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Editorial

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It is important to note that in the mid-1800s, studies by Ignaz Semmelweis in Vienna, Austria, and Oliver Wendell Holmes in Boston, USA, established that hospital-acquired diseases were transmitted via the hands of Healthcare workers. As a consequence, Semmelweis recommended that hands be scrubbed in a chlorinated lime solution before every patient contact and particularly after leaving the autopsy room. Unfortunately, both Holmes and Semmelweis failed to observe a sustained change in their colleagues' behaviour. In particular, Semmelweis experienced great difficulties in convincing his colleagues and administrators of the benefits of this procedure. In the light of the principles of social marketing today, his major error was that he imposed a system change (the use of the chlorinated lime solution) without consulting the opinion of his collaborators. Also people are more resistant to change in the system. But following the implementation of this measure, the mortality rate fell dramatically to 3% in the clinic most affected and remained low thereafter. This caused a major paradigm shift in the field of hand hygiene. And today it is one of the major concerns to eliminate Nosocomial Infection.

In the section mini review, WHO Guidelines on Hand Hygiene in Healthcare is discussed. Health care-associated infection (HCAI) is a major problem for patient safety and its surveillance and prevention must be a first priority for settings and institutions committed to making health care safer.

In the section current trends we are going to explore various aspects of Environmental Monitoring in Pharmaceutical industry. It is necessary to follow these guidelines in the areas like clean-rooms for drug fill/finish, formulation tank rooms, laminar flow hoods, biological safety hoods, isolators, glove boxes, molding machines, kit assembly lines, Intravenous compounding areas and sterile packaging.

In profile segment covers biography of Subhash Mukhopadhyay (physician). His feat was recognized posthumously and was given belated recognition as the Indian physician who in 1986 was "officially" regarded as being the first doctor to perform in-vitro fertilization in India.

Chlamydia trachomatis will be discussed in the Bug of the month segment. It is an obligate intracellular human pathogen and Gram-negative. It can cause numerous disease states in both men and women. Both sexes can display urethritis, proctitis (rectal disease and bleeding), trachoma, and infertility. The bacterium can cause prostatitis and epididymitis in men.

Did You Know emphasizes on Proteus syndrome, which is a complex disorder consisting variably of disproportionate, asymmetric overgrowth of body parts; cerebriform connective tissue nevi; epidermal nevi; vascular malformations of the capillary, venous, and lymphatic types; and dysregulated adipose tissue. Serious complications may ensue, such as pulmonary embolism, cystic lung disease, and various neoplasms.

Best Practices segment will encompass aseptic media-fill testing, which is used to quantify the aseptic technique of compounding personnel or processes and to ensure that the processes used are able to produce a sterile product without microbiological contamination.

JHS team thanks all our readers for their support and contribution. Feedback and suggestions are always invited.

WHO Guidelines on Hand Hygience in Health Care

Definition of terms

Antiseptic handwashing. Washing hands with soap and water, or other detergents containing an antiseptic agent.

Antiseptic handrubbing (or handrubbing). Applying an antiseptic handrub to reduce or inhibit the growth of microorganisms without the need for an exogenous source of water and requiring no rinsing or drying with towels or other devices.

Hand antisepsis/decontamination/degerming. Reducing or inhibiting the growth of microorganisms by the application of an antiseptic handrub or by performing an antiseptic handwash.

Hand care. Actions to reduce the risk of skin damage or irritation.

Handwashing. Washing hands with plain or antimicrobial soap and water.

Hand cleansing. Action of performing hand hygiene for the purpose of physically or mechanically removing dirt, organic material, and/or microorganisms.

Hygienic hand antisepsis. Treatment of hands with either an antiseptic handrub or antiseptic handwash to reduce the transient microbial flora without necessarily affecting the resident skin flora.

Hygienic handrub. Treatment of hands with an antiseptic handrub to reduce the transient flora without necessarily affecting the resident skin flora. These preparations are broad spectrum and fast-acting, and persistent activity is not necessary.

Hygienic handwash. Treatment of hands with an antiseptic handwash and water to reduce the transient flora without necessarily affecting the resident skin flora. It is broad spectrum, but is usually less efficacious and acts more slowly than the hygienic handrub.

Surgical hand antisepsis/surgical hand preparation. presurgical hand preparation. Antiseptic handwash or antiseptic handrub performed preoperatively by the surgical team to eliminate transient flora and reduce resident skin flora. Such antiseptics often have persistent antimicrobial activity. Surgical handscrub (bing)/ presurgical scrub refer to surgical hand preparation with antimicrobial soap and water. Surgical handrub (bing) refers to surgical hand preparation with a waterless, alcohol-based handrub.

The burden of health care-associated infection

Health care-associated infection (HCAI) is a major problem for patient safety and its surveillance and prevention must be a first priority for settings and institutions committed to making health care safer.

Health care-associated infection in developed countries

In developed countries, HCAI concerns 5–15% of hospitalized patients and can affect 9–37% of those admitted to intensive care units (ICUs). Recent studies conducted in Europe reported hospital-wide prevalence rates of patients affected by HCAI ranging from 4.6% to 9.3%. According to data provided by the Hospital in Europe Link for Infection Control through Surveillance (HELICS) (http://helics.univ-lyon1.fr/ helicshome.htm), approximately 5 million HCAIs are estimated to occur in acute care hospitals in Europe annually, representing around million extra days of hospital stay and a corresponding economic burden of €13–24 billion. In general, attributable mortality due to HCAI in Europe is estimated to be 1% (50 000 deaths per year), but HCAI contributes to death in at least 2.7% of cases (135 000 deaths per year). The estimated HCAI incidence rate in the USA was 4.5% in 2002, corresponding to 9.3 infections per 1000 patient-days and 1.7 million affected patients; approximately 99 000 deaths were attributed to HCAI. The annual economic impact of HCAI in the USA was approximately US $6.5 billion in 2004.

Burden of health care-associated infection in developing countries

The magnitude of the problem is particularly relevant in settings where basic infection control measures are virtually nonexistent. This is the result of the combination of numerous unfavorable factors such as understaffing, poor hygiene and sanitation, lack or shortage of basic equipment, and inadequate structures and overcrowding, almost all of which can be attributed to limited financial resources. In addition to these specific factors, an unfavorable social background and a population largely affected by malnutrition and other types of infection and/or diseases contribute to increase the risk of HCAI in developing countries. Under these conditions, thousands of infections – in particular due to hepatitis B and C viruses and human immunodeficiency virus (HIV) transmission – are still acquired from patients, but also from HCWs through unsafe use of injections, medical devices and blood products, inadequate surgical procedures, and deficiencies in biomedical waste management. In one-day prevalence surveys recently carried out in single hospitals in Albania,Morocco,Tunisia,and the United Republic of Tanzania,HCAI prevalence rates were 19.1%, 17.8%, 17.9%, and 14.8%, respectively. Given the difficulties to comply with the USA Centers for Disease Control and Prevention (CDC) definitions of nosocomial infection,the most frequently surveyed type of infection is SSI, which is the easiest to define according to clinical criteria. The risk for patients to develop SSI in developing countries is significantly higher than in developed countries (e.g. 30.9% in a paediatric hospital in Nigeria,23% in general surgery in a hospital in the United Republic of Tanzania,and 19% in a maternity unit in Kenya).

Historical perspective

In the mid-1800s, studies by Ignaz Semmelweis in Vienna, Austria, and Oliver Wendell Holmes in Boston, USA, established that hospital-acquired diseases were transmitted via the hands of HCWs. In 1847, Semmelweis was appointed as a house officer in one of the two obstetric clinics at the University of Vienna Allgemeine Krankenhaus (General Hospital). He observed that maternal mortality rates, mostly attributable to puerperal fever, were substantially higher in one clinic compared with the other (16% versus 7%).He also noted that doctors and medical students often went directly to the delivery suite after performing

autopsies and had a disagreeable odour on their hands despite handwashing with soap and water before entering the clinic. He hypothesized therefore that "cadaverous particles" were transmitted via the hands of doctors and students from the autopsy room to the delivery theatre and caused the puerperal fever. As a consequence, Semmelweis recommended that hands be scrubbed in a chlorinated lime solution before every patient contact and particularly after leaving the autopsy room. Following the implementation of this measure, the mortality rate fell dramatically to 3% in the clinic most affected and remained low thereafter.

Unfortunately, both Holmes and Semmelweis failed to observe a sustained change in their colleagues' behaviour. In particular, Semmelweis experienced great difficulties in convincing his colleagues and administrators of the benefits of this procedure. In the light of the principles of social marketing today, his major error was that he imposed a system change (the use of the chlorinated lime solution) without consulting the opinion of his collaborators. Despite these drawbacks, many lessons have been learnt from the Semmelweis intervention; the "recognize-explain-act" approach has driven many investigators and practitioners since then and has also been replicated in different fields and settings. Semmelweis is considered not only the father of hand hygiene, but his intervention is also a model of epidemiologically driven strategies to prevent infection.

Normal bacterial flora on hands

In 1938, Price established that bacteria recovered from the hands could be divided into two categories, namely resident or transient. The resident flora (resident microbiota) consists of microorganisms residing under the superficial cells of the stratum corneum and can also be found on the surface of the skin. Staphylococcus epidermidis is the dominant species, and oxacillin resistance is extraordinarily high, particularly among HCWs. Other resident bacteria include S. hominis and other coagulase-negative staphylococci, followed by coryneform bacteria (propionibacteria, corynebacteria, dermobacteria, and micrococci). Among fungi, the most common genus of the resident skin flora, when present, is Pityrosporum (Malassezia) spp. Resident flora has two main protective functions: microbial antagonism and the competition for nutrients in the ecosystem. In general, resident flora is less likely to be associated with infections, but may cause infections in sterile body cavities, the eyes, or on non-intact skin.

