Chapter 6
Epidemiology of COVID-19: Special Emphasis on Nanoscience and Its Implications

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Abstract Coronavirus disease 2019 (COVID-19) is a highly contagious pathogenic viral infection caused by SARS-Cov-2. Coronavirus seems to have taken a popular role in the twenty-first century. The first instance of COVID-19 which was reported in Hubei province, Wuhan, China, has now spread to the entire world by human-to-human transmission. The World Health Organization (WHO) declared this infectious disease as a pandemic. Currently this pandemic has created a global health crisis. In this chapter, we analysed the epidemiological characteristics, i.e. occurrence, distribution and transmission of disease in different countries, laboratory diagnosis, prevention, control and treatment of COVID-19. The main objective of this chapter is to provide the latest insights over nanotechnology and its implications in the diagnosis, treatment, prevention and control of COVID-19. In this direction, several emerging issues such as optical biosensor nanotechnology, respiratory masks, Nanofibers Membrane Technology, etc. We are in opinion that this chapter will provide useful insights towards understanding the role of nanotechniques to combat COVID-19.

Keywords COVID-19 · Occurrence · Transmission · Prevention · Control and treatment · Nanotechnology

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6.1 Introduction

Coronavirus disease is a pathogenic viral infection and is highly contagious caused by SARS-CoV-2 (Wikipedia 2020). It is an RNA virus that causes disease in animals and mammals. This coronavirus disease is also called as COVID-19 pandemic. These viruses are responsible for respiratory tract infections which may range from mild to lethal. These viruses have a positive-sense SS RNA as their genome with an outer envelope and nucleocapsid in the form of helical symmetry. This is enclosed by an icosahedral protein shell. The size of the genome of coronavirus compasses roughly 26 to 32 kilobases, one of the biggest RNA virus among the other RNA viruses (Fig. 6.1). Coronaviruses are enormous, for the most part round, once in a while pleomorphic (variable fit as a fiddle), particles with spherical surface projections (Goldsmith et al. 2004). The normal distance of the infectious particle is around 125 nm. The virus envelope in electron micrographs seems to be a distinct pair of electron-dense shells. Envelope comprises of a lipid bilayer, in which the film (M), envelope (E) and spike (S) auxiliary proteins are tied down (Lai and Cavanagh 1997). Nucleocapsid contains numerous duplicates of N (Nucleocapsid) protein, are bound to the positive sense single-stranded RNA genome in a constant dots on-a-string-type testimony. The lipid bilayer envelope, film proteins, and nucleocapsid ensure the infection when it is exterior the host cell (Neuman et al. 2011).
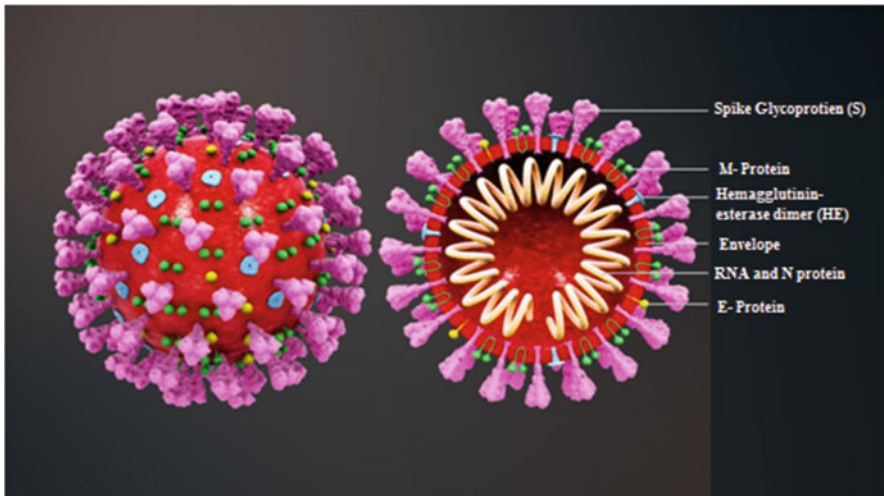
Fig. 6.1 The structure of coronavirus (Wikimedia 2020)

6.2 Epidemiology

Epidemiology is defined as the study of disease spread and examination of the diffusion and determinants of wellbeing-related states or occasions in indicated population and utilization of investigation to the control of medical issues. The word epidemiology is derived from a Greek language in which *epi* means upon, *demos* indicates the people and *logos* mean study of (Last 2001). Epidemiology has its underlying foundations in the examination of what comes upon a populace. The following are the important steps in the epidemiology:

(i) *Disease occurrence*: While there are numerous proportions of disease frequency, epidemiologists frequently gauge the disease occurrence in a population as incidence and prevalence of the infection. The key contrast between these two measures is the hour of ailment beginning.

