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The Role of Molecular Biology for National Defense related to Bioterrorism and Biological Warfare Threat

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ABSTRACT:*Indonesia is a very large country and it has lots of threats that threaten Indonesia, including military and non-military threats. One of the non-military threats that threaten it is biological warfare, including bioterrorism. Biological warfare is the use of organisms or any biological agent and toxin that could bring disease and death to humans, crops, and livestock. Bioterrorism itself is the intentional use and release of any organisms to bring negative effects to death in humans, crops, and livestock in intention to make the terror.Technology continues to develop in the world, including molecular biology technology. The rapid development of biological sciences, on the other hand, has many impacts on life, both positive and negative impacts. Molecular biology could be a useable tool for national defenses, not only to prevent outbreaks that could occur due to bioterrorism or biological warfare but also to overcome them. The purpose of this paper is to explain the role of molecular biology for national defense-related to bioterrorism and biological warfare.*

KEYWORDS:*Bioterrorism, Biological Agents, Biological Warfare, National Defence*

I. INTRODUCTION

Biological warfare is the use of organisms including microorganisms and toxins that could bring disease and death to humans, crops, and livestock(DaSilva, 1999). Otherwise, the intentional release of any organisms (viruses, bacteria, etc.) including toxinsto bring negative effects from illness to death in humans, plants, crops, also livestock with intent to make terror or intimidate for a certain political objective is called bioterrorism(Interpol, 2021). Bioterrorism and biological warfare both use bioweapons to do the job. Biological weapons areeasy to use, non-detectable, easy to transport, and easy to disperse (DaSilva, 1999). Bioterrorism can attack any country and at any time, including Indonesia.

Indonesia is a very large country, in terms of land, sea, and air. Therefore, many threats threaten Indonesia. These threats include military threats and non-military threats (Indonesian Defense White Paper). If the threat cannot be handled properly, it can certainly endanger the integrity of the Indonesian state. The development of technology here is a factor that also acts as a threat to Indonesia's security and defense. Technology is growing rapidly in Indonesia and the world, including the development of molecular biology sciences. This technological advancement in molecular biology, if it is used by irresponsible people, would certainly be dangerous for the public and also have implications for national, regional, and international security (Kementerian Pertahanan RI, 2017).

Technology continues to develop in the world, including molecular biology technology. The development of genetic technology and molecular biology occurs very quickly, starting from the discovery of

the structure of DNA to genetic engineering. The rapid development of biological sciences, on the other hand, has many impacts on life, both positive and negative impacts. The misuse of biological sciences is carried out, for example by the presence of bioterrorism cases in several locations in the world, as in the case of anthrax spores that were spread through envelopes in the US in 2001 (Soeliongan, 2020).

Molecular biology is one of the biology fields that study biological molecules that is essential in the cellular metabolism process such as carbohydrate, nucleic acids, protein, and lipid and its derivatives(Nature, 2021). Molecular biology could be a useable tool for national defenses, not only to prevent outbreaks that could occur due to bioterrorism or biological warfare but also to overcome them. The purpose of this paper is to explain the role of molecular biology for national defense-related to bioterrorism and biological warfare.

II. RESEARCH METHODOLOGY

This paper is descriptive qualitative research using the literature review approach. A literature review is one of the research methods that analyze and review previous references, such as books, journals, and any other research findings in line with the research subject. Descriptive qualitative means, the author will describe the phenomenon regarding the research subject that has been held(Sarwono, 2006).

III. LITERATURE REVIEW

3.1.1. Early and Modern Bioterrorism and Biological Warfare

Biological warfare and bioterrorism have been around for a long time in the world. Biological warfare activities have been carried out during the Peloponnesians war in 430-426 BC. In that war, there was an infection from *Salmonella enterica* which was suspected to have originated from the Spartans who poisoned water reservoirs with these bacteria (Papagrigorakis, et al., 2013). In the middle of the black death epidemic (the mid-1300s), the tartars used the infected corpses, then threw them at the enemy city walls. In addition, the spread of plague is also carried out by mice and fleas for the spread of bubonic plague. In 1763, bioterrorism was also carried out during the war between Europeans and the Pontiac Tribe (Indians). During the war, General Jeffrey Amherst used the smallpox virus to attack the Indians. Almost 95% of the native American population death due to smallpox infection and other infectious diseases (Clark & Pazdernik, 2016).

