International Journal of Pharmacy and Biological Sciences
ISSN: 2321-3272 (Print), ISSN: 2230-7605 (Online)
IJPBS | Volume 9 | Special Issue 2| 50-56
Proceedings of National Seminar on "Health, Hygiene, and Sanitation"
Held at Little Flower Degree College, Uppal, Hyderabad, India, 26th and 27th April 2019
| Review Article | Biological Sciences |Open Access |MCI Approved|
|UGC Approved Journal|

Management and Disposal of Microbiological and Carcinogenic Agents in Laboratories- A Review

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Received: 15 Apr 2019 / Accepted: 20 Apr 2019 / Published online: 01 May 2019
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Abstract
Over the few past decades there are some considerable reports on laboratory acquired infections by the workers and researchers working with pathogenic agents like meningococci, HIV, hepatitis-C, dengue virus etc. The accidental infections acquired by the lab workers are to be evaluated and set periodical standards to prevent such incidences. The practical work at under graduation in Microbiology involves handling pathogenic microbes and potential carcinogenic agents. There is a need to develop awareness right from under graduation level for pupils pursuing Microbiology as one of their elective. The present review is an attempt to bring awareness among the readers about the biosafety levels and the methods used to manage and dispose hazardous microbiological and carcinogenic agents in educational and research institutes. The current study is expected to be helpful in establishing biologically safe laboratories in educational and research institutes. Certain chemicals used in industries and labs act as carcinogens. Carcinogenic chemical substances are regulated by the Occupational Safety and Health Administration (OSHA). Carcinogenic chemical waste materials generated is hazardous hence, treated properly. Laboratory decontamination and destruction of carcinogens in laboratory wastes must be carried out after the conduct of the experiment.

Keywords
Biosafety, laboratory acquired infections, carcinogens, laboratory-waste-disposal

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1.INTRODUCTION
Laboratory biosafety is the term used to describe the containment principles, technologies and practices that are implemented to prevent unintentional exposure to pathogens and toxins or their accidental release. This eventually includes the management and disposal of microbiological and carcinogenic waste produced in the laboratories in the course of their work. Another guiding force for laboratories is laboratory biosecurity which refers to personal and institutional security a measure to prevent the misuse, theft, loss or intentional release of pathogens or toxins [1,8].

The objective of biosafety program is protection of laboratory workers and containment of potentially harmful agents. Containment means use of safe methods, use of equipment and facilities to manage infectious agents in and around the work area. The lab workers must follow the basic elements of containment such as hands on training and proficiency in handling hazardous agents, strict adherence to microbiological practices and techniques and awareness about potentially hazardous agents in the

laboratory [2]. The ways of infection in a laboratory include contact with eyes, mucous membrane, inhalation, ingestion and direct contact with insects or animals. The risk of lab-acquired infections have been increased over the past two decades due to the emergence of various viral out brakes like Ebola, Zika, SARS, Chikungunya, Japanese Encephalitis etc[2-6]. A major means of transmission is aerosol, a suspension of infectious substance of solid or liquid particles in air, small enough to remain airborne for longer periods. After inhalation they usually get deposited in the lower respiratory tract [1,8].

A better understanding of management and disposal of laboratory waste can be achieved by emphasizing on the required biosafety setup to prevent laboratory acquired hazards [9].

2. BIOSAFETY LEVELS

Based on the degree of hazard caused by microbial agents labs were divided into four biosafety levels where the protective practices increase with each level. Similarly, the microorganisms used in the laboratories are also classified into four major risk groups. The biosafety level 1 labs work with least dangerous agents requiring fewest precautions, while biosafety level 4 labs have strict methods as they deal with agents that are very dangerous to human health. Each biosafety level has prescribed barriers to protect against microorganisms. According to Phillips and Runkle the designing of laboratories should include two barriers namely: primary and secondary barriers. The primary barrier includes physical or personal protective equipment used by the lab workers such as gloves, mask or special breathing apparatus. Whereas, the secondary barriers are structural aspects of the laboratory which make the working environment safer against the pathogenic organisms which include special areas for working like laminar air flow, sinks for hand washing, biosafety chambers, special air ventilation patterns designed to prevent contamination of adjacent rooms and other workers [8].

2.1. Biosafety level 1: Microbes of risk group 1 with no threat to healthy humans are handled in BSL-1 labs. Eg: *Bacillus subtilis, Naeglaria gruberi*, non-pathogenic E. *coli* etc. The standard practices in biosafety level 1 are frequent hand washing before leaving the laboratory and after removing blouses Limited access to work area no smoking eating drinking or storage of food in the laboratory care to minimize aerosols decontamination of work area before and after use of mechanical pits decontamination of laboratory ways special containers to dispose needles and sharp objects maintenance of rodents and insect control program and use of personal protective equipments like loves mask I protection for face shield coats etc [10].

