



BIOSAFETY AND BIOSECURITY OF LAB AND HOSPITAL ACQUIRED INFECTIONS

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Abstract: *Microbes have the ability to transmit and reproduce. Pathogenic microbes when released and spread in the environment can cause infectious diseases. This release can be natural, accidental, or intentional. Whatever might be the cause of release it can cause devastation and destruction of not just human health but the entire system of the affected region. It is, therefore, very important to handle these microbes with utmost precautions to avoid any such situation. When released either intentionally or accidentally the best response is to limit its transmission by adopting preventive measures. Most of the lab acquired infections (LAIs) are bacterial and viral in nature. Infectious agents having a potential hazard to cause LAIs are bacillus anthracis, Francisella tularensis, Brucella spp., yersinia pestis, smallpox, VHF agents, and botulinum. Small doses of these agents can be controlled under BSL2 while dealing with large quantities requires BSL3 practices. Hospital-Acquired infections (HAIs) can be transmitted via direct or indirect contact, droplet transmission, and air. Pathogens encountered causing HAIs are usually bacteria, viruses, and mites. The transfer of pathogenic agents in healthcare personnel can be avoided by treating them with vaccines whenever such a risk is expected. They should also be given PPEs and trained to use them in an effective manner. All the hygiene and sterilization procedures should be strictly followed. The cleansing of surgical instruments and the physical environment in hospitals is also very important to prevent HAIs.*

Keywords: infectious diseases, pathogens, bacterial, viral, lab acquired infections, Spanish flu

Introduction

Nearly, 1400 species of microbes are known to be of possible threat to humans (Taylor *et al.*, 2001). Release of microbes in the environment causes the epidemic. This release can be as a result of natural mechanism, unintentional release or intentional release. The epidemic of diseases caused by infectious agents has been recorded since 500BC when a typhoid fever like unknown disease 'the plague of Athens' killed almost 100,000 people. The history of Europe has a number of incidents of plagues ranging from Antonine plague that killed 30% of its population to the Black Death that finished 70% of the population. This left the cities deserted and whose record was only found through archeology (Morens *et al.*, 2009; Eitzens and Takafyuji, 1997). An epidemic that crosses boundaries and occurs worldwide, effects people on large scale is a pandemic." This is how pandemic is defined internationally (Harris, 2000). The pandemic of influenza, AIDS, severe acute respiratory syndrome (SARS), plague, west Nile disease, cholera, small pox etc. are the well-known pandemics of human history (Qiu and Chu 2019). Among these influenza has been the worst of all the pandemics. Since 1500s this pandemic occurs periodically three times in a

century i.e. more or less after every 10 to 15 years (Qiu and Chu 2019). During the 20th century the 1st pandemic was in the year 1918 to 1919 which was named as Spanish flu, this pandemic destroyed the lives of more than 20 million people (Morens *et al.*, 2009). This according to WHO is the most severe pandemic of the world history (WHO, 2011). Then second pandemic named Asian flu was in 1957 to 1958, killed almost million deaths and then again in 1968-1969 in Hong Kong occurred third pandemic of influenza and almost one million people died of it (Qiu and Chu 2019).

Of the 21st century major epidemic outbreaks were hanta virus pulmonary syndrome, H5N1 influenza, the Middle East respiratory syndrome, H1N1 influenza and the Ebola virus disease (Gostin *et al.*, 2006). Ebola caused the death of more than 11,000 (Maurice, 2016). In 21st century the first influenza pandemic was of H1N1virus of 009 which killed more than 18000 people worldwide. Microbial forensics deals with bioterrorism by first identifying the source of disease causing biological agent and then associating that act of release to a specific individual or group. Microbial forensics need to improve its competence so that differentiation among unintentional release, natural outbreaks and bio

crimes can be done. It must provide satisfactory quality evidence to carry out legal proceedings (Carus, 2001). Examples of events of bioterrorism include the use of smallpox on South American groups in 15th century with clothes contaminated by variola (Eitzen *et al.*, 1997; Christopher *et al.*, 1997). Also smallpox was used in French-Indian war on the native Indian groups that were unfriendly with British (Christopher *et al.*, 1997; Henderson, *et al.*, 1999).

