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Surveillance systems for Bioterrorism: A Global Perspective

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Abstract -Introduction - Bioterrorism is a constant threat to global health. It is imperative to update the surveillance systems for every country by sharing the experience from other countries. Surveillance systems not only help in the early detection of the threat but also elicit a timely response. Thus, the review intended to summarize the information available in the public domain pertaining to the surveillance systems of different countries.
Methodology - A Systematic approach was utilized to search articles from standard databases.
Results- Twenty-two articles were found in standard databases, mainly about the USA, UK, and Poland.
Conclusion - Different countries have effective surveillance systems for bioterrorism. Technology is upgraded regularly, and effective committees are formed that function to monitor the systems. However, due to the period of dormancy of biological warfare, it is difficult to prepare a sustainable system. Thus, these systems have to be incorporated with the surveillance of other infectious diseases to improve the utility of the resources invested in these systems.

1. Introduction -

According to the CDC, Bioterrorism involves intentionally releasing viruses, bacteria, or toxins to harm people, livestock, or crops. Bioterrorism is a constant threat to health at a global level.[1]
It disrupts a civilian population or a government and imposes panic amongst the masses. Every country endeavors to protect itself from bioterrorism and employs appropriate measures and systems for responding to such an emergency. It is imperative to update the status of surveillance systems for every country regularly. This review intends to summarize the surveillance systems which exist around the globe for bioterrorism.

2. Methodology - A systematic search was conducted pertaining to literature on bio terrorism and surveillance in the databases of Google Scholar and PubMed to summarize this article. The MESH terms used for the search included bioterrorism, biological warfare, biosecurity, and surveillance. The Boolean Operators included AND and OR. We could identify 22 articles and book chapters in relation to the subject in the past two decades.

"If the public health system is a body, then surveillance is the sensory organ for the same." [2]
With the emergence of the new infectious diseases, it is important to update the health of this sensory organ, as, medical/public health, political, and legal responses would depend on the early detection of the pathogen associated with an intentional release. The Centers for Disease Control and Prevention (CDC) has developed three categories of biological agents, prioritized according to their potential for bioterrorist use and the severity of disease they may produce.

Category A:

These agents present the greatest threat and can lead to widespread fatalities. Examples include anthrax, botulism, plague, smallpox, etc.

Category B:
These agents are less dangerous than Category A but still pose a significant threat. Examples include brucellosis and certain foodborne illnesses.

Category C:
These agents are currently not common, but they have the potential to become a threat in the future. Examples include the Nipah virus and the Hantavirus. [3]
Pathogens with a potential for biological warfare are constantly monitored in different countries through infectious diseases surveillance, syndromic surveillance, environmental surveillance, and laboratory surveillance. Some countries like China also employ internet-based surveillance, as in the case of the second wave of COVID-19, but the chances of receiving responses from the paucisymptomatic population are higher with such tools. Surveillance systems fortify the early detection of these pathogens and facilitate a timely response. They assist in responding to the bioterrorism attacks, i.e., they help with the preparedness phase, early warning phase, notification phase, response phase, and recovery phase. [4]

Difference in Epidemics and Bioterrorism
There is a narrow line between a natural outbreak and bio terrorism. Methods are available to distinguish between the two, however, four available methods are closely related. Although insufficiency of data might be expected during an epidemic, the simpler methods, such as the Dembek et al. method and the Radosavljevic and Belojevic method, may be useful for a fast orientation. The Grunow and Finke method is more complex and most effective after an epidemic. The Radosavljevic method is the most detailed and allows for further differential analysis of a UEE (unusual epidemic event). According to the precautionary principle, if the results of these epidemiological methods point to a highly probable bioterrorist attack, counter-terrorist measures should be applied before completing the microbial forensics, which may be time-consuming. The Radosavljevic method is the most comprehensive and enables distinction between a biological attack, a sudden emergence of a new or re-emerging illness, an unintentional release of a pathogen, and a naturally occurring outbreak of an endemic disease that could resemble bioterrorism or biological warfare.[5]

3. Surveillance -
Surveillance in health care refers to the continual systematic collection, analysis, interpretation, and proclamation of data. Active monitoring serves as a major combat tool for biological warfare.[6]

Functions of basic surveillance include (1) detecting cases of disease in specific populations and reporting the information, (2) analyzing and confirming reported case information to detect outbreaks, (3) providing timely and appropriate responses at the local/regional level to allow appropriate national level prevention and control of disease outbreaks, and (4) providing epidemiologic intelligence information to assist in long-term management of public health and health-care policies and programs. [7]

3.1 What is syndromic surveillance?
Syndromic surveillance is a public health monitoring method that collects and analyzes health-related data in real-time (or near real-time) to detect and respond to potential disease outbreaks or other public health threats before diagnoses are confirmed.
Syndromic surveillance is a public health monitoring approach that involves near real-time collection, analysis, interpretation, and dissemination of health-related data, primarily focusing on symptoms and clinical signs reported by patients and clinicians before diagnoses are confirmed. Its fundamental goal

is to detect illness clusters early, enabling timely public health action even before laboratory confirmation or clinical diagnosis.