2.2. Biosafety level 2: Working in biosafety level 2 laboratories have a risk of accidental infections when the workers are exposed to the infectious microorganisms. These organisms may enter through eyes, nose, ingestion and infected needles. However, these agents do not cause legal infections and are not airborne. These organisms may cause infection in immuno-compromised patients and infections caused by these microorganisms can be prevented by immunization and can be treated by the available antibiotics. Microbes of risk group 2 like measles virus, Salmonella sp., Toxoplasma, Clostridium botulinum, hepatitis-B and other blood borne pathogens are handled here. The risk of accidental infection can be minimized by following standard practices of biosafety level 1 laboratories and few other procedure such as restricted access during conduction of work by hazard warning signs outside the laboratory surveillance of lab persons with appropriate immunization special training in handling hazardous agents and construction of biosafety cabinets [10].

In biosafety level 2 laboratories secondary barriers should include autoclaving of lab glassware in addition to biosafety level 1 secondary barriers. The microorganisms transmitted through aerosol may be studied at biosafety level 2 for diagnostic purpose only. Further experimental requires biosafety level 3 laboratory conditions [9].

2.3. Biosafety level 3: The BSL 3 laboratory deals with microorganisms transmitted through inhalation and are those lethal in their infections. Microbes of risk group 3 like *Mycobacterium tuberculosis, St. Louis encephalitis virus, Francisella tularensis, Coxiella burnetii* are handled here. In 2002 state laboratory worker in USA was reportedly cut his finger while disconnecting a bird 2 test for West Nile virus 4 days later he had symptoms of fever, myalgia, hot flashes and recurring sweats. Another common lab acquired infection is Tularemia transmitted while handling infected rabbits [11].

2.4. Biosafety level 4: Dangerous and exotic agents that pose high risk of life-threatening disease transmitted by aerosol are found in biosafety level-4. Viruses with unknown risk of transmission and having no available therapy or vaccines are also handled here. Eg: Microbes of risk group 4 like Marburg virus, Ebola virus, Congo-Crimean hemorrhagic fever and Lassa fever [11].

Table 1: Comparation on facilities provided at different biosafety levels.

Facility	BSL-1	BSL-2	BSL-3	BSL-4
Isolation of laboratory	No	No	Yes	Yes
Room sealable for decontamination	No	No	Yes	Yes
Ventilation:				
➢ Inward airflow	No	Desirable	Yes	Yes
➢ Controlled ventilating system	No	Desirable	Yes	Yes
➢ HEPA filtered air exhaust	No	No	Yes/No	Yes
Double door entry	No	No	Yes	Yes
Airlock				
Airlock with shower	No	No	No	Yes
Effluent treatment	No	No	Yes/No	Yes
Autoclave				
➢ On site	No	Desirable	Yes	Yes
➢ In laboratory room	No	No	Desirable	Yes
➢ Double-ended	No	No	Desirable	Yes
Biological safety cabinets	No	No	Desirable	Yes
Personnel safety monitoring capability	No	No	Desirable	Yes

3. STERILIZATION AND DISINFECTION

A basic knowledge of disinfection and sterilization is essential for biosafety in the laboratories since heavily solid items cannot promptly be disinfected or sterilized. It is important to understand the fundamental cleaning prior to disinfection. Cleaning involves removal of dirt, organic matter and things from the glassware and other items used in the laboratory. Cleaning also includes washing, mopping, drying, vacuuming, with soap or detergent. Pre-cleaning is essential to achieve a proper disinfection or sterilization. Many germicidal products claim activity only on pre-cleaned items. Pre-cleaning must be carried out with care to avoid exposure to infectious agents. many types of chemicals are used as disinfectant and antiseptics. The germicidal activity of many chemicals is faster and better at higher temperatures at the same time higher temperatures can accelerate their evaporation and also degenerate them. Special care is needed in use and storage of such chemicals in tropical regions. Many of these germicides are harmful to human beings and to the environment. They should be stored, handled and disposal with care following manufacturer instructions [7].

The most commonly used classes of chemical germicides are chlorine releasing compounds like sodium hypochlorite solution, calcium hypochlorite, sodium dichloroisocyanurate and chloramine, formaldehyde, glutaraldehyde, phenolic compounds, quaternary ammonium compounds, alcohols, iodine and Iodophores and hydrogen peroxide [10].