During the World War 1, some say that Germans sent cattle and horses infected with *B. anthracis* and *P. pseudomallei* to USA and other countries (Eitzen *et al.*, 1997; Stockholm *et al.*, 1994). The 'unit 731' of Japanese bio-warefare program used to test the prisoners of war with pathogenic agents like *Yersinia pestis*, *Shigella* spp, *Vibrio cholera*, *Neisseria meningitides*, *B. anthracis* (Eitzen *et al.*, 1997). Due to this testing almost 10,000 prisoners died between 1932 and 1945, these were the prisoners of World War 2 (Riedel, 2004). In April 1979, the anthrax epidemic started spreading in a city of Russia called Sverdlovsk. Death of livestock started happening in that area. Human anthrax cases there were as result of eating the meat of infected livestock. When investigated by US and European intelligence, they characterized it as the accident release of spores of anthrax (Riedel, 2004).

Before March 1995, using the anthrax and botulin toxin three unsuccessful bioterrorism attempts were made by cult in Japan and before that in 1992 the members of cult made another bioterrorism attempt using Ebola virus in Zaire (Christopher *et al.*, 1997; Caudle, *et al.*, 1997). But no sufficient evidence was collected by Japanese intelligence, only little information collected was made available to public (Riedel, 2004). During 2001 in US the attack by letters of anthrax was another example of bioterrorism. All the current cases at that time were as a result of indirect or direct contact with these letters (Lin *et al.*, 2016). Due to all such attempts of bioterrorism it becomes difficult to differentiate if the epidemic is naturally occurring or an act of bioterrorism (Riedel, 2004). Either the outbreak is accidental or intentional; in both the cases it is important to identify the source of release to ensure public health safety by stopping the further release of microbe. Formation of federal bureau investigation in united stated began microbial forensics in 1990s. The unit called hazardous materials response unit (HMRU) was made to deal with events suspected of bioterrorism. Forensics must be able to answer leader's questions such as the source of biological agent, law enforcement and public health by help of forensic science. The information should be of such

evidence that is acceptable by the audience as well (Riedel, 2004).

World's economy and region's stability both gets effected by the spread of these infectious diseases since these communicable agents easily cross boundaries, as happened earlier in case of HIV, H5N1, H1N1, SARS epidemic and Spanish flu pandemic (Lin *et al.*, 2016; Davies, 2013). Apart from economy and health, pandemics also influence social behavior, political moments, transport, education, agriculture, tourism, animal health and financial sector (Davies, 2013). The certain characteristics that must be present in a biological agent to cause pandemic or to act as an agent of bioterrorism are its pathogenicity, possibly high mortality rate and its ability to cause such an infectious disease that is difficult to treat. Other characters may include its ability to reproduce and spread rapidly and its stability under normal conditions. Communication is of great importance in the prevention and control of pandemics (Philip, 2002). The number of people it would affect would greatly depend upon its route of transmission. Definitely if the agent is airborne is would affect greater number of people in small period of time (Philip, 2002). If the agent transmission is by water or food then it would possibly affect specific groups of people. Other routes of transmission may include blood, body fluids, some insect vectors and medicines (Kruse *et al.*, 1991). Prevention of the spread of these biological agents depends upon its route of transmission (Philip, 2002).

Lab-acquired Infections

Mostly lab acquired infections are due to isolates of new infectious agents shown from experience (Kruse *et al.*, 1991). The factor that risk of infectious agent exposure to lab workers is negligible as compared to other health care workers groups (HCW), but that risk is greater in employees of clinical and research laboratories rather than in the general population. It suggests that unique risks are often linked with the laboratory workspace. At first, it was observed that laboratory-acquired infections are mainly due to bacteria, rickettsia and viruses. Many of these agents were transferred by air so it led to the use and development of biosafety cabinets with laminar flow and HEPA filters. According to this observation, it was thought again that lab associated infections are mostly because of the viruses which transfer mostly through contact and not by bacteria (Kiley, 1992).

