Mini Review

BIOMEDICAL Journal of Scientific & Technical Research

ISSN: 2574 -1241

DOI: 10.26717/BJSTR.2022.41.006609

Pandemic Prevention

Abas Khan[1], Mohd Sarwar Mir[2] and Ruksana Hamid[3]*

[1]*Senior Resident, hospital adminstration, SKIMS, India*

[2]*Resident Medical Officer, SKIMS, India*

[3]*Medical officer and anesthesiologist, JK health, India*

***Corresponding author:** Ruksana Hamid, Medical officer and Anesthesiologist, JK health, India

ARTICLE INFO

Received: January 03, 2022

Published: January 31, 2022

Citation: Abas Khan, Mohd Sarwar Mir, Ruksana Hamid. Pandemic Prevention. Biomed J Sci & Tech Res 41(3)-2022. BJSTR. MS.ID.006609.

ABSTRACT

Pandemic prevention is the organization and management of preventive measures against pandemics. Those include measures to reduce causes of new infectious diseases and measures to prevent outbreaks and epidemics from becoming pandemics.

Introduction

Measures

Infrastructure and International Development: Robust, collaborating public health systems that have the capacity for active surveillance for early detection of cases and to mobilize their health care coordination capacity may be required to be able stop contagion promptly. After an outbreak there is a certain window of time during which a pandemic can still be stopped by the competent authorities isolating the first infected and/or fighting the pathogen. A good global infrastructure, consequent information exchange, minimal delays due to bureaucracy and effective, targeted treatment measures can be prepared. 2012 it has been proposed to consider pandemic prevention as an aspect of international development in terms of health-care infrastructure and changes to the pathogen-related dynamics between humans and their environment including animals. Often local authority carers or doctors in Africa, Asia or Latin America register uncommon accumulations (or clusterings) of symptoms but lack options for more detailed investigations. Scientists state that "research relevant to countries with weaker surveillance, lab facilities and health systems should be prioritized" and that "in those regions, vaccine supply routes should not rely on refrigeration, and diagnostics should be available at the point of care".

Technologies

Pathogen Detection and Prediction: In a 2012 study it is claimed that "new mathematical modelling, diagnostic, communications, and informatics technologies can identify and report hitherto unknown microbes in other species, and thus new risk assessment approaches are needed to identify microbes most likely to cause human disease". The study investigates challenges in moving the global pandemic strategy from response to pre-emption. Some scientists are screening blood samples from wildlife for new viruses. The international Global Virome Project (GVP) aims to identify the causes of fatal new diseases before emergence in human hosts by genetically characterizing viruses found in wild animals. The project aims to enlist an international network of scientists to collect hundreds of thousands of viruses, map their genomes, characterize and risk-stratify them to identify which ones to pay attention to.

However, some infectious disease experts have criticized the project as too broad and expensive due to limited global scientific and financial resources and because only a small percentage of the world's zoonotic viruses may cross into humans and pose a threat. They argue for prioritizing rapidly detecting diseases when they cross into humans and an improving the understanding of their mechanisms. A successful prevention of a pandemic from specific viruses may also require ensuring that it does not re-emerge – for instance by sustaining itself in domestic animals. Pathogen detection mechanisms may allow the construction of an early warning system which could make use of artificial intelligence surveillance and outbreak investigation. Edward Rubin notes that after sufficient data has been gathered artificial intelligence could be used to identify common features and develop countermeasures and vaccines against whole categories of viruses.

It might be possible to predict viral evolution using machine learning. In April 2020 it was reported that researchers developed a predictive algorithm which can show in visualizations how combinations of genetic mutations can make proteins highly effective or ineffective in organisms – including for viral evolution for viruses like SARS-CoV-2.` In 2021, pathogen researchers reported the development of machine learning models for genome-based early detection and prioritization of high-risk potential zoonotic viruses in animals prior to spillover to humans which could be used for virus surveillance for (i.a.) measures of "early investigation and outbreak preparedness" and, according to the study, would have been capable of predicting SARS-CoV-2 as a high-risk strain without prior knowledge of zoonotic SARS-related corona viruses. An artificial "global immune system"-like technological system that includes pathogen detection may be able to substantially reduce the time required to take on a biothreat agent.