Modern biological warfare started in World War I (WW1), the German used biological agents to infect Allied horses with *Burkholderia mallei* and anthrax. The French army also used *Burkholderia mallei* to infect German horses. During this time, biological agents began to be used to infect animals, no longer to be used to infect humans. During the second world war (WW2), the Japanese unit 731 conducted experiments by infecting Chinese prisoners of war with various infectious diseases, such as cholera, hemorrhagic fever, and venereal disease. Japan also dropped "flea bombs" on cities in China. In 1969, the US turned anthrax and tularemia into biological weapons(Clark & Pazdernik, 2016).

Nowadays, biological warfare is more carried out by terrorist groups or even carried out by "lone wolves". In 1984, the Rajneesh cult poisoned food for 750 people in Oregon by infecting salad bars with *Salmonella*, for political reasons(Clark & Pazdernik, 2016).Then in 1995 in Japan, the Aum Shinrikyo group used sarin gas mixed with anthrax virus. Recently in 2001, there was a terror attack in the US using anthrax spore powder through envelopes, that killed 5 people (Soeliongan, 2020).Biological warfare and bioterrorism nowadays not only affect humans but also livestock and crops. So far, some scientists have stated that the terrorist group cannot commit a greater crime of bioterrorism, based on recent days facts. However, this cannot be underestimated, because there are still many biological agents that have the potential to be developed and armed.

3.2. Biological Agents

Biological agents are organisms that can affect human health to a certain degree or even death (US Department of Labor, 2021). Biological agents may have the ability to spread from one person to another either directly or indirectly (using a vector or not using a vector). Biological agents are generally found in nature, there are lots of natural diseases that also potential to be used as biological agents and it is also possible to enhance them using genetic engineering. Five factors determine a biological agent can be used as a biological agent for bioterrorism and biological warfare such as preparation, dispersal, persistence, incubation time, and the laboratory.According to US Army in Clark &Pazdernik 2016, biological agents that could be used in bioterrorism and biological warfare must fulfill certain requirements such as;

1) It would produce death, disability, and damage.
2) Capable to produce economically and materially available.
3) Stable during production, storage, and transport.
4) Could be disseminated easily and efficiently.
5) Spreading stably after dissemination.

Centers for Disease Control and Prevention (CDC) classified a variety of viruses, bacteria, and toxins that are considered effective for biological agents in biological warfare and bioterrorism into 3 groups or categories (Table 1)(Vaseashta, 2013).

Table 1. CDC-List for Potential Agent in Biological Warfare and Bioterrorism

Categories	Characteristics	Biological Agents	
A	• Easy to spread and transmit from person to person. • Cause a high number of deaths. • Could cause public panic and social chaos. • Require special action to protect public health.	**Bacteria:**	
		Anthrax	*Bacillus anthracis*
		Plague	*Yersinia pestis*
		Tularemia	*Francisellatularensis*
		Viruses:	
		Smallpox	*Variola major*
		Filoviruses	Ebola hemorrhagic fever Marburg hemorrhagic fever
		Arenaviruses	Lassa fever
		Toxins:	
		Botulinum toxin	*Clostridium botulinum*
B	• Moderately easy to spread. • Cause a moderate number of morbidity and low mortality. • Need diagnostic capacity and surveillance enhancement.	**Bacteria:**	
		Brucellosis	*Brucella sp.*
		Glanders	*Burkholderia mallei*
		Melioidosis	*Burkholderiapseudomallei*
		Q fever	*Coxiella burnetti*
		Food or waterborne enteric diseases	*Salmonella, Shigella dysentriae, Vibrio cholerae*
		Viruses:	
		Alphaviruses	Venexuelan encephalomyelitis
		Toxins:	

