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Review

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Bioterrorism and Biosecurity

September 23, 2016: The activities of several extremist groups worldwide have been focused on methods to inflict high mass casualty incidents. They seek weapons of mass destruction which they would not hesitate to deploy into densely populated regions in America or anywhere in the world. Fortunately, the level of security guarding nuclear arsenals is high and the required security clearances and ongoing government surveillance over key personnel working in the nuclear weapons industry is also high. The control over nuclear weapons and raw materials makes it difficult, but not impossible, for a group of determined extremists to acquire essential materials and technical skills to build a nuclear device or buy an operational one on the black market.

However, a far less secured and less government regulated industry with equal potential for high mass casualty incidents exist in virology laboratories throughout the world today. Advances in virology have far surpassed existing public policy controls and government regulatory safeguards that would serve to secure laboratories at reasonably the same level as the nuclear weapons industry. Laboratories are not closely regulated and key scientists have not been vetted and cleared by extensive background screening procedures or kept under the close surveillance protocols as they were during the Manhattan Project while developing the first atomic bomb during WWII.

To some readers this commentary may just be dismissed as alarmist. It is nonetheless important to understand that the technology to create deadly viruses is available; and, dangerous pathogens could be under development now in any of the many unregulated laboratories operated by unsupervised scientists. International public policy and global multinational government regulation have not kept pace with the advances in biological sciences. It is assumed that scientists regulate themselves; however, if any scientist who is also an extremist either religiously or politically engineers a novel virus or reanimates an extinct virus as scientists have been doing with the Spanish Flu virus that killed an estimated 100 million people worldwide in 1918, they will have a potential weapon of mass destruction in terms of mass casualties. Ask the U.S. CDC why they keep the deadly smallpox virus alive and on hand in their laboratories in Atlanta, Georgia? Further, what security clearance investigations have been conducted on the U.S. CDC scientists and what ongoing security surveillance protocols have been implemented to ensure their compliance with high level bio-hazard security risk procedures?

Scientists who are working in biosyn research are designing novel viruses in laboratories as small as a single car garage that have the potential for high infectious rates and high case fatality rates. CRSPR cas9 technology is available without regulatory restrictions and is capable of manipulating the genome of existing or bioengineered microscopic organisms altering them to become designer pathogens posing a dangerous public health risk. The laboratory equipment and technology are available for sale at reasonable cost without government regulation controlling the means for someone with the requisite skill and knowledge to create new viruses with the intention for release on populations. It is easier to buy this new technology than it is to buy a gun in America. Who is minding the store today?

The Science of the New Age of Terror: Bioterror or Biological Warfare

Some viruses and biological agents are potentially dangerous if not secured properly in high security laboratory conditions. This paper concerns the risks of bioterrorism or the intentional release of a dangerous biological organism; and, is increasingly necessary in view of global insecurity and the ongoing quest by some groups for means of causing mass casualties.

A critical appraisal of these potential new population health risk issues could help prevent international viral storm epidemics that could be intentionally inflicted on densely populated areas of the world. The Ebola virus, Marburg virus and Small Pox are devastatingly infectious viruses with exceedingly high case fatality rates. And, to date, attempts have been made to acquire them by groups with ulterior motives. Today, more than ever before in history, scientists have the technology and the requisite skill to engineer a dangerous novel virus or reanimate a formerly extinct virus into an even more infectious disease organism with an even higher case fatality rate than that which existed in nature. The cost of this new technology is within the means of trained biological scientists and can be procured without government oversight or regulation.

The Influenza virus is unique in its ability to recombine and evolve into highly pathogenic unique strains. Genetic engineering has selectively enhanced the transmissibility hence the need to be current with this virus and as well as many others. Since no broad spectrum vaccine exists for all viruses, it is important to consider the possibilities for the development of a bioweapon and enforce measures to prevent or mitigate any intentional release. Public health systems globally must prepare to detect a pandemic early and respond promptly. Developing countries need to prepare for a potential public health emergency as there is increased traffic across international borders resulting from high volume international travel. Potentially harmful viruses do not respect international boundaries and they travel at the speed of air travel; and early in the infection stage, they can be virtually undetected and carried by passengers on any airplane to a destination of intended impact.