A system of that sort would also include a network of well-trained epidemiologists who could be rapidly deployed to investigate and contain an outbreak. Funding for the United States' PREDICT government research program that sought to identify animal pathogens that might infect humans and to prevent new pandemics was cut in 2019. Funding for United States' CDC programs that trained workers in outbreak detection and strengthened laboratory and emergency response systems in countries where disease risks are greatest to stop outbreaks at the source was cut by 80% in 2018. Despite recent advances in pandemic modeling, experts using mostly experience and intuition are still more accurate in predicting the spread of disease than strictly mathematical models.

Crispr-Based Immune Subsystems: In March 2020 scientists of Stanford University presented a CRISPR-based system, called PAC-MAN (Prophylactic Antiviral Crispr in human cells), that can find and destroy viruses *in vitro*. However, they weren't able to test PAC-MAN on the actual SARS-CoV-2, use a targeting-mechanism that uses only a very limited RNA-region, haven't developed a system to deliver it into human cells and would need a lot of time until another version of it or a potential successor system might pass clinical trials. In the study published as a preprint they write that it could be used prophylactically as well as therapeutically. The CRISPR-Cas13d-based system could be agnostic to which virus it's fighting so novel viruses would only require a small change. In an editorial published in February 2020 another group of scientists claimed that they have implemented a flexible and efficient approach for targeting RNA with CRISPR-Cas13d which they have put under review and propose that the system can be used to also target SARS-CoV-2 in specific.

There have also been earlier successful efforts in fighting viruses with CRISPR-based technology in human cells. In March 2020 researchers reported that they have developed a new kind of CRISPR-Cas13d screening platform for effective guide RNA design to target RNA. They used their model to predict optimized Cas13 guide RNAs for all protein-coding RNA-transcripts of the human genome's DNA. Their technology could be used in molecular biology and in medical applications such as for better targeting of virus RNA or human RNA. Targeting human RNA after it's been transcribed from DNA, rather than DNA, would allow for more temporary effects than permanent changes to human genomes. The technology is made available to researchers through an interactive website and free and open source software and is accompanied by a guide on how to create guide RNAs to target the SARS-CoV-2 RNA genome. Scientists report to be able to identify the genomic pathogen signature of all 29 different SARS-CoV-2 RNA sequences available to them using machine learning and a dataset of 5000 unique viral genomic sequences. They suggest that their approach can be used as a reliable real-time option for taxonomic classification of novel pathogens.

Testing and Containment: Timely use and development of quick testing systems for novel virus in combination with other measures might make it possible to end transmission lines of outbreaks before they become pandemics. A high discovery-rate is important for tests. For instance this is the reason why no thermal scanners with a low discovery-rate were used in airports for containment during the 2009 swine flu pandemic.[39] The German program Infect Control 2020 seeks to develop strategies for prevention, early recognition and control of infectious diseases. In one of its projects "HyFly" partners of industry and research work on strategies to contain chains of transmission in air traffic, to establish preventive countermeasures and to create concrete recommendations for actions of airport operators and airline companies. One approach of the project is to detect infections without molecular-biological methods during passenger screening. For this researcher of the Fraunhofer-Institute for cell therapy and immunology are developing a non-invasive procedure based on ion-mobility spectrometry (IMS).