		Ricin toxin Epsilon toxin Enterotoxin B	*Ricinus communis* *Clostridium perfringens* *Staphylococcus*
C	pathogens that have just emerged and have the potential to be developed for mass dissemination.	Nipah virus Hantaviruses Flaviviruses Multidrug resistant tuberculosis	Yellow fever, Dengue fever

One of which biological agents that have already been used as a bioweapon is Anthrax. Anthrax is a disease caused by the bacterium Bacillus anthracis. Anthrax is often used as a weapon because spores from anthrax are easy to find in nature and can be produced in the lab and can last a long time in the environment. Anthrax can easily be used as a weapon because it is easily removed without many people knowing. Anthrax spores can be incorporated in the form of powder, spray, food, and even water. Spores are so microscopic that they cannot be recognized, seen, smelled, or tasted. Anthrax is already being used as a biological weapon as was the case in the United States when anthrax was put in envelopes. The spread of anthrax spores in 2001 caused 5 deaths (CDC, 2021).

In addition to bacteria and viruses, toxins can also be used as bioweapons. Toxins are biomolecular compounds produced by an organism, such as bacteria, protists, fungi, plants, or animals. These molecules can induce certain effects on other organisms if inhaled, injected, ingested, or absorbed(Dorner & Rummel, 2015). Certain toxins could affect the nervous system and interfere with its electrical impulses, for example, botulinum toxin. There are other types of toxins that can damage cell membranes so that they interfere with certain organs or tissues' function. The effects of these types of toxins are usually irreversible and can cause permanent damage to the body.Compared with other pathogenic biological agents, biological toxins are classified as bioterrorism factors, because toxins are not infectious and cannot reproduce on their own. In certain doses, biological toxins can cause lethal death(Janik, et al., 2019). A biological toxin is one of the ways that terrorists are very interested in being used in their actions. Biological toxins are very easy to obtain. The equipment used for bacterial culture and extraction for toxin harvesting has a low price, is easy to obtain and the process can be done at home(Johnson, et al., 2001).

3.3. Genetics and Molecular Biology Role in Bioterrorism and Biological Warfare

The development of science and biology is happening very rapidly. Molecular biology and biotechnology also continue to develop, starting from the discovery of DNA, genes to genetic engineering. Genetic engineering is a technique used to artificially modify and transfer genetic material from one organism to another or from one species to another. This technology is used to change the transcription results of certain genes so that the desired protein product is produced. We could also design desired organisms for our use ranging from research activities to pharmaceutical and industrial uses. Genetic recombinant technic is used widely, opening lots of industry especially in the pharmaceutical field and also increasing the human way of life, because of new drugs or vaccines developed. For example, synthetic insulin that has been produced that help people with diabetes, smallpox vaccine, until COVID-19 vaccine that would be a breakthrough during COVID-19 pandemic to save millions (National Research Council Committee).

However, this significant improvement in molecular biology also has a dual-use research dilemma. The use of science helps to improve the human standard of living, on the other hand, the same knowledge and research can be misused and cause harm. Genetic engineering could engineer pathogens to be more lethal than before. One case from a Soviet germ warfare facility that modified the smallpox virus and made a variety of artificial smallpox mutants and hybrids. Another case is the mousepox case. Mousepox is a smallpox-related virus and only infects mice.The virulence of the virus differs depending on the strain of the mice. Genetically

resistant mice rely more on cell-mediated immunity (Natural killer cells and cytotoxic T-cells) than antibodies. Then, the researchers inserted a human gene for cytokine interleukin-4 (IL-4) into the mousepox virus. The hypothesis is that modifying the virus would stimulate antibodies production and increase balanced immune response. The results were the opposite of the hypothesis, the new modified virus has greater virulence than before. The new modified virus killed all of the genetically resistant mice and 50% of mice that got the smallpox vaccine. Excess IL-4 gene expression suppressed natural killer cells and cytotoxic T cells and failed to increase antibody response (Clark & Pazdernik, 2016).

