



Review Article

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Most Current Microbial Terror to Humanity - A Review

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Abstract

Current, on-going microbial terror to humanity needs public enlightenment. Unknown to most people, it is the 18th such terror in recorded human history. First noticed in Wuhan (China) in early December 2019 as atypical pneumonia reported in a cluster of patients, and later discovered to be caused by a new coronavirus, called SARS-CoV-2, best known by WHO's terminology, COVID-19. Routes of transmission are droplets, aerosols and fomites, close face-to-face contacts, and spread by asymptomatic, pre-symptomatic and symptomatic carriers. Symptoms and signs are typically an influenza-like syndrome: rigours, fatigue, high-fever, dry-cough, shortness of breath, fatigue, myalgia, headache, weakness, less commonly, nausea, vomiting, and diarrhea. Complications include pneumonia, acute respiratory disease syndromes necessitating supplemental oxygen, acute liver, kidney, and cardiac injuries, that necessitates intensive-care units. Diagnosis is by detection of SARS-CoV-2 via reverse transcription PCR testing. Clinical management involves providing supportive care to relief aforementioned symptoms, supporting vital organ functions, treating secondary bacterial infections, and managing critically ill-patients in ICUs. Socio-economic effects include forced restrictions, quarantine, testing, vaccination and travel bans; globally as of October 01, 2021: economy shrunk by 3.5 per cent, with monumental financial loss of over \$21, 000,000,000,000; world total infected individuals = 234,707,794; confirmed death = 4,800,466; recovered cases = 211,514,975; day new cases = 146, 944; day new deaths = +3,036. USA, India, Brazil, UK, Russia, Turkey and France topped the list of casualties in that order; Nigeria is 98th in the list; daily details obtainable from: www.worldometers.info/coronavirus. Succor is that about 270 vaccines are presently in production; six are in use.

Introduction

Terror is defined as a person or thing that causes very great fear; while humanity is noted as human beings collectively [1]; this topic therefore touched the most current microbe that causes very great fear to human beings collectively. Many microbes have indeed time immemorial brought such issue of serious health and deep survivability concern to humanity. Many of them assumed pandemic level. Some caused huge economic, social, material and human resources lost. Notwithstanding, some that were merely regional or sporadic were not neglected out of fear from the fact that the world is now what is termed a "global village" due to more intense easier travels, immigrations and emigrations; consequently, the

great risk of neglecting such sporadic case Others that did not, and probably may not assume a pandemic, were also neither dismissed unconcern by other nationals because of both the social stigma and the terror of pain from its affliction – should they or their our people get infected should they visit such area or regions.. Usually, the one of most concern are usually those that are pandemic. Table1 show the timeline of the historical pandemic ones.

Most Current Microbial Terror

The most current microbial terror to humanity is the Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) virus that is causing the worldwide severe acute respiratory syndrome



coronavirus-2 diseases best known as Coronavirus disease 2019 (COVID-19). The disease was declared a pandemic globally by the World Health Organization on March 11, 2020.

Etiologic agent

The etiologic agent, SARS-CoV-2 is a very highly pathogenic novel virus that is a beta CoV of the Family *Coronaviridae* which usually causes respiratory symptoms that resemble common cold. Like all the coronaviruses, it belongs to the Family: *Coronaviridae*. This family consists of four genera: Alpha-coronaviruses, Beta-coronaviruses, Gamma-coronaviruses and Delta-coronaviruses [2]. Structurally, they are enveloped, positive-sense, single-stranded ribose-nucleic acid (RNA) viruses. Their genome encodes non-structural proteins and 4 structural proteins that include the membrane, spike, envelope and nucleocapsid proteins.

Pathogenically, they infect a wide range of animals and humans. The human ones (HCoVs) cause seasonal respiratory tract

infections/diseases, and to a lesser extent, gastroenteritis. Human coronaviruses-229E (HCoV-229E) and Human coronaviruses-OC43 (HCoV-OC43) that belong to the Genus Alpha-coronavirus, are the causative agents of common cold [3]. Human coronaviruses-NL63 (HCoV-NL63) and Human coronaviruses-NKU1 (HCoV-HKU1), which are members of the Genus Beta-coronavirus, cause more severe, though rarely fatal, upper and lower respiratory tracts infections/diseases [3]. Further, the Genus Beta-coronavirus also include three very highly pathogenic viruses [(i.e. Severe acute respiratory syndrome coronavirus (SARS-CoV), Middle East respiratory syndrome coronavirus (MERS-CoV), and the Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) - the etiological agent of the most current microbial terror to humanity of this topic, i.e. Coronavirus disease 2019 (best known as COVID-19)] that elicit severe paroxysm of pneumonia in humans [4], as indicated in Table 1.