Transient flora (transient microbiota), which colonizes the superficial layers of the skin, is more amenable to removal by routine hand hygiene. Transient microorganisms do not usually multiply on the skin, but they survive and sporadically multiply on skin surface. They are often acquired by HCWs during direct contact with patients or contaminated environmental surfaces adjacent to the patient and are the organisms most frequently associated with HCAIs. Some types of contact during routine neonatal care are more frequently associated with higher levels of bacterial contamination of HCWs' hands: respiratory secretions, nappy/diaper change, and direct skin contact. The transmissibility of transient flora depends on the species present, the number of microorganisms on the surface, and the skin moisture. The hands of some HCWs may become persistently colonized by pathogenic flora such as S. aureus, Gram-negative bacilli, or yeast. Normal human skin is colonized by bacteria, with total aerobic bacterial counts ranging from more than 1×10^6 colony forming units (CFU)/cm^2 on the scalp, 5×10^5 CFUs/cm^2 in the axilla, and 4×10^4 CFU/cm^2 on the abdomen to 1×10^4 CFU/cm^2 on the forearm. Total bacterial counts on the hands of HCWs have ranged from 3.9×10^4 to 4.6×10^6 CFU/cm^2. Fingertip contamination ranged from 0 to 300 CFU when sampled by agar contact methods. Price and subsequent investigators documented that although the count of transient and resident flora varies considerably among individuals, it is often relatively constant for any given individual.

Transmission of pathogens by hands

Transmission of health care-associated pathogens from one patient to another via HCWs' hands requires five sequential steps:

1) Organisms are present on the patient's skin, or have been shed onto inanimate objects immediately surrounding the patient.

The number of organisms such as S. aureus, Proteus mirabilis, Klebsiella spp. and Acinetobacter spp. present on intact areas of the skin of some patients can vary from 100 to 106 CFU/cm^2 gowns, bed linen, bedside furniture and other objects in the immediate environment of the patient become contaminated with patient flora. Contamination of the inanimate environment has also been detected on ward handwash station surfaces and many of the organisms isolated were staphylococci Tap/faucet handles were more likely to be contaminated and to be in excess of benchmark values than other parts of the station.

2) Organisms must be transferred to the hands of HCWs.

Nurses could contaminate their hands with 100–1000 CFU of Klebsiella spp. during "clean" activities such as lifting patients; taking the patient's pulse, blood pressure or oral temperature; or touching the patient's hand, shoulder or groin. cultured the hands of nurses who touched the groin of patients heavily colonized with P. mirabilis and found 10–600 CFU/ml in glove juice samples. Estimating the frequency of HCWs' glove contamination with methicillin resistant S. aureus (MRSA) after contact with a colonized patient, HCWs were intercepted after a patient-care episode and cultures were taken from their gloved hands before handwashing had occurred; 17% (confidence interval (CI) 95%) of contacts with patients, a patient's clothing or a patient's bed resulted in transmission of MRSA from a patient to the HCWs' gloves. In another study involving HCWs caring for patients with vancomycin-resistant enterococci (VRE), 70% of HCWs contaminated their hands or gloves by touching the patient and the patient's environment.

3) Organisms must be capable of surviving for at least several minutes on HCWs' hands.

Enterococcus faecalis and E. faecium survive for at least 60 minutes on gloved and ungloved fingertips. Pseudomonas aeruginosa and Burkholderia cepacia are transmissible by handshaking for up to 30 minutes when the organisms are suspended in saline, and up to 180 minutes when they are suspended in sputum. Shigella dysenteriae type 1 showed its capacity to survive on hands for up to 1 hour. Survival percentages for rotavirus at 20 minutes and 60 minutes after inoculation were 16.1% and 1.8%, respectively. Bacterial contamination increases linearly over time. In the absence of hand hygiene action, the longer the duration of care, the higher the degree of hand contamination.

4) Handwashing or hand antisepsis by the HCW must be inadequate or entirely omitted, or the agent used for hand hygiene inappropriate.

In a laboratory-based study, it was found that using only 1 ml of liquid soap or alcohol-based handrub yielded lower log

reductions (greater number of bacteria remaining on hands) than using 3 ml of product to clean hands. The findings have clinical relevance since some HCWs use as little as 0.4 ml of soap to clean their hands. A comparative, crossover study of microbiological efficacy of handrubbing with an alcohol-based solution and handwashing with an unmedicated soap was conducted. The study results were: 15% of HCWs' hands were contaminated with transient pathogens before hand hygiene; no transient pathogens were recovered after handrubbing, while two cases were found after handwashing. Another comparative study of three hand hygiene agents (62% ethyl alcohol handrub, medicated handwipe, and handwashing with plain soap and water) in a group of surgical ICUs was conducted. The impact of ring wearing on hand contamination was also studied. The results showed that hand contamination with transient organisms was significantly less likely after the use of an alcohol-based handrub compared with the medicated wipe or soap and water. Ring wearing increased the frequency of hand contamination with potential health care-associated pathogens.

5) The contaminated hand or hands of the caregiver must come into direct contact with another patient or with an inanimate object that will come into direct contact with the patient.

Cross-transmission of organisms occurs through contaminated hands. Factors that influence the transfer of microorganisms from surface to surface and affect cross-contamination rates are type of organism, source and destination surfaces, moisture level, and size of inoculum. Contaminated hands could contaminate a clean paper towel dispenser and vice versa. The transfer rates ranged from 0.01% to 0.64% and 12.4% to 13.1%, respectively. Fingers contaminated with norovirus could sequentially transfer virus to up to seven clean surfaces, and from contaminated cleaning cloths to clean hands and surfaces. Contaminated HCWs' hands have been associated with endemic HCAIs. Endemic S. marcescens was transmitted from contaminated soap to patients via the hands of HCWs. During an outbreak investigation of S. liquefaciens, BSI, and pyrogenic reactions in a haemodialysis centre, pathogens were isolated from extrinsically contaminated vials of medication resulting from multiple dose usage, antibacterial soap, and hand lotion. VRE could be transferred from a contaminated environment or patients' intact skin to clean sites via the hands of HCWs in 10.6% of contacts. Several HCAI outbreaks have been associated with contaminated HCWs' hands. An outbreak of multidrug-resistant A. baumannii documented identical strains from patients, hands of staff, and the environment. The outbreak was terminated when remedial measures were taken. Contaminated HCWs' hands were clearly related to outbreaks among surgical and neonatal patients.

Preparations used for hand hygiene

Alcohols

Most alcohol-based hand antiseptics contain either ethanol, isopropanol or n-propanol, or a combination of two of these products. Concentrations are given as either percentage of volume (= ml/100 ml, abbreviated % v/v), percentage of weight (= g/100 g, abbreviated % m/m), or percentage of weight/volume (= g/100 ml, abbreviated % m/v). Studies of alcohols have evaluated either individual alcohols in varying concentrations (most studies), combinations of two alcohols, or alcohol solutions containing small amounts of hexachlorophene, quaternary ammonium compounds (QAC), povidone-iodine, triclosan or CHG.

The antimicrobial activity of alcohols results from their ability to denature proteins. solutions containing 60–80% alcohol are most effective, with higher concentrations being less potent. paradox results from the fact that proteins are not denatured easily in the absence of water.

Alcohols have excellent in vitro germicidal activity against Gram-positive and Gram-negative vegetative bacteria (including multidrug-resistant pathogens such as MRSA and VRE), M. tuberculosis, and a variety of fungi.

However, they have virtually no activity against bacterial spores or protozoan oocysts, and very poor activity against some non-enveloped (non-lipophilic) viruses.

Chlorhexidine

CHG, a cationic bisbiguanide, was developed in the United Kingdom in the early 1950s and introduced into the USA in the 1970s. base is barely soluble in water, but the digluconate form is water-soluble. The antimicrobial activity of chlorhexidine appears to be attributable to the attachment to, and subsequent disruption of cytoplasmic membranes, resulting in precipitation of cellular contents. The antimicrobial activity of Chlorhexidine is not seriously affected by the presence of organic material, including blood. A scrub agent based on CHG (4%) was shown to be significantly more effective to reduce bacterial count than povidone iodine (7.5%) scrub agent. Chlorhexidine has significant residual activity. Addition of low concentrations (0.5–1%) of chlorhexidine to alcohol-based preparations results in significantly greater residual activity than alcohol alone.

Triclosan

Triclosan (chemical name 2,4,4'–trichloro-2'-hydroxydiphenyl ether) is known commercially as Irgasan DP-300. It is a nonionic, colourless substance developed in the 1960s; it is poorly soluble in water, but dissolves well in alcohols. Concentrations ranging from 0.2% to 2% have antimicrobial activity. Triclosan has been incorporated in detergents (0.4% to 1%) and in alcohols (0.2% to 0.5%) used for hygienic and surgical hand antisepsis or preoperative skin disinfection; it is also used for antiseptic body baths to control MRSA. This agent is incorporated into some soaps (at a 1% w/v concentration) and a variety of other consumer products (deodorants, shampoos, lotions, etc.), as well as being integrated also into various dressings and bandages for release over time onto the skin.

Triclosan enters bacterial cells and affects the cytoplasmic membrane and synthesis of RNA, fatty acids, and proteins. Recent studies suggest that this agent's antibacterial activity is attributable in large part to binding to the active site of enoylacyl carrier protein reductase.

Triclosan has a fairly broad range of antimicrobial activity. inhibitory concentrations (MICs) range from 0.1 to 10 g/ml, while minimum bactericidal concentrations are 25–500 g/ml. Triclosan's activity against Gram-positive organisms (including MRSA) is greater than against Gram-negative bacilli, particularly P. aeruginosa. agent possesses reasonable activity against mycobacteria and Candida spp., but has little activity against filamentous fungi and most viruses of nosocomial significance. Triclosan (0.1%) reduces bacterial counts on hands by 2.8 log10 after a 1-minute hygienic handwash.