Decontamination of the laboratory area, its furniture and equipments requires a combination of liquid and gaseous disinfectants. The surfaces can be decontaminated using the solution of sodium hypochlorite and equipments can be decontaminated by fumigation with formaldehyde gas generated by heating paraformaldehyde or boiling formaldehyde. This is highly dangerous process that requires specially trained personals. All openings in the room should be sealed with masking tape before the gas is generated. Fumigation should be conducted at an ambient temperature of 21 degree centigrade and relative humidity of 70 percentage. After fumigation area must be ventilated thoroughly and the person entering for ventilating should wear protective masks. The fumigation of small areas require special equipment to generate the hydrogen peroxide vapours [11].

Heat is the most common method of decontamination of pathogens. Dry heat is totally non-corrosive and is used to process many items of laboratories, which can withstand temperature of 160-180 degree centigrade for 2-4 hours. Moist heat is a most effective method used for sterilization of laboratory glassware in the form of autoclaving.

Burning or incineration is also a form of dry heat. Incineration is useful for disposal of animal waste as well as anatomical and other laboratory waste with or without decontamination. Incineration of infectious material is an alternative to autoclaving. A proper incineration requires an effective means of temperature control and secondary burning chamber [7].

Table2: Uses of disinfectants in laboratories.

Disinfectant	Use	Applied Conditions
Sodium hypochlorite	Disinfection of glassware contaminated with blood and body fluids	Should be used in well ventilated areas Protective clothing must be worn while handling undiluted Not to be mixed with strong acids to avoid release of chlorine gas Corrosive to metals
Bleaching powder (7gm/litre of water with 70% available chlorine, may be used in place of liquid bleach if liquid bleach is not available)	Toilets, bathrooms	Should be used in well ventilated areas Protective clothing must be worn while handling undiluted Not to be mixed with strong acids to avoid release of chlorine gas Corrosive to metals
Alcohol (70%) Isopropyl alcohol, ethyl alcohol, methylated spirit	Smooth metal surfaces, tabletops and tabletop on which sodium hypochlorite cannot be used	Flammable, toxic, to be used in well ventilated areas, avoid inhalation To be kept away from heat sources, electrical equipment, flames, hot surfaces Should be allowed to dry completely
Chlorhexidine Combined with alcohol or detergents	Disinfection of skin and hands	Most commercially available preparations contain large amounts of alcohol (70%) and are flammable. Do not use them or store them near a flame, heater, or electrical device. ➢ Apply in a well-ventilated place.

4. BIOLOGICAL WASTE MANAGEMENT AND DISPOSAL

The waste generated from laboratories is a potential reservoir of pathogenic microorganisms and requires appropriate handling. The commonest documented transmission of infection from waste to health care workers is through contaminated needles. Infectious waste can transmit numerous diseases in the community and also to those who handle waste. Besides, the increasing use of disposables in health care is also posing an additional burden on the waste management facility. It is extremely important that the unscrupulous reuse of these disposable items is prevented.

Disposal of biological waste includes two major steps firstly segregation of waste and secondly treatment and disposal [8].

4.1. Waste segregation at point of generation

The laboratory waste requires management at every step from generation, segregation, collection, transportation, storage, and treatment to final disposal. Approximately 25% of the waste generated in health care units is infectious. Therefore, if not segregated properly, the entire waste becomes infectious, increasing the overall cost of waste management. The most practical approach to the management of biomedical waste is to identify and segregate infectious waste, which would in turn

drastically reduce the cost of the waste disposal in health care settings.

Biomedical waste should be segregated into containers or bags at the point of generation. This includes placing different types of waste in different containers or colour-coded-bags at the site of generation. Proper segregation should identify waste according to source and type of disposal or disinfection.

As per the Bio-Medical Waste Management Rules, 2016, the biomedical waste is categorized into four distinguished with colors namely:

- Yellow category: Human anatomical waste, Animal anatomical waste, Soiled waste, expired or discarded medicines, Chemical waste, Chemical liquid waste, discarded contaminated beddings and Microbiology, biotechnology and other clinical waste,
- Red category: includes contaminated recyclable waste,
- White category: includes waste sharps including metals,
- Blue category: includes glassware and metallic body implants.

The color-coded bags as per national norms need to be placed in appropriate containers with the appropriate label/logo e.g. biohazard symbol for infectious waste. Puncture proof containers made of plastic or metal with a biohazard symbol, in blood collection areas, injection trolleys, nursing stations and operation theatres should be made available for collecting metallic wastes. Syringes should be either mutilated or needles should be cut and or stored in tamper proof, leak proof and puncture proof containers for sharps storage. The liquid chemical waste collected at source is pre-treatment or neutralization prior to mixing with other effluent generated from health care facilities. Color coded bags used for collection of segregated waste must be free of chlorine. Solid waste is collected in leak-resistant heavy-duty bags. Coloured bags made of non-chlorinated plastic with biohazard sign and labels mentioning date and details of waste are to be used. The bags are tied tightly after they are three-fourth full [8,10].