- Automated and continuous data acquisition, allowing for near real-time monitoring and early warning of potential public health threats like infectious disease outbreaks, heat illness, or opioid overdoses
- Application for early detection, situational awareness during public health events, reassurance when no widespread health problems are detected, and flexibility to respond to various public health demands, including bioterrorism, environmental incidents, and mass gatherings

Syndromic monitoring focuses on the early symptom (prodrome) period before clinical or laboratory confirmation of a particular disease and uses both clinical and alternative data sources. Strictly defined, syndromic surveillance gathers information about patients' symptoms (e.g., cough, fever, or shortness of breath) during the early phases of illness. However, in practice, certain syndromic surveillance systems collect surrogate data indicating early illness (e.g., school or work absenteeism data or veterinary data such as unexpected avian deaths or other potential precursors of human illness). Alternative data sources have potential problems, including a presumed low specificity for syndromes of interest, high probability of influence by factors unrelated to personal health (e.g., weather or holidays), and difficulty in retracing data aberrations to individual patients. Despite these qualifiers, the optimal system might be one that integrates data from multiple sources, potentially increasing investigators' confidence in the relevance of an alert from any single data source. The analytic challenge in using syndromic surveillance for outbreak detection is to identify a signal corresponding to an outbreak or cluster amid substantial "background noise" in the data. Syndromic surveillance systems use an array of aberration-detection methods to identify increases in syndromes above predetermined thresholds. However, signal-detection methods have not yet been standardized. Temporal and spatio-temporal methods have been used to assess day-to-day and day and place variability of data from an expected baseline.
Response protocols for investigating syndromic surveillance alerts are under development by multiple programs. Obstacles to effective, efficient follow-up include the difficulty of predicting how well the syndromes themselves correlate with target diseases under surveillance; the extremely low positive predictive value of any given signal based on the high level of system sensitivity; and investigators' relative lack of experience with syndromic surveillance under real-world conditions.

Programmatic requirements for effective signal response (e.g., documented procedures; staff with appropriate expertise; 24-hour/day, 7-day/week analysis and response; and plans for information dissemination) are complex. Certain circumstances surrounding an alert might prompt rapid investigation, including clustering of cases by location, severe symptoms, unexplained deaths, sudden, substantial case numbers, simultaneous alerts from multiple data sources, or restriction of an alert to a particular population (e.g., age group or sex). Diagnostic confirmation is a paramount step in investigating alerts, particularly given the nonspecific nature of certain syndrome categories. Developing protocols to address alerts from data sources in which individual cases are unidentifiable (e.g., over-the-counter medication sales) is particularly challenging. Although syndromic surveillance's ability to detect a terrorism-related outbreak earlier than traditional surveillance remains unknown, it will likely be useful for defining the scope of an outbreak, providing reassurance that a large-scale outbreak has not occurred, and conducting surveillance of noninfectious health problems (e.g., monitoring nicotine replacement therapy sales following tobacco-tax increases). However, integral components of syndromic surveillance require additional research and evaluation, including the following:

• Defining optimal data sources.
• Evaluating appropriate syndromic definitions.
• Standardizing signal-detection methods.

- Developing minimally acceptable response protocols.
- Clarifying the use of simulation data sets to test systems; and
- Advancing the debate regarding resource commitment for syndrome versus traditional surveillance.
- On a broader policy level, defining the role of academic partners in bridging any potential analytic gaps, defining the role and scope of a national syndromic data repository, and developing policy for integrating laboratory testing and laboratory information systems with syndromic surveillance are on the horizon.[8]

Syndromic surveillance has been created for early detection, to monitor the temporal-spatial spread of an outbreak, and to provide prompt data for immediate analysis and feedback to public health authorities. It supports the timely decision-making process for countermeasure procedures. The framework of the syndromic surveillance system requires a proper electronic infrastructure to be built. Electronic data will augment the concern for data privacy, trained personnel, etc.[9]