(ii) *Incidence*: Incidence can be evaluated utilizing information from a disease registry data or a partner preliminary. There is a certain suspicion of a timeframe, for example, new cases within a month.

(iii) *Prevalence*: Prevalence measures the new and existing cases of a disease or outcome. Since prevalence tallies both new and existing cases, the term of the sickness influences the commonness.

Infections with a long span will be more pervasive than those with shorter term. Ceaseless, nonlethal conditions are more predominant than conditions with high mortality. Prevalence of a disease is legitimately identified with the span of the infection (CDC 2020).

## 6.3 Disease Occurrence and Distribution of COVID-19

In 2019, December the primary instance of coronavirus illness 2019 was accounted for in Wuhan, Hubei Province, China, during an outbreak of viral pneumonia. Since December 2019, patients with unexplained pneumonia have been found in Wuhan, Hubei Province, China. On 7th January 2020, Chinese specialists affirmed that the reason was a novel coronavirus that had not been recently distinguished, unique in relation to different coronaviruses, for example, Middle East respiratory syndrome coronavirus (MERS-CoV) in 2012 to 2015 and severe acute respiratory syndrome coronavirus (SARS-CoV) in 2003 (He et al. 2020). A large number of underlying cases were related to direct exposure to live markets, while ensuing cases were most certainly not. This further notified that infection spreads to human-to-human transmission through contacts, respiratory droplets, various discharges, etc.; on 21st January 2020, the National Health Commission of the People's Republic of China declared 2019-nCoV pneumonia as a class B irresistible infection, by considering the category A infectious disease as a reference (Wang et al. 2020a). In China, 11,791 cases were affirmed, and 17,988 cases were associated in 34 regions similarly as with 24:00, 31st January 2020. Gradually the number of cases attained peak

stage in the month of February, and downfall of cases was observed in late March; as of 12th May 2020, the total number of cases recorded were 82,919, and the number of deaths were 4,633. The irresistible respiratory infection COVID-19 has spread quickly inside China and to neighbouring nations and throughout the world in a very short period of time. The first affirmed coronavirus cases outside China happened on 20th January 2020.

On 21st January 2020, the very first case was reported in Washington State of the United States (Holshue 2020). The continuous COVID-19 pandemic was affirmed at the United States in January 2020. On 25th February, the Centers for Disease Control and Prevention (CDC) cautioned the Americans to get ready for a nearby outbreak (Taylor 2020). A national crisis was proclaimed by President Trump on 13th March (Liptak 2020). The alarm in other countries of the world was not gigantic, but rather the number of the contaminated individuals in different nations of the world was additionally expanded. Among these nations South Korea, Japan, Iran, Saudi Arabia, Afghanistan, Ireland, Brazil, Pakistan, India, Russia, Kuwait, Qatar, the United Arab Emirates and France were top nations of the world.