Molecular biology also has lots of positive impacts on human life, for example with molecular biology technic we could identify various pathogens easily. Using molecular biology technology we could analyze DNA, RNA, Protein, and other molecules to identify the disease-causing pathogen. With this technology, we could run molecular diagnostics easily and in a shorter time rather than using conventional culturing methods. Polymerase Chain Reaction (PCR) technology could help us in diagnosing some diseases. During the COVID-19 pandemic, real-time qPCR is the golden standard for diagnosing someone who got infected by the Sars-Cov-2 Virus(Long, et al., 2020). The molecular technic also helps us with the development of the COVID-19 vaccine (Forni & Mantofani, 2021). Without the real-time q-PCR technology and the vaccine, it would be harder for us to control the spreading of the Sars-Cov-2 virus. The application of this technology helps us to survive during the pandemic. The need for genetics and molecular biology technic is a must, evolvement, and development of genetics and molecular biology science is unavoidable to help human life.

3.4. Genetics and Molecular Biology Role for National Defense

Analysis of potential threats that will enter the country, must be carried out carefully and accurately, including analyzing the threat of biological warfare. The development of existing molecular genetic technology can help to analyze threats that will occur and can determine policy directions that can be taken. Molecular biology has taken an important role, for example, to overcome this recent COVID-19 threat. Using molecular biology technology such as real-timeqRT-PCR, we could detect the COVID-19 virus. Real-time qRT-PCR detects the genetic material of the virus that infects human bodies. The genetic material of the virus inside the infected human bodies will be amplified so that the machine will detect the virus. Real-time qRT-PCR technology developed at ChariteInstitute of Virology in Germany and the WHO introduced this technology in January 2020 and the additional protocols were reported by the Chinese Centre for Diseases Control and Prevention, University of Hongkong, and the US Centre for Disease Control and Prevention. Using this technology, we have high specificity and sensitivity for identifying SARS-CoV-2 (COVID-19 virus) isolated from the patient(Chung, et al., 2021).

Besides real-time qRT-PCR, there is a sequencing technology that helps to sequence the genetic material of the virus to make sure and identify the variant type. Next genome sequencing (NGS) is also important to find the origin and intermediate host of the COVID-19 virus(Chen, et al., 2021).Early diagnosis of certain diseases, enables us to prepare a specific treatment and implementation of public health protocols to protect every citizen so that national defense can be maintained(Chung, et al., 2021).

The Indonesian National Army (TNI) consists of three dimensions, which are land, sea, and air. Each dimension of the Indonesian national army has its specificity and specification of the field of work. Supporting a strong TNI certainly requires qualified human resources for their respective fields of work. The concept of the right human resources for the right field of work is a concept that must be applied to support the strength of the Indonesian national army. In addition to using competency tests, education, and training, the positioning of soldiers can also be done using molecular genetic analysis techniques of each soldier's genetic material. One of the roles of genetics and molecular biology for defense is as a screening tool for soldiers. Information on genetic soldiers can be obtained during the recruitment process, later the genetic material will be analyzed and identified whether certain diseases can hinder the performance of the candidate soldiers. For example, it is associated with a deficiency of glucose 6-phosphate dehydrogenase which can interfere with the metabolism of certain drugs, for example, malaria drugs. If the soldier is placed in a location that is prone to malaria, it will certainly be fatal.

In addition, screening can also be done to see cases of sickle cell anemia or to see individuals who carry a mutation in the RYR1 gene that makes the candidate more susceptible to heat-related injury. Candidates will not be immediately disqualified if they have anomalous medical conditions but can be specified to certain work units so that their potential can still be developed to the maximum. Genetic information based on proper genetic screening will certainly build the capacity and capability of the TNI's human resources(Castro, et al., 2016).

IV. CONCLUSIONS

Molecular biology could be a useable tool for national defenses, not only to prevent outbreaks that could occur due to bioterrorism or biological warfare but also to overcome them. Molecular biology also could be used for recruitment and maintaining the strength of Tentara Nasional Indonesia (TNI). Genetic information based on proper genetic screening will certainly build the capacity and capability of the TNI's human resources to maintain Indonesia's national defense.

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