Table 1: Timeline, pathogen, and vectors of the past pandemics.

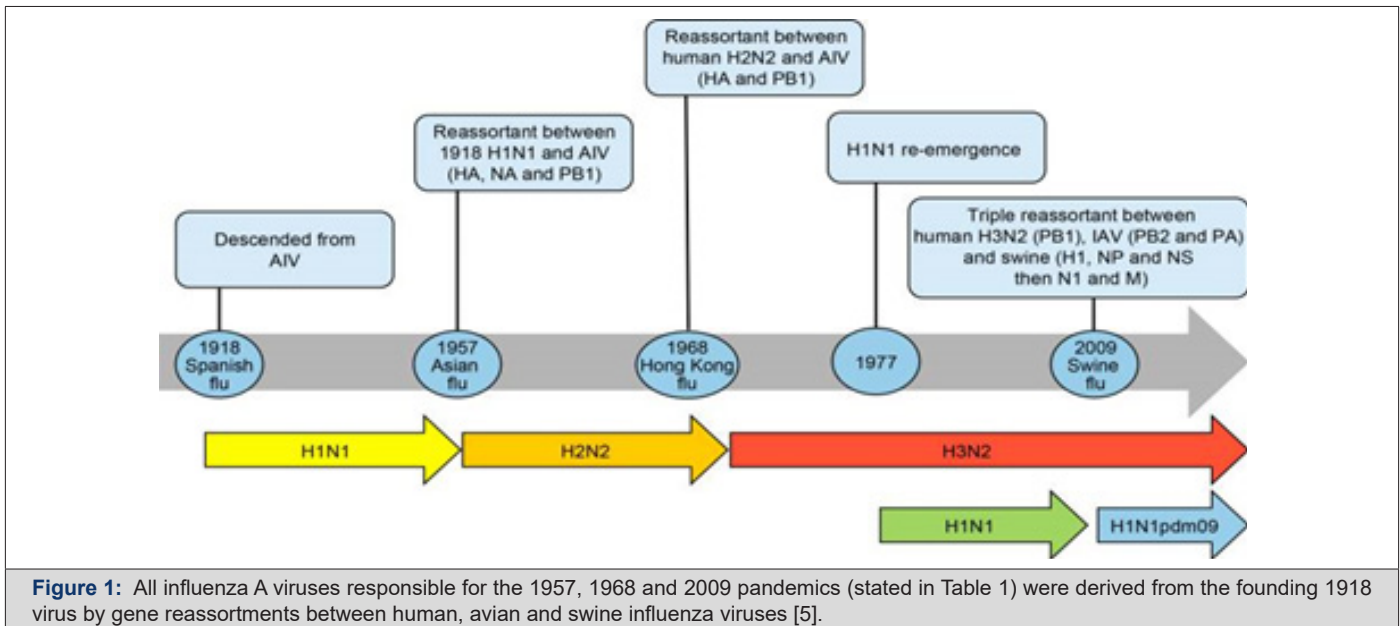
S/No	Years	Pandemics	Pathogens	Vectors
1	541-543	Plague of Justinian	<i>Yersinia pestis</i>	Fleas associated to wild rodents
2	1347-1351	Black Death	<i>Yersinia pestis</i>	Fleas associated to wild rodents
3	1817-1824	First cholera pandemic	<i>Vibrio cholerae</i>	Contaminated water
4	1827-1835	Second cholera pandemic	<i>Vibrio cholerae</i>	Contaminated water
5	1839-1856	Third cholera pandemic	<i>Vibrio cholerae</i>	Contaminated water
6	1863-1875	Fourth cholera pandemic	<i>Vibrio cholerae</i>	Contaminated water
7	1881-1886	Fifth cholera pandemic	<i>Vibrio cholerae</i>	Contaminated water
8	1885-ongoing	Third plague	<i>Yersinia pestis</i>	Fleas associated to wild rodents
9	1889-1893	Russian flu	Influenza A/H3N8?	Avian?
10	1899-1923	Sixth cholera pandemic	<i>Vibrio cholerae</i>	Contaminated water
11	1918-1919	Spanish flu	Influenza A/H1N1	Avian
12	1918-1919	Spanish flu	Influenza A/H1N1	Avian
13	1961-ongoing	Seventh cholera pandemic	<i>Vibrio cholerae</i>	Contaminated water
14	1968-1970	Hong Kong flu	Influenza A/H3N2	Avian
15	2002-2003	Severe acute respiratory syndrome (SARS)	SARS-CoV	Bats, palm civets
16	2009-2010	Swine flu	Influenza A/H1N1	Pig
17	2015-ongoing	Middle East respiratory syndrome (MERS)	MERS-CoV	Bats, dromedary camels
18	2019-ongoing	COVID-19	SARS-CoV-2	Bats, pangolins?