The infection was affirmed to have spread to Brazil on 25th February 2020 when a man from São Paulo tested positive for the infection (Brasil confirma 2020). Starting on 2nd June 2020, 555,383 cases have been affirmed in the nation, causing 31,199 deaths. As of June 2020, Brazil has the second-most noteworthy number of affirmed COVID-19 cases on the planet behind the United States (Wikipedia 2020). The infection spread to Russia on 31st January 2020, when two Chinese residents in Tyumen, Siberia, and Chita, Russian Far East tested positive for the infection, with the two cases being contained. Russia was generally late in enduring a serious outbreak; however it now has become the nation with the third-most cases on the planet, after the United States and Brazil (Wikipedia 2020). As per official figures starting on 3rd June, Russia has 432,277 affirmed cases; 195,957 recuperations; 5,215 passings; and over 11.4 million tests performed. The city of Moscow is as of now the most influenced government subject. The contamination spread from Italy on 2nd March, prompting extra estimates, for example, dropping occasions; shutting schools, theatres and galleries; closing the fringe; and announcing a non-working period which kept going up to 11th May, has been expanded twice. The continuous COVID-19 pandemic was first declared and spread to Spain on 31st January 2020, when a German visitor tested positive for SARS-CoV-2 in La Gomera, Canary Islands (Sanidad confirma 2020). As of 2nd June 2020, there have been 239,932 declared cases and 27,127 deaths (Actualización n° 165 2020). The real number of cases was viewed as a lot higher, and the same number of individuals with just mellow or no side effects was probably not going to have been tested (Lau et al. 2020; Linde et al. 2020). The progressing COVID-19 pandemic spread to the United Kingdom in late January 2020. Starting on 3rd June 2020, there have been 279,856 declared cases and 39,728 deaths (Wikipedia 2020) shown in Fig. 6.2a and b.

The COVID-19 pandemic in India is a part of the overall pandemic of coronavirus ailment 2019 (COVID-19) brought about by SARS-CoV-2. The first instance of COVID-19 in quite a while, which began from China, was accounted on 30th January 2020. Starting on 8th June 2020, the MoHFW has affirmed a sum of
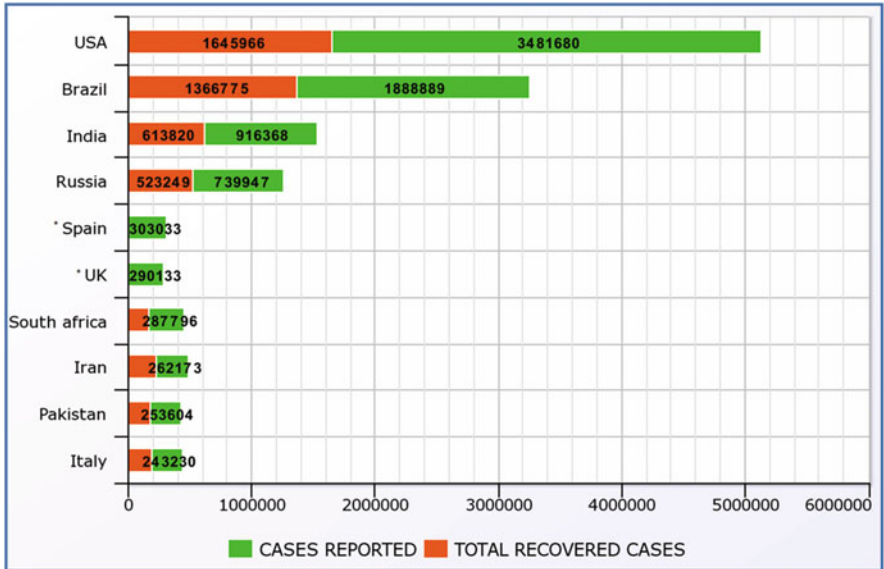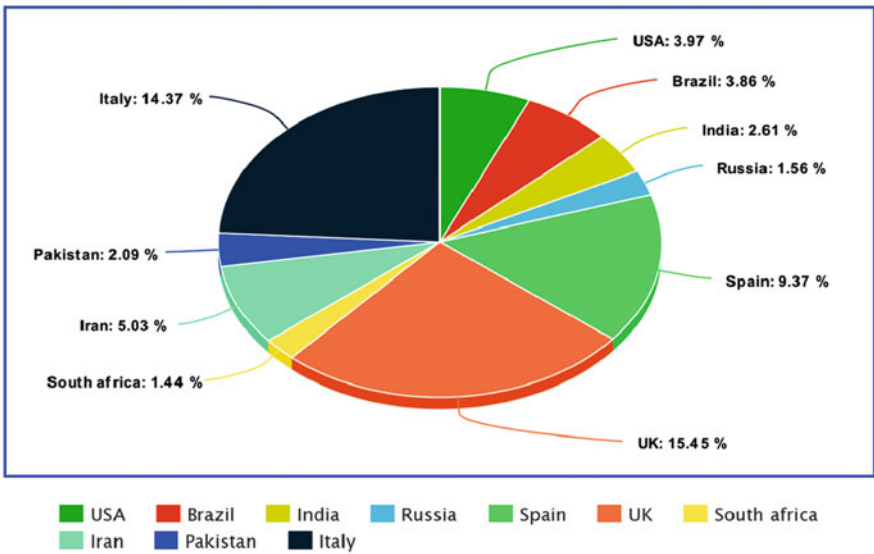
Fig. 6.2 Disease transmission details of coronavirus in various countries (Worldometer 2020 as updated till 16th July 2020). (**a**) Information about recovery and reported cases in various countries *(Spain and UK total recovered data is not available). (**b**) Percentage of deaths in various countries