Iodine and iodophors

Iodine has been recognized as an effective antiseptic since the 1800s, though iodophors have largely replaced iodine as the

active ingredient in antiseptics because iodine often causes irritation and discolouring of skin.

Iodine molecules rapidly penetrate the cell wall of microorganisms and inactivate cells by forming complexes with

amino acids and unsaturated fatty acids, resulting in impaired protein synthesis and alteration of cell membranes. are composed of elemental iodine, iodide or triiodide, and a polymer carrier (complexing agent) of high molecular weight.

The amount of molecular iodine present (so-called "free" iodine) determines the level of antimicrobial activity of iodophors. "Available" iodine refers to the total amount of iodine that can be titrated with sodium thiosulfate. 10% povidoneiodine formulations contain 1% available iodine and yield free iodine concentrations of 1 ppm.

Combining iodine with various polymers increases the solubility of iodine, promotes sustained-release of iodine, and reduces skin irritation. The most common polymers incorporated into iodophors are polyvinyl pyrrolidone (povidone) and ethoxylated nonionic detergents (poloxamers). antimicrobial activity of iodophors can also be affected by pH, temperature, exposure time, concentration of total available iodine, and the amount and type of organic and inorganic compounds present (e.g. alcohols and detergents). The concentrations used in antiseptics, iodophors are not usually sporicidal. Iodophors demonstrated poor persistent activity. The in vivo antimicrobial activity of iodophors is significantly reduced in the presence of organic substances such as blood or sputum. iodine has been found to be less effective than alcohol 60% (v/v) and hydrogen peroxide 3% and 5% on S. epidermidis. Iodophor antiseptics have become contaminated with Gram-negative bacilli as a result of poor manufacturing processes and have caused outbreaks or pseudo-outbreaks of infection. outbreak of P. cepacia involving 52 patients in four hospitals in New York over six months was attributed to the contamination of a 10% povidone iodine solution used as an antiseptic and disinfectant solution.

Surgical hand preparation: state-of-the-art

Objective of surgical hand preparation

Surgical hand preparation should reduce the release of skin bacteria from the hands of the surgical team for the duration of the procedure in case of an unnoticed puncture of the surgical glove releasing bacteria to the open wound. contrast to the hygienic handwash or handrub, surgical hand preparation must eliminate the transient and reduce the resident flora. It should also inhibit growth of bacteria under the gloved hand. Rapid multiplication of skin bacteria occurs under surgical gloves if hands are washed with a non-antimicrobial soap, whereas it occurs more slowly following preoperative scrubbing with a medicated soap.

The skin flora, mainly coagulase-negative staphylococci, Propionibacterium spp., and Corynebacteria spp., are rarely responsible for SSI, but in the presence of a foreign body or necrotic tissue even inocula as low as 100 CFU can trigger such infection. The virulence of the microorganisms, extent of microbial exposure, and host defence mechanisms are key factors in the pathogenesis of postoperative infection, risk factors that are largely beyond the influence of the surgical team. Therefore, products for surgical hand preparation must eliminate the transient and significantly reduce the resident flora at the beginning of an operation and maintain the microbial release from the hands below baseline until the end of the procedure.

Required time for the procedure

Scientists compared hand bacterial counts after 3-minute and 5-minute scrubs with seven different formulations. showed that the 3-minute scrub could be as effective as the 5-minute scrub, depending on the formula of the scrub agent. Scrubbing for longer than 2 minutes did not confer any advantage. This study recommended a 4-minute scrub for the surgical team's first procedure and a 2-minute scrub for subsequent procedures.

Surgical hand preparation with alcohol-based handrubs

Several alcohol-based handrubs have been licensed for the commercial market frequently with additional, long acting compounds (e.g. chlorhexidine gluconate or quaternary ammonium compounds) limiting regrowth of bacteria on the gloved hand. antimicrobial efficacy of alcohol based formulations is superior to that of all other currently available methods of preoperative surgical hand preparation. Numerous studies have demonstrated that formulations containing 60–95% alcohol alone, or 50–95% when combined with small amounts of a QAC, hexachlorophene or chlorhexidine gluconate, reduce bacterial counts on the skin immediately post-scrub more effectively than do other agents.

Technique for the application of surgical hand preparation using alcohol-based handrub

The application technique has not been standardized throughout the world. The WHO approach for surgical hand preparation requires the six basic steps for the hands as for hygienic hand antisepsis, but requires additional steps for rubbing the forearms. The hands should be wet from the alcohol-based rub during the whole procedure, which requires approximately 15 ml depending on the size of the hands. One study demonstrated that keeping the hands wet with the rub is more important than the volume used. Once the forearms and hands have been treated with an emphasis on the forearms – usually for approximately 1 minute – the second part of the surgical handrub should focus on the hands, following the identical technique as outlined for the hygienic handrub. The hands should be kept above the elbows during this step.

Required time for the procedure

For many years, surgical staff frequently scrubbed their hands for 10 minutes preoperatively, which frequently led to skin damage. Surgical hand antisepsis using an alcohol-based handrub required 3 minutes.

Surgical handscrub with medicated soap or surgical hand preparation with alcohol-based formulations, both methods are suitable for the prevention of SSIs. However, although medicated soaps have been and are still used by many surgical teams worldwide for presurgical hand preparation, it is important to note that the antibacterial efficacy of products containing high concentrations of alcohol are far more superior than that of any medicated soap presently available.

Environmental Monitoring in Pharmaceutical Industry

Environmental Monitoring (E/M) 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, isolators, glove boxes, molding machines, kit assembly lines, Intravenous (IV) compounding areas and sterile packaging.

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 veracity that a clean room is functioning as designed and being properly maintained. Surface and air monitoring exhibit the asepsis of the product manufacturing operation.

In aseptic processing, one of the most important laboratory controls is the environmental monitoring program. This program provides meaningful information on the quality of the aseptic processing environment (e.g., when a given batch is being manufactured) as well as environmental trends of ancillary clean areas. Environmental monitoring should promptly identify potential routes of contamination, allowing for implementation of corrections before product contamination occurs.

Evaluating the quality of air and surfaces in the cleanroom environment should start with a well-defined written program and scientifically sound methods. The monitoring program should cover all production shifts and include air, floors, walls, and equipment surfaces, including the critical surfaces that come in contact with the product, container, and closures. Written procedures should include a list of locations to be sampled. Sample timing, frequency, and location should be carefully selected based upon their relationship to the operation performed. Samples should be taken throughout the classified areas of the aseptic processing facility (e.g., aseptic corridors, gowning rooms) using scientifically sound sampling procedures. Sample sizes should be sufficient to optimize detection of environmental contaminants at levels that might be expected in a given clean area.

It is important that locations posing the most microbiological risk to the product be a key part of the program. It is especially important to monitor the microbiological quality of the critical area to determine whether or not aseptic conditions are maintained during filling and closing activities. Air and surface samples should be taken at the locations where significant activity or product exposure occurs during production. Critical surfaces that come in contact with the sterile product should remain sterile throughout an operation. When identifying critical sites to be sampled, consideration should be given to the points of contamination risk in a process, including factors such as difficulty of setup, length of processing time, and impact of interventions. Critical surface sampling should be performed at the conclusion of the aseptic processing operation to avoid direct contact with sterile surfaces during processing. Detection of microbial contamination on a critical site would not necessarily result in batch rejection. The contaminated critical site sample should prompt an investigation of operational information and data that includes an awareness of the potential for a low incidence of false positives.

Environmental monitoring methods do not always recover microorganisms present in the sampled area. In particular, low-level contamination can be particularly difficult to detect. Because false negatives can occur, consecutive growth results are only one type of adverse trend. Increased incidence of contamination over a given period is an equal or more significant trend to be tracked. In the absence of any adverse trend, a single result above an action level should trigger an evaluation and a determination about whether remedial measures may be appropriate. In all room classes, remedial measures should be taken in response to unfavorable trends.

All environmental monitoring locations should be described in SOPs with sufficient detail to allow for reproducible sampling of a given location surveyed. Written SOPs should also address elements such as (1) frequency of sampling, (2) when the samples are taken (i.e., during or at the conclusion of operations), (3) duration of sampling, (4) sample size (e.g., surface area, air volume), (5) specific sampling equipment and techniques, (6) alert and action levels, and (7) appropriate response to deviations from alert or action levels.

Establishing Levels and a Trending Program

Microbiological monitoring levels should be established based on the relationship of the sampled location to the operation. The levels should be based on the need to maintain adequate microbiological control throughout the entire sterile manufacturing facility. One should also consider environmental monitoring data from historical databases, media fills, cleanroom qualification, and sanitization studies, in developing monitoring levels. Data from similar operations can also be helpful in setting action and alert levels, especially for a new operation.

Environmental monitoring data will provide information on the quality of the manufacturing environment. Each individual sample result should be evaluated for its significance by comparison to the alert or action levels. Averaging of results can mask unacceptable localized conditions. A result at the alert level urges attention to the approaching action conditions. A result at the action level should prompt a more thorough investigation. Written procedures should be established, detailing data review frequency and actions to be taken. The quality control unit should provide routine oversight of near-term (e.g., daily, weekly, monthly, quarterly) and long-term trends in environmental and personnel monitoring data.

Trend reports should include data generated by location, shift, room, operator, or other parameters. The quality control unit should be responsible for producing specialized data reports (e.g., a search on a particular isolate over a year period) with the goal of investigating results beyond established levels and identifying any appropriate follow-up actions. Significant changes in microbial flora should be considered in the review of the ongoing environmental monitoring data.

