cetylpyridinium chloride (CPC), Benzethonium chloride (BZT). The cationic nature of the surfactants is not typically consistent with the world of non-ionic and anionic charges, and they disrupt cell membranes of bacteria and viruses. Permanently charged quaternary ammonium cations include: Alkyltrimethylammonium salts: cetyltrimethylammonium bromide (CTAB) and cetyltrimethylammonium chloride (CTAC).

Quaternary ammonium compounds

Quaternary ammonium compounds (QACs) were first introduced in 1917 and are probably the best known cationic surface-active agents. Cationic surfactants are used as the active ingredient in disinfectants.

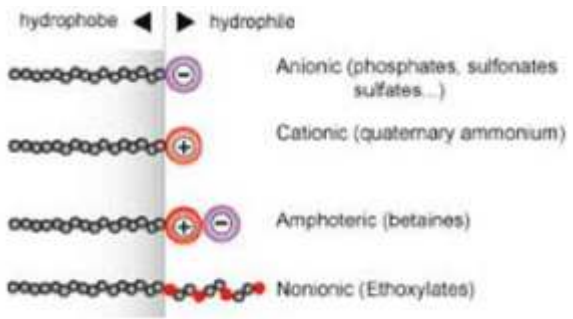
Cationic detergents are a group of alkyl- or aryl-substituted quaternary ammonium compounds (eg, benzalkonium chloride, benzathonium chloride, cetylpyridinium chloride) with an ionizable halogen, such as bromide, iodide, or chloride. The major site of action of these compounds appears to be the cell membrane, where they become adsorbed and cause changes in permeability. The activity of older quaternary ammonium compounds is reduced by hard water and by porous or fibrous materials (eg, fabrics, cellulose sponges) that adsorb them. They are also inactivated by anionic substances (eg, soaps, proteins, fatty acids, phosphates). Therefore, they are of limited value in the presence of blood and tissue debris. However, newer dialkyl quaternary ammonium compounds (fourth generation, including dodecyl dimethyl ammonium bromide, dioctyl dimethyl ammonium bromide, etc) purportedly remain active in hard water and are tolerant of anionic residues. Fifth-generation quaternaries are mixtures of the fourth generation with the second generation and demonstrate greater biocidal activity under conditions of high soil load, making them useful disinfectants in barns and footbaths. Quaternary ammonium compounds are effective against most bacteria, enveloped viruses, some fungi (including yeasts), and protozoa but not against nonenveloped viruses, mycobacteria, and spores. Aqueous solutions of 1:1,000 to 1:5,000 have good antimicrobial activity, especially at slightly alkaline pH, and are commonly used for disinfection of noncritical instruments and hard surface cleaning. When applied to skin, they may form a film under which microorganisms can survive, which limits their reliability as antiseptics. Concentrations >1% are injurious to mucous membranes.

Octenidinedihydrochloride is a cationic surfactant used increasingly in Europe as an alternative to quaternaries, chlorhexidine, and iodophores for skin, mucous membrane, and wound antisepsis.

Zwitterionic surfactants

Zwitterionic (amphoteric) surfactants have both cationic and anionic centers attached to the same molecule. The anionic part can be variable and include sulfonates, as in the sultaines CHAPS (3-[(3-Cholamidopropyl)dimethylammonio]-1-

propanesulfonate). Betaines such as cocamidopropyl betaine have a carboxylate with the ammonium. The cationic part is based on primary, secondary, or tertiary amines or quaternary ammonium cations. Zwitterionic surfactants are often sensitive to pH and will behave as anionic or cationic based on pH. Fast dry ("coacervation") latex traffic paints are based on this concept, with a drop in pH triggering the latex in the paint to coagulate.



Representation of the 4 types of surfactants.

In pharmacy

A wetting agent is a surfactant that, when dissolved in water, lowers the advancing contact angle, aids in displacing an air phase at the surface, and replaces it with a liquid phase. Examples of application of wetting to pharmacy and medicine include the displacement of air from the surface of sulfur, charcoal, and other powders for the purpose of dispersing these drugs in liquid vehicles; the displacement of air from the matrix of cotton pads and bandages so that medicinal solutions can be absorbed for application to various body areas; the displacement of dirt and debris by the use of detergents in the washing of wounds; and the application of medicinal lotions and sprays to surface of skin and mucous membranes.

Pharmaceutical forms

Human body produce different types of surfactant in different parts of body or it's organs for different purposes. Pulmonary surfactant is produced in lungs in order to facilitate breathing by increasing total lung capacity, TLC, and lung compliance. In respiratory distress syndrome or RDS surfactant replacement therapy help patients have normal respiration after using pharmaceutical forms of the surfactants. One of the most important pharmaceutical pulmonary surfactant is Survanta (beractant) or its generic form Beraksurf produced by Abbvie and Tekzima respectively.