256,611 cases; 1,24,430 recuperations (counting 1 movement); and 7,200 passings in the nation. India at present has the biggest number of affirmed cases in Asia, with the quantity of all-out affirmed cases penetrating the 100,000 blemish on 19th May and 200,000 on 3rd June. India's case casualty rate is moderately lower at 2.80%, against the worldwide 6.13%, starting on 3rd June (Wikipedia 2020).

The infection was first declared and spread to Italy on 31st January 2020, when two Chinese vacationers in Rome tested positive for the infection (Covid-19—Situazione in Italia 2020). Starting on 7th June 2020, Italy has 35,262 dynamic cases, one of the most noteworthy in the world. Overall there have been 234,998 declared cases and 33,899 passings (a pace of 561 passings for each million population, while there have been 165,837 recuperations or dismissals (Wikipedia 2020). By 7th June, Italy had tested around 2,627,000 people. Due to the set number of tests played out, the genuine number of contaminated individuals in Italy, as in different nations, is assessed to be greater than the official check (Aggiornamento 2020; Flaxman et al. 2020; Lau et al. 2020; CNBC 2020). On 27th January 2020, the principal case in Germany was affirmed and contained close to Munich, Bavaria (Erster Fall 2020). Most of the cases in January and early February started from a similar car parts producer as the primary case. On 25th and 26th February, various cases identified with the Italian flare-up were distinguished in Baden-Württemberg. A huge group connected to a festival occasion was framed in Heinsberg, North Rhine-Westphalia, with the primary demise covered on 9th March 2020 (Kreis Heinsberg 2020; Hamburg, Hamburger Abendblatt 2020; Robert Koch Institute 2020). Starting on 8th June 2020, the RKI has formally detailed 184,193 cases, 8,674 passings and around 1,69,600 recoveries (Table 6.1) (Robert Koch Institute Covid-19 dash board 2020).

In the same manner, the COVID-19 pandemic affected lakh of people in Iran, Saudi Arabia, France and Pakistan.

As of 8th June 2020 (10:00am CET), more than 6.9 million cases were reported globally, with 401,000 fatalities. On 14th May to 8th June, over 1.5 million cases were diagnosed. Even though containment as well as mitigation measures have been intensified and efforts to develop disease-modifying pharmacologic compounds are being carried out, COVID-19 continues to spread.

6.4   Laboratory Diagnosis of COVID-19

The COVID-19 pandemic has majorly affected clinical microbiology research facilities in the previous a while. The laboratory diagnosis of COVID-19 is presently being performed using two tests: viral tests and antibody tests. The viral test determines whether you have a current disease, and the antibody test determines if you have an infection in the past. An antibody test may not indicate that you have an ongoing infection, because it can take 1 to 3 weeks' time after infection to produce anticorps. Having antibodies to the virus that triggers COVID-19 may provide defence against the virus being infected again. Rapid and reliable identification of