Laboratory safety practices with specific agents

(i) *Bacillus anthracis*

Bacillus anthracis is bacterial specie which is present in many clinical samples, including cerebrospinal fluid (CSF), blood, pleural fluid, wound exudates,

sputum and infrequently in urine and feces. The major hazards to lab personnel are indirect or direct contact of infectious inoculation culture with intact or broken skin. Screening of environmental samples lead to the hazard of aerosol infections exposure. To control the spread of culture and clinical specimen of *Bacillus anthracis*, BSL2 practices along with containment facilities and equipment are enough. But if we are working with high loads of cultures for which there is high potential of aerosol spread, including suspect powder, then we apply BSL3 conditions (Lin *et al.*, 2016; David, 2003).

(ii) *Francisella tularensis*

F. tularensis is commonly spread through air and an easy cause for lab acquired infections. *Francisella tularensis* is nearly present in all clinical specimens. However, in most cases, large amount of liquid cultures of *Francisella tularensis* are handled in research facilities. Hazards include accidental ingestion of the culture, direct contact of infectious culture with the mucous membranes or skin. Manipulation of cultures can be exposed through the air in the form of droplets and can cause infection. Among all the biggest risk to lab workers comes with the manipulation of cultures. For the safe handling of *Francisella tularensis*, practices of BSL2 and containment equipment is suitable but more accurate with BSL3 when handling cultures (Gilchrist *et al.*, 1992; Lin *et al.*, 2016; David, 2003).

(iii) *Brucella spp.*

The most vulnerable laboratory-acquired infection reported is the infection of Brucellosis because only a small dose of it can cause infection. The sources of Brucellosis spread include blood, semen, CSF fluid and seldom, urine. Hazards associated with the spread of this infectious agent are either the direct contact or indirect contact of Brucellosis with mucous membrane or skin, or accidental ingestion of air droplets generated during culture manipulation. Laboratory safe handling is working with Brucellosis in BSL2 and clinical safe handling in BSL3 are recommended (Lin *et al.*, 2016; David, 2003).

(iv) *Yersinia pestis*

Y. pestis is not a usual cause of lab acquired infections. The chances of its spread are rare. Samples of *Yersinia pestis* include blood, CSF fluid, feces, sputum, urine and bubo fluid. Hazard of *Yersinia pestis* spread to lab personnel include exposure to infectious aerosols or droplets of manipulated cultures, accidental ingestion or inoculation and direct contact of infectious cultures with skin or mucous membrane. With small sample sizes, BSL2 is recommended for the safe handling of *Yersinia pestis* but at large sample sizes with high potential of spread through air droplets, BSL3

practices are recommended to carry out (Gilchrist *et al.*, 1992; Lin *et al.*, 2016; David, 2003).

(v) Smallpox virus

Smallpox virus has a very high potential of spread to lab personnel therefore, very high precautions are undertaken for its safety. The main sources of smallpox virus are respiratory excretions and tissues and smallpox lesion crusts or fluids. The primary hazards include exposure not infectious aerosol dispersal, accidental ingestion or parenteral inoculation, or direct or indirect contact with broken skin or mucous membrane. At clinical level, if there are mild or high symptoms of smallpox present in a patient, doctors should immediately contact state health department prior to collect the specimen. The lab personnel who is previously vaccinated against small should only be allowed to collect samples. Testing of patients with very high risk and potential of smallpox should be done by National laboratory of D level. BSL2 conditions are enough for testing patients with low risks of smallpox infection. In any case smallpox is not identified by testing, immediately contact with local or state level health departments (Lin *et al.*, 2016; David, 2003).

