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Biosafety in the Era of Emerging Infections

Anuradha De*

M.B.B.S., M.D. in Microbiology
Former Professor, T. N. Medical College & BYL Nair Ch. Hospital, Mumbai, INDIA

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***Corresponding author**: Anuradha De, M.B.B.S., M.D. in Microbiology Former Professor, T. N. Medical College & BYL Nair Ch. Hospital, Mumbai, INDIA. Email: dranuradhade@gmail.com

Abstract

Emerging microbial threats need to be met with deliberative actions such as improved surveillance and outbreak response measures. It is a challenging task and the role of the laboratory in diagnosis and research of emerging diseases are indispensable. Development and implementation of laboratory biosafety principles is therefore critical as part of a response for preparedness to future outbreaks of emerging infections. Any comprehensive approach to biosafety needs to be based on a combination of administrative controls, standard operating procedures, engineering controls, personal protective equipment and appropriate professional training of Health Care Workers (HCWs) at Community and Healthcare facility Centers. The concept of biosafety self-protection must be emphasized, so that HCWs can protect themselves from diseases and avoid spreading them.

Introduction

Biosafety refers to the prevention and control measures taken to reduce risk factors leading to infectious diseases and/or to eliminate pathogenic microorganisms and their potential toxins. The World Health Organization's 2006 publication defines Laboratory Biosafety as "the containment principles, technologies and practices that are implemented to prevent the unintentional exposure to pathogens and toxins, or their accidental release". Merriam Webster's online dictionary reports the first use of the term "**Biorisk"** in 1966, defined as "the containment of extremely pathogenic organisms (such as viruses) usually by isolation in secure facilities to prevent their accidental release especially during research". The concept of **Biocontainment** is related to laboratory biosafety and pertains to microbiology laboratories in which the physical containment of pathogenic organisms or agents is required, usually by isolation in environmentally and biologically secure cabinets or rooms, to prevent accidental infection of workers or release into the surrounding community during scientific research.

Biosecurity encompasses a set of preventive strategies designed to reduce the menace of transmission of infectious diseases in crops and livestock, isolated pests, or genetically modified organisms (GMOs).

Over the past years, a broad spectrum of pathogenic agents, such as bacteria, fungi, viruses, parasites, or genetically modified organisms, gained a substantial concern due to their profound biological as well as ecological risks, to tackle biosafety/biosecurity and biocontainment issues. Emerging infections require biosafety awareness and procedures. In 2015, the MERS outbreak in Korea focused on HCWs and their ability to self-protect from infectious materials. Human error and poor technique contribute to unnecessary exposure and compromise the best safeguards set into place for protection. All Health Care Workers (HCWs) must recognize and adopt biosafety concepts and guidelines to keep them safe from newly emerging highly infectious diseases such as SARS, MERS, Ebola, Zika, SARS CoV-2, etc.

Emerging Infections

Table 1 shows the important emerging infections and their characteristics. Emerging foodborne and waterborne diseases accounts for 20 million cases in the world annually. Incidence

is increasing - half of all known food borne pathogens have been discovered during the past 25 years. Most commonly associated organisms are Enterohemorrhagic *Escherichia coli*, *Vibrio cholerae* and *Campylobacter* spp.

Table 1: Important Emerging Infections and their Characteristics

Infection	Year	Characteristics
Nipah Virus	1998-1999 2001, 2007 May 2018 September 2023	First outbreak in Malaysia. Outbreaks in West Bengal. Outbreak in Kozhikode and Malappuram in Kerala. Sixth outbreak in India. Zoonotic disease spreading from fruit bats. Fatality rate is 45%–75%.
Severe Acute Respiratory Syndrome (SARS)	In 2003	Started from Guangdong Province in Central China (1,511 cases with 57 deaths). In Canada, Singapore, and Vietnam, between 40% to 57% of cases were reported among HCWs working in the respiratory disease research laboratory.
Avian Influenza (H5N1)	Since November 2003	Affected 60 countries across Asia, Europe, Middle East and Africa. Globally mortality rate linked to influenza A H5N1 infection is 53%. Greater than 220 million birds killed by this virus or culled to prevent further spread.
Swine Flu (H1N1)	Since April 2009	WHO declared public health emergency. May 16th 2009, India reported the first confirmed case.
Zika Virus	In 1952 In 2015	First human case was detected. An epidemic of Zika virus occurred in South America, Central America and in the Caribbean.
Ebola Hemorrhagic Fever	As of January 31, 2016	28,639 cases of Ebola virus disease and 11,316 deaths. WHO reported that HCWs were 21 to 32 times more likely to be infected by Ebola than general adults. Characterized by high mortality (30%–90%).
Middle East Respiratory Syndrome (MERS-CoV)	May 2012 Since September 2012	First case in a farmer from Bahrain. 1638 laboratory confirmed cases of MERS-CoV cases globally in 26 countries, including 587 MERS-CoV - related deaths.
Severe Acute Respiratory Syndrome Coronavirus 2 (SARS CoV-2)	In Dec 2019 11th March, 2020	Began in Wuhan, China. Declared a pandemic by World Health Organization. Total cases worldwide till 7th December 2023 were 698,957,477 with 6,948,104 deaths. Records of infections in medical workers and family clusters and evidence of human-to-human transmission.