Origins

Wuhan, a city in China became the epicenter of the outbreak of COVID-19 in December 2019. Details of the origin of all the coronaviruses need be noted first. This is because just as the past pandemic descendants of the 1918 pandemic virus were the cause of almost all seasonal influenza A epidemics worldwide (Figure 1), COVID-19 is being traced to other severe respiratory disease syndromes, including common cold; notwithstanding that they belong to the same family. Figure 1 shows the descendant of all influenza A viruses responsible for the 1957, 1968 and 2009

pandemics (as indicated in Table 1) were also derived from the founding 1918 virus by gene reassortments between human, avian and swine influenza viruses [5].

Severe acute respiratory syndrome coronavirus (SARS-CoV) first originated in Guangdong province of People Republic of China in 2003. Bats are implicated as the likely natural reservoir [6], while palm civets were suggested as the intermediary hosts before being disseminated to human beings [7]. Within one week, the causative agent was identified [8,9].



According to WHO (2003), in the 2002–2003 outbreak, altogether 8437 SARS-CoV infections were reported in 29 countries in North America, South America, Europe and Asia, but less than 10% (813) were noted fatal. The modes of transmission then, were mainly nosocomial, at the rates of 33–42%, but at the rates of 22–39% between family members [10]. Unlike the current sister SARS-CoV-2, cases identification, isolations followed by contact tracing and surveillance proved effective in containing the threat extending globally, with the eradication of the virus in 7 months.

Ge et al. [11] noted that some SARS-CoV-like viruses found in bats had been proven to be able to infect human cells without prior adaptation, which indicates that SARS could re-emerge in the future. Probably this observation was not taken with the seriousness it deserved that was why the world found herself in this present conundrum. Just ten years after the first emergence of severe acute respiratory syndrome coronavirus (SARS-CoV), Middle East Respiratory Syndrome coronavirus (MERS-CoV) was reported in Jeddah, Kingdom of Saudi Arabia. The animal reservoirs of MERS-CoV are bats, while the camels have been suggested as the intermediary hosts. Due to advances in molecular diagnostic tools the etiological agent was identified within weeks of global spread [12]. According to WHO, (2020c) between 2012 and 2020, 2,519 cases of MERS-CoV, confirmed in the laboratory, with at least 866 deaths were reported in 27 countries. All cases were linked to persons in the Arabian Peninsula or who had returned from traveling in MERS-CoV endemic areas. According to Hui et al. [13], almost 50% of MERS-CoV cases were due to nosocomial transmission to inpatients, health care workers and visitors.

MERS-CoV is still circulating nowadays. According to Sikkema et al. [14], the ubiquity of infected dromedary camels close to

humans [15] and the continuing zoonotic transmission may explain why MERS-CoV continues to cause intermittent sporadic cases, community clusters and nosocomial outbreaks.

It was in early December 2019, that an atypical pneumonia were reported in a cluster of patients in Wuhan, China and were later shown to be caused by a new coronavirus, called SARS-CoV-2 [16] whereas the disease is referred to as COVID-19 by World Health Organization. The animal reservoirs were suspected to be bats by [17] proposed that pangolins could be the animal hosts that transmit the virus to humans but the intermediary host, if any, has not yet been definitely identified.

Nature of Microbial Terrorism

Transmission and incubation period

According to Seto WH et al. [18], the major routes of transmission of SARS-CoV were droplets, aerosols and fomites, especially in close face-to-face contact. Its infection can be spread by asymptomatic, pre-symptomatic, and symptomatic carriers. It has low infectivity and long incubation period; the average time from exposure to symptom onset is 5 days, and 97.5% of people who develop symptoms do so within 11.5 days [19]. However, because it is a respiratory tract infection, and it is highly transmissible, it quickly became a global threat

Disease, symptoms and signs

Manifestations of COVID-19 include asymptomatic carriers and fulminant disease characterized by sepsis and acute respiratory failure. Approximately 5% of patients with COVID-19, and 20% of those hospitalized, experience severe symptoms necessitating intensive care; more than 75% of patients hospitalized require supplemental oxygen [19].