Table 6.1 Disease transmission details of coronavirus in various countries

Country	Cases reported	Total deaths reported	Total recovered cases	Transmission classification	Total population
USA	3,481,680	138,291	1,645,966	Community transmission	331,081,677
Brazil	1,888,889	72,950	1,366,775	Community transmission	212,620,008
India	916,368	23,952	613,820	Clusters of cases	1,380,530,110
Russia	739,947	11,614	523,249	Clustered cases	145,937,175
*Spain	303,033	28,406	N/A	Community transmission	46,775,564
*UK	290,133	44,830	N/A	Community transmission	67,900,637
South Africa	287,796	4,172	160,693	Community transmission	5,933,662
Iran	262,173	13,211	227,561	Community transmission	84,033,003
Pakistan	253,604	5,320	178,737	Cluster of cases	221,037,609
Italy	243,230	34,967	196,016	Community transmission	60,457,891
Saudi Arabia	237,803	2,283	183,048	Cluster of cases	34,833,307
Germany	200,451	9,139	186,000	Cluster of cases	83,795,199
Bangladesh	190,057	2,424	105,523	Community transmission	164,752,852
France	172,377	30,029	78,820	Community transmission	65,279,649
Canada	108,155	8,790	72,485	Community transmission	37,755,152
China	83,650	4,634	78,719	Cluster of cases	1,439,323,776
Iraq	81,575	3,345	52,621	Community transmission	40,251,640
Indonesia	78,572	3,710	39,050	Community transmission	273,634,614
Philippines	57,545	1,603	20,796	Community transmission	109,635,041
Kuwait	56,174	396	46,897	Cluster of cases	4,272,860
UAE	55,198	396	46,418	Community transmission	9,894,897
Singapore	46,630	26	42,988	Cluster of cases	5,852,170
Israel	41,325	368	19,989	Pending	9,197,590
Afghanistan	34,740	1,048	22,456	Cluster of cases	38,956,620
Switzerland	33,016	1,968	29,800	Community transmission	8,657,154
Japan	21,686	982	18,545	Cluster of cases	126,459029
Australia	10,250	108	8,035	Cluster of cases	25,511,086
Malaysia	8,729	122	8,526	Cluster of cases	32,381,446

Worldometer (2020) as updated till 16th July 2020
*Spain and UK total recovered data is not available—N/A

COVID-19 is critical for community and hospital monitoring of outbreaks (CDC 2020). Current coronavirus diagnostic tests include reverse transcription polymerase chain reaction (RT-PCR), real-time RT-PCR (rRT-PCR) and reverse transcription loop-mediated isothermal amplification (RT-LAMP) tests; RT-LAMP has equal sensitivity to rRT-PCR, which is very precise used for MERS-CoV detection (Bhadra et al. 2015; Chan et al. 2015; Huang et al. 2018).

6.4.1   RT-PCR

RT-PCR is a diagnostic test which uses specimens of nasal swab, tracheal aspirate or bronchoalveolar lavage (BAL). Collection of upper respiratory samples through nasopharyngeal and oropharyngeal swabs is the primary and preferred method for diagnosis. The use of bronchoscopy as a diagnostic method for COVID-19 is not recommended since the generated aerosol poses a significant risk to both patients and healthcare staff. Bronchoscopy would only be used for incubated patients if the upper respiratory tests are negative and other diagnostic methods will alter the clinical management considerably. Bronchoscopy can, however, be suggested when clinical and safety conditions are met and for unclear diagnosis (Wang et al. 2020b). Alternatively, tracheal aspiration and non-bronchoscopic BAL may be used in incubated patients to collect respiratory specimens (WHO 2020). SARS-CoV-2 RNA was extracted from upper and lower respiratory tract specimens, and the virus was isolated from upper respiratory tract secretions and BAL specimens in a cell culture; however, limited RNA data is available. In a set of cases by Zou et al., SARS-CoV-2 RNA levels were found to be higher in upper respiratory tract samples (as shown by lower nose period threshold values), and the first 3 days after symptom onset and elevated SARS-CoV-2 RNA levels were also observed in asymptomatic patient samples obtained from upper respiratory tract samples (Zou et al. 2020). Several studies have shown that SARS-CoV-2 RNA in the blood and stool specimens can also be detected. It is possible that viral RNA will be detectable for weeks, as seen in some instances of SARS-CoV or MERS-CoV infection. The specificity of the RT-PCR test appears to be very high although, particularly in asymptomatic patients, false-positive results may occur due to swab contamination (Memish et al. 2014; Rodriguez-Morales et al. 2020; Zumla et al. 2015; Chan et al. 2004; Cheng et al. 2004; Hung et al. 2004; Peiris et al. 2003). The sensitivity levels are not explicit, but are estimated at around 66–80%.The validity of tests in asymptomatic persons in close contact with symptomatic persons is much less clear; the rate of positivity could exceed 50% without symptoms or confirmed infection (Ai et al. 2020). A single negative test does not preclude SARS-CoV-2 infection, especially in highly exposed individuals where the test is performed using a nasopharyngeal swab specimen and at the onset of the infection (Zhuang et al. 2020).

