Int Microbiol (2001) 4: 113–115
DOI 10.1007/s101230100023

BOOK REVIEWS

Mercedes Berlanga

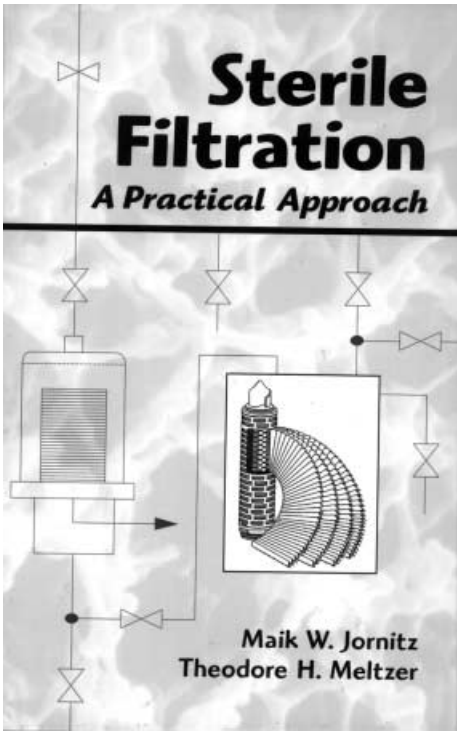
Maik W. Jornitz, Theodore H. Meltzer: Sterile filtration. A practical approach

Marcel Dekker, New York, 2001. 624 pp, 23.5×15.5 cm (ISBN: 0-8247-0282-4) U.S. $ 195

Published online: 21 September 2001

Sterilization is vital in today's civilization. Before it existed, food could not be kept without spoiling, except by drying or salting. Surgery resulted in infections and death in a very large percentage of cases. Today, we buy cartons of milk and fruit juices that keep for months without refrigeration. Flash heating, chemical sterilizants and filtration bring about these modern-day marvels. In medical and dental practice, the instruments used in surgery and the gloves, gowns, drapes, dressings and solutions are rendered sterile. Pharmaceutical companies sterilize many products. Microbiological laboratories require that cultures, containers, media and equipment be sterilized, so that only the desired organisms that are inoculated will grow and all others will be eliminated. "Sterilization," as we practice it, began little more than 100 years ago. Certain empirically based practices, however, have been known since early historical times. In biblical and medieval times, fire was used to destroy clothes and corpses of diseased persons. Sterilization by filtration has been observed from early times. Techniques such as filtration through sand, fine gravel, cloth bags and porous clay vessels were all reasonably effective for clarifying and/or purifying water. The dangers inherent in impure supplies were well recognized during the eighteenth and nineteenth centuries, when cholera and typhoid fever swept through highly populated areas. Improvements in purification methods were almost entirely related to filtration.

Sterilization is any process designed to eliminate entirely microorganisms from a material or medium. It should not be confused with disinfection, sanitation (cleaning plus disinfection) or pasteurization, which are intended to kill or inactivate microorganisms, but which may not necessarily entirely destroy or eliminate all of them. Books describe how sterilization may be accomplished using heat, chemicals, radiation or filtration.



Can filtration be considered a sterilization mechanism? Initially, 0.45 μm-rated filters were used for sterilizing purposes, i.e. the retention of *Serratia marcescens*, but they failed to retain *Brevundimonas (Pseudomonas) diminuta*. This microorganism was used to validate the 0.2/0.22 μm-rated filter; but again, it became obvious that the 0.22-μm filter was not universally effective in providing sterile effluent. Using 0.1 μm instead of 0.22 μm was suggested as a sensible measure to ensure the removal of organisms smaller than *B. diminuta*. Nevertheless, organisms that penetrate 0.22 μm-rated membranes are not necessarily retained by 0.1 μm-rated filters. What happens with viruses? Ultrafilters retain bacteriophages 0.04 μm in size. The definition of

M. Berlanga
University of Barcelona, Barcelona, Spain

filtration is: a separative practice wherein fluids, whether liquids or gases, are ''freed'' of their suspended particulates (microorganisms). The result of eliminating microorganisms from a filtrate depends on the filter (porous grade) type used; and thus, in my opinion, filtration would not be considered as a sterilizing mechanism.

''Sterilization filtration. A practical approach'' is organized into nine chapters that essentially describe contamination prevention and sterile product manufacturing. Sterilizing-grade filters are found in product manufacturing, utilities systems and product testing. In each of these roles, the filter is vital. Filtration science is a complex and dynamic discipline, which is subject to misunderstanding and misapplication. Only with a thorough understanding of the scientific principles of filtration can wise development and operational and regulatory judgments be made.