Symptoms and signs typically include an influenza-like syndrome with rigours, fatigue and high fever, dry cough, shortness of breath, fatigue, myalgia, headache, weakness, rhinorrhea, anosmia and ageusia. Less common symptoms include nausea, vomiting, and diarrhea.

In about 20-30% cases, the disease advances to an atypical pneumonia, with shortness of breath due to poor oxygen exchange in the alveoli which requires management of the patient in ICU or mechanical ventilation. Quite a number of such patients also developed watery diarrhea and shedding the active virus.

Complications

Among hospitalized patients, common complications include pneumonia, acute respiratory disease syndromes (ARDS), acute liver injury, cardiac injury, prothrombotic coagulopathy, acute kidney injury and neurologic manifestations. Critically ill patients could also develop a cytokine storm and a macrophage activation syndrome. According to [20], in 60–90% of hospitalized patients, co-morbidities (e.g. hypertension, diabetes, cardiovascular disease, chronic pulmonary disease, chronic kidney disease, malignancy and chronic liver disease) are present.

Pathogenicity and pathogenesis

Bastard et al. & Zhang Q et al. [21,22] reported that impaired Type I interferon response to be involved in patients with life-threatening COVID-19.

Prognosis

80% of laboratory-confirmed cases are mild symptoms; about 14-19% of patients are hospitalized, but only 3-5% of such cases require transfer to ICU, usually due to hypoxemic respiratory failure; and, among the 3-5%, 29-91% necessitates invasive mechanical ventilation.

There is no protective immunity against this virus as well as effective antiviral drugs and, until almost one year vaccines were lacking. Respiratory failure was the most common cause of death among patients infected with the disease.

Mortality

The case-fatality rate for COVID-19 varies markedly by age; in general, mortality rate among hospitalized patients is approximately 15–20% whereas it is as high as 40% in patients requiring intensive care unit (ICU) admission [19].

According to Wilson et al. [23], the global estimated case mortality rate is about 0.25 to 3.0%; 0.02% in patients aged 20-49 years; about 0.5% for patients aged 50-69 years and greater than 5.4% for patients aged more than 80 years. According to Rowley et al. [24] children have milder symptoms predominantly limited to the upper respiratory tract; though, a rare multisystem inflammatory syndrome has been reported. The current rate and degrees of

casualties can be found in the web site: www.worldometers.info/coronavirus (which is a live statistics and coronavirus news tracking of the number of confirmed cases, recovered patients, tests, and death toll due to COVID-19).

Diagnosis

Diagnosis is made by detection of SARS-CoV-2 via reverse transcription polymerase chain reaction testing, although false-negative test results may occur in up to 20% to 67% of patients; however, this is dependent on the quality and timing of testing.

Radiographic and laboratory abnormalities, such as lymphopenia and elevated lactate dehydrogenase, are common, but nonspecific [19].

Treatments

The treatment procedure for COVID-19 disease, like MERS-CoV, is the clinical management of the patients, consisting mainly in providing supportive care for the relief of pain and fever, (and other symptoms), supporting vital organ functions and treating concomitant or secondary bacterial infections with antibiotics [26]. Critically ill patients required to be managed in intensive-Care units (ICU).

Further, because of absence of adequate vaccines and vaccination, in addition to unavailable pharmaceutical treatments, the impact of COVID-19 is being mitigated by the use of non-pharmaceutical interventions. Treatment for individuals with COVID-19, as indicated includes best practices for supportive management of acute hypoxic respiratory failure; more than 75% of patients hospitalized require supplemental oxygen [19].

Emerging data indicate that dexamethasone therapy reduces 28-day mortality in patients requiring supplemental oxygen compared with usual care (21.6% vs 24.6%; age-adjusted rate ratio, 0.83 [95% CI, 0.74-0.92]) and that remdesivir improves time to recovery (hospital discharge or no supplemental oxygen requirement) from 15 to 11 days. In a randomized trial of 103 patients with COVID-19, convalescent plasma did not shorten time to recovery. Ongoing trials are testing antiviral therapies, immune modulators, and anticoagulants [19].

Other Effects of the microbial terror

The most current microbial terror, SARS-CoV-2 has, and is still having many devastating healths, economics and social horrors on human beings collectively all over the world. The healths, socio- and socio-economic impacts of the COVID-19 pandemic are household word, to all ages, all over the world.