Biorisk assessment for working with emerging infections

Increased biorisk is faced by workers when handling emerging infections with high viral loads and which involves aerosol-generating methodology. Biorisk assessment is one of the key principles of biosafety. It is a very important process that includes identification, the probability of occurrence and the severity of a potential adverse effect on human health or the environment associated with a specific use of a pathogen or GMO. It identifies the hazardous characteristics of an infectious organism, the activities that could lead to exposure, the chances of contracting a disease after an exposure and the consequences of an infection.

The **AMP model** for biorisk management stands for assessment, mitigation and performance. It implies that control measures (mitigation) should be based on a substantive risk assessment (assessment) and also that the effectiveness and suitability of the control measures be evaluated (performance). Biorisk mitigation controls or reduces the possibility of accidental exposure or unauthorised access to harmful microbes with the use of safety equipment, personal protective equipment (PPE) and behavioral practices.

This model determines the appropriate biosafety levels to be implemented, the level of risk (the route of spread, stability in the environment, presence in various body sites, sample types and the number of cases likely to be encountered) and safety practices for the work. Laboratory-specific issues of biorisk concern include sample collection and handling, the kind of tests and instruments used, sample disposal and storage, and disposal of biohazardous waste. Risk of exposure is also faced during decontamination and repair of instruments. Risks to laboratory personnels should be reduced to minimum by the provision of appropriate equipment, PPE, procedures and an adequate level of training. It minimizes risk and provides a safe working environment. Once performed, risk assessments should be reviewed routinely and revised when required.

Special attention should be given to the genetic modification of emerging viruses, that become modified in

increased transmissibility in humans and the potency to cause human pandemic threats. High-efficiency particulate air (HEPA)-filtered respirators or powered air-purifying respirators (PAPR) are essential for the safe handling of viruses, which have the potential of human infection. Table 2 shows the classification of infectious microorganisms by Risk Group.

Table 2: Classification of Infectious Microorganisms by Risk Group

Risk Group Classification	WHO, Lab Biosafety Manual, 2004
Risk Group 1	**(No or low individual and community risk)** A microorganism unlikely to cause human or animal disease.
Risk Group 2	**(Moderate individual risk; low community risk)** A pathogen that can cause human or animal disease but is unlikely to be a serious hazard to lab workers, the community, livestock or environment. Lab exposures may cause serious infection, but effective treatment and preventive measures are available and the risk of spread of infection is limited.
Risk Group 3	**(High individual risk; low community risk)** A pathogen that can cause serious human or animal disease but does not ordinarily spread from one infected individual to another. Effective treatment and preventive measures are available.
Risk Group 4	**(High individual risk; high community risk)** A pathogen that usually causes serious human or animal disease and can be readily transmitted from one individual to another directly or indirectly. Effective treatment and preventive measures are not usually available.

Biosafety Levels

There are four biosafety levels. Each level has specific controls for containment of microbes and biological agents. The primary risks that determine levels of containment are infectivity, severity of disease, transmissibility and the nature of work conducted. Table 3 shows the risk group and biosafety levels used for emerging viruses.

Table 3: Risk group & Precautions for Emerging Viruses

Virus	Risk Group	Recommended precaution
Zika Dengue	2	BSL2
Hanta HIV H1N1 H5N1 West Nile Chikungunya Japanese encephalitis SARS CoV-2 MERS-CoV	3	BSL2 for diagnostic purposes; BSL3 for virus propagation
Hendra Nipah Ebola Marburg Crimean-Congo hemorrhagic fever Junin Lassa	4	BSL4 for all work

Biosafety level (BSL-2) differs from BSL-1 because laboratory personnel receive specific training in handling pathogenic agents and are supervised by scientists competent in handling infectious agents and associated procedures; access to the laboratory is restricted when work is being conducted; and all procedures are done in BSC Class I.

Safety controls within a BSL-3 laboratory include the use of PPE, including goggles and gloves (respirators may also be required); The use of solid-front wraparound gowns, scrub suits and/or coveralls is often required; Access to a hands-free sink and eyewash station should be available near the exit; and all procedures are done in BSC Class II.