4.2. Treatment and disposal

The biomedical waste treatment and disposal facilities are not to be established in the premises of the laboratories unless a common bio-medical waste treatment facility is not available within a distance of 75kms. Highly infectious bio-medical waste generated shall be pre-treated by equipment like autoclave, incinerator or microwave before handing over or segregated. The heads of common bio-medical waste treatment facility shall set up requisite biomedical waste treatment equipment like incinerator, autoclave or microwave, shredder and effluent treatment plant as a part of treatment, prior to commencement of its operation. The standards for treatment and disposal of bio-medical wastes must be complied with the handling and disposal of all the mercury waste and lead waste [12].

Provision must be made within the premises of health care facility for a safe, ventilated and secured location for storage of segregated biomedical waste in colored bags or containers, inaccessible to scavengers and protected against insects, birds, animals and rain, to ensure that there is no secondary handling, pilferage of recyclables, or inadvertent scattering or spillage by animals. The bio-medical waste from such place or premises should be directly transported to the authorized common bio-medical waste treatment facility for the appropriate treatment and disposal [12].

Untreated human anatomical waste, animal waste, soiled waste and biotechnology waste shall not be stored beyond a period of 48 hrs.

All health care workers and others involved in handling of biomedical waste are protection against diseases including Hepatitis B and Tetanus by immunization [12].

5. CARCINOGENIC AGENTS MANAGEMENT AND DISPOSAL

5.1 Carcinogens: Disorder of cells in the body is known as Cancer. A group of cells that fail to respond to the normal control mechanism and continue to divide without need. The new growths are called tumours or neoplasia and may be either "benign" or "malignant". A "benign" tumour is one that remains localised whereas "malignant" tumours invade neighbouring tissues, enter blood vessels, lymphatic vessels and other spaces and can be carried to other areas of the body to form new tumours called "secondaries" or "metastases".

There are so many causes for Cancer, one of which is the adverse effects of certain substances on the cells of the body either directly or via their metabolites. Other reasons may be smoking, sexual promiscuity and low fiber diet.

The factors bearing the risk of cancer developing are dose, duration of exposure, latency, co-factors and the route of entry.

Dose

Some carcinogens are extremely potent and can induce cancer at very low dose levels in a susceptible species. There is often no knowledge available about the lower threshold of dose below which cancer will not occur. The probability that cancer will result is usually proportional to the dose, except that very high doses may have more immediate toxic effects.

Duration of Exposure

Unlike radiation protection control, there is no simple way of monitoring individual exposure to chemical

carcinogens. A single exposure to a carcinogen may be sufficient to induce cancer.

Latency

With carcinogens, there is no immediate indication that harm has resulted from exposure, unless the agent has some other toxic effect. Long intervals generally elapse between exposure to carcinogens and the appearance of tumours resulting from the exposure. Intervals of two or three decades are not unusual.

Co-factors

Some carcinogenic agents are unable to produce cancer alone. Subsequent exposure to another agent is necessary to amplify or promote the initial carcinogenic injury.

Routes of Entry

Carcinogens can enter the human body by mouth into the gut, by inhalation into the lungs and by skin contact. The resulting cancers do not necessarily appear at the site of entry, because carcinogens require chemical transformation in the body into their active form. Carcinogens are chronic toxins. They cause damage after repeated or long-duration exposure.

5.2 Carcinogenic lab chemicals:

As per OSHA (The Occupational Safety and Health Administration) and International Agency for Research on Cancer (IARC) the chemicals recognized and anticipated to be carcinogenic in nature 2-acetylaminofluorene, 3,3'-dichlorobenzidine and its salts, 4-aminodiphenyl, 4-dimethylaminoazobenzene, 4-nitrobiphenyl, Alpha-naphthylamine, Benzidine and its salts, Beta-naphthylamine, Beta-propiolactone, Bis-chloromethyl ether, Ethyleneimine, Methyl chloromethyl ether and N-nitrosodimethylamine (13). Other additional carcinogens are Acrylonitrile, Arsenic, Benzene, Butadiene, Cadmium, Carbon tetrachloride, Formaldehyde, Ethylene dibromide
Ethylene oxide, Methylene chloride (Dichloromethane), Methylenedianiline and Vinyl chloride.