Health

As of March 2021, Marchisio [26] estimated that 100 million people have contracted the virus worldwide and over 2.2 million died from the disease. According to www.worldometers.info/

coronavirus (which is a live statistics and coronavirus news tracking website of the number of confirmed cases, recovered patients, tests, and death toll due to COVID-19), as of today, October 01, 2021, the world total number of infected individuals = 234,707,794, with a total confirmed death = 4,800,466, presently totally recovered cases = 211,514,975; today's total world new cases = 146, 944; new deaths = +3,036. In Nigeria, as of October 01, 2021, the total number of confirmed cases is 205,779, including 295 for today; the total number of confirmed deaths is 2,721 including 20 for today.

The coronavirus COVID-19 is affecting 221 countries and territories. The reported cases and death by country or territory each day is reset after midnight GMT+0 and the list of countries and their regional classification is based on the United Nations Geoscheme. USA, India, Brazil, UK, Russia, Turkey and France topped the list number and degrees of infected cases in that order, with Samoa, (3) Saint Helena (2) and Micronesia (1) in that descending order; Nigeria is the number 98 in the list.

Social effects (Restrictions, travel bans, quarantine, forced vaccination and testing)

Nobody in this generation will ever live to forget the bitter tastes of the resultant social constraints generated by the COVID-19 pandemic. Besides, the disgusting lockdown restraints forced down on the populace as is done to prisoners, other annoying impositions include being forced to run test against ones will, forced to wear facemasks against wishes, constrained to unwilling social distance, restrained from intimate close contact whether as handshakes or public embrace, prevented to travel to places against ones choices, unable to go on routine vacations, conferences, seminars, symposia, church, mosque, etc;. even dignitaries are forced to self-quarantine for obvious reasons; there have even been many cases that even when one present vaccination certificate on arrival to another country, among other reasons such as "coming from an epicenter or an endemic zone," the one will still be quarantined for two weeks!! Two unplanned weeks, restrained in a foreign country, before the one can now go for the business that made the person to travel!! The most importantly boiling one presently is the issue of forced vaccination for which otherwise calls for stiff consequences.

Economy

According to the International Monetary Fund, as of March 2021, the global economy shrunk by 3.5 per cent last year [26], with monumental financial lost of over 21 trillion (\$21, 000,000,000,000) United States' dollars, which represents the gravest global recession since the Second World War. This was because the pandemic was trailed by supply-chain disruptions and inflation, which usually were among the top-three risks to national economic growth and development.

Machiso [26] summarized the gloomy situation as follows, I quote: what is today still considered by many as primarily a health

and economic crisis may soon become a long-term development crisis, if the world does not act promptly. The economic impacts of COVID-19 are likely to lead to an enduring increase in global poverty and food insecurity. The World Bank estimates that COVID-19 has pushed an additional 88 to 115 million people into extreme poverty last year. According to The State of Food Security and Nutrition in the World 2020 report, the pandemic may have added between 83 and 132 million people to the total number of undernourished in the world in 2020. In this scenario, without assistance, low-income developing countries are the most vulnerable: they are already particularly vulnerable to external shocks, and they have limited resources and weak institutional capacity to support their economies in the face of a shock. Within these countries, rural communities are the most vulnerable, as they are often not covered by economic safety nets, and their livelihoods primarily depends on activities that have been significantly affected by the measures countries have implemented to contain the pandemic – e.g. remittances from migrant labour, production and sale of agricultural products, unquote.

Diseases, most especially the respiratory tract infections like COVID-19, have no geographic boundaries, nor respect political borders, and the effects of a possible global food crisis will affect everyone without distinction; if not nutritionally, it could come as violence arising as insecurity from starving stomachs. In Nigeria, it is already coming up as insurgencies of various forms: banditry, kidnapping for ransom, cattle rustling, herdsmen violence, Boko haram, Shiite group problems, etc; if they consume available food in West Africa and Africa, like the Mediterranean migrants, they would also seek solace in Europe and the entire world like ISIS and Al Qaeda, etc. So, besides donating free vaccines to the most vulnerable in individual countries, of course the entire worlds need the vaccine – as well as food and other nutrients.

Outlook on the pandemic crisis

According to Mckinsey and Company Strategy and Corporate Finance [27] and their coronavirus effect on global economic sentiment of September 29, 2021 survey, eighteen months into the COVID-19 pandemic, executives' responses to their latest McKinsey Global Survey suggest that they believe the economy is on track toward a recovery; and throughout 2021, their views have, on average, been consistently positive.