Surveillance and Mapping

Viral Hotspots and Zoonotic Genomics: Monitoring people who are exposed to animals in viral hotspots – including via virus monitoring stations – can register viruses at the moment they enter human populations - this might enable prevention of pandemics. The most important transmission pathways often vary per underlying driver of emerging infectious diseases such as the vector-borne pathway and direct animal contact for land-use change – the leading driver for emerging zoonoses by number of emergence events as defined by Jones et al. (2008). 75% of the reviewed 1415 species of infectious organisms known to be pathogenic to humans account for zoonoses by 2001. Genomics could be used to precisely monitor virus evolution and transmission in real time across large, diverse populations by combining pathogen genomics with data about host genetics and about the unique transcriptional signature of infection. The "Surveillance, Outbreak Response Management and Analysis System" (SORMAS) of the German Helmholtz-Zentrum für Infektionsforschung (HZI) and Deutsches Zentrum für Infektionsforschung (DZIF), who collaborate with Nigerian researchers, gathers and analyzes data during an outbreak, detects potential threats and allows to initiate protective measures early. It's meant specifically for poorer regions and has been used for the fight against a monkeypox outbreak in Nigeria.

Syndromic Surveillance and Border Control: Expert on infectious diseases at the Johns Hopkins Center for Health Security, Amesh Adalja states that the most immediate way to predict a pandemic is with deeper surveillance of symptoms that fit the virus' profile. The scientific and technological ways of quickly detecting a spillover could be improved so that an outbreak can be isolated before it becomes an epidemic or pandemic. David Quammen states that he heard about the idea to develop technology to screen people at airport security points for whether or not they carry an infectious disease ten years ago and thought it was going to be done by now. Thermometers whose measurement data is directly shared via the Internet and medical guidance apps have been used to plot and map unusual fever levels to detect anomalous outbreaks. Various forms of data-sharing could be added to health care institutions such as hospitals so that e.g. anonymized data about symptoms and incidences found to be unusual or characteristic of a pandemic threat could enable high-resolution "syndromic surveillance" as an early warning system. In 1947, the World Health Organization established such a global network of some hospitals. Such sharing and off-site evaluation of symptoms and possibly related medical data may have complementary benefits such as improving livelihoods of workers who work with livestock and improving the accuracy, timeliness, and costs of disease prognoses.

Mutation Surveillance: In December 2020 during the COVID-19 pandemic national and international officials reported mutated variants of SARS-CoV-2, including some with higher transmissibility and worldwide spread. While mutations are common for viruses and the spread of some of the virus' mutations have been tracked earlier, mutations that make it more transmittable or severe can be problematic. Resources for disease surveillance have improved during the pandemic so that medical systems around the world are starting to be equipped to detect such mutations with genomic surveillance in a manner relevant to pandemic mitigation and the prevention of sub-pandemics of specific variants or types of variants. As of December 2020, contemporary measures such as COVID-19 vaccines and medications seem to be effective in the treatment of infections with the tracked mutated variants compared to earlier forms that are closer to the original virus/es.

Policy and Economics: A 2014 analysis asserts that "the window of opportunity to deal with pandemics as a global community is within the next 27 years. Pandemic prevention therefore should be a critical health policy issue for the current generation of scientists and policymakers to address. A 2007 study warns that "the presence of a large reservoir of SARS-CoV-like viruses in horseshoe bats, together with the culture of eating exotic mammals in southern China, is a time bomb. The possibility of the reemergence of SARS and other novel viruses from animals or laboratories and therefore the need for preparedness should not be ignored". The US' National Security Council Directorate for Global Health Security and Biodefense, which worked on preparing for the next disease outbreak and preventing it from becoming an epidemic or pandemic, was closed in 2018.

Environmental Policy and Economics: Some experts link pandemic prevention with environmental policy and caution that environmental destruction as well as climate change drives wildlife to live close to people. For instance the WHO projects that climate change will also affect infectious disease occurrence. A 2016 study reviews literature on the evidences for the impact of climate change on human infectious disease, suggests a number of proactive measures for controlling health impacts of climate change and finds that climate change impacts human infectious disease via alterations to pathogen, host and transmission. Studies have shown that the risk of disease outbreaks can increase substantially after forests are cleared. According to Kate Jones, chair of ecology and biodiversity at University College London, the disruption of pristine forests driven by logging, mining, road building through remote places, rapid urbanisation and population growth is bringing people into closer contact with animal species they may never have been near before, resulting in transmission of diseases from wildlife to humans.