Syndromic surveillance systems can potentially be used to detect a bioterrorist attack earlier than traditional surveillance, by virtue of their near real-time analysis of relevant data. Receiver operator characteristic (ROC) curve analysis using the area under the curve (AUC) as a comparison metric has been recommended as a practical evaluation tool for syndromic surveillance systems, yet traditional ROC curves do not account for timeliness of detection or subsequent time-dependent health outcomes. This study demonstrates the importance of accounting for mortality, morbidity and costs in the evaluation of syndromic surveillance systems. Incorporating these outcomes into the ROC curve analysis allows for more accurate identification of the optimal method for signaling a possible bioterrorist attack.[10]

However, the cost of the surveillance system would depend on the active or passive surveillance, the type of pathogen under surveillance, and the response of the system.[11]

4. Surveillance system in the US

Since 1878, the National Notifiable Disease Surveillance System (NNDSS) has been the basic surveillance system in the US. It is a passive surveillance system reporting a pathogen either through a clinician or a lab investigation report. The information is transferred from the local/ state level to the CDC. Data is scrutinized at every local/state, and federal level to investigate any unusual patterns of disease. Data is published weekly as well as annually for notifiable diseases. Council of State and Territorial Epidemiologists (CSTE), in collaboration with the CDC, recommends that the health conditions be notifiable through NNDS. Quarantinable diseases are considered notifiable at all levels of the system following the international regulations. e.g., cholera, diphtheria, infectious tuberculosis, plague, potential pandemic influenza viruses, SARS, smallpox, yellow fever, and viral hemorrhagic fevers. The rest of the diseases are considered notifiable according to the state laws. Reporting of notifiable diseases may be mandated by the legislature, state health officer or epidemiologist, the board of health, or some combination thereof. Some diseases like Smallpox Pox although eradicated, are still kept under surveillance at all levels due to their potential for biowarfare. On the other hand, outbreaks irrespective of the pathogen are considered notifiable by many states. Epidemiologic Surveillance Projects is a fully interactive computer-based reporting system. It was renamed as the National Electronic Telecommunications System for Surveillance (NETSS). De-identified data is transmitted weekly at the federal level of the CDC from all 50 state health departments as well as from New York City, Washington, D.C., and five U.S. territories. To fortify the timely dissemination of information, the CDC/Agency for Toxic Substances and Disease Registry (ATSDR) Steering Committee on Public Health Information and Surveillance System convened to give its recommendations. The National Electronic Disease Surveillance System (NEDSS) will also assist in the ongoing analysis of trends and detection of emerging public health problems and provide information for setting public health policy. The NEDSS architecture will eventually replace the NETSS reporting format. NEDSS currently resides within the Public Health Information Network (PHIN) initiative and serves as its public health surveillance component. NEDSS was deployed in 16 states by 2007, and the rest of the states developed their surveillance web-based systems, which were NEDSS compatible. Surveillance systems working towards rare events like bioterrorism are costly to maintain. It has been reported in research that the active surveillance and response phase is the most cost-consuming in surveillance. Surveillance is difficult to maintain in terms of time, finances, and vastly underappreciated human resources. To overcome these difficulties, the systems should be developed to detect new infectious diseases and VPDs, thus, the period of dormancy for the bioterrorism activity can be neglected. Surveillance activities also offer an added advantage of estimation of morbidity and mortality due to a bioagent. It helps in planning and tailoring the interventions required for combating the bioagent. It can also help in the documentation of adverse events for antimicrobial prophylaxis (e.g., Anthrax) or vaccination campaigns (e.g., Influenza).