Biosurfactants

Biosurfactants are surface-active substances synthesised by living cells. Interest in microbial surfactants is due to their diversity, environmentally friendly nature, possibility of large-scale production, selectivity, performance under extreme conditions, and potential applications in environmental protection.A few of the popular examples of microbial biosurfactants includes Emulsan produced by Acinetobacter calcoaceticus,Sophorolipids produced by several yeasts belonging to candida and the starmerella clade, and Rhamnolipid produced by Pseudomonas aeruginosa etc.

Biosurfactants enhance the emulsification of hydrocarbons, have the potential to solubilise hydrocarbon contaminants and increase their availability for microbial degradation. The use of chemicals for the treatment of a hydrocarbon polluted site may contaminate the environment with their by-products, whereas biological treatment may efficiently destroy pollutants, while being biodegradable themselves. Hence, biosurfactant-producing microorganisms may play an important role in the accelerated bioremediation of hydrocarbon-contaminated sites. These compounds can also be used in enhanced oil recovery and may be considered for other potential applications in environmental protection. Other applications include herbicides and pesticides formulations, detergents, healthcare and cosmetics, pulp and paper, coal, textiles, ceramic processing and food industries, uranium ore-processing, and mechanical dewatering of peat.

Several microorganisms are known to synthesise surface-active agents; most of them are bacteria and yeasts. When grown on hydrocarbon substrate as the carbon source, these microorganisms synthesise a wide range of chemicals with surface activity, such as glycolipid, phospholipid, and others. These chemicals are synthesised to emulsify the hydrocarbon substrate and facilitate its transport into the cells. In some bacterial species such as Pseudomonas aeruginosa, biosurfactants are also involved in a group motility behavior called swarming motility.

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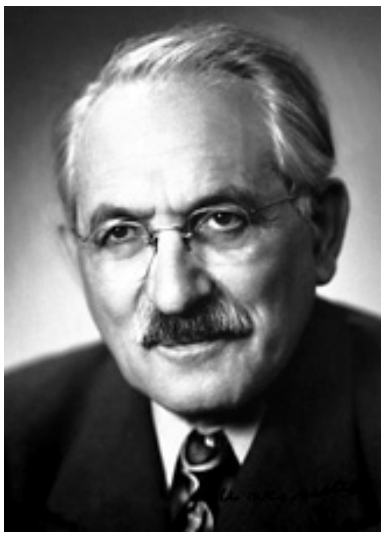
Selman Abraham Waksman



Selman Abraham Waksman (1888-1973) was born in the rural Ukrainian town of Novaya Priluka. The town and its nearby villages were surrounded by a rich black soil that supported abundant agricultural life. Although Waksman did not do much farming as a child, the chemistry of the fertile soil incited a curiosity in him that would eventually influence the direction of his future endeavors.

In 1910, after completing his matriculation diploma, Waksman followed the example of several relatives and migrated to the United States. He worked for a few years on a family farm in New Jersey and then enrolled in Rutgers College. There he studied bacteria in culture samples from successive soil layers, which resulted in his introduction to the actinomycetes. These bacteria became an enduring interest that Waksman studied for both his Master's and Doctorate degrees and on which he would eventually become a major expert.

After receiving his doctorate from the University of California, Berkeley, in 1918, Waksman secured a position at the Rutgers Bacteriology Department where he continued his research on soil microflora. Several years later, a young French biologist named Rene Dubois joined his laboratory. By 1927, Dubois was studying the one-on-one effects of soil organisms in decomposing cellulose and was beginning an approach that would lead to modern antibiotics. In collaboration with Oswald Avery at the Rockefeller Institute Hospital, Dubois isolated a soil bacterium that could attack the capsular polysaccharide of *Streptococcus pneumoniae*. This discovery inspired Waksman to look for more pre-existing antibacterial organisms in soil samples.

By 1940, Waksman and H. Boyd Woodruff had devised a technique for identifying natural substances with antibacterial properties. The screening was done by looking for growth inhibition zones around single colonies of systematically isolated soil microbes, grown under a variety of culture conditions, and then testing the inhibition on specifically targeted pathogenic bacteria.

The first true antibiotic Waksman identified was from *Actinomyces antibioticus*, a member of the actinomycetes family. The microbe produced a substance, actinomycin, that had both bacteriostatic and bactericidal properties. Waksman and Woodruff determined that actinomycin could be separated with petroleum ether into two constituents, an orange-red colored actinomycin A and a colorless actinomycin B. Actinomycin A had strong bacteriostatic and bactericidal properties whereas actinomycin B displayed only bactericidal characteristics.

In the *Journal of Biological Chemistry* (JBC) Classic reprinted here, Waksman and Max Tishler, who was featured in a previous JBC Classic, describe the nature and properties of actinomycin A. The pair found that actinomycin is a quinine-like pigment with a molecular formula of either $C_{41}H_{56}N_8O_{11}$, $C_{37}H_{50}N_7O_{10}$, or $C_{36}H_{49}N_7O_9 \cdot ½H_2O$. The compound is highly active against various gram-positive bacteria but less active against gram-negative organisms. Unfortunately, Waksman and Tishler also discovered that actinomycin is extremely toxic to experimental animals and thus of little therapeutic value.