An August 2020 study published in Nature concludes that the anthropogenic destruction of ecosystems for the purpose of expanding agriculture and human settlements reduces biodiversity

and allows for smaller animals such as bats and rats, who are more adaptable to human pressures and also carry the most zoonotic diseases, to proliferate. This in turn can result in more pandemics. In October 2020, the Intergovernmental Science-Policy Platform on Biodiversity and Ecosystem Services published its report on the 'era of pandemics' by 22 experts in a variety of fields and concluded that anthropogenic destruction of biodiversity is paving the way to the pandemic era and could result in as many as 850,000 viruses being transmitted from animals – in particular birds and mammals – to humans. The increased pressure on ecosystems is being driven by the "exponential rise" in consumption and trade of commodities such as meat, palm oil, and metals, largely facilitated by developed nations, and by a growing human population.

According to Peter Daszak, the chair of the group who produced the report, "there is no great mystery about the cause of the Covid-19 pandemic, or of any modern pandemic. The same human activities that drive climate change and biodiversity loss also drive pandemic risk through their impacts on our environment." Stanford biological anthropologist James Holland Jones notes that humanity has "engineered a world where emerging infectious diseases are both more likely and more likely to be consequential", referring to the modern world's prevalent highly mobile lifestyles, increasingly dense cities, various kinds of human interactions with wildlife and alterations of the natural world. Furthermore, when multiple species that are not usually next to each other are driven to live closely together new diseases may emerge. Research shows that abundant animals, plants, insects, and microbes living in complex, mature ecosystems can limit the spread of disease from animals to people. The United Nations is formulating nature-focused action plans that could help to stop the next pandemic before it starts.

These strategies include conserving ecosystems and wilderness that are still untouched by human activity, and restoring and protecting significant areas of land and ocean (i.e. through protected areas). Protected areas (which may hold wildlife) also limits human presence and/or limits the exploitation of resources (including non-timber forest products such as game animals, fur-bearers). An article by the World Economic Forum states that studies have shown that deforestation and loss of wildlife cause increases in infectious diseases and concludes that the recovery from the COVID-19 pandemic should be linked to nature recovery, which it considers economically beneficial. A report by FAIRR global investor network found that more than 70% of the biggest meat, fish and dairy producers were in danger of fostering future zoonotic pandemics due to lax safety standards, closely confined animals and the overuse of antibiotics. Some have recommended food system-change, behaviour change, different lifestyle choices and altered consumer spending including moving away from factory farming and towards more plant-based diets. Some traditional medicines (i.e. traditional African medicine, TCM) still use animal-based substances.

Since these can trigger zoonosis, a possible prevention could be changes to handbooks for practitioners of such traditional medicines (i.e. exclusion of animal-based substances). Senior adviser and veterinary epidemiologist at the National Food Institute at the Technical University of Denmark Ellis-Iversen states that in agricultural animal health "outbreaks of exotic disease in well-regulated countries rarely get big because we identify and control them right away". New York City's Bronx Zoo's head veterinarian Paul Calle states that usually emerging infectious diseases from animals are the result from wildlife consumption and distribution on a commercial scale rather than a lone person hunting to feed their family. Dennis Caroll of the Global Virome Project states that the "extractive industry — oil and gas and minerals, and the expansion of agriculture, especially cattle" are the biggest predictors of where spillovers can be seen.