Infection severity can be estimated through a standard real-time RT-PCR set-up that usually runs through 35 cycles, meaning that around 35 billion new copies of the

viral DNA sections are created from each virus strand present in the sample by the end of the process.

6.4.2 TrueNat Testing

Current PCR tests can distinguish a wide variety of pathogens in real time, with clear results, while the chain reaction is in progress. TrueNat is a chip-based, portable RT-PCR computer which was originally developed by Goa-based startup Molbio Diagnostics as a portable device for tuberculosis. The platform is on its way to becoming one of COVID-19's principal diagnostic tools as India seeks to increase its testing capacity. The new versions of the TrueNat system will detect a coronavirus SARS-CoV-2 enzyme (called RdRp) located in the RNA (First post 2020).

6.4.3 Antibody Tests

Antibody testing (or serological testing) is a bloodstream protein test to see whether a person was affected with COVID-19. A diseased person would have unique antibodies to certain pathogens to which they were exposed. As part of a bigger cycle, the immune system develops antibodies to protect itself against an infection. In comparison to a nasal or throat swab test that searches for genetic signatures of the body's virus, an antibody test looks for signs of the body's reaction to the virus. Antibodies are found in the blood, and either a finger prick or a blood sample taken with a needle produces a blood sample. In an antibody test, two different forms of an antibody are sought: IgM antibodies against SARS-CoV-2, which evolve in an infection early on IgG antibodies to SARS-CoV-2, often discovered after someone recovered from the infection. With respect to COVID-19 diagnosis, RT-PCR and TrueNat antibody tests are varied in their strengths and limitations. The advantage of antibody tests is to provide clarification as to their COVID-19 status for authorities and individuals. This test also gives the information related to infection rate, prevention, control and treatment of COVID-19. As part of the vaccine-enabled response, antibodies are produced faster and more abundantly. Antibody testing is crucial for determining who had the virus, particularly when a number of infected people do not appear to have any symptoms. An antibody test will yield results in less than an hour. The test can be used 7 to 10 days after someone has been contaminated, although it does have a greater percentage of error than swab tests. Antibody tests that look for IgM antibodies are typically quick finger prick tests that can deliver results in less than 20 minutes. But IgG testing requires a blood sample to be sent to a laboratory—a process that could take a week to produce results. IgG tests are more accurate than quick IgM tests, but don't provide as much detail about anyone being infected with COVID-19.

False negatives and false positives: The various test kits currently in use are a necessity—but they are also products of fast-track acceptance and production of COVID-19 science, where demand and pace for public health are the focus (First post 2020).

6.4.4   Antigen Test

Antigen tests look for different proteins present only in the virus, which is regarded as 'foreign' by the body's immune response. Most COVID-19 antigen tests target the 'spike protein' that studs the surface of the coronavirus. In this examination, a swab from the nose is obtained, where there is a high likelihood that virus particles are present. The swab is first dipped into a virus-inactivating solution and then moved to a test sheet. The test strip houses antibodies binding and holding coronavirus proteins in place as the fluid spreads. Checking for antigens has some primary benefits. One of the major benefits of using antigen test is that it decreases the pressure of relying on only RT-PCR tests to classify patients with COVID-19. These tests are also inexpensive compared to RT-PCR, costing around Rs 450 per test. The following are the boundaries of antigen selection. Antigen test can only disclose whether a person is currently experiencing SARS-CoV-2 infection. Antigens shall not be present before or after the infection has passed. Because antigen detection does not require any amplification processes of the virus or its genetic material, a swab sample can have too little antigen to detect. This may result in a false-negative outcome. To confirm a true negative for COVID-19, a negative test should be followed up by the more reliable RT-PCR test as a precaution. Accuracy is the single biggest issue with antigen checks, which as a diagnostic method are much less sensitive than RT-PCR (First post 2020).