Waksman followed this initial failure with a comprehensive program of screening actinomycetes for their ability to produce antibacterials. He identified more than 20 new natural inhibitory substances, including streptomycin and neomycin, and proposed the now standard term “antibiotics” for this class of natural growth inhibitors.

With his discovery of streptomycin in 1944, Waksman initiated a collaboration with Merck and Company. Tishler led the microbiological group that developed the fermentation process for producing bulk quantities of streptomycin. As a result of his success in developing manufacturing processes for products such as streptomycin, riboflavin, cortisone, vitamin B_{12}, and penicillin, Tisher eventually became the first president of the Merck Sharp & Dohme Research Laboratory Division of Merck & Co. Inc. and remained there until 1970, running the research programs.

Waksman patented and licensed his promising antibiotics, but rather than keeping the money for himself, he gave 80% of his patent earnings to Rutgers University. In 1951 he established an Institute of Microbiology in association with Rutgers, the construction of which was completed in 1954. The institute was endowed and supported by the generous assignment of 80% of Waksman's streptomycin patent royalties to Rutgers. Waksman's philanthropic nature was further evident when he established the Foundation for Microbiology in 1951 and assigned one-half of his 20% personal royalties for its support.

During his lifetime, Waksman received some 66 awards and 22 honorary degrees for his scientific work. He was elected to the National Academy of Sciences in 1942. However, Waksman's greatest honor came when he won the Nobel Prize in physiology or medicine in 1952 “for his discovery of streptomycin, the first antibiotic effective against tuberculosis.” This distinction earned him the title of “Father of Antibiotics” and gained him well deserved recognition for his philanthropy and contributions to science and medicine.

Funny quotes

- My son wanted to know what it's like to be married. I told him to leave me alone and when he did I asked him why he was ignoring me.

- My wife's cooking is so bad we usually pray after our food.

- My wife told me she needs more space. I said no problem and locked her out of the house.

- A 60 year old millionaire is getting married and throws a big wedding reception.
  His friends are quite jealous and in a quiet moment one of them asks him how did he land such a hot 23 year old beauty?
  "Simple," grins the millionaire, "I faked my age."
  His friends are really amazed and ask him how much he said.
  "Well", he replied. "I said I was 87!"

- A little boy looks at his mum at a wedding and says, "Mummy, why is the girl dressed all in white?"
  His mum answers, "The girls is called a bride and she is in white because she's very happy and this is the happiest day of her life."
  The boy nods and then says, "OK, and why is the boy all in black?"

- An elderly couple talk in the evening:
  "Honey, I'm so sorry that I let out my anger at you so often. How do you manage to stay so calm with my foul moods?"
  "I always go and clean the toilet when that happens."
  "And that helps?"
  "Yes, because I'm using your toothbrush."

- Honey, do you think I gained weight?
  -
  No, I think the living room got smaller.

- Honey, what will you give me for our 25th anniversary?
  -
  A trip to Thailand?
  -
  Wow, that's awesome, and for our 50th anniversary?
  -
  Then I pick you up again.

- A man noticed his credit card has been stolen - but he never reported it. The thief was still spending considerably less than his wife."

- A man and his wife have to go to a doctor. The doctor asks, "Do you share the same blood group?"
  The husband replies, "We must by now. She's been sucking my blood for years."

- Arguing with the wife is a lot like trying to read the Terms of Use on the internet. In the end you just give up and go "I Agree".

Bifidobacteria

Bifidobacteria are a group of bacteria that normally live in the intestines. They can be grown outside the body and then taken by mouth as medicine.

Bifidobacteria are commonly used for diarrhea, constipation, an intestinal disorder called irritable bowel syndrome, for preventing the common cold or flu, and lots of other conditions, but there is no good scientific evidence to support many of these uses.

How effective is it?

Natural Medicines Comprehensive Database rates effectiveness based on scientific evidence according to the following scale: Effective, Likely Effective, Possibly Effective, Possibly Ineffective, Likely Ineffective, Ineffective, and Insufficient Evidence to Rate.

The effectiveness ratings for BIFIDOBACTERIA are as follows:

Possibly effective for...