Prevention and controls

Until an effective vaccine is available, the primary methods to reduce spread are wearing of face masks, observation of social distancing, and prompt contact tracing. Monoclonal antibodies and hyper immune globulin may provide additional preventive strategies [19]. Because of the low infectivity and long incubation period, the disease provided good time for implementation of series of prevention and control measures that can allows containing its

widespread so as to prevent transmission. These measures are:

Isolation

Besides COVID-19, isolation is a very effective prevention and control measure to so many infectious diseases; it has been efficient in the past pandemics, and even in many other isolated endemic diseases like leprosy, Ebola, tuberculosis, and interestingly United Kingdom uses it for even malaria; if one is diagnosed for malaria in UK, the one is isolated until radical cure is achieved on the patient before discharge from quarantine. The reason for that is obvious: not to allow the patient give another mosquito(es)' bites(s) any plasmodia to suck and spread in their soil.

In the case of COVID-19, all visitors, whether from COVID-19 epicenter or not, are isolated and quarantined for 14 days (peak of the incubation period) until they are tested negative at the end of the quarantine. Effectiveness of this measure is that it prevents importation of the virus to another country.

Testing

The importance of testing is obvious. For instance, students returning to schools are all tested for the virus in order to be reassured that they are not infected thereby ensure not to transmitting it to other students, members of staff and visitors of their various institutions. This has a high degree of reassurance of preventing transmission; detected infected persons are thereby isolated and treated, and make sure they are no longer transmitting the virus before they are discharged from the isolation centres.

Contact tracing

Because of it is a respiratory tract infection it, contact tracing was not as successful as in contagious diseases like Ebola; besides, it has a very high rapid transmission rate, so its spread was by arithmetical and geometrical progression beyond capacity of tracing contacts, so it did not took time to become worldwide threat, more than any pandemic in human history.

Physical distancing

Like contact tracing, because it is a respiratory tract infection, physical distancing as a preventive measure has limitations. The only saving grace is that, since it is a very heavy virus, it is not carried too far when coughed out into air by carriers or patients, and it usually quickly falls onto the ground within two meters. Therefore, maintaining social distancing of, at least, that two metres, is a degree of security from contacting the virus (and other respiratory tract infections in general) from air.

Community sanitations

This, as a measure to protect the uninfected ones from those infected, who may have disseminated the virus include fumigations of public environments, face mask wearing by absolutely everybody (especially in public places), coughing into elbow/disposables by

everybody at home and at public places, particularly in the public), etc. are all degrees of preventive measures from dissemination, rather than being absolute sanitation or sterilization procedures. Vaccination or immunization is inclusive but will be treated as a special chapter below.

Fumigation of public places such as schools, markets, malls, public transport systems and places (e.g. rail stations, motor parks, etc), even streets, to a degree kills the disseminated viruses, depending on the efficiency of the fumigators and the fumigants. Yet, they are all degrees of preventive measures from dissemination rather than being absolute sanitation or sterilization procedures.

Facemask wearing by everyone surely also will help prevent the afflicted from dissemination of the virus and infecting the healthy ones, as well as preventing the otherwise healthy ones from getting themselves inhaling the virus and thereby getting infected. It also depends on the type and efficiency of the individual facemasks; however, COVID-19 viruses have spikes unlike so many other microbes of respiratory tract infections, so can easily stick to the facemasks and restrict inhalation by the wearer, if well used. Though, makes and types were heavily abused up to the moment, and many much lesser effective makes and models are presently in circulation.

Personal hygiene

This, as a measure to protect oneself from the disseminated virus or from potential carriers or the diseased includes washing hands with sanitizer/soap regularly, face mask wearing in public places, coughing into elbows at home and at public places, not touching of nose-mouth-eyes and ears with unwashed/un-sanitized hands, and vaccination.

Washing hands with sanitizer/soap regularly, especially after returning home or from public places or meetings is a very valuable personal preventive measure. This is because inadvertent contact with the virus by touch are thereby destroyed and prevented from being disseminated to your immediate self/person, food, loved ones, friends, and relations.

Facemask wearing has been addressed in the chapter above

Coughing into elbows at home and at public places, like in wearing of facemask, prevent you (potentially infected, asymptomatic, pre-symptomatic, and symptomatic carriers) from disseminating the disease to the public, which include your loved ones, friends, and relations. It is also a very fair degree of community sanitation and personal hygiene that can highly assist in the prevention and control of the virus and respiratory tract infections in general.

Because the portal of entry of the COVID-19 virus into the host is primarily through the facial orifices (nose primarily, possible though the mouth eyes and ears) not touching of nose-mouth-eyes

and ears with unwashed/un-sanitized hands is strongly advocated as a preventive measure from infecting oneself.