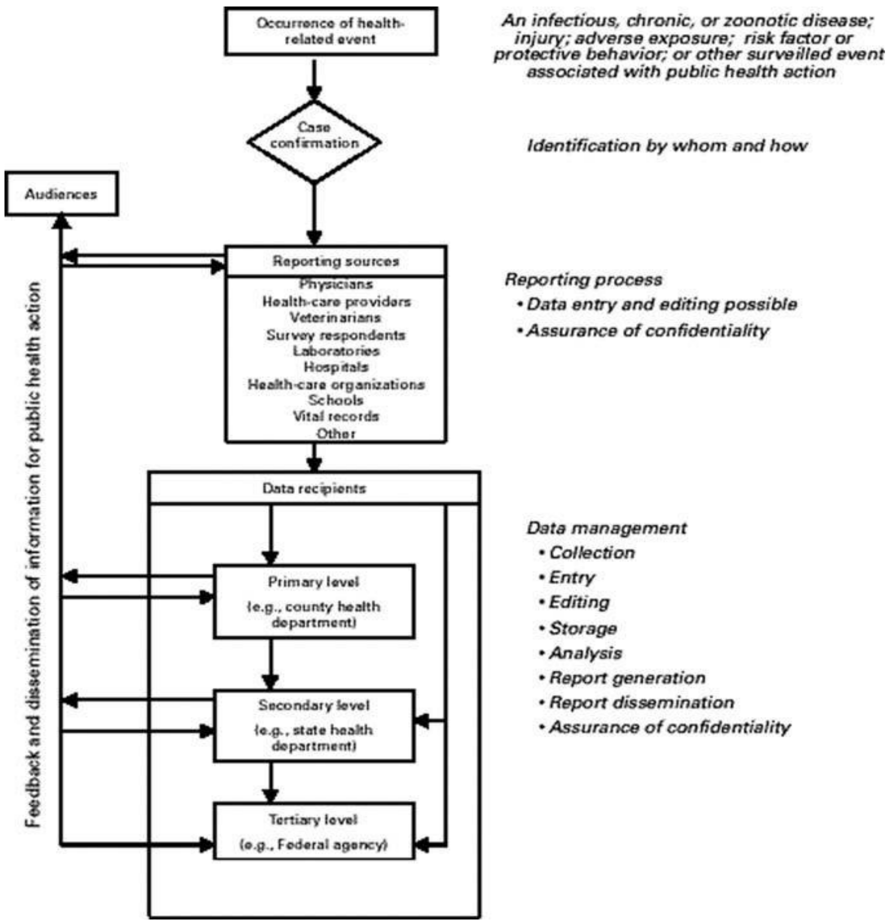

Fig. 1 Simplified flow chart for a generic surveillance system Centers for Disease Control and Prevention. Updated Guidelines for Evaluating Public Health Surveillance Systems: Recommendations from the Guidelines Working Group. MMWR 2001;50(RR-13):8 [12]

5. Surveillance system in Europe

Intentional release of Anthrax spores in the US and the discovery of Ricin, a potentially fatal substance in London, reminded the agencies to have a strong action plan against bioterrorism. The Ottawa initiative of 7th Nov 2001, also called for a global action to strengthen the public health response towards biological, chemical, and radio nuclear terrorism. The Commission launched a series of

coordinated actions across civil protection, health, enterprise (pharmaceuticals), research, nuclear and transport, and energy fields. It also improved the coordination between the Member States for the evaluation of Chemical, Biological and Radio-Nuclear (CBRN) risks, alerts and intervention, the storage of means of intervention, and in the field of research. Thus, it was undertaken to develop and establish effective surveillance, familiarize clinicians with the syndromes to look out for, disseminate case management guidelines, put in place effective arrangements for prompt notifications to the authorities in charge of collecting and evaluating epidemiological information, and coordinate public health responses. It also decided that the necessary laboratory expertise, technology, and capacity must be built to deal with the high-risk agents. In case of an event, the states must be prepared to provide physical protection and assistance. The health system should be prepared enough to take preventive and therapeutic actions, such as decontaminating exposed persons, taking swabs for analysis, administering prophylactic treatments, etc. The systems should be able to elicit a multi-sectoral response. The deployment of a response will help a state cope with the event of an attack.
In the EU, a program for biological and chemical agent attacks was coded as BICHAT. The program had four objectives -

1. **To set up an alert and information exchange mechanism** – A Health Security Committee would be responsible for using the Rapid Alert System (RAS-BICHAT), which involves the rapid release of information related to biological and chemical agents. This committee exchanges information on health-related threats, preparedness and response plans, and crisis management strategies.
2. **To develop the capability for detecting and identifying biological and chemical agents** that might be used in attacks, New diagnostics should be continuously developed to monitor emerging infections. Agents with the potential for biological warfare are prioritized for surveillance. Export control arrangements were also established for a list of biological and chemical agents. If laboratory capacity is insufficient in any state, member states must share their resources.
3. **To create a database on medicine stocks and health services** – There should be a standby facility to make medicines and healthcare services available during an attack.
4. **To establish rules and disseminate guidance on responding to attacks from a health perspective**, including coordinating the EU response and linking with third countries and international organizations. In 2007, the Council extended the mandate of this health security initiative by three years.