- **Constipation.** Early research shows that taking the bifidobacteria species Bifidobacterium breve can reduce constipation in children. Other research shows that taking Bifidobacterium animalis subsp. lactis BB-12 reduces constipation in adults with mild constipation. Some research shows that taking Bifidobacterium longum BB536 reduces constipation in some adults. But conflicting results exist.
- **Helicobacter pylori (H. pylori) infection.** Taking probiotics containing bifidobacteria and lactobacilli bacteria can reduce side effects such as diarrhea and taste disturbances caused by medication used to treat Helicobacter pylori infections.
- **Irritable bowel syndrome (IBS).** Taking probiotics appears to help with symptoms of IBS. However, the specific type of probiotic might be important. Taking the bifidobacteria species Bifidobacterium infantis 35624 (Align or Bifantis, Proctor & Gamble) for 8 weeks can reduce symptoms of IBS. Also, taking a specific product containing species of Bifidobacterium, Lactobacillus, and Streptococcus (VSL#3) seems to decrease bloating in people with IBS. However, taking a combination of Lactobacillus paracasei subsp. paracasei, Lactobacillus acidophilus La5, and Bifidobacterium lactis BB-12 does not improve IBS symptoms.
- **A complication after surgery for ulcerative colitis called pouchitis.** Taking a specific product containing a combination of Bifidobacterium, Lactobacillus, and Streptococcus (VSL#3) by mouth seems to help prevent pouchitis after surgery for ulcerative colitis.
- **Airway infections.** Research shows that using probiotics containing bifidobacteria might help prevent airway infections such as the common cold in otherwise healthy people. But the specific type of probiotic seems be important. Some research shows that taking Bifidobacterium bifidum reduces the number of college students who experience a cold or the flu. But taking Bifidobacterium longum subsp. infantis doesn't seem to work in these people. Other research shows that taking a combination product containing Lactobacillus acidophilus and Bifidobacterium (HOWARU Protect) with milk helps prevent cold and flu symptoms in young children who attend day-care centers. Another study shows that taking a product containing Lactobacillus acidophilus and Bifidobacterium bifidum (Infloran, Berna) reduces the risk of colds in school-aged children. But taking the bifidobacteria species Bifidobacterium animalis subsp. lactis does not reduce the risk of airway infections in hospitalized children and teens.
- **Diarrhea in infants (rotaviral diarrhea).** Taking Bifidobacterium bifidum seems to help prevent rotaviral diarrhea when used with other bacteria such as Streptococcus thermophiles or Bifidobacterium animalis subsp. lactis BB-12.
- **Traveler's diarrhea.** Taking Bifidobacterium seems to help prevent traveler's diarrhea when used with other bacteria such as Lactobacillus acidophilus, Lactobacillus bulgaricus, or Streptococcus thermophilus.
- **Ulcerative colitis.** Research shows that taking specific products containing combinations of Bifidobacterium, Lactobacillus, and Streptococcus (VSL#3) or Bifidobacterium breve, Bifidobacterium bifidum, and Lactobacillus acidophilus (Yakult Co., Japan) helps control symptoms and prevent their recurrence in people with ulcerative colitis.

Possibly ineffective for...

- **Diarrhea caused by antibiotics.** A large study shows that taking a combination of Bifidobacterium bifidum, Bifidobacterium lactis, and Lactobacillus acidophilus does not prevent diarrhea in people taking various antibiotics such as penicillin. Also, taking Bifidobacterium longum does not seem to prevent diarrhea in people taking the antibiotic clindamycin. But one early study shows that taking Bifidobacterium longum reduces stool frequency and stomach discomfort in people taking the antibiotic erythromycin.
- **Diarrhea due to an infection with the bacteria Clostridium difficile.** A large study shows that taking a combination of Bifidobacterium bifidum, Bifidobacterium lactis, and Lactobacillus acidophilus does not reduce diarrhea in elderly people with Clostridium difficile infection.
- **Mortality of premature babies.** Adding Bifidobacterium breve to infant formula does not reduce the risk of death in premature babies.
- **Infant development.** Giving formula containing Bifidobacterium longum BL999 plus prebiotics, or giving Bifidobacterium longum BB536 plus Lactobacillus rhamnosus or Lactobacillus paracasei, does not seem to improve growth in infants.
- **Blood infection (sepsis).** Adding Bifidobacterium breve to infant formula does not reduce the risk of sepsis in premature babies.

Insufficient evidence to rate effectiveness for...