(vi) VHF agents

Hemorrhagic fevers also pose greater risks of lab acquired infections to the lab personelles. Samples of this infectious agent are urine, blood, semen, throat and respiratory excretions. Infectious aerosol exposure, unintentional ingestion or parenteral inoculation and exposure of mucous membrane with infectious air droplets are primary hazards of spread of VHF agents. Safe handling of VHF agents is carried out with BSL3 practices and appropriate PPEs to lab personnel. After consultation, specimen from patients suspected with VHF agents should be send to National Laboratory for testing procedures (Lin *et al.*, 2016; David, 2003).

(vii) Botulism

Botulinum also poses a threat to lab infections. Sources are feces, serum, environmental samples, gastric juice and food. Primary hazards include direct contact of mucous membrane or broken skin with botulinum toxins and through the ingestion of toxins along the respiratory tract. Safe handling of botulinum toxins is carried out in BSL2 with a face shield or mask. Manipulated cultures are treated under BSL3 (Gilchrist *et al.*, 1992; Lin *et al.*, 2016; David, 2003).

Management of laboratory accidents

A safety plan is the most careful approach to identify the potential hazards and risks of laboratory accidents and exposures to infectious agents. Thus, minimizing the cause of lab accidents or potential exposure (Gilchrist *et al.*, 1992). All the management and

control programs are planned according to that infectious agent while keeping in view all its risk assessments (David, 1995). If there occur an accidental exposure, it should be reported immediately to the safety officer and the supervisor. After the accident, instant medical care is sent to give first aid to lab personnel and to control the exposure of the infectious agent. Following are the investigation of the accident to determine the risk factor and source of exposure, specially, in the case blood borne pathogens. On the subject of risk assessment of infection, confidential medical consultation with the employee is arranged so to get more information about the potential of transmission of infection to the family members, future supervision and medication, the need of prophylaxis and helpful actions that could be taken in the future to prevent the accidental exposure of infectious material. If the patient is infected with the blood borne pathogen e.g. HIV virus or any type of hepatitis virus, the action plan is dependent on the status and level of infection of the patient. Employee health manual should cover the management plan of already occurred lab accidents and also the expected future lab exposures based on the frequency of that infectious agent to cause disease in population and also its types which are under use in industrial and research projects (David, 1995).

Hospital-acquired Infections

Hospital acquired infections (HAIs) is an important safety issue for health stability givers and their patients. Considerations of being unhealthy, death rates, longer stay at hospitals, and thus the increased costs are also important in this regard. Therefore, measures should be taken to make the health care institutions as safe as they possibly could be by getting rid of such infections (Plowman *et al.*, 1999; Wenzel, 1995). HAIs are caused by a variety of sources. These include viruses, other microorganisms such as bacteria and fungi as the possible factors. Significant reasons that cause vulnerability to HAIs are the instruments used for cannulation, drug delivery for therapy and contact with infectious fluids from the patient's body during supportive healthcare procedures. The Centers for Disease Control and Prevention (CDC) has given an alarming approximate figure of two million people being affected by HAIs each year out of which almost 100,000 lose their lives due to it (Deoine *et al.*, 2009).

Sources of infectious agents

The factors causing infections are usually traced back to human sources, but physical environment also plays a considerable role in transmission. Human carriers and sources include. Patients, health care

providers, family members and other visitants. These sources may be carrying infections in active form, or the pathogens may be harboring in the incubation time in them or they may be acutely or chronically affected by those pathogens which are deposited in their respiratory system or gut. The naïve set of disease-causing organisms in such tracts may also be a factor in causing HAIs (Siegel *et al.*, 2007).