Written procedures should define the system whereby the most responsible managers are regularly informed and updated on trends and investigations.

Disinfection Efficacy

The suitability, efficacy, and limitations of disinfecting agents and procedures should be assessed. The effectiveness of these disinfectants and procedures should be measured by their ability to

ensure that potential contaminants are adequately removed from surfaces.

To prevent introduction of contamination, disinfectants should be sterile, appropriately handled in suitable containers and used for no longer than the predefined period specified by written procedures. Routinely used disinfectants should be effective against the normal microbial vegetative flora recovered from the facility. Many common disinfectants are ineffective against spores. For example, 70 percent isopropyl alcohol is ineffective against Bacillus spp. spores. Therefore, a sound disinfectant program also includes a sporicidal agent, used according to a written schedule and when environmental data suggest the presence of sporeforming organisms.

Disinfection procedures should be described in sufficient detail (e.g., preparation, work sequence, contact time) to enable reproducibility. Once the procedures are established, their adequacy should be evaluated using a routine environmental monitoring program. If indicated, microorganisms associated with adverse trends can be investigated as to their sensitivity to the disinfectants employed in the cleanroom in which the organisms were isolated.

Monitoring Methods

Industries that have their clean room facilities monitored do so to ensure their desired/required quality standards are met. The areas that are sampled in a manufacturer's clean room include:

Acceptable methods for monitoring the microbiological quality of the environment include:

Methods of Air sampling in a Clean Room

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. 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.

What is Air Sampling?

- Air Sampling is used to quantify specific chemical, biological and physical agents that may present in occupational environment.
- Biological Air Sampling is routinely used to monitor the populations of air borne particles of the surrounding area.
- In the context of microbiological assessment air sampling is the collection of air borne microbial contaminants that may impact on product spoilage, product safety and human health.

Significance Of Air Sampling

- Measures the number of viable air borne particles (i.e. the concentration of microorganisms in the air).
- Evaluation of the effectiveness of control methods.
- Compliance status with respect to various occupational health standards.
- Routine surveillance.

There are two principle means of monitoring the microbiological population of the air, active air monitoring and passive air monitoring. Both have a part to play, but active sampling methods have become an essential environmental monitoring tool, especially in the pharmaceutical and medical device sectors.

1. Active Air Monitoring

Assessing microbial quality of air should involve the use of active devices including but not limited to impaction, centrifugal, and membrane (or gelatin) samplers. Each device has certain advantages and disadvantages, although all allow testing of the number of organisms per volume of air sampled. We recommend that such devices be used during each production shift to evaluate aseptic processing areas at carefully chosen locations. Manufacturers should be aware of a device's air monitoring capabilities, and the air sampler should be evaluated for its suitability for use in an aseptic environment based on collection efficiency, cleanability, ability to be sterilized, and disruption of unidirectional airflow.20 Because devices vary, the user should assess the overall suitability of a monitoring device before it is placed into service. Manufacturers should ensure that such devices are calibrated and used according to appropriate procedures.

Air Sampler

Environmental Monitoring is a must in the pharmaceutical industry.

The FDA guidelines for Aseptic Processing from September 2004 suggests that the air sampler should be evaluated based on collection efficiency, cleaning ability, ability to be sterilized and disruption of unidirectional air flow. Further devices have to be calibrated and used according to appropriate procedures.

A specific Standard for the purpose of Environmental Monitoring is ISO 14698 Biocontamination control. It is a valid worldwide published standard, and is mandatory in Europe as there is a reference in the EU GMP Guide.

Types of Air Sampler

Sieve Impactor: This acts by aspiration of air through the sieves at the top of the sampler. The apparatus consists of a container designed to accommodate a petri dish containing growth medium. The cover of the unit is perforated and a vacuum pump draws a volume of air through the cover. The particles in the air containing microorganisms impact on the agar medium. It works on well-known Andersen's sieve impaction principle.

Centrifugal Sampler: Centrifugal samplers create a centrifugal force, which causes particles and microorganisms to impact the medium at a rate dependent on the size of the particle.

Slit-to-Agar Air Sampler: This sampler draws a known volume of air by vacuum through a slit opening and then accelerated and directed toward the surface of a petri dish containing growth media.

Gelatin Filter Sampler: In this air sampler air is sampled at a programmable flow rate and passes through a gelatin membrane filter, which captures the microbes.

2. Passive Air Monitoring (Settling Plates)

In Pharmaceutical industry all manufacturing activities are carried out in clean areas as recommended by FDA guidelines. Different standards of clean room are used.

Eg- Class 100, Class 10,000, Class 1,00,000

According to USP chapter<1116> microbial limits for sterile products are as follows:

Class	CFU/m^3 Air
100	<3
10,000	<20
100,000	<100

Class 100- all sterile fillings (Injectables/eye drops) are carried out.

Class 10,000- Manufacturing activities like blending mixing,

filtration, stirring and punching of tablets.

Class 1,00,000- Air locks, Packing area, manufacturing of non-injectable product.

Environmental monitoring by settling plate

Passive monitoring is usually done using 'settle plates' – standard Petri dishes containing appropriate (usually non-selective) culture media that are opened and exposed for a given time and then incubated to allow visible colonies to develop and be counted. Settle plates are very limited in their application since they are only really capable of monitoring viable biological particles that sediment out of the air and settle onto a surface over the time of exposure. They will not detect smaller particles or droplets suspended in the air and they cannot sample specific volumes of air, so the results are not quantitative. They are also vulnerable to interference and contamination from non-airborne sources and the agar growth medium in the plates may deteriorate if they are exposed for too long. Settle plates may easily become overgrown in heavily contaminated conditions and interpretation of the data they produce can be difficult.

Their value in critical areas will be enhanced by ensuring that plates are positioned in locations posing the greatest risk of product contamination. As part of methods validation, the quality control laboratory should evaluate what media exposure conditions optimize recovery of low levels of environmental isolates. Exposure conditions should preclude desiccation (e.g., caused by lengthy sampling periods and/or high airflows), which inhibits recovery of microorganisms. The data generated by passive air sampling can be useful when considered in combination with results from other types of air samples.

On the other hand, settle plates are inexpensive and easy use, requiring no special equipment. They are useful for qualitative analysis of airborne microorganisms and the data they produce may detect underlying trends in airborne contamination and provide early warning of problems. They are also useful for directly monitoring airborne contamination of specific surfaces. In an environment such as a low risk food factory, settle plates may provide an adequate means of monitoring biological air quality.

Requirements

Dehaydrated Culture Media- Soyabean Casein Digest Agar

Microorganisms (ATCC Culture)- S.aureus 25923 and C.albicans 10231

Equipments

- Autoclave
- Incubator

Procedure

- Prepare sterile plates of Soyabean Casein Digest Agar.
- Expose the plates in specified area as per respective protocol.
- After exposure as per specified time incubate one set at 37±2 ^{0}C and set another set at 25 -30 ^{0}C for 5 days.
- Count the number of colonies from both sets.

  1stset will give bacterial colonies.

  2ndset will give Yeast/Mould colonies.
- Count the colonies from both sets and calculate final CFU value.
- Incubate one sterile plate of SCDA at 37±2 ^{0}C and another at 25 - 30 ^{0}C for 5 days. (Negative control).
- Incoculate one SCDA Plate with 24 hours old culture of S.aureus incubate at 37±2^{0}C for 5 days. Inoculate another SCDA Plate with 24 hours old culture C.albicans incubate at 25-30 ^{0}C for 5 days. (Positive Control).

Interpretation

- Negative Control Plates should remain sterile till end of the incubation period.
- Positive Control Plates should give growth of standard colonies.

Methods for surface monitoring in a Clean Room

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 called Trypticase Soy Agar (TSA) and Sabouraud Dextros 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^{0}C which is mainly the optimal growing temperature for most environmental bacteria, and 20-25^{0}C which is the optimal growing temperature for most mold and yeast species.

1. Contact Plates- as mentioned above are special Petri dishes which contain sterile growth medium 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.

2. Swabs- are sterile and stored in a suitable sterile liquid. The swabs are rubbed over the test surface. The microbiologist can determine the type of microorganisms on the swab by subculturing 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.

How Personnel are monitored in a Clean Room?...

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 asses 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.

Contact Plates - Personnel in critical areas may be monitored for microbial contamination utilizing 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.

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Subhash Mukhopadhyay

(Physician)

Early life

He was born on January 16, 1931 in Hazaribag, Bihar (now in Jharkhand), India. He studied and graduated (in 1955) with an honours degree in physiology from the Calcutta National Medical College. He later earned a doctorate from the University of Calcutta in 1958 reproductive physiology under the stewardship of Prof. Sachchidananda Banerjee, followed by a second doctorate from the University of Edinburgh in 1967 in reproductive endocrinology.

Career

The country's first successful in-vitro fertilization to produce "Durga" alias Kanupriya Agarwal--second test tube baby in the world--was performed by Dr Subhash Mukhopadhyay on October 3, 1978. The Calcutta-based doctor got belated recognition eight years later but it was tragically late.

The world's first test tube baby Louise Brown was born just three months earlier on July 25, 1978 in the UK when Edwards' efforts were crowned by success.

Some of his remarkable achievements are- 1) Used HMG for ovarian stimulation for IVF, 2) First to use transvaginal approach for ovum pick up, 3) First to cyropreserve human embryos, 4) First to transfer embryo in a subsequent untreated cycle.

Durga's birth was caught in ethical and moral controversies with the West Bengal government even denouncing Mukhopadhyay's claim that he had created history in India. The physician's achievements were not recognised at first.