- **Scaly, itchy skin (eczema).** Some research shows that giving Bifidobacterium animalis subsp. lactis BB-12 by mouth reduces eczema severity in infants. However, giving Bifidobacterium longum BL999 along with Lactobacillus rhamnosus does not seem to prevent eczema in infants with a family history of the condition.
- **Celiac disease.** In children with newly diagnosed celiac disease, taking Bifidobacterium longum CECT 7347 as part of a gluten-free diet does not improve stomach and intestinal symptoms compared to diet alone.
- **Infections related to chemotherapy treatment.** Early research shows that taking specific products containing Bifidobacterium longum and Lactobacillus acidophilus (Morinaga Bifidus) or Bifidobacterium infantis, Lactobacillus acidophilus, and Enterococcus faecalis (Levenin) does not prevent yeast infections in people with leukemia who are undergoing chemotherapy.
- **High cholesterol.** Early research shows that drinking milk containing Lactobacillus acidophilus 145 and Bifidobacterium longum BB536 reduces "bad" low-density lipoprotein (LDL) cholesterol in people with high cholesterol. But it also seems to reduce "good" high-density lipoprotein (HDL) cholesterol.
- **Japanese cedar pollen allergy.** Some research shows that taking Bifidobacterium longum BB536 during pollen season might reduce nose and eye symptoms of Japanese cedar pollen allergy. But conflicting results exists. Also, this strain of bifidobacteria does not seem to reduce sneezing or throat symptoms associated with Japanese cedar pollen allergy.
- **A type of infection in the lining of the intestine caused by bacteria (necrotizing enterocolitis; NEC).** One study shows that taking Bifidobacterium infantis along with Lactobacillus acidophilus helps prevent NEC in critically ill infants. But giving formula containing Bifidobacterium breve BBG-001 to premature infants does not help prevent NEC.
- **Preventing infections after exposure to radiation.** Early research shows that antibiotic-resistant Bifidobacterium longum can help improve short-term survival in the treatment of radiation sickness. In combination with antibiotics, bifidobacteria appear to help prevent dangerous bacteria from growing and causing a serious infection.
- **Aging.**
- **Breast pain, possibly due to infection (mastitis).**
- **Cancer.**
- **Lactose intolerance.**
- **Liver problems.**
- **Lyme disease.**
- **Mumps.**
- **Replacing beneficial bacteria removed by diarrhea.**
- **Stomach problems.**
- **Other conditions.**

More evidence is needed to rate bifidobacteria for these uses.

How does it work?

Bifidobacteria belong to a group of bacteria called lactic acid bacteria. Lactic acid bacteria are found in fermented foods like yogurt and cheese. Bifidobacteria are used in treatment as so-called "probiotics," the opposite of antibiotics. They are considered "friendly" bacteria and are taken to grow and multiply in areas of the body where they normally would occur. The human body counts on its normal bacteria to perform several jobs, including breaking down foods, helping the body take in nutrients, and preventing the take-over of "bad" bacteria. Probiotics such as bifidobacteria are typically used in cases when a disease occurs or might occur due to a kill-off of normal bacteria. For example, treatment with antibiotics can destroy disease-causing bacteria, but also normal bacteria in the GI (gastrointestinal) and urinary tracts. The theory is that taking Bifidobacterium probiotics during antibiotic treatment can prevent or minimize the death of good bacteria and the take-over by bad bacteria.

Are there safety concerns?

Bifidobacteria are LIKELY SAFE for adults and children when taken by mouth appropriately. In some people, treatment with bifidobacteria might upset the stomach and intestine, causing diarrhea, bloating and gas.

Special precautions & warnings:

Pregnancy and breast-feeding: There is not enough reliable information about the safety of taking bifidobacteria if you are pregnant or breast-feeding. Stay on the safe side and avoid use.
Weakened immune system: There is some concern that "probiotics" might grow too well in people with a weak immune system and cause infections. Although this has not occurred specifically with bifidobacteria, there have been rare cases involving other probiotic species such as Lactobacillus. If you have a weakened immune system (e.g., you have HIV/AIDS or are undergoing cancer treatment), check with your healthcare provider before using bifidobacteria.

Are there interactions with medications?

Antibiotic drugs

Antibiotics are used to reduce harmful bacteria in the body. Antibiotics can also reduce friendly bacteria in the body. Bifidobacteria are a type of friendly bacteria. Taking antibiotics along with bifidobacteria might reduce the effectiveness of bifidobacteria. To avoid this interaction, take bifidobacteria products at least two hours before or after antibiotics.

Are there interactions with herbs and supplements?

There are no known interactions with herbs and supplements.

Are there interactions with foods?

There are no known interactions with foods.

What dose is used?

The following doses have been studied in scientific research:

ADULTS

BY MOUTH:

- **For constipation:** 1-10 billion cells of Bifidobacterium animalis subsp. lactis BB-12 daily for 4 weeks have been used. 2-20 billion cells of Bifidobacterium longum BB536 daily for 1 week have also been used.

- **For irritable bowel syndrome (IBS):** 1 billion cells of Bifidobacterium infantis 35624 (Align or Bifantis) daily in a malted milk drink has been used for 8 weeks. A specific probiotic product containing 450 billion cells of a combination of Bifidobacterium, Lactobacillus, and Streptococcus (VSL#3) has been used for 8 week.
- **For airway infections:** 3 billion cells of Bifidobacterium bifidum R0071 have been used daily for 6 weeks.
- **For a complication after surgery for ulcerative colitis called pouchitis:** a dose of up to 3 trillion cells consisting of species of Lactobacillus, Bifidobacterium, and Streptococcus (VSL#3) has been given once daily for up to 12 months.
- **For Helicobacter pylori treatment:** 5 billion cells of Bifidobacterium lactis and Lactobacillus acidophilus daily for 1 week has been used.
- **For ulcerative colitis:**
  - o 100 mL per day of a specific fermented milk product (Yakult, Yakult Honsha Co., Ltd.) containing at least 10 billion cells of Bifidobacterium breve, Bifidobacterium bifidum, and Lactobacillus acidophilus strains per dose has been used daily for up to 12 weeks.
  - o 3 grams of a specific combination probiotic containing living freeze-dried bacteria species including Lactobacillus, Bifidobacterium, and Streptococcus (VSL#3) has been used twice daily.