Bioterrorism

Filoviruses and smallpox are dangerous viruses which are a major threat to any nation; indeed, the world swarms with viral zoonoses. Some genetically-engineered viral proteins that can be transfected exist and this reality underscores the need for governments globally to monitor the activities of laboratories with genetic engineering capabilities. Genetic fingerprinting forensic studies; and the use of genomics for manipulation of agents including viruses are critical [1]. The threat of emerging infections and bioterrorist attacks has heightened the need for a more sensitive, specific, and timely pandemic disease surveillance system [2,3]. Many countries in the developing world are not prepared even as they rely on the importation of biological and medical supplies. In the event of an intentional pandemic attack, the magnitude of human deaths in these unprepared areas would be significant.

The primary purpose of reporting diseases is to trigger appropriate public health response so casualty figures are reduced and public fears allayed [4]. Continual virus global movement has prevailed because of failure to identify early the vertebrate reservoir and effectively and quickly quarantine infected animals or humans [5]; and in part, because of the lack of ecological data supporting or refuting any alternative modes of transmission [6].

Recently, the U.S. Centers for Disease Control and Prevention has funded the development of electronic laboratory reporting (Jorgensen, 1997). A more thorough understanding of the pitfalls of such existing reporting systems can provide insights into the development and implementation of new methods in infectious disease surveillance. With recent funding for activities to defend public health against terrorism and naturally occurring diseases, development of automated reporting systems has accelerated [7].

Reverse Genetics

Artificial generation of influenza A [8], B [9], and C [10] viruses are now possible through dynamic systems that rely on intracellular synthesis of influenza viral RNAs by a cellular enzyme called RNA polymerase I that transcribes ribosomal RNA in the nucleus of eukaryotic cells. Influenza viral segments are encoded by cDNAs flanked by the RNA polymerase

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I promoter and the RNA polymerase I terminator or a ribozyme sequence. RNA polymerase I transcription in transfected cells results in the efficient synthesis of RNA transcripts with defined 5' ends whereas the integrity of the 3' ends is achieved using the nucleotide-specific RNA polymerase I terminator [11] or a self-cleaving ribozyme [8]. RNA polymerase I transcripts are neither capped nor polyadenylated therefore they exactly resemble influenza viral transcripts. Cells are transfected with eight plasmids to provide all eight viral RNAs, as well as four plasmids for the expression of the polymerase and NP proteins that are required to initiate viral replication.

Although this approach requires the co-transfection of cells with 12 plasmids, it is highly efficient and routinely yields 108 plaque-forming units of influenza A virus per mL of cell culture supernatant. In one modification, both the RNA polymerase I transcripts (for vRNA synthesis) and the RNA polymerase II transcripts (for mRNA synthesis) are derived from the same template [9], which reduces the number of plasmids required for virus generation to eight. In another modification, the eight RNA polymerase I transcription units for the eight viral RNAs were combined [11], allowing the generation of the entire viral genome from a single plasmid.

These dynamic biological systems revolutionized influenza virus research by allowing researchers to study the functions of viral proteins, their contributions to the viral life cycle, and role in pathogenesis and host range restriction. They are invaluable tools for the generation of influenza virus vaccines and vaccine vectors. In fact, reverse genetics has permitted the generation of inactivated and live vaccine strains for H5N1 viruses that could not have been produced by conventional approaches. Fouchier and other researchers from the Erasmus Medical Center Rotterdam, The Netherlands in September 2011 announced they had successfully engineered a mutant form of influenza H5N1 (avian influenza) that was transmissible by respiratory route between ferrets. Given that ferrets' immune response to influenza is considered to be similar to the response in humans, the studies suggest that the engineered H5N1 is likely to be transmissible from human-to-human.

The researchers suggested that the transmissible flu they had created remained as lethal as the original strain on which their work had been carried out. A strain estimated to be fatal in ~30-60% of cases in humans [12-14]. Several months later it became widely known that a second research group, led by University of Tokyo and University of Wisconsin Professor Yoshihiro Kawaoka similarly had engineered a mammal-to-mammal transmissible form of H5N1 [15,16].