The removal of organisms from their suspension (liquid or gas) by filtration can be accomplished by the use of proper filters under appropriate filtration conditions. Not all filters are suitable for this purpose; and perhaps no filter is dependable under all circumstances. The nature of the pores and the composition of the matrices containing and positioning them are central to the filtration process. The size and number of the pores, their size distribution, the number of restrictive pores, their shapes and spatial disposition are described in Chapter 1 (''Filter porosity: its genesis and character''). Although filter pores govern filtration applications, the matrix must have adequate mechanical properties, such as tensile strength, elongation and elasticity, to maintain its geometry and to be impervious to the differential pressure applied at the given operational temperature (Chapter 2, ''The polymeric matrix and its influence''). The polymers most widely used in microporous membrane preparations are polyvinylidene fluoride, the polyamides (nylons), the cellulose acetates, polytetrafluoroethylene, polysulfone and polycarbonate. Formerly widely employed, membranes of cellulose nitrate are now essentially confined to laboratory use, as are track-etched polycarbonates.

Cleaning agents and sanitation of membranes are discussed extensively in Chapter 3 (''Membrane fouling, cleaning, and sanitation''). Specific procedures for system sanitation must be considered thoroughly prior to use. Chemical incompatibilities between the agent and the system components, selectivity of the disinfectants for the problem organisms and the toxic effects of the agent and its residuals must all be assessed.

The rate of fluid flow through the filter is of operational interest (Chapter 4, ''Flow and pressure, flow decay, and filter sizing''). The flow rate, as commented above, is related directly to the effective filtration area. The flow rate of the fluid through the filter also depends on the thickness of the filter and on its total porosity, in terms of pore sizes and their disposition. The fluid viscosity and hence its temperature influences the flow rate and the rate of filter blockage. For most fluids, flow through the filter pores also varies directly with the differential pressures applied. The mechanisms of particle (organism) removal from both liquids and gases are detailed in Chapters 5 and 6, respectively (''Mechanisms of particle removal from liquids'', ''Mechanisms of particle removal from air and other gases''). The sieve retention mode of particle capture is the most evident in common filtration; and it occurs whenever a particle is too large to pass through a filter pore. It is a geometric or spatial restraint. Adsorptive retention such as Van der Waal's forces, hydrogen-bonding and hydrophobic forces are also implicated in the removal of organisms.

Chapter 7 (''Filter integrity testing'') describes the United States Food and Drug Administration (FDA) regulation guidelines for the appropriate integrity (i.e. pore structure) test of a filter, which is used before and after filtration to ensure and prove the safety of filtrate products. Another major issue, which is discussed in Chapter 8 (''Cartridges, cartridge holder, and their care'') is the sanitary design of cartridge holders to avoid organism-contamination of both filters and products. Sterilization is the process by which all viable forms of microorganisms are destroyed; and thus the sterility of a product can be described in terms of a ''probability of a survivor'' or ''sterility assurance level''. The practical goal of the sterilization process is to sterilize products that have only a remote chance of containing viable microorganisms. Biological indicators are used to demonstrate sterility assurance. Bacterial indicators used to monitor sterilization processes involving steam heat include *Bacillus stearothermophilus*; and *B. subtilis* var. *niger* is used for ethylene oxide and dry heat. Chapter 9 deals with the ''Validation of filtrative sterilization''. The 0.45 μm-rated filter was validated for sterilizing purposes by the retention of *S. marcescens*, but it failed to retain *Brevundimonas diminuta*. The FDA, in its guidelines on sterile drug products produced by aseptic processing, defined the sterilizing filter as one that is capable of withstanding challenges of 1×10^7 *B. diminuta*/cm^2 of a filter surface with a pore size of 0.2/0.22 μm. ''Sterilizing'' membranes are most often the last barrier between a non-sterile atmosphere and the ''sterile'' product or equipment. Although the food industry has been aware of the importance of supplying clean air to their process plants, most of the advances in this area have come primarily from hospital designs. The provision of clean air in hospitals and the electronic industry are especially critical. In hospitals, it prevents the dissemination of nosocomial infections; and in the electronic industries, even very small particles can become ''killer particles'', bridging electronic circuits and destroying the element. Filtration is the most commonly employed technique to control airborne contamination. Filtration eliminates microorganisms mechanically without causing selective effects in microorganisms such as resistance to chemical products.

''Sterile filtration. A practical approach'' describes the principles of filtration, emphasizing the most significant facts and concepts about this technique. Figures

and tables facilitate comprehension, but some information is repeated in different chapters. The main conclusion after reading this book is that it may not be possible to designate a single filter rating to serve as a sterilizing grade for all the possible organisms that can be encountered. Filtration conditions and cartridge holders may determine the successful elimination of particles embedded in fluids. It is a specific and technical book, especially recommended to those responsible for microbial risk assessment in the pharmaceutical, electronic and food industries and in hospitals.