CHILDREN

BY MOUTH:

- **For constipation:** 1-100 billion cells of a specific Bifidobacterium breve powder (Yakult, Yakult Honsha Co., Ltd.) once daily for 4 weeks has been used in children aged 3-16 years.
- **For airway infections:** 120 mL of milk containing 5 billion cells each of Lactobacillus acidophilus and Bifidobacterium (HOWARU Protect, Danisco) has been used twice daily in children aged 3-5 years.
- **Diarrhea in infants (rotaviral diarrhea):** Bifidobacterium bifidum combined with Streptococcus thermophilus has been used in infants and children up to 3 years-old.
- **Ulcerative colitis:** Up to 1.8 trillion cells consisting of species of Lactobacillus, Bifidobacterium, and Streptococcus (VSL#3) has been used daily for up to 1 year in children 1-16 years-old.

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Impetigo

Impetigo is a bacterial infection that involves the superficial skin. The most common presentation is yellowish crusts on the face, arms, or legs. Less commonly there may be large blisters which affect the groin or armpits. The lesions may be painful or itchy. Fever is uncommon.

It is typically due to either *Staphylococcus aureus* or *Streptococcus pyogenes*. Risk factors include attending day care, crowding, poor nutrition, diabetes mellitus, contact sports, and breaks in the skin such as from mosquito bites, eczema, scabies, or herpes. With contact it can spread around or between people. Diagnosis is typically based on the symptoms.

Prevention is by hand washing, avoiding people who are infected, and cleaning injuries. Treatment is typically with antibiotic creams such as mupirocin or fusidic acid. Antibiotics by mouth, such as cephalexin, may be used if large areas are affected. Antibiotic-resistant forms have been found.

Impetigo affected about 140 million people (2% of the world population) in 2010. It can occur at any age, but is most common in young children. In some places the condition is also known as "school sores". Without treatment people typically get better within three weeks. Complications may include cellulitis or poststreptococcal glomerulonephritis. The name is from the Latin *impetere* meaning "attack".

Signs and symptoms

Contagious impetigo

This most common form of impetigo, also called nonbullous impetigo, most often begins as a red sore near the nose or mouth which soon breaks, leaking pus or fluid, and forms a honey-colored scab, followed by a red mark which heals without leaving a scar. Sores are not painful, but they may be itchy. Lymph nodes in the affected area may be swollen, but fever is rare. Touching or scratching the sores may easily spread the infection to other parts of the body. Skin ulcers with redness and scarring also may result from scratching or abrading the skin.

Bullous impetigo

Bullous impetigo, mainly seen in children younger than 2 years, involves painless, fluid-filled blisters, mostly on the arms, legs, and trunk, surrounded by red and itchy (but not sore) skin. The blisters may be large or small. After they break, they form yellow scabs.

Ecthyma

Ecthyma, the nonbullous form of impetigo, produces painful fluid- or pus-filled sores with redness of skin, usually on the arms and legs, become ulcers that penetrate deeper into the dermis. After they break open, they form hard, thick, gray-yellow scabs, which sometimes leave scars. Ecthyma may be accompanied by swollen lymph nodes in the affected area.

Causes

Impetigo is primarily caused by *Staphylococcus aureus*, and sometimes by *Streptococcus pyogenes*. Both bullous and nonbullous are primarily caused by *S. aureus*, with *Streptococcus* also commonly being involved in the nonbullous form.

Predisposing factors

Impetigo is more likely to infect children ages 2–5, especially those that attend school or day care. 70% of cases are the nonbullous form and 30% were the bullous form. Other factors can increase the risk of contracting impetigo such as diabetes mellitus, dermatitis, immunodeficiency disorders, and other irritable skin disorders. Impetigo occurs more frequently among people who live in warm climates.

Transmission

The infection is spread by direct contact with lesions or with nasal carriers. The incubation period is 1–3 days after exposure to *Streptococcus* and 4–10 days for *Staphylococcus*. Dried streptococci in the air are not infectious to intact skin. Scratching may spread the lesions.

Diagnosis

Impetigo is usually diagnosed based on its appearance. It generally appears as honey-colored scabs formed from dried serum, and is often found on the arms, legs, or face. If a visual diagnosis is unclear a culture may be done to test for resistant bacteria.

Differential diagnosis

Other conditions that can result in symptoms similar to the common form include contact dermatitis, herpes simplex virus, discoid lupus, and scabies.

Other conditions that can result in symptoms similar to the blistering form include other bullous skin diseases, burns, and necrotizing fasciitis.