Pharmaceutical industries must have the capacity to address issues of availability, production capability, storage, and distribution of medicines in case of an emergency. It was recommended to stockpile medications like antibiotics during a bio terrorist attack. In case of a lack, the same can be shared with the member states. e.g. stockpile assessment of smallpox vaccines was carried out. The Commission/pharmaceutical industry task force and the Member States have highlighted the need to establish a stockpile of smallpox vaccines, antibiotics, and antivirals at a community level. Some medicines, like smallpox vaccines, were stockpiled in addition to the national stock. A research and development expert group was also set up for civil protection. A response initiated through the surveillance system must mobilize actors and resources from multiple sectors, like food safety, animal safety, plant safety, and water safety. Collaboration of laboratories, training for health staff, and the development of risk management and communication methods should also be planned. The commission cooperates bilaterally with WHO, the council, and NATO to exchange information related to chemical, biological, and radio-nuclear activities. [13]

6. Surveillance system in Poland

AFRP has emphasized modernizing, securing, and maintaining structures in the field of medicine related to the intentional release of a biological agent. WMD (Weapons of mass destruction) are treated with utmost attention. Thus, military, diagnostic, Biological Safety Level (BSL)-1 and BSL-2 microbiological laboratories have been established. These labs are supported by the military scientific research institutes. The Epidemiological Response Centre of the AFRP at Warsaw is equipped with a wide range of BSL-1, BSL-2, and mobile infrastructure, and includes an extensive array of BSL-1, BSL-2, and mobile microbiological laboratories. The center is equipped with an Epidemiological Crisis Team designed for the decontamination of people within a contamination zone, yet remains part of the field hospital comprising an infectious disease ward and isolation department, together with qualified medical staff trained in bioterrorist events. As the center is stationary, it serves a purpose of coordination with the Central Contamination Analysis Centre of the Armed Forces of the Republic of Poland, which deals with the identification and diagnosis of chemical and radiological contamination in samples obtained from contaminated areas and of unknown origin. Another military research center equipped with a BSL-3 laboratory is the Biological Threat Identification and Countermeasure Centre of the Military Institute of Hygiene and Epidemiology in Poland. Currently, the Center’s priority research focuses on the detection and neutralization of pathogens and toxins that can be used as biological weapons. Furthermore, the center creates detailed diagnostic procedures for the AFRP for identifying biological agents. The Military Health Inspectorate in AFRP includes a center for Preventive medicine. Military Centers of Preventive Medicine carry out, among other activities, tasks related to anti-epidemic protection, health and hygienic protection, anti-epizootic protection, epidemiological response, and detection of biological risk factors for the Ministry of Defence in regions under their responsibility. The task of the Biological Recognition Teams is to travel to areas where the suspected use of potential biological weapons has been reported and safely retrieve samples from the contaminated area for further diagnosis. While maintaining international standards, all available lab facilities have a qualified staff in microbiology. The Early Warning Subsystem operates under constant operational readiness.

To diagnose the contamination Poland uses latest technologies like immunochromatographic tests, laser induced fluorescence technology of BIODES, National contamination detection and alert systems and Hand Held Assays, LRBSDS (Long Range Biological Standoff Detection System) and R.A.P.I.D. system (Ruggedized Advanced Pathogen Identification Device), based on polymerase chain reaction (PCR) techniques.

The triage methodology for a bio event depends upon exposure, duration, or infectiousness. The complete population falls under the 5 SEIRV categories for triage.

There are rules for notification and cooperation in the event of a threat of a dangerous infectious disease or bioterrorism, a scheme for dealing with suspicious shipments, and procedures for dealing with cases of smallpox, anthrax, and botulism. Twenty-five hospitals have also been appointed to care for patients with particularly dangerous infectious diseases, as well as transport units for the evacuation of these patients, and 10 laboratories of provincial health and epidemiological stations, which have been proposed for inclusion in the NATO network of reference laboratories. Smallpox vaccines have been purchased with funds budgeted for the Minister of Health, and lists of persons from particular risk groups to be vaccinated in the event of an emergency have been prepared. A 24h communication system has also been introduced between the Chief Health Inspectorate and voivodeship state health inspectors, as well as at the voivodeship level, between organizational units of the State Health Inspectorate.
An increase in the IEC activities is needed for the common masses about the threats and the remedial actions. Current organizational capabilities at an administrative level should be assessed, including the technical and financial resources. More strategic plans should be developed for National risk management. 14

7. Conclusion

However, this review is limited by the information disclosed by the different countries in the public domain. With the emergence of several biological weapons, it has become a mandate to utilize international cooperation, latest technologies for surveillance, appropriately trained medical and non-medical teams, epidemiologists, preventive physicians, observation units, equipped laboratories, vaccination centers, communication methods, hospitals for hospitalization and well researched triage systems to prepare for any bio event. Every country must invest in biodefense in terms of finance and human resources. Depending upon the population dynamics and immigration in a country/city, it is prone to an attack of bioterrorism. Although such events are rare but creating integrated public health systems for surveillance and response would create more robust, sustainable, and cost-effective health systems for early detection of weapons for mass destruction.

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