Vaccinations and Vaccines

Vaccination

Vaccination can be defined as the acquisition of an applied types of artificially acquired active immunoprophylaxis through various forms of vaccines, which are antibody stimulants or agents (such as live-attenuated or killed-attenuated microorganisms, or fractionated part of microorganism or toxoids (i.e. detoxified toxins - technically not including immune serum, known as Convalescent Plasma Proteins) that are administered into otherwise healthy individuals/host, in order to artificially stimulates specific antibodies production in the body of the recipient; so as to protect such susceptible person(s) against specific diseases.

Immunization is the process of the use of vaccines, toxoids and immune sera to protect otherwise susceptible people against specific disease; it confer various type of immunity on the recipients depending on type of immunization and mode of its acquisition which may be active or passive; likewise either passive or active immunity could be artificial or naturally acquired.

Vaccines

Vaccines (Tables 2-4) are one of the most significant advances in human medicine for reducing the spread and effects of infectious disease; they have been used to contain epidemics and are a useful strategy in reducing pandemic mortality [28]. The process of using them is known as vaccination, and the affection of its usage is known as immunization

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Vaccines (Tables 2-4), therefore, are defined as various forms of antibody stimulants or agents [such as live-attenuated (i.e. vector-based live-attenuated), killed-attenuated microorganisms, fractionated part of microorganism, and toxoids (i.e. detoxified products)], which when practically administered into a host, artificially stimulates specific antibodies production in the body of the recipient; (e.g. Polio vaccine, smallpox vaccine, BCG, etc.), so as to protect such susceptible person(s) against specific diseases.

The development of a COVID-19 vaccine was more rapid than that of any other vaccine; within less than 12 months after the beginning of the pandemic, teams had developed vaccines that could be deployed for protection of the population [29]. Under normal conditions, especially as it was with other past vaccines, to develop a safe and reliable vaccine usually takes many years because it must undergo very closely monitored clinical trials. Even before they are formulated and marketed, and obviously for fear of adverse health reason, the vaccines must obtain stringent regulatory approval from the country of manufacture by a national regulatory authority.

However, the safety assessment processes were not affected, and the experiments adhered to the same stringent legal standards as other vaccine tests [30].

Qualities of a good vaccine

- I. Ability to elicit a strong immune response that results in long-lasting neutralizing antibodies to the specific pathogen (SARS-CoV-2 in this case);
- II. Capacity to stimulate potent T-lymphocyte immunity to inhibit a specific pathogen (in this case, viral replication);
- III. Capacity to develop specific memory T-cells against the pathogen in order to prevent reinfection;
- IV. Capability to protect against both clinical illness and transmission of the specific pathogen, thus disrupting the process of pandemic dissemination from person to person;
- V. Possession of little or no side effect
- VI. Possession of minimal significant adverse events (SAEs) at the injection site or systemically; adverse host responses should be blocked.
- VII. Further, the duration of vaccine immunity is vital to maintaining herd immunity, estimated at 50% to 67%; without population immunity, in the absence of intervention and considering all individuals similarly vulnerable and contagious [31].

Israel was the first country to demonstrate that the COVID-19 vaccines had an effect on viral transmission of SARS-CoV-2 in society; by February 2021, more than 84 percent of her people aged 70 and over had received two doses, making the country the global leader in vaccines; their number of severe the disease cases and deaths dropped dramatically [32].

Thereafter, approximately 120 SARS-CoV-2 vaccines [19]; about 270 COVID-19 vaccines [33], are presently in varying phases of production, many using similar technology of already used vaccines, others using novel approaches. Each of the vaccine that has been granted or is being considered for temporary licensing were validated in trials involving over 20,000 patients, and with months of safety evidence collected.

As of May 2021, about 1.3 billion vaccine doses have been distributed globally, an average of 17 doses per 100 individuals (<https://www.nytimes.com/interactive/2021/world/covid-vaccinations-tracker.html>). Further, there are significant disparity among vaccine systems in various nations, with several countries unable to record even a single dose; some others fully vaccinated (i.e. have received all doses prescribed by the vaccination protocol); as of May 10, 2021 they are in the web site: 'https://covid-nma.com/dataviz/'

Presently associated issues with COVID-19 vaccines and vaccination

A. Currently, because vaccines are presently scarce worldwide, majority of countries concentrated their early vaccination programs on high-risk populations such as the clinically vulnerable (i.e. people in their 60s, 70s, and older; and front-line staff such as doctors and nurses [30].