Prevention

To prevent spread of impetigo to other people the skin and any open wounds should be kept clean. Care should be taken to keep fluids from an infected person away from the skin of a non-infected person. Washing hands, linens, and affected areas will lower the likelihood of contact with infected fluids. Sores should be covered with a bandage. Scratching can spread the sores; keeping nails short will reduce the chances of spreading. Infected people should avoid contact with others and eliminate sharing of clothing or linens.

Treatment

For generations, the disease was treated with an application of the antiseptic gentian violet. Today, topical or oral antibiotics are usually prescribed. Mild cases may be treated with bactericidal ointment, such as mupirocin. In 95% of cases, a single antibiotic course results in resolution in children. It has been advocated that topical antiseptics are not nearly as efficient as antibiotics, and therefore should be avoided.

More severe cases require oral antibiotics, such as dicloxacillin, flucloxacillin, or erythromycin. Alternatively, amoxicillin combined with clavulanate potassium, cephalosporins (first-generation) and many others may also be used as an antibiotic treatment. Alternatives for people who are seriously allergic to penicillin or infections with MRSA include doxycycline, clindamycin, and SMX-TMP. When streptococci alone are the cause, penicillin is the drug of choice.

When the condition presents with ulcers, valacyclovir, an antiviral, may be given in case a viral infection is causing the ulcer.

Alternative medicine

There is not enough evidence to recommend alternative medicine such as tea tree oil or honey.

Prognosis

Without treatment people typically get better within three weeks. Complications may include cellulitis or poststreptococcal glomerulonephritis. Rheumatic fever does not appear to be related.

Epidemiology

Globally, impetigo affects more than 162 million children in low to middle income countries. The rates are highest in countries with low available resources and is especially prevalent in the region of Oceania. The tropical climate and high population in lower socioeconomic regions contribute to these high rates. Children under the age of 4 in the United Kingdom are 2.8% more likely than average to contract impetigo; this decreases to 1.6% for children up to 15-years-old. As age increases, the rate of impetigo declines, but all ages are still susceptible.

Wound Management in Diabetic Foot Ulcers-Part 1

DFU wound management

Practitioners must strive to prevent DFUs developing elsewhere on the foot or on the contralateral limb and to achieve limb preservation.

The principle aim of DFU management is wound closure17. More specifically, the intention should be to treat the DFU at an early stage to allow prompt healing.

The essential components of management are:

- Treating underlying disease processes,
- Ensuring adequate blood supply ,
- Local wound care, including infection control ,
- Pressure of floading.

Effective foot care should be a partnership between patients, carers and healthcare professionals. This means providing appropriate information to enable patients and carers to participate in decision making and understand the rationale behind some of the clinical decisions as well as supporting good self-care.

TREATING THE UNDERLYING DISEASE PROCESSES

Practitioners should identify the underlying cause of the DFU during the patient assessment and, where possible, correct or eliminate it.

- Treating any severe ischaemia is critical to wound healing, regardless of other interventions. It is recommended that all patients with critical limb ischaemia, including rest pain, ulceration and tissue loss, should be referred for consideration of arterial reconstruction.
- Achieving optimal diabetic control. This should involve tight glycaemic control and managing risk factors such as high blood pressure, hyperlipidaemia and smoking. Nutritional deficiencies should also be managed.
- Addressing the physical cause of the trauma. As well as examining the foot, practitioners should examine the patient's footwear for proper fit, wear and tear and the presence of any foreign bodies (such as small stones, glass fragments, drawing pins, pet hairs) that may traumatise the foot1 . When possible and appropriate, practitioners should check other footwear worn at home and at work (eg slippers and work boots).

ENSURING ADEQUATE BLOOD SUPPLY

A patient with acute limb ischaemia is a clinical emergency and may be at great risk if not managed in a timely and effective way.

It is important to appreciate that, aside from critical limb ischaemia, decreased perfusion or impaired circulation may be an indicator for revascularisation in order to achieve and maintain healing and to avoid or delay a future amputation.

OPTIMISING LOCAL WOUND CARE

The European Wound Management Association (EWMA) states that the emphasis in wound care for DFUs should be on radical and repeated debridement, frequent inspection and bacterial control and careful moisture balance to prevent maceration. Its position document on wound bed preparation suggests the following TIME framework for managing DFUs.

1: Wound bed preparation and TIME framework
Wound bed preparation is not a static concept, but a dynamic and rapidly changing one
There are four components to wound bed preparation, which address the different pathophysiological abnormalities underlying chronic wounds
The TIME framework can be used to apply wound bed preparation to practice

- Tissue debridement
- Inflammation and infection control
- Moisture balance (optimal dressing selection)
- Epithelial edge advancement.

Tissue debridement

There are many methods of debridement used in the management of DFUs including surgical/sharp, larval, autolytic and, more recently, hydrosurgery and ultrasonic.

Debridement may be a one-off procedure or it may need to be ongoing for maintenance of the wound bed. The requirement for further debridement should be determined at each dressing change. If the wound is not progressing, practitioners should review the current treatment plan and look for an underlying cause of delayed healing (suchas ischaemia, infection or inflammation) and consider patient concordance with recommended treatment regimens (such as not wearing offloading devices or not taking antidiabetic medication).