Facing social ostracization, bureaucratic negligence, reprimand and insult from the government and refusal to allow him to attend international conferences, the physician committed suicide in his Calcutta residence on June 19, 1981.

The physician was subjected to repeated questioning by a committee formed by the West Bengal government. The committee said the doctor's work was bogus.

His feat has since been posthumously recognised. He has been given belated recognition as the Indian physician who in 1986 was "officially" regarded as being the first doctor to perform in-vitro fertilization in India.

Eight years after the birth of 'Durga', India's second Test-tube baby Harsha was born. Indira Hinduja was the gynaecologist responsible for the birth of Harsha Chawda at the state-run hospital K.E.M. Hospital in Mumbai on August 16, 1986. Some records say that Harsha is the 'first' Test-tube baby because of the controversy involving Mukhopadhayay.

Like Brown's birth, Durga's birth had caused public debate, criticism and even social professional ostracism of those involved in initiating life outside the body.

Harsha's birth opened up the much-sought opportunity for treating couples incapable of natural reproduction. The ICMR estimates at least 10 per cent of couples in India face infertility. Apart from factors like low sperm count, infections and erectile dysfunction in males, damaged fallopian tubes, low egg production and fibroids in females, lifestyle changes have also adversely affected fertility. In Vitro Fertilisation (IVF) is a complex process in which the ovum is fertilised outside the body and the fertilised egg is then implanted to the uterus.

Presently, there are more than 400 IVF clinics in India that even treat those coming from abroad due to the comparatively lower costs and, in some cases, for Indian donor eggs.

Mukhopadhyaya's life and death has been the subject of countless newspaper reviews and inspired the Hindi movie 'Ek Doctor Ki Maut' (Death of a doctor), directed by Tapan Sinha.

Kumar is currently active in setting up a research institute in reproductive biology in memory of Mukhopadhyay.

Late recognition

According to Scientific records, “Harsha” (born 16 August 1986) become the first human test tube baby of India. The credit for this achievement went to T.C Anand Kumar, Director of IRR (ICMR). In 1997, he went to Kolkata to participate in a Science Congress. It was there that all the research documents of Mukhopadhyay were handed over to him. After meticulously scrutinising and having discussions with Durga’s parents, he became certain that Mukhopadhyay was the architect of first human test tube baby in India. This eminent scientist once mentioned in a journal on ‘A critique of Mukherjee ’s technique’: “The brief description given by Mukherjee in his letter dated 19 October 1978 to the Director of Health Services, Government of West Bengal, the reports he gave over the television interviews and reported in the lay press describe how Mukherjee carried out the procedure of in vitro fertilization.

In the ‘Dictionary of Medical Biography,’ published by World Foundation, enlists names of 1100 Medical Scientists from 100 countries around the world for their path breaking contributions to the medical science. Only three names found their place in that dictionary from the city of Kolkata. The names are: Sir Ronald Ross, U.N. Bramhachari and Dr. Mukhopadhyay. What is more ridiculous is that after his death, in 1983, one by one three scientists Howard Jones, Gleicher and Trounson (Australia) in three separate research claimed the invention of Human test tube baby. Dr. Subhas Mukherjee is still respected and remembered as someone who invented the most efficient process for the birth of test tube babies. In Sao Paulo, during the eve of 30 years completion of IVF, Brazilian Medical Society recognized and honored him for his incredible achievements.

Dr. Subhas Mukherjee's life and work was published in the "Dictionary of Medical Biography" by Wellcome Trust Centre for the History of Medicine at UCL, London England. Edited by W. F. Bynum and Helen Bynum and published Greenwood Press, Westport, CT 06881. ISBN 0-313-32881-1.

Enjoy the humour

A distraught patient phoned her doctor's office. Was it true, the woman wanted to know, that the medication the doctor had prescribed was for the rest of her life? She was told that it was. There was a moment of silence before the woman continued, "I'm wondering, then, just how serious my condition is, because this prescription is marked NO REFILLS."

Evolution of medicine
I have a headache ...
2000 BC - Eat this root.
1000 AD - That root is infected. say this prayer.
1850 AD - That prayer is superstition. drink this potion.
1940 AD - That potion is snake oil. swallow this pill.
1985 AD - That pill is ineffective. take this antibiotic.
2000 AD - That antibiotic is artificial. eat this root.

Customer: "How much is that banana for?"
Shopkeeper: "10 rupees?
Customer: "Can you sell it to me for 6 rupees?"
Shopkeeper: "At that rate, you'll only get the banana peel!"
Customer: "Okay… I'll buy the banana for 4 rupees, but you can keep the peel!"

The doctor took his patient into the room and said,
"I have some good news and some bad news."
The patient said, "Give me the good news."
"They're going to name a disease after you."

70 Year Old Tom went to the Doctor for a Check up.
Days later the Doctor sees Tom with a Gorgeous Young Woman and says, Wow, Aren't you really Doing Great.?!
Tom : I'm just doing what You Said, Doc. You said "Get a Hot Mamma and Be Cheerful".
Doc.: God. I Only Said, "you've Got a Heart Murmur: Be Careful".

A salesman was demonstrating unbreakable combs in a department store. He was impressing the people who stopped by to look by putting the comb through all sorts of torture and stress.
Finally to impress even the skeptics in the crowd, he bent the comb completely in half, and it snapped with a loud crack.
Without missing a beat, he bravely held up both halves of the 'unbreakable' comb for everyone to see and said, "And this, ladies and gentlemen, is what an unbreakable comb looks like on the inside."

A software manager, a hardware manager, and a marketing manager are driving to a meeting when a tire blows. They get out of the car and look at the problem.
The software manager says, "I can't do anything about this - it's a hardware problem."
The hardware manager says, "Maybe if we turned the car off and on again, it would fix itself."
The marketing manager says, "Hey, 75% of it is working - let's ship it!"

Touch-screen monitors

Touch-screen monitors have become more and more commonplace as their price has steadily dropped over the past decade. There are three basic systems that are used to recognize a person's touch:

- Resistive
- Capacitive
- Surface acoustic wave

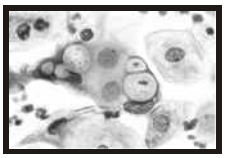
The resistive system consists of a normal glass panel that is covered with a conductive and a resistive metallic layer. These two layers are held apart by spacers, and a scratch-resistant layer is placed on top of the whole setup. An electrical current runs through the two layers while the monitor is operational. When a user touches the screen, the two layers make contact in that exact spot. The change in the electrical field is noted and the coordinates of the point of contact are calculated by the computer. Once the coordinates are known, a special driver translates the touch into something that the operating system can understand.

In the capacitive system, a layer that stores electrical charge is placed on the glass panel of the monitor. When a user touches the monitor with his or her finger, some of the charge is transferred to the user, so the charge on the capacitive layer decreases. This decrease is measured in circuits located at each corner of the monitor. The computer calculates, from the relative differences in charge at each corner, exactly where the touch event took place and then relays that information to the touch-screen driver software. One advantage that the capacitive system has over the resistive system is that it transmits almost 90 percent of the light from the monitor, whereas the resistive system only transmits about 75 percent. This gives the capacitive system a much clearer picture than the resistive system.

On the monitor of a surface acoustic wave system, two transducers (one receiving and one sending) are placed along the x and y axes of the monitor's glass plate. Also placed on the glass are reflectors - they reflect an electrical signal sent from one transducer to the other. The receiving transducer is able to tell if the wave has been disturbed by a touch event at any instant, and can locate it accordingly. The wave setup has no metallic layers on the screen, allowing for 100-percent light throughput and perfect image clarity. This makes the surface acoustic wave system best for displaying detailed graphics (both other systems have significant degradation in clarity).

Another area in which the systems differ is in which stimuli will register as a touch event. A resistive system registers a touch as long as the two layers make contact, which means that it doesn't matter if you touch it with your finger or a rubber ball. A capacitive system, on the other hand, must have a conductive input, usually your finger, in order to register a touch. The surface acoustic wave system works much like the resistive system, allowing a touch with almost any object -- except hard and small objects like a pen tip.

As far as price, the resistive system is the cheapest; its clarity is the lowest of the three, and its layers can be damaged by sharp objects. The surface acoustic wave setup is usually the most expensive. Most of the Instruments in biological segments with touch-screen interface are generally the resistive type.



Chlamydia Trachomatis

Chlamydia trachomatis, an obligate intracellular human pathogen, is one of three bacterial species in the genus Chlamydia. C. trachomatis is a Gram-negative bacteria, therefore its cell wall components retain the counter-stain safranin and appear pink under a light microscope. The inclusion bodies of Chlamydia trachomatis were first described in 1907, the Chlamydia trachomatis agent was first cultured in the yolk sacs of eggs by Feifan Tang et al in 1957. Also, there are diagnostic isolation of Chlamydia, including TRIC agent, from the eye, genital tract, and rectum. C. trachomatis includes three human biovars: trachoma (serovars A, B, Ba or C), urethritis (serovars D-K), and lymphogranuloma venereum (LGV, serovars L1, 2 and 3). Many, but not all, C. trachomatis strains have an extra-chromosomal plasmid.

Identification

Chlamydia species are readily identified and distinguished from other chlamydial species using DNA-based tests. Most strains of C. trachomatis are recognized by monoclonal antibodies (mAbs) to epitopes in the VS4 region of MOMP. However, these mAbs may also cross-react with two other Chlamydia species, C. suis and C. muridarum.