B. When the vaccination become more widely available, vaccination programs should extend to include younger generations in order to forestall asymptomatic transmission that will lead to significant relapses in the prevention and control of the virus, because it is more prevalent in younger age groups; in this way dissemination of the virus is restricted, hence potentially protecting the most vulnerable people [30,31].

C. Presently, few adverse effects have been recorded from SARS-CoV-2 vaccine clinical trials, and the efficacy and efficiency of those that have been extensively tested appear very encouraging.

D. The only other significant issue with COVID-19 vaccines is the manufacturing capability and capacity; given that billions of people will be vaccinated, will the production companies be able to meet up?

E. Besides qualities of a good vaccine already addressed, in terms of logistics, the optimal vaccine for COVID-19:

F. Should be simple to deliver; ideally in a single dose of the smallest volume available (many of the presently approved ones require booster doses)

G. Should be simple to manufacture and scale-up (almost all the presently available COVID-19 vaccines are manufactured with high-tech researches and procedures which are beyond the reach of third-world countries. Probably that is the reason why Nigeria and non of the black African countries have been able to research and produce even one).

H. Should be simple to transport and store (almost all the presently approved ones require high-tech refrigeration and storages, which is mostly below 0oCelsius).

Conclusion and Recommendations

Conclusion

i. Globally as of October 01, 2021: economy shrunk by 3.5 per cent, monumental financial lost of over 21 trillion (\$21,000,000,000,000) USA dollars; world total infected individuals = 234,707,794; confirmed death = 4,800,466; recovered cases = 211,514,975; day new cases = 146, 944; day new deaths = +3,036. USA, India, Brazil, UK, Russia, Turkey and France topped the list of casualties in that order; Samoa, (3) Saint Helena (2) and Micronesia (1) in same descending order; Nigeria = 98 in the list

(www.worldometers.info/coronavirus). Nigeria case for October 01, 2021: total confirmed infected = 205,779; day-case = 295; total confirmed deaths = 2, 721, day-case = 20.

ii. Because it is a novel virus and a new disease, many aspects of transmission, infection, pathogenicity, pathogenesis, and treatment are not yet fully unclear.

iii. Advances in prevention and effective management will need much more basic and clinical investigations, researches and literature publications, public health and clinical interventions and experiences.

iv. Because of increased contacts between humans and animals through breeding, hunting, wet markets and trade of exotic pets also favor the risk of spillover of zoonotic pathogens; the spread of infectious diseases is thus expected to increase due to human activities and their effects on the environment; epidemics and pandemics therefore will also occur more frequently and will represent new challenges for public health.

v. Succor is that about 270 vaccines are presently in production; six (Comminarty, Moderna, Vaxzevria, Janssen (Ad26. COV2.S), Sputnik V and CoronaVac) are in use.

Recommendations

A. The time of onset and the pathogen that will cause the next pandemic are not predictable, like when Ge et al. [13] noted that some SARS-CoV-like viruses found in bats had been proven to be able to infect human cells without prior adaptation, which indicates that SARS could re-emerge in the future; but this advise was not patently heeded.

B. Therefore, pandemic preparedness plans should first anchor on implementations to control human-to-human transmission of the pathogen before emphasizing on those non-pharmaceutical interventions;

C. Ideally, non-pharmaceutical interventions should adequately control the spread of an infection while minimizing societal and economic disruption;

D. Risks of resurgence can follow once these non-pharmaceutical interventions are lifted, as it is happening in many parts of the world as of October 01, 2021;

E. Once available, rapid testing together with contact tracing [34] and isolation of infected individuals should be put in place for a more effective response.

F. Furthermore, pharmaceutical interventions should include rapid point-of-care diagnostic tests [35], biomarkers for disease stratification [36], broad spectrum antimicrobials/antivirals obtained through in silico drug repurposing [37] or by the use of drugs targeting host cells.

G. As well, new platforms for accelerated vaccine development and production [38-45] should be developed to improve the global response to the pandemic.

H. Increased viral replication provides further chances for SARS-CoV-2 variants to evolve, like the delta-variant just did; as a result, vaccine production may be hampered if the virus later develops resistance to the spike glycoprotein most currently used to create the vaccine; therefore, vaccinations should be engineered to attack multiple viral locations, so as to minimize the chance of a mutated virus evading existing immunity [46-53].

Conflict of Interest

The authors hereby declare that the research was conducted without any commercial or financial relationships that could be construed as a potential conflict of interest.

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