Sharp debridement

No one debridement method has been shown to be more effective in achieving complete ulcer healing. However, in practice, the gold standard technique for tissue management in DFUs is regular, local, sharp debridement using a scalpel, scissors and/or forceps. The benefits of debridement include:

- Removes necrotic/sloughy tissue and callus
- Reduces pressure
- Allows full inspection of the underlying tissues
- Helps drainage of secretions or pus
- Helps optimise the effectiveness of topical preparations
- Stimulates healing.

Sharp debridement should be carried out by experienced practitioners (eg a specialist podiatrist or nurse) with specialist training.

Practitioners must be able to distinguish tissue types and understand anatomy to avoid damage to blood vessels, nerves and tendons. They should also demonstrate high-level clinical decision-making skills in assessing a level of debridement that is safe and effective. The procedure may be carried out in the clinic or at the bedside.

Ulcers may be obscured by the presence of callus. After discussing the plan and expected outcome with the patient in advance, debridement should remove all devitalised tissue, callus and foreign bodies down to the level of viable bleeding tissue. It is important to debride the wound margins as well as the wound base to prevent the 'edge effect', whereby epithelium fails to migrate across a firm, level granulation base.

Sharp debridement is an invasive procedure and can be quite radical. Practitioners must explain fully to patients the risks and benefits of debridement in order to gain their informed consent. One small study piloting an information leaflet showed that many patients did not understand the procedure despite having undergone debridement on several previous occasions.

Vascular status must always be determined prior to sharp debridement. Patients needing revascularisation should not undergo extensive sharp debridement because of the risk of trauma to vascularly compromised tissues. However, the 'toothpick' approach may be suitable for wounds requiring removal of loose callus45. Seek advice from a specialist if in doubt about a patient's suitability.

Other debridement methods

While sharp debridement is the gold standard technique, other methods may be appropriate in certain situations:

- As an interim measure (eg by practitioners without the necessary skill sets to carry out sharp debridement; methods include the use of a monofilament pad or larval therapy)
- For patients for whom sharp debridement is contraindicated or unacceptably painful
- When the clinical decision is that another debridement technique may be more beneficial for the patient
- For patients who have expressed another preference.

Larval therapy The larvae of the green bottle fly can achieve relatively rapid, atraumatic removal of moist, slimy slough, and can ingest pathogenic organisms present in the wound69. The decision to use larval debridement must be taken by an appropriate specialist practitioner, but the technique itself may then be carried out by generalist or specialist practitioners with minimal training.

Larval therapy has been shown to be safe and effective in the treatment of DFUs. However, it is not recommended as the sole method of debridement for neuropathic DFUs as the larvae cannot remove callus.

A recent review of debridement methods found some evidence to suggest that larval therapy may improve outcomes when compared to autolytic debridement with a hydrogel.

Hydrosurgical debridement This is an alternative method of wound debridement, which forces water or saline into a nozzle to create a high-energy cutting beam. This enables precise visualisation and removal of devitalised tissue in the wound bed.

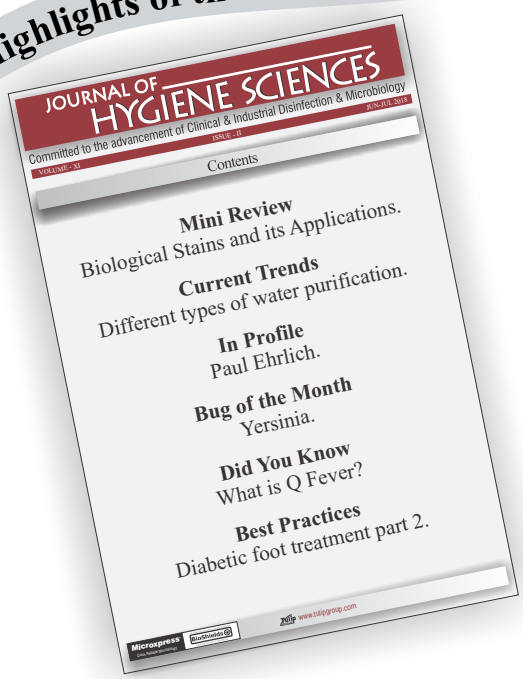
Autolytic debridement This is a natural process that uses a moist wound dressing to soften and remove devitalised tissue. Care must be taken not to use a moisturedonating dressing as this can predispose to maceration. In addition, the application of moisture-retentive dressings in the presence of ischaemia and/or dry gangrene is not recommended.

Not debriding a wound, not referring a patient to specialist staff for debridement, or choosing the wrong method of debridement, can cause rapid deterioration with potentially devastating consequences.

Reference:

National Institute for Health and Clinical Excellence. Diabetic foot problems: inpatient management of diabetic foot problems. Clinical guideline 119. London: NICE, 2011.

Highlights of the coming issue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