Counter bioterrorism measures

Identification of viral sources, surveillance, disease reporting, early detection and management of a bioterrorism attack are means of preventing and mitigating mass casualties in bioterrorist epidemics. As the popular saying goes; to be forewarned is to be forearmed, giving advance notice of an impending virus outbreak. There is hope that the tools and the imaginations of molecular biology will find the means to prepare some effective biological defense [7]. There is also a possibility of linking rapid detection to rapid responses through vaccine and therapeutic antibody development in an attempt to abort epidemics caused by new viruses while as it rages [17].

Decisions about the treatment or prophylaxis of emerging infections must take into account the effect on patients' health and the potential risks such as a mother's health and that of the fetus. In preparation for bioterrorism emergencies, the U.S. government stockpiled medications and vaccines, rated by the FDA, as one of the categories B through X indicating they could pose risks to the fetus or that insufficient information exists to evaluate their potential fetal risk. Some are routine healthcare products like ciprofloxacin, gentamicin and doxycycline while others are reserved for emergency preparedness and response activities, and for deployed military personnel such as small pox and anthrax vaccines [18].

Some emergency response medications and vaccines fall outside of the FDA labeling system because they are not licensed by the FDA. Some are newly developed and still in pre-licensure clinical trials; others are no longer licensed and pre-date the classification system [18].

In an emergency with high risk of life-threatening exposure to an infectious pathogen, vaccinations and prophylaxis when available will be used for pregnant women despite unknown risks to the fetus. Other measures that can protect persons who are unable or choose not to receive vaccination or prophylactic medications include; selective or mass population quarantine for prevention of exposure to persons who may be infected, avoiding public gatherings and restricting travel to affected areas [18]. Since public health does not have the power to order any type of quarantine, it will be decisions made by public administration and the political will of government executives such as governors and the President and global heads of state to issue a mandated enforceable order for quarantine.

A plan by multi-national scientists to conduct research on enhancing mutating H7N9 avian flu to mimic person to person spread was greeted with controversy, following the backlash of similar research on H5N1 in 2011. In letters published in Science and Nature journal, Fouchier and colleagues from a dozen research centers in the US, Hong Kong and Britain outlined plans for what they called gain-of-function research to create potentially stronger strains, including ones that might easily spread through the air between laboratory animals. They opined it was promising research which could highlight the most important mutations for public health officials to watch and monitor the natural spread of the virus or determine how to manufacture vaccines.

The Obama Administration tightened oversight of research involving dangerous germs while the U.S. Department of Health and Human Services announced an extra step. It is expected that in addition to scientific review, researchers proposing to create easier-to-spread strains of the new H7N9 will have to pass special review by a panel of experts weighing risks and potential benefits [19]. However, since the technology is readily available cheaply without a security clearance or government license, could scientists globally engage in various dangerous genome altering experiments even while under the surveillance of international governments?

A complication of the new science of genetic engineering is that the cost of doing these risky procedures are much lower than the cost of developing other weapons of mass destruction; and, anyone with the requisite skill, and a reasonably small investment in laboratory equipment, could be engineering a novel virus that could be catastrophically dangerous if intentionally released into densely populated regions of the world; and, they could do it given the current existing weak to nonexistent governmental controls to prevent such dangerous experiments.

Public health priority

In the event of outbreaks, masses of people will fall ill and likely die, hence the need for improved public health community measures and deployment of adequate resources toward developing a local, regional, national, and global response plan. The second reason this should be considered a top public health priority is that such outbreaks overlap with preparedness for naturally occurring outbreaks of other communicable diseases. The core functions of public health are assessment, policy development, and assurance; therefore, the public health system is tasked with providing ongoing surveillance of infectious diseases as well as ensuring that populations and communities have access to health services when necessary. The infrastructure to promptly identify and respond to naturally occurring infectious disease outbreaks if synchronized will help in this regard [20].

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