Biotechnology Research and Development Regulation: Toby Ord, author of the book The Precipice: Existential Risk and the Future of Humanity which addresses this issue, puts into question whether current public health and international conventions, and self-regulation by biotechnology companies and scientists are adequate. In the context of the 2019–2020 coronavirus pandemic Neal Baer writes that the "public, scientists, lawmakers, and others" "need to have thoughtful conversations about gene editing now". Ensuring the biosafety level of laboratories may also be an important component of pandemic prevention. This issue may have gotten additional attention in 2020 after news outlets reported that U.S. State Department cables indicate that, although there may be no conclusive proof at the moment, the COVID-19 virus responsible for the COVID-19 pandemic may, possibly, have accidentally come from a Wuhan (China) laboratory, studying bat coronaviruses that included modifying virus genomes to enter human cells, and determined to be unsafe by U.S. scientists in 2018, rather than from a natural source.

As of 18 May 2020, an official UN investigation into the origins of the COVID-19 virus, supported by over 120 countries, was being considered. United States' president Donald Trump claimed to have seen evidence that gave him a "high degree of confidence" that the novel coronavirus originated in the Chinese laboratory but did not offer any evidence, data or details, contradicted statements by the United States' intelligence community and garnered a lot of harsh criticism and doubts. As of 5 May, assessments and internal sources from the Five Eyes nations indicated that the coronavirus outbreak being the result of a laboratory accident was "highly unlikely", since the human infection was "highly likely" a result of natural human and animal interaction. Many others have also criticized statements by US government officials and theories of laboratory

release. Virologist and immunologist Vincent R. Racaniello said that "accident theories – and the lab-made theories before them – reflect a lack of understanding of the genetic make-up of Sars-CoV-2."

Virologist Peter Daszak stated that an estimated 1–7 million people in Southeast Asia who live or work in proximity to bats are infected each year with bat coronaviruses. In January 2021, the WHO's investigations into the origin of COVID-19 was launched. In early 2021, the hypothesis of a laboratory cause of the pandemic received renewed interest and expert consideration due to renewed media discussion. Martin Rees, author of the book Our Final Hour which also addresses this issue, states that while better understanding of viruses may allow for an improved capability to develop vaccines it may also lead to an increase in "the spread of 'dangerous knowledge' that would enable mavericks to make viruses more virulent and transmissible than they naturally are". Different accelerations and priorizations of research may however be critical to pandemic prevention. A multitude of factors shape which knowledge about viruses with different use-cases, including vaccine-development, can be used by whom. Rees also states that "the global village will have its village idiots, and they will have global range".

Food Markets and Wild Animal Trade: In January 2020 during the SARS-CoV 2 outbreak experts in and outside China warned that wild animal markets, where the virus originated from, should be banned worldwide. On January 26 China banned the trade of wild animals until the end of the coronavirus epidemic at the time. On February 24 China announced a permanent ban on wildlife trade and consumption with some exceptions.[103] Some scientists point out that banning informal wet markets worldwide isn't the appropriate solution as fridges aren't available in many places and because much of the food for Africa and Asia is provided through such traditional markets. Some also caution that simple bans may force traders underground, where they may pay less attention to hygiene and some state that it's wild animals rather than farmed animals that are the natural hosts of many viruses. UN biodiversity chief, bipartisan lawmakers and experts have called for a global ban of wet markets and wildlife trade. Jonathan Kolby cautions about the risks and vulnerabilities present in the massive legal wildlife trade.

International coordination The Global Health Security Agenda (GHSA) a network of countries, international organizations, NGOs and companies that aim to improve the world's ability to prevent, detect, and respond to infectious diseases. Sixty-seven countries have signed onto the GHSA framework. Funding for the GHSA has been reduced since the launch in 2014, both in the US and globally. In a 2018 lecture in Boston Bill Gates called for a global effort to build a comprehensive pandemic preparedness and response system. During the COVID-19 pandemic he called upon world leaders to "take what has been learned from this tragedy and invest in systems to prevent future outbreaks". In a 2015 TED Talk he warned that "if anything kills over 10 million people in the next few decades, it's most likely to be a highly infectious virus rather than a war". Numerous prominent, authoritative, expert or otherwise influential figures have similarly warned about elevated, underprepared or contemporary risks of pandemics and the need for efforts on an "international scale" long before 2015 and since at least 1988 [1-3].