C. trachomatis is an obligate intracellular pathogen and can cause numerous disease states in both men and women. Both sexes can display urethritis, proctitis (rectal disease and bleeding), trachoma, and infertility. The bacterium can cause prostatitis and epididymitis in men. In women, cervicitis, pelvic inflammatory disease (PID), ectopic pregnancy, and acute or chronic pelvic pain are frequent complications. C. trachomatis is also an important neonatal pathogen, where it can lead to infections of the eye (trachoma) and pulmonary complications. Chlamydia trachomatis is the single most important infectious agent associated with blindness; approximately 600million worldwide suffer C. trachomatis eye infections and 20million are blinded as a result of the infection. C. trachomatis may be treated with any of several antibiotics: azithromycin, erythromycin or doxycycline/tetracycline.

Chlamydia infection

Chlamydia infection is a common sexually transmitted infection (STI) in humans caused by the bacterium Chlamydia trachomatis. The term Chlamydia infection can also refer to infection caused by any species belonging to the bacterial family Chlamydiaceae. C. trachomatis is found only in humans. Chlamydia is a major infectious cause of human genital and eye disease. Chlamydia infection is one of the most common sexually transmitted infections worldwide; it is estimated that about 1 million individuals in the United States are infected with chlamydia.

C. trachomatis is naturally found living only inside human cells. Chlamydia can be transmitted during various means of sexual intercourse, and can be passed from an infected mother to her baby during vaginal childbirth. Between half and three-quarters of all women who have a chlamydia infection of the neck of the womb (cervicitis) have no symptoms and do not know that they are infected. In men, infection of the urethra (urethritis) is usually symptomatic, causing a white discharge from the penis with or without pain on urinating (dysuria). Occasionally, the condition spreads to the upper genital tract in women (causing pelvic inflammatory disease) or to the epididymis in men (causing epididymitis). If untreated, chlamydial infections can cause serious reproductive and other health problems with both short-term and long-term consequences.

Chlamydia conjunctivitis or trachoma is a common cause of blindness worldwide. The World Health Organization (WHO) estimates that it accounted for 15% of blindness cases in 1995, but only 3.6% in 2002.

Signs and symptoms Genital disease

Chlamydial cervicitis in a female patient is characterized by mucopurulent cervical discharge, erythema, and inflammation. Male patients may develop a white, cloudy or watery discharge from the tip of the penis. Women Chlamydial infection of the neck of the womb (cervicitis) is a sexually transmitted infection which is asymptomatic for about 50-70% of women infected with the disease. Of those who have an asymptomatic infection that is not detected by their doctor, approximately half will develop pelvic inflammatory disease (PID), a generic term for infection of the uterus, fallopian tubes, and/or ovaries. PID can cause scarring inside the reproductive organs, which can later cause serious complications, including chronic pelvic pain, difficulty becoming pregnant, ectopic (tubal) pregnancy, and other dangerous complications of pregnancy.

Chlamydia is known as the "Silent Epidemic" because in women, it may not cause any symptoms in 75% of cases, and can linger for months or years before being discovered. Symptoms that may occur include unusual vaginal bleeding or discharge, pain in the abdomen, painful sexual intercourse (dyspareunia), fever, painful urination or the urge to urinate more frequently than usual (urinary urgency).

In men, chlamydia shows symptoms of infectious urethritis (inflammation of the urethra) in about 50% of cases. Symptoms that may occur include: a painful or burning sensation when urinating, an unusual discharge from the penis, swollen or tender testicles, or fever. Discharge, or the purulent exudate, is generally less viscous and lighter in color than for gonorrhea. If left untreated, it is possible for chlamydia in men to spread to the testicles causing epididymitis, which in rare cases can cause sterility if not treated within 6 to 8 weeks. Chlamydia is also a potential cause of prostatitis in men, although the exact relevance in prostatitis is difficult to ascertain due to possible contamination from urethritis.

Conjunctivitis due to chlamydia.

Chlamydia conjunctivitis or trachoma was once the most important cause of blindness worldwide, but its role diminished from 15% of blindness cases by trachoma in 1995 to 3.6% in 2002. The infection can be spread from eye to eye by fingers, shared towels or cloths, coughing and sneezing and eye-seeking flies. Newborns can also develop chlamydia eye infection through childbirth. Using the SAFE strategy (acronym for surgery for in-growing or in-turned lashes, antibiotics, facial cleanliness, and environmental improvements), the World Health Organisation is aiming for the global elimination of trachoma by 2020 (GET 2020 initiative).

Rheumatological conditions

Chlamydia may also cause reactive arthritis (reiter's syndrome) - the triad of arthritis, conjunctivitis and urethritis (inflammation of the urethra) - especially in young men. About 15,000 men develop reactive arthritis due to chlamydia infection each year in the U.S., and about 5,000 are permanently affected by it. It can occur in both sexes, though is more common in men.

Perinatal infections

As many as half of all infants born to mothers with chlamydia will be born with the disease. Chlamydia can affect infants by causing spontaneous abortion; premature birth; conjunctivitis, which may lead to blindness; and pneumonia. Conjunctivitis due to chlamydia

typically occurs one week after birth (compared with chemical causes (within hours) or gonorrhea (2–5 days)).

Other conditions

Chlamydia trachomatis is also the cause of lymphogranuloma venereum, an infection of the lymph nodes and lymphatics. It usually presents with genital ulceration and swollen lymph nodes in the groin, but it may also manifest as proctitis (inflammation of the rectum), fever or swollen lymph nodes in other regions of the body.

Pathophysiology

Chlamydiae have the ability to establish long-term associations with host cells. When an infected host cell is starved for various nutrients such as amino acids (for example, tryptophan), iron, or vitamins, this has a negative consequence for Chlamydiae since the organism is dependent on the host cell for these nutrients. Long-term cohort studies indicate that approximately 50% of those infected clear within a year, 80% within two years, and 90% within three years.

The starved chlamydiae enter a persistent growth state wherein they stop cell division and become morphologically aberrant by increasing in size. Persistent organisms remain viable as they are capable of returning to a normal growth state once conditions in the host cell improve.

There is much debate as to whether persistence has in vivo relevance. Many believe that persistent chlamydiae are the cause of chronic chlamydial diseases. Some antibiotics such as β-lactams can also induce a persistent-like growth state, which can contribute to the chronicity of chlamydial diseases.

Screening for women

For sexually active women who are not pregnant, screening is recommended in those under 25 and others at risk of infection. Risk factors include a history of chlamydial or other sexually transmitted infection, new or multiple sexual partners, and inconsistent condom use. For pregnant women, guidelines vary: screening women with age or other risk factors is recommended by the U.S. Preventive Services Task Force (USPSTF) (which recommends screening women under 25) and the American Academy of Family Physicians (which recommends screening women aged 25 or younger). The American College of Obstetricians and Gynecologists recommends screening all at risk, while the Centers for Disease Control and Prevention recommend universal screening of pregnant women. The USPSTF acknowledges that in some communities there may be other risk factors for infection, such as ethnicity. Evidence-based recommendations for screening initiation, intervals and termination are currently not possible. There is no universal agreement on screening men for chlamydia.

In England and Wales the NHS National Chlamydia Screening Programme (NCSP) aims to- Prevent and control chlamydia infection through early detection and treatment of asymptomatic infection; Reduce onward transmission to sexual partners; Prevent the consequences of untreated infection; Test at least 25 percent of the sexually active under 25 population annually.

Through the programme chlamydia testing is available for free to men and women under 25 in a range of local venues including Contraceptive and Sexual Health Clinics, Community Pharmacy, General Practice and in some areas postal testing is available.

Diagnosis

The diagnosis of genital chlamydial infections evolved rapidly from the 1990s through 2006. Nucleic acid amplification tests (NAAT), such as polymerase chain reaction (PCR), transcription mediated amplification (TMA), and the DNA strand displacement amplification (SDA) now are the mainstays. NAAT for chlamydia may be performed on swab specimens collected from the cervix (women) or urethra (men), on self-collected vaginal swabs, or on voided urine. Urine and self-collected swab testing facilitates the performance of screening tests in settings where genital examination is impractical. At present, the NAATs have regulatory approval only for testing urogenital specimens, although rapidly evolving research indicates that they may give reliable results on rectal specimens.

Because of improved test accuracy, ease of specimen management, convenience in specimen management, and ease of screening sexually active men and women, the NAATs have largely replaced culture, the historic gold standard for chlamydia diagnosis, and the non-amplified probe tests. The latter test is relatively insensitive, successfully detecting only 60-80% of infections in asymptomatic women, and often giving falsely positive results. Culture remains useful in selected circumstances and is currently the only assay approved for testing non-genital specimens.

Treatment

C. trachomatis infection can be effectively cured with antibiotics once it is detected. Current Centers for Disease Control guidelines provide for the following treatments: Azithromycin 1 gram oral as a single dose, or Doxycycline 100 milligrams twice daily for seven to 14 days. Tetracycline, Erythromycin, Ciprofloxacin 500 milligrams twice daily for 3 days. Agents recommended for pregnant women include erythromycin or amoxicillin. β-lactams are not suitable drugs for the treatment of chlamydia. While they have the ability to halt growth of the organism (i.e. are microbistatic), these antibiotics do not eliminate the bacteria. Once treatment is stopped, the bacteria will begin to grow once more.

Research

Recent phylogenetic studies have revealed that Chlamydia likely shares a common ancestor with cyanobacteria, the group containing the endosymbiont ancestor to the chloroplasts of modern plants, hence, Chlamydia retains unusual plant-like traits, both genetically and physiologically. In particular, the enzyme L,L-diaminopimelate aminotransferase, which is related to lysine production in plants, is also linked with the construction of chlamydia's cell wall. The genetic encoding for the enzymes is remarkably similar in plants, cyanobacteria, and Chlamydia, demonstrating a close common ancestry. This unexpected discovery may help scientists develop new treatment avenues: if scientists could find a safe and effective inhibitor of L,L-diaminopimelate aminotransferase, they might have a highly effective and extremely specific new antibiotic against chlamydia.