Biosafety Level 4 is required for work with dangerous and exotic agents that pose a high individual risk of aerosol-transmitted laboratory infections and life-threatening disease that is frequently fatal, for which there are no vaccines or treatments, or a related agent with unknown risk of transmission. Laboratory staff must have specific and thorough training in handling extremely hazardous, infectious agents. All staff must be competent in handling infectious agents and procedures requiring BSL-4 containment. The laboratory supervisor should control access within the BSL-4 laboratory in accordance with institutional policies. There are two models for BSL-4 laboratories – Cabinet Laboratory (all handling of infectious agents and infected animals must be performed in Class III BSCs) and Suit Laboratory (personnel must wear a positive pressure protective suit). BSL-4 builds upon the standard practices, procedures, containment equipment and facility requirements of BSL-3. However, BSL-4 cabinet and suit laboratories have special engineering and design features to prevent microorganisms from being disseminated into the environment and personnel. The BSL-4 Cabinet laboratory is distinctly different from a BSL-3 laboratory containing a Class III BSC. India's most advanced BSL-4 category laboratory National Institute of Virology in Pune, Maharashtra was established in 2012.

Biosafety Cabinets

There are three classes of Biosafety Cabinets (BSCs) – Class I, Class II and Class III. Table 4 shows the characteristics of different classes of BSCs. Class II BSC is further divided into Types A1, A2, B1, B2 and C1. Depending on inlet flow velocity and % of HEPA filtered air recirculated, Class 2 BSC is further divided into: Type A1 – 30% exhausted to room; Type A2 – 30% exhausted to outside; Type B1 – 70% exhausted to outside; Type B2 – 100% exhausted to outside. Gaseous decontamination of working areas is only required at BSL3 and BSL4 and that also in particular cases. The primary methods for decontamination of BSC are the use of formaldehyde gas, the vapor phase of hydrogen peroxide and chlorine dioxide gas.

Table 4: Characteristics of Classes of Biosafety Cabinets (BSCs)

Class of BSC	Characteristics
Class I BSC	Ventilated cabinet with inward airflow and air exhausted through HEPA filters to outside. CDC Hood protects personnel and environment. Room air is drawn in through the front opening at a minimum velocity of 0.38 m/s. Front opening allows operator's arms to reach the work surface inside the cabinet, while observing the work area through a glass window. Obsolete for the past several decades.
Class II BSC	Provides an inward airflow to protect personnel. Protects personnel, product and environment. Exhaust HEPA filtered air to protect environment from particulate and aerosol hazards. HEPA filtered (sterile) air flows over the work surface. Working with infectious agents in Risk Groups 2 and 3. In Gr 4, when positive pressure suits are used.
Class III BSC	HEPA filter provides particulate-free, but somewhat turbulent airflow within the work environment. Require special ventilation systems. Long heavy-duty rubber gloves attached in a gas tight manner to allow manipulation of materials isolated inside. HEPA filtered air flows over the work surface Usually installed in maximum containment laboratories with controlled access.

Preventive Measures

Biosafety must be introduced at the hospital to safeguard all Health Care Workers (HCWs) from these emerging infections. In a high containment (BSL3) facility, the essential elements for containment include good microbiological techniques, specialized safety practices and procedures (management of contaminated samples, sample transportation), safety equipment and containment devices (often called primary barriers) with the design and construction of proper laboratory facilities (often called secondary barriers) to protect persons inside and outside the facility. In the US, the CDC has offered online Biosafety training for emergency room HCWs dealing with emerging infectious disease patients since the Ebola outbreak in 2014. Developed by Johns Hopkins University, the training includes PPE preparation and emergency room guidelines to assist HCWs dealing with infected patients. Three internationally recognized regulatory agencies, i.e., WHO, FAO (Food and Agriculture Organization) and OIE (World Organization for Animal Health), published biosafety guidelines to assist developing countries in the publication of their biosafety manuals. These manuals train HCWs using a standardized training package to improve biosafety awareness and also well-organized and proper biosafety and biosecurity precautions.

Biohazards can be minimized and controlled by implementation of nationally and internationally certified protocols and hazards-free laboratory procedures by maintaining the following principles: Primary and secondary barriers; Personal and procedural barriers; Protective barriers; Proper microbiological techniques; Proper culture handling procedures; Proper (bio)-waste management; Disposing

anatomical biomedical waste and animal carcasses by incineration; Adequate facilities such as appropriate sterilization or decontamination services; adequate protection and deprotection steps; Specialized education, training programs and first aid awareness of laboratory workers.