Some have provided suggestions for organizational or coordinative preparedness for pandemic prevention including a mechanism by which many major economic powers pay into a global insurance fund which "could compensate a nation for economic losses if it acts quickly to close areas to trade and travel in order to stop a dangerous outbreak at its source" or, similarly, sovereign or regional-level epidemic-insurance policies. International collaboration including cooperative research and information-sharing has also been considered vital. According to Senator Dianne Feinstein called for the creation of a new interagency government entity, the Center for Combating Infectious Disease which would combine analytical and operational functions "to oversee all aspects of preventing, detecting, monitoring, and responding to major outbreaks such as coronavirus" and get provided with data and expertise by the Centers for Disease Control and Prevention. John Davenport advises to abandon widespread libertarian ideology which, according to him, "denies the importance of public goods or refuses to recognize their scope."

According to the CDC, investing in global health security and improving the organization's ability to prevent, detect, and respond to diseases could protect the health of American citizens as well as avert catastrophic costs. Dennis Carroll argues for a "marriage" between scientific discovery and political decision-making and policy formulation. Artificial induction of immunity and/or biocides. Outbreaks could be contained or delayed – to enable other containment-measures – or prevented by artificial induction of immunity and/or biocides in combination with other measures that include prediction or early detection of infectious human diseases. In a preprint published on March 24, 2020 researchers suggested that the unique transcriptional signature of SARS-CoV-2 in the human immune system may be responsible for the development of COVID-19: SARS-CoV-2 did not induce the antiviral genes that code for type I and type III interferons. This could be relevant for the development or repurposing of treatments [4-6].

Vaccination: Development and provision of new vaccines usually takes years. The Coalition for Epidemic Preparedness Innovations, which was launched in 2017, works on reducing the time of vaccine-development. The Global Health Innovative Technology Fund (GHIT) is a public-private partnership fund which involves a

national government, a UN agency, a consortium of pharmaceutical and diagnostics companies, and international philanthropic foundations to accelerate the creation of new vaccines, drugs and diagnostic tools for global health. It is unclear whether vaccines can play a role in pandemic prevention alongside pandemic mitigation. Nathan Wolfe proposes that pathogen detection and prediction may allow establishing viral libraries before novel epidemics emerge – substantially decreasing the time to develop a new vaccine. Public health surveillance expert and professor at Harvard University, John Brownstein says that "vaccines are still our main weapon". Besides more rapid vaccine development it may also be possible to develop more broader vaccines. Misinformation and misconceptions about vaccines including about their side-effects may be a problem.

Culling: Experts warned that depleting the numbers of species by culling to forestall human infections reduces genetic diversity and thereby puts future generations of the animals as well as people at risk while others contend that it's still the best, practical way to contain a virus of livestock.

Prevention Versus Mitigation: Pandemic prevention seeks to prevent pandemics while mitigation of pandemics seeks to reduce their severity and negative impacts. Some have called for a shift from a treatment-oriented society to a prevention-oriented one. Authors of a 2010 study write that contemporary "global disease control focuses almost exclusively on responding to pandemics after they have already spread globally" and argue that the "wait-and-respond approach is not sufficient and that the development of systems to prevent novel pandemics before they are established should be considered imperative to human health". Peter Daszak comments on the COVID-19 pandemic, saying "the problem isn't that prevention was impossible, It was very possible. But we didn't do it. Governments thought it was too expensive. Pharmaceutical companies operate for profit". The WHO reportedly had mostly neither the funding nor the power to enforce the large-scale global collaboration necessary to combat it. Nathan Wolfe criticizes that "our current global public health strategies are reminiscent of cardiology in the 1950s when doctors focused solely on responding to heart attacks and ignored the whole idea of prevention".

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ISSN: 2574-1241

DOI: 10.26717/BJSTR.2022.41.006609

Ruksana Hamid. Biomed J Sci & Tech Res

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