5.3 Limitations of exposures [13,15]:

According to OSHA regulations for 12 specific chemicals the permeable limit of exposure are:

Acrylonitrile -1 ppm for 8 hr TWA
Arsenic compounds -10 ug/M3 for 8hr
Benzene - 0.5 ppm for 8 hr TWA
1,3-butadiene -above 0.5 ppm for 8 hr
Cadmium 2.5 ug/M3 over 8 hr
Chromium+6 compounds above 2.5 ug/M3 for 8 hr
1,2-dibromo-3-chloropropane above 1 ppb for 8 hr
Ethylene oxide 0.5 ppm for an 8 hr
Formaldehyde above 30 ug/M3 8hr TWA for 30 days.
Methylene chloride 12.5 ppm 8hr
Methylenediamine .005ppm (5 ppb) 8hr TWA
Vinyl chloride 0.5 ppm TWA 8hr

5.4 Disposal

Carcinogenic chemical waste materials generated must be treated as a hazardous waste. The empty container must be rinsed three times with a COMPATIBLE solvent and leave opened in the back of the hood overnight. Solvent rinses and water rinse must be disposed of as hazardous waste. As an alternative, unrinsed empty containers can be disposed of through EH&S as hazardous waste. The unrinsed empty containers must be capped. incompatible waste streams should not be mixed. Decontamination of the empty container in order to use it for other purposes is not permitted.

Users should properly segregate, package and label all solid and liquid wastes contaminated with carcinogens. Use of incineration is also one of the best methods to decontaminate the carcinogenic material [15]. Under no circumstance should carcinogenic or highly toxic chemicals be disposed of down drains or into the atmosphere [16].

5.5 Cleaning and Decontamination

Lab-specific information on decontamination may be included in the protocol or procedure section. Individuals must wear personal protection equipment. Laboratory work surfaces must be cleaned at the conclusion of each procedure and at the end of each work day. Upon leaving the designated work area, personal protective equipment worn if any must be removed. Washing of hands, forearms, face and neck must be done. At the end of each project, thorough decontaminate of the designated area should be done, before resuming normal laboratory work in the area.

5.6 Laboratory decontamination and destruction of carcinogens in laboratory wastes.

The following methods of decontamination and destruction of carcinogens in laboratory wastes are based on procedures published by the International Agency for Research on Cancer (IARC).

Organic compounds, including carcinogens, can be destroyed by sodium dichromate in a strong solution of sulphuric acid. One to two days is generally considered sufficient time for the destruction of chemicals when a freshly prepared reagent is used. By then all material should have dissolved in the reagent and can be rinsed away with water.

Carcinogens that oxidise readily can be destroyed with milder agents such as saturated solution of potassium permanganate in acetone. This solution is suitable for the destruction of hydrazines or compounds containing isolated carbon-carbon double bonds. Concentrated or 50 per cent aqueous sodium hypochlorite can also be used as an oxiding agent.

Carcinogens that are alkylating, arylating or acrylating agents can be destroyed by reaction with nucleophiles such as water, hydroxyl ions, ammonia,

thiols and thiosulfate. The reaction of alkylating agents varies greatly, however, and is influenced by the solubility in the reaction medium. The complete reaction can be facilitated by dissolving the agents in ethanol or similar solvents.

Methyl methanesulfonate and ethyl methanesulfonate are moderately soluble in water and can be destroyed in 10% thiosulfate solution. Special care should be taken, however, when gram or greater quantities of these compounds and other highly reactive reagents have to be destroyed. Large volumes of aqueous bicarbonate solutions are recommended in preference to 10% thiosulfate solutions which may cause violent reactions.

Ethyleneimine and its derivatives can be destroyed by acid-catalysed hydrolysis or by thiosulfate buffered to pH 5.

Cyclophosphamide can be destroyed by potassium hydroxide in methanol.

N-Methyl-N'-nitro-N-nitrosoguanidine (MNNG) is slowly hydrolysed in water [16,17]

6. CONCLUSION AND DISCUSSION

Emergence of laboratory acquired diseases due to mishandling or improper diposal practices in research centers and industries can be prevented by providing appropriate laboratory setup depending upon the risk factors and strict adherence to the norms of OSHA, CDC, WHO or NCDC.

Laboraticians are to be trained on annual basis and are to be ensured about the consequences of accidental exposure or misuse of hazardous microbial and chemical agents. There is a need to standardize and implement disposal techniques as a part of procedure or protocol at college and universities. The laboratories established in colleges and universities should maintain biosafety level-2 through the required level is biosafety level-1 in order to create awareness and prevent unscrupulous means of infection or lethal ailments by hazardous agents.

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