Modes of Transmission and their control

Direct contact transmission

As mentioned previously the infected fluids from a patient's body can infect the healthcare providers. Blood or other such fluids can meet the patient via mucous membrane (Rosen 1997) or exposed areas such as cuts and wounds on the skin (Beltrami *et al.*, 2003). Mites from the body of a patient suffering scabies are transmitted to the skin surface of a healthcare provider by just a direct contact with the patient's skin for example the on contact without gloves (Obasanjo *et al.*, 2001; Andersen *et al.*, 2000). Similarly, a caregiver can be infected with whitlow on hand or fingers after direct handling of an HSV patient when giving oral treatment to a patient especially in the absence of gloves. On the other hand, HSV can be transferred to a patient from the pathogen carrying hands of a caregiver with no gloves and contamination with herpetic whitlow (Avitzur and Amir, 2002).

Indirect contact transmission

Infections can spread by the hands of health caregivers if they do not follow the proper hand hygiene procedures between treating more than one patient. Pathogens from one patient may be transmitted to the other by the contaminated hands or healthcare instruments of the healthcare personnel (Duckro *et al.*, 2005). The healthcare devices are another factor of indirect contact transmission leading to HAIs. These can include temperature monitoring thermometers, glucose measuring apparatus etc. If these instruments have come into contact with an infected person and are contaminated with the patient's body fluids such as blood or saliva and then they are not properly sanitized before being used for other patients they can definitely transmit the pathogens from one patient to the other (Brooks *et al.*, 1992). Moreover, patients in early ages may exchange toys in the pediatric spaces. These toys if contaminated can become a reason for the spread of diseases especially those associated with respiratory tracts. They may contain viruses such as RSV (respiratory syncytial virus) or infectious bacteria such as *Pseudomonas aeruginosa* and many others (Agerton *et al.*, 1997; Hall and Douglas, 1980). Healthcare devices such as stethoscope and other surgical apparatus can carry and transmit pathogens if

not properly cleansed and sterilized before use from one patient to another. Some of these might have manufacturing shortcomings that inhibit efficient disinfection processes and thus are a potential tool of transmission of HAIs (Srinivasan *et al.*, 2003).

Droplet Transmission

Pathogen containing droplets that can be inhaled are generated during coughing, sneezing or simply talking of a patient (Papineni and Wolfenden, 1997; Wells, 1934). They can also be produced during oral procedures such as suction, endotracheal procedures, cough treatments, chest therapies and cardiopulmonary processes (Loeb *et al.*, 2004). Epidemiological researches prove this method of transmission via droplets (Gilchrist *et al.*, 1992; Fowler *et al.*, 2004). Other experimental studies and aerosol science have also mounted evidence proving such transmission (Gehanno *et al.*, 1999). Conventionally, the region of high risk is within 3 feet of the infected patient and this is based on epidemiological and experimental researches of some infections (Valenzuela *et al.*, 1991; Bassinet *et al.*, 2004). Using face masks within this distance and otherwise around patients has proved to be useful in getting rid of such transfers of HAIs via droplets. In the light of above facts, it is important to wear face masks with 6 to 10 feet or while entering the vicinity of an infected patient especially when the risk of such virulent pathogenic infections is inevitable (Feigin *et al.*, 1982). Some of the disease causing pathogens that are transferred by this method include *Neisseria meningitidis* (Dick *et al.*, 1992; Duguid, 1946), Rhinovirus (Papineni and Rosenthal, 1997), *Bordetella pertussis* (Christie *et al.*, 1995), group A streptococcus (Hamburger and Robertson, 1948), *Mycoplasma pneumonia* (Steinberg *et al.*, 1969), influenza (Weinstein *et al.*, 2003) and adenovirus (Musher, 2003), SARS related corona virus (SARS-CoV) *etc.* (Seto *et al.*, 2003; Varia *et al.*, 2003).