Disinfection

Correct disinfection is essential for interrupting the environmental spread of emerging pathogens in the laboratory. Some virus species are resistant to harsh environmental conditions and are able to remain infectious on surfaces over long periods of time, thereby presenting high resistance to disinfection. Potassium hydroxide- and sodium hydroxide-based alkaline detergents, peracetic acid, acetic acid-based disinfectants and gaseous hydrogen peroxide are known to have capacity to inactivate several viruses. They offer virucidal efficacy and can provide for a very high level of protection. Zika virus is killed by potassium permanganate at 0.5%, 24 hours of contact with ether and temperatures above 60 °C but is not inactivated by 10% ethanol.

The virus inactivation mechanisms of several common virucidal agents consist of treatments with ultraviolet (UV) radiation, singlet oxygen and hypochlorous acid, whereas chlorine dioxide and heat interrupt the process of host cell recognition for virus binding. Due to the presence of essential lipids in their envelope, enveloped viruses are considerably more susceptible to virucidal chemicals. Among the nonenveloped viruses, those with a smaller particle size are less susceptible than those of a larger size.

Personal protection

Personal Protective Equipment (PPE), such as impermeable gloves, coats, gowns, cuffed gowns or disposable coverall suits, long-sleeved shoe covers, boots, face masks, eyes protection or goggles, are generally used in the handling of emerging diseases. The use of respirators is an important consideration in diagnostic and research settings, where aerosols pose a high risk of infection to workers.

Some recommended practices related to personal protection include:

- Wearing laboratory coveralls, gowns or uniforms during work in the laboratory
- Wearing appropriate gloves for all procedures that may involve direct or accidental contact with potentially biohazardous materials and removing gloves aseptically after use, followed by washing hands
- Washing hands after handling infectious materials before leaving the laboratory working areas
- Not wearing open-toed footwear in laboratories
- Not eating, drinking, smoking and handling contact lenses
- Not storing human foods or drinks in the laboratory
- Not storing used protective laboratory clothing in the same compartment as street clothing.
- Vaccination may provide a higher level of personal protection.

All procedures involving the manipulation of infectious materials must be conducted within biological safety cabinets or other physical containment devices. When procedures cannot be performed in a BSC, alternate containment equipment should be used.
Decontamination of work surfaces after completion of work and after any spill or splash of potentially infectious material are required with appropriate disinfectant.

Special safety practices and facilities for BSL-4 Laboratory

- Laboratory personnel and support staff must be provided with appropriate occupational medical service including medical surveillance and available immunizations for agents handled or potentially present in the laboratory.
- A system must be established for reporting and documenting laboratory accidents, exposures, employee absenteeism and for the medical surveillance of potential laboratory-associated illnesses.
- A BSL-4 laboratory specific biosafety manual must be prepared in consultation with the Laboratory Supervisor and the Biosafety Advisor. The biosafety manual must be available and accessible. Personnel are advised of special hazards and are required to read and follow instructions on practices and procedures. Prior to beginning a study, appropriate policies and procedures must be developed and approved. The Biosafety Officer and/or other applicable committees are responsible for review of protocols and policies to prevent hazardous exposures to personnel.
- A complete clothing change is required in the BSL-4 operation. All persons leaving the BSL-4 laboratory are required to take a personal body shower.

Hazmat suit

A Hazmat Suit (hazardous materials suit) is a piece of personal protective equipment that consists of an impermeable whole-body garment worn as protection against hazardous materials. With self-contained breathing apparatus (SCBA). They are used by emergency medical technicians, paramedics, researchers, specialists cleaning up contaminated facilities and workers in toxic environments. These suits provide protection from:

- Chemical agents, through the use of appropriate barrier materials like Teflon, heavy PVC or rubber.
- Nuclear agents, possibly through radiation shielding in the lining, and also by preventing direct contact with or inhalation of radioactive particles or gas.
- Biological agents, using powered air purifying respirators with full hoods and protective suits to prevent exposure (level C protection).

The air is usually pumped into the suit at positive pressure with respect to the surroundings as an additional protective measure against the introduction of dangerous agents into a potentially ruptured or leaking suit. Use is usually limited to short duration of up to two hours.

Conclusion

It is important to understand the dynamics of the microbe holistically to develop ways to control it. Policies must be reviewed regarding the utilization of wild birds and animals as a source of food. Cooperation of government agencies, public health authorities and healthcare professionals throughout the world is critical for managing these infectious diseases. The government should establish legal devices to strengthen biosafety in the bioresearch field. The government must validate higher biosafety security level facilities and provide designated Institutional Biosafety Committees and Biosafety Officers for controlling research facilities. Research Centers should establish guidelines for safe management of highly dangerous pathogens in accordance with the new laws regarding epidemic diseases & their prevention and training according to the guidelines.

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