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Proteus Syndrome

Proteus syndrome is a complex disorder consisting variably of disproportionate, asymmetric overgrowth of body parts; cerebriform connective tissue nevi; epidermal nevi; vascular malformations of the capillary, venous, and lymphatic types; and dysregulated adipose tissue. Serious complications may ensue, such as pulmonary embolism, cystic lung disease, and various neoplasms. Somatic mosaicism, lethal in the nonmosaic state, is the best working hypothesis. Although Proteus syndrome data are consistent with this hypothesis, it has not been proven. The etiology is unknown to date. Diagnostic criteria are emphasized because misdiagnosis of Proteus syndrome is common. Proteus syndrome, also known as Wiedemann's syndrome (named after the German paediatrician Hans-Rudolf Wiedemann). Proteus syndrome is highly variable, and is named after the Greek sea-god Proteus, who could change his shape. The condition appears to have been first described in the American medical literature by Drs. Samia Temtamy and John Rogers in 1976. Dr. Michael Cohen described it in 1979, only a few more than 200 cases have been confirmed worldwide, with estimates that about 120 people are currently alive with the condition. As attenuated forms of the disease may exist, there could be many people with Proteus syndrome who remain undiagnosed. Those most readily diagnosed are also the most severely disfigured.

Proteus syndrome is a progressive condition wherein children are usually born without any obvious deformities. Tumors and skin and bone growths appear as they age. The severity and locations of these various asymmetrical growths vary greatly but typically the skull, one or more limbs, and soles of the feet will be affected. There is a risk of premature death in affected individuals due to deep vein thrombosis and pulmonary embolism caused by the vessel malformations that are associated with this disorder. Because of carrying excess weight and enlarged limbs, arthritis and muscle pain may also be symptoms — as is the case for Mandy Sellars, a woman living with a form of Proteus syndrome. Further risks may occur due to the mass of extra tissue — Joseph Merrick, the most famous sufferer of Proteus syndrome, himself died when the weight of his head dislocated his neck while asleep.

The disorder itself does not uniformly cause learning impairments: the distribution of intelligence deficits among sufferers of Proteus syndrome appears higher than that of the general population, although this is difficult to determine with statistical significance. In addition, the presence of visible deformity may have a negative effect on the social experiences of the sufferer, causing cognitive and social deficits.

Frequency

Proteus syndrome is believed to be exceedingly rare, with less than 100 confirmed affected individuals reported worldwide. This suggests that prevalence is less than 1 case per 1,000,000 live births.

Prevalence based on Sex

Males are almost twice as likely to be affected as females and also appear to be at greater risk for thrombosis as females.

Genetics

Manifestations probably result from somatic mosaicism for a dominant lethal gene, but the gene locus has yet to be identified. Because hyperplasia and hypoplasia often occur together, another hypothesis suggests that the postzygotic event that results in these clinical manifestations is embryonic somatic recombination leading to at least 3 subsets of cells. These subsets include normal, overgrowth (pleioproteus), and atrophy (elattoproteus) cells. Reports of discordance for Proteus syndrome in monozygotic twins supports the theory that the condition arises postzygotically.

In 2011 researchers determined the cause of Proteus syndrome. In 26 of 29 patients who met strict clinical criteria for the disorder Lindhurst et al. identified an activating mutation in AKT1 kinase in a mosaic state gene. This mutation was not present in more than 1,000 persons who were unaffected by this disorder. Previous research had suggested the condition linked to PTEN on chromosome 10, while other research pointed to chromosome 16. Prior to the determination of the cause of the disease in 2011, other researchers expressed doubt regarding the involvement of PTEN or GPC3.

Diagnosis

The following are the 3 general criteria necessary for clinical diagnosis without regard to specific clinical features: Lesions follow a mosaic distribution or pattern. Problems follow a progressive course. The disorder appears to be sporadic (ie, not inherited).

Diagnostic confirmation also requires the presence of manifestations listed under the following categories: Category A (1 required) - Connective tissue nevus, Category B (2 required), Epidermal nevus.

Disproportionate overgrowth of one or more of the following: limbs, digits, cranium, vertebrae, external auditory meatus, spleen, or thymus. Bilateral ovarian cystadenomas or a parotid monomorphic adenoma in a patient younger than 20 years. Category C (all 3 required): Lipomas or focal atrophy of adipose tissue; Capillary, venous, or lymphatic malformation; Facial features including dolichocephaly, a long face, down-slanting palpebrae, ptosis, depressed nasal bridge, anteverted nares, and open mouth position while at rest.

Treatment

A team of doctors in Australia have trial tested the drug Rapamycin in the treatment of a patient said to have Proteus syndrome and have found it to be an effective remedy. However, the diagnosis of Proteus syndrome in this patient has been questioned by others.

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Media-Fill Test

'Sterile' is a powerful word, with harsh legal implications surrounding non-compliance. Global regulatory authorities would define sterile as 'free of viable organisms', and sterility assurance has become one of the most scrutinised areas of pharmaceutical and medical device manufacture. The favoured method of production of sterile pharmaceutical products includes a terminal sterilisation process, such as autoclaving or irradiation. Since it is not practical to examine every unit for confirmation of sterility, terminal sterilisation processes use biological indicators (BIs) to provide levels of sterility assurance. BIs are substrates carrying high loads of resistant micro-organisms, at levels far greater than the bioburden of the load being sterilised. If everything on the BI is killed, it is reasonable to assume that the load is also free of viable organisms and can be deemed sterile. However, many therapeutic agents would not withstand terminal sterilisation, so aseptic manufacture and aseptic filling processes are required.

Aseptic processing used to produce sterile parenteral drug products and Active Pharmaceutical Ingredients (APIs) involves the handling of pre-sterilised products in a highly controlled environment. Using the BI correlation approach is not applicable here, as aseptic processing involves ensuring a great deal of process control, with sensitive handling of products until they are sealed within their final containers.

All efforts are made to minimise the risk of contamination:

- Filling and support areas are engineered to minimise contamination
- Air in critical areas is supplied at point-of-use as high-efficiency particulate air (HEPA) filtered, laminar flow air at a velocity sufficient to sweep particles away from the filling and closing areas
- Positive air pressure is used to prevent ingress of airborne contamination: anything that can be sterilised must be rendered sterile before it can be taken into the clean area where the process is performed
- Human intervention is kept to a minimum
- Cleaning is thorough and validated
- Disinfection practices are tight and validated
- Monitoring is done to prove the process and environment are under control

Despite such measures, contamination is an ever-present threat, since there will always be a risk that materials and surfaces may carry organisms, and inefficiencies in air filtration may pose a risk. The largest source of potentially viable contamination comes from people – the operators running the filling process. Aseptic processing is a process being operated in a controlled – but not sterile – environment; the probability of non-sterility cannot be calculated. The industry works to recognised, accepted contamination levels, so the probability of viable contamination is recognised and calculated. Routine sampling for sterility testing is not sensitive enough to detect such low level contamination. Sample numbers are too small, and only gross contamination is likely to be detected. Pharmaceutical manufacturers, therefore, need other means of guaranteeing the quality of their product. This is why process simulations (media fills) – supported by environmental monitoring and other related processes – are required. These are used to demonstrate control of the process to the industry standard for allowable contamination levels.

UNITED STATES PHARMACOPEIA (USP) GENERAL CHAPTER <797>: PHARMACEUTICAL

Compounding – Sterile Preparations recommends minimal requirements for personnel training and evaluation in aseptic manipulation skills. These guidelines apply to all organizations that prepare compounded sterile preparations (CSPs), and are enforceable by the FDA, individual state boards of pharmacy, and accreditation organizations. The aim of USP Chapter <797> is to set consistent compounding standards and increase patient safety.

What is a media-fill test?

Aseptic media-fill testing is used to quantify the aseptic technique of compounding personnel or processes and to ensure that the processes used are able to produce a sterile product without microbiological contamination. During this test, a microbiological growth medium, such as soybean-casein digest medium (SCDM), also known as trypticase soy broth (TSB), is substituted for the actual drug product to simulate admixture compounding. This process simulation, normally includes exposing the microbiological growth medium to product contact surfaces of equipment, container closure systems, critical environments, and process manipulations to closely simulate the same exposure that the product itself will undergo. After using TSB instead of actual drug product to prepare a simulated sterile preparations (CSP), the final container is then incubated and checked for turbidity, which indicates the presence of microbial contaminants. Results are then interpreted to assess the potential for a unit of drug product to become contaminated during actual operations (e.g., start-up, sterile ingredient additions, aseptic connections, filling, closing). Environmental monitoring data from the process simulation can also provide useful information for the processing line evaluation.

Process simulation studies should be designed to emulate the routine production process as closely as possible, including formulation, filtration and filling stages. Processes will vary in relation to the type of product to be filled, e.g. liquid or solid dosage forms, and each process simulation is a unique event whereby extrapolation of outcomes cannot be directly linked to actual process contamination rates.

The study will be performed using microbiological growth media in place of active pharmaceutical ingredients (API). Microbiological growth medium, such as soybean casein digest medium, should be used. Use of anaerobic growth media (e.g., fluid thioglycollate medium) should be considered in special circumstances. The media selected should be demonstrated to promote growth of gram-positive and gram-negative bacteria, and yeast and mold (e.g., USP indicator organisms). The QC laboratory should determine if USP indicator organisms sufficiently represent production-related isolates. Environmental monitoring and sterility test isolates can be substituted (as appropriate) or added to the growth promotion challenge. Growth promotion units should be inoculated with a <100 CFU challenge. If the growth promotion testing fails, the origin of any contamination found during the simulation should nonetheless be investigated and the media fill promptly repeated (The cause of the growth promotion failure should also be investigated.) The production process should be accurately simulated using media and conditions that optimize detection of any microbiological contamination. Each unit should be filled with an appropriate quantity and type of microbial growth medium to contact the inner container closure surfaces (when the unit is inverted or thoroughly swirled) and permit visual detection of microbial growth. Some drug manufacturers have expressed concern over the possible contamination of the facility and equipment with nutrient media during media fill runs. However, if the medium is handled properly and is promptly followed by the cleaning, sanitizing, and, where necessary, sterilization of

equipment, subsequently processed products are not likely to be compromised.