Airborne Transmission

Pathogens and other infectious agents can spread through long distances by the movements of air particles and waves. These pathogens may then be inspired by the vulnerable persons who do not have any direct contact with the infected patient (Coronado *et al.*, 1993; Bloch *et al.*, 1985). This type of transfer of pathogens can only be stopped by using particular air treating and ventilating methods such as AIIRs to inhibit the spread and removal of such disease-causing pathogens (LeClair *et al.*, 1980). The pathogens which can be removed via this procedure include Rubeola virus. Other infectious agents that can be stopped include *Mycobacterium tuberculosis* (Riley *et al.*, 1959; Beck-Sague *et al.*, 1992), measles (86) as well as the chickenpox virus called Varicella-

zoster virus (87). Moreover, respiratory protective equipment that is certified by NIOSH such as N95 or a better respirator is endorsed for the healthcare providers who enter AIIR so that infections with pathogenic agents such as *Mycobacterium tuberculosis* can be prevented (GiHaleychrist *et al.*, 1989).

Response to bioterrorism

Various bioterrorism events in the past enabled the scientist and researchers devise an effective way to deal with bioterrorism attack. This response includes two steps (Erenler *et al.*, 2018) early detection of the biological agent, (Vatansever *et al.*, 2013) emergency role of various healthcare and laboratory departments (Erenler *et al.*, 2018).

Detection

Various methods of decontamination and detection have been developed and applied recently due to which this step has shown significant progress (Vatansever *et al.*, 2013). Huge burden may rise on the healthcare system since many people can get infected in quite a small period of time (Keim *et al.*, 1999). Know how about the biological agents to the professionals of healthcare are stimulated by the US Center of Disease Control as this would help escape the logistic problems and the problem of lack of resources and medication. A new program is been made 'bioterrorism preparedness and response program' in association of the government organizations and the healthcare staff for the immediate response and detection in case of a bio crime act (Vatansever *et al.*, 2013). Preservation of adequate resources, starting immediate appropriate response and the possibility of occurrence of minimal casualties are all dependent on the early detection of bio crime. Sometimes the symptoms of biological agent used in bio crime are similar to everyday disease symptoms and can be mistaken with them that is way enough knowledge about warfare agents is very essential (Busl *et al.*, 2012). Determination of a bio crime agent has a strong relationship with the maintenance of suspicion strong index (Kman *et al.*, 2012). Existence of these agents is rapidly and accurately determined these days because of the newly developed technologies. These new techniques and technologies are easy to use, portable and are efficient enough to detect multiple agents at a time to identify the bioterrorism agent in small amounts is also very important and for this the development of sensor based on nucleic acid are under research (Thavaselvam *et al.*, 2010).

Responsibilities of emergency sectors

A safe communication between the infectious disease workers, infection control workers and emergency room staff in the hospitals should be developed by

the advisory of health network and regular meetings should be conducted to share the current situation information and the effective response that should be opted. New programs to cope up with the situation should be formed (Thavaselvam *et al.*, 2010). Training of the health workers by various training programs would increase the number of people that would deal with the emergency and would prove useful (Olson *et al.*, 2010). The condition of developing countries is the worst when such infection spread and so there is a greater need to increase the emergency personnel. Training may be given either online or in person (Chandler *et al.*, 2008). Funding, space and staff needed to cope up with the emergency must be asked from general public that is capable. Keeping in context the type of outbreak help should be asked from other sectors such as police, intelligence, forensics, law enforcement agencies and customs. These should work in collaboration with environmental, public, social and animal health organizations (Posid *et al.*, 2013). Simultaneously the scientist and researchers should start working on the development of vaccines and antibody serum as these two are most effective treatments in case of infectious diseases (Martensson *et al.*, 2010).

Conclusion

Once these infectious agents get spread, no one can determine the destruction it would cause so it is best to safely handle these agents by various methods discussed above so that its chances of release are minimized. If an epidemic has spread, the immediate preventive measures one can take is to minimize its transmission by adopting various methods depending upon its route of transmission. Obviously it is impossible to prevent the initial cases of the epidemic because of the lack of information but once the preventive measures become defined by the researches, the spread can become limited by the responsible and mature public response.

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