Modern culture media, designed for media fill trials, possess certain attributes that facilitate process simulations; they will be irradiated making them suitable for introduction into compounding areas, will dissolve in cold water and have known filtration performance as standard broth can be slow to filter or block the filter.

How is a media-fill test prepared?

USP Chapter <797> provides examples of media-fill test procedures that are considered an adequate representation of each of the three risk levels – low, medium, and high – assigned to CSPs.

Media is generally available in sterile vials and bags, and as sterile and nonsterile powder. Each organization should review the types of sterile compounding performed and mimic their own procedure as closely as possible. For example, the USP low- and medium-risk media-fill examples do not specifically mention the use of a sterile, lyophilized powder for reconstitution as part of the process. If any organization reconstitutes antibiotics from lyophilized powder in vials, this should be included in their media-fill validation process. The media-fill tests should mimic the most challenging or stressful conditions that might be encountered during the preparation (and sterilization, when applicable) of CSPs. Additionally, be sure to clear the compounding area of any real patient compounding records, labels, and drug vials, to assure that the TSB media will not be dispensed in error to a patient. Table 1 for the suggested examples listed in the current proposed revisions to USP Chapter <797>.

CSP Risk Level	Example of Media-Fill Test Procedure
Low	Within an ISO Class 5 environment, transfer, with same sterile 10-mL syringe and needle or dispensing pin, three sets of four 5-mL aliquots of sterile SCDM into three separate 30-mL sterile vials.
Medium	Within an ISO Class 5 environment, transfer six 100- mL aliquots of sterile SCDM by gravity through separate tubing sets into separate evacuated sterile containers. Arrange the six containers as three pairs, and use a sterile 10-mL syringe and 18-gauge needle to exchange two 5-mL aliquots of medium from one container to the other in the pair. Then, inject a 5-mL aliquot from each container into a sterile 10-mL clear vial (three total), using a sterile 10-mL syringe and vented needle or pin.
High	Dissolve 3 g of non-sterile commercially available SCDM powder in 100 mL of non-bacteriostatic water to make a 3% non-sterile solution. Withdraw 25 mL of the medium into each of three 30-mL syringes and transfer 5 mL from each syringe into separate sterile 10-mL vials. (These vials are positive controls and will generate exponential microbial growth, for comparison). Next, in an ISO Class 5 environment, affix a 0.2-micron filter and 20-gauge needle to the previously prepared syringes and inject 10 mL from each syringe into three separate 10-mL sterile vials. Repeat for three more vials, affix sterile adhesive seal, and label.

How is the prepared final container of media incubated?

The USP Chapter <797> Proposed Revisions indicate that vials should be incubated within a range of 20 to 35°C for 14 days. "Positive" test, is indicated by visible turbidity in the medium on or before 14 days. The American Society for Microbiology (ASM) asserts that in their "experience and opinion a range of 32°C ± 2°C covers a broader spectrum of potential contaminants and pathogens". Therefore, a temperature range of 30 to 35°C would likely be acceptable to both the USP and ASM as a range of incubator temperature. It is suggested that a "media-fill results log" be kept, with results documented at days seven and 14 of the incubation process.

What does a turbid or "positive"media test mean?

A positive test could indicate that the compounding employee needs additional training and instruction regarding aseptic technique. Often, simple touch contamination can be the culprit, but a turbid test could also indicate that the controlled cleanroom environment was negatively compromised, possibly due to a malfunctioning blower/motor in a laminar air flow workstation (LAFW) or biological safety cabinet (BSC) or a leak in a hood or cleanroom HEPA-filter. In addition, for highrisk compounding, a positive test could indicate that the integrity of the sterilizing 0.2-micron filter was compromised.

What should be analyzed if the media-fill test is positive?

As part of the aseptic media-fill validation process, written policies and procedures should describe how your organization will meet the USP Chapter <797> requirements and provide employees with a step-by-step process for the media-fill activity. It is suggested that each employee performing media-fill activities have a "mentor" for the activity – someone to verbalize the instructions, step-by-step throughout the activity, and to provide additional observation of aseptic technique. Additionally, the written policy should define the steps to take if a media-fill is positive. Recommended steps include re-training of aseptic technique (with a mentor) and a repeat media-fill test. If tests continue to indicate microbial contamination, further testing of the hoods and cleanroom environment may be necessary. If highrisk compounding is performed during the media-fill, filter integrity may need to be examined as a potential culprit. If environmental air sampling is being performed on a weekly (high-risk) or monthly (low- or medium-risk) basis, review these results to see if any compelling trends are noticed in relation to areas where the positive media-fill activity was performed. All corrective actions and re-testing should be documented as part of the overall quality assurance process.

Along with other quality assurance measures, a robust media-fill program is a necessary step to validate processes of organizations that prepare CSPs. Media-fill testing is just one part of a necessary overall quality assurance program.

Alone, it may not provide enough data to fully validate compounding, but it is an important step in the overall pharmacy quality assurance process.

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Sterile Ready Prepared Media Plate…….

Microxpress is proud and happy to present latest range of **Sterile Ready Prepared Media Plate** in service of the customer.

Microxpress manufacturing setup for Sterile Ready Prepared Plates has been designed as per current GMP (Good Manufacturing Practice) guidelines. The modern set up encompasses manufacturing rooms of class 10000, plate filling carried out in class 100 with Laminar Air flow. Qualified dedicated team of well trained personnel in aseptic and microbiology techniques to handle this critical manufacturing process. Well equipped state of the art automated machines for media preparation and plate filling designed for speed with accuracy.

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Cat no.	Product (Plate size : 90mm x 15mm)
SP000304	Chocolate Agar Plate
SP000303	Chromogenic UTI Agar Plate
SP000308	Dey Engley Neutralizing Agar Plate
SP000504	MacConkey Agar without Crystal Violet, NaCl and with 0.5% Sodium Taurocholate plate
SP000507	Mueller Hinton Agar Plate
SPG000507	Mueller Hinton Agar Plate (γ- irradiated)
SP000508	Mueller Hinton Agar with 5% Sheep Blood Plate
SP000601	Nutrient Agar Plate
SP000101	5% Sheep Blood Agar Plate
SP000903	Sabouraud Dextrose Agar Plate
SPG000903	Sabouraud Dextrose Agar Plate (γ- irradiated)
SP000908	Soyabean Casein Digest Agar Plate
SPG000908	Soyabean Casein Digest Agar Plate (Triple Layer Pack, γ- irradiated)
SP000909	Soyabean Casein Digest Agar with β Lactamase Plate (Triple Layer Pack, γ- irradiated)
SP001001	Tryptone Soya Agar with Lecithin and Polysorbate 80 Plate
SPG001001	Tryptone Soya Agar with Lecithin and Polysorbate 80 Plate (Triple Layer Pack, γ- irradiated)

NOTE: Also available all Harmonized Media Plate (Sterile Ready Plate) as triple wrapped gamma Irradiated.

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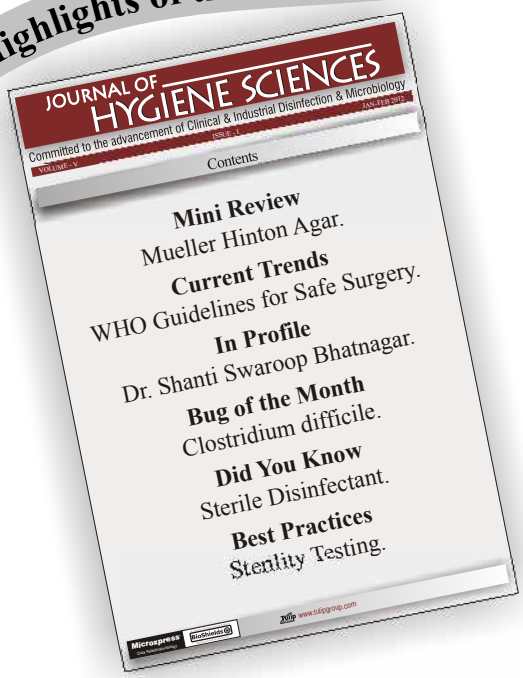
APPLICATIONS :
Medical: In Hospitals, Nursing homes, Medical colleges, Pathological laboratories for Inter-operative irrigation. Pre & post surgery skin and mucous membrane disinfection. Post-operative dressings. Surgical & non-surgical wound dressings. Surgical Bath/Sitz bath. Routine antisepsis during minor incisions, catheterization, scopy etc. First aid. Surface disinfection.
Industrial: In Pharmaceutical industry, Food & beverage industry, Hotel industry etc. General surface disinfection. Eliminating biofilms.

USAGE DIRECTIONS :

Surgical, postoperative, non surgical dressings	–	Use undiluted
Pre & post surgery, skin cleaning & disinfection	–	Use undiluted
Surgical/Sitz bath	–	Add 50 ml of NUSEPT™ in 1L of water & use
Antisepsis during minor incisions, catheterization,	–	Use undiluted scopy, first aid, bites, cuts stings etc
Midwifery, nursery & sickroom	–	Use undiluted
General surface disinfection	–	Add 100 ml of NUSEPT™ in 1L of water and gently mop the floor or surfaces

Highlights of the coming issue



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