6.4.5   Nanotechnology Approaches for Diagnosis of COVID-19

Nowadays nano-based products are being developed and install for the containment, diagnosis and treatment of COVID-19 (Future markets 2020). Nanosensors are now a reality, showing great ability to detect extremely low concentrations of bacteria and viruses and thus alert clinicians even before symptoms have shown or on patients with very low viral loads. As several nations around the world struggle with the rising number of cases involving coronavirus, the monitoring of suspected carriers is also being increased. A broad range of detection kits are in the production line, among which the ground-breaking rapid nanogold-based test will ease the burden on healthcare systems caused by the COVID-19 pandemic (Lu et al. 2020).

A recent review paper (*ACS Nano*, 'Diagnosing COVID-19: Disease and Detection Tools') discusses the existing nanotechnology-based diagnostic methods, e.g. nucleic acid and computed tomography testing) and potential new techniques (e.g. protein and point-of-care testing).

It allows researchers to move beyond architecture to advance their technologies. Although tremendously helpful for the current pandemic, it would be useful to build plug-and-play diagnostics to handle the outbreak of SARS-CoV-2 to avoid potential epidemics too (Nanowerk 2020).

When nanoparticles enter a biological system, such as human blood, they come into contact with different biomolecules, such as proteins, instantly; such biomolecules form a coating layer on the surface of the nanoparticles—the so-called biomolecular corona—thus giving the nanoparticles a special biological identity, which may be very different from the surface of the pure nanoparticles. Researchers have also shown that disease-specific corona protein can be used in conjunction with advanced classifiers for early detection and screening of cancers (Nanowerk 2020).

6.4.5.1 Magnetic Levitation (MagLev)

The MagLev approach may furnish useful insights into measuring protein density in solution for a better awareness of the protein's physicochemical properties. As long as various diseases produce substantial difference in the plasma proteome, the levitation development and patterns of plasma proteins may hold some information on an individual's health conditions. More precisely, MagLev's optical images of levitated proteins subjected to machine learning examination provide useful information on the health status of the individual (Nanowerk 2020).

6.4.5.2 Optical Biosensor Nanotechnology

A new device based on optical biosensor nanotechnology would allow the coronavirus to be extracted directly from patient samples within 30 minutes approximately without the need for centralized laboratory tests. The latest technique could quickly establish if a patient is infected by coronavirus or influenza virus. The initiative should be used for more than the present pandemic and for the treatment of humans. The new biosensor tool will also be used to examine various forms of coronavirus present in reservoir animals, such as fleas, to detect and track the possible evolution of these viruses and to prevent future human outbreaks (Hu et al. 2020).

Scientists from the University of Maryland School of Medicine (UMSOM) have developed an experimental COVID-19 diagnostic test that can visually detect the virus' presence in 10 minutes. This uses a simple assay that includes plasmonic nanoparticles in gold to detect a shift in colour when the virus is present.

Based on our preliminary findings, we conclude that as early as the first day of infection this exciting new test can detect RNA material from the virus. Nevertheless, more studies are required to confirm whether this is actually the case, said study

leader Dipanjan Pan, PhD, UMSOM Professor of Diagnostic Radiology and Nuclear Medicine and Pediatrics (Sciencedaily 2020).

The test does not require the use of any specialized laboratory methods for research, such as those widely used to amplify DNA. The authors published their research last week in nanotechnology journal *ACS Nano* of the American Chemical Society. When a patient obtains a nasal swab or saliva sample, the RNA is extracted from the sample through a simple process which takes about 10 minutes. To detect a particular protein, the test uses a highly specific molecule that is bound to the gold nanoparticles. This protein is part of the genetic code the novel coronavirus is related to. Once the biosensor binds to the gene sequence of the virus, by turning the liquid reagent from purple to blue, the gold nanoparticles react. This RNA-based research looks very promising in terms of virus detection. The ground-breaking solution yields results without the need for an extensive laboratory facility. While further clinical trials are needed, the manufacturing and processing of this test will be much less costly than a typical COVID-19 laboratory study; it does not require laboratory equipment or specialized staff to conduct the test and interpret the results. If this new test meets the FDA standards, it may potentially be used as a monitoring tool to track any outbreak of infections in day-care centres, nursing homes, college campuses and work places (Tectales 2020).

6.5 Prevention and Control of COVID-19

Because presently no vaccine is available to prevent coronavirus disease (COVID-19), preventing exposure to this virus is the only way to prevent illness. Because the primary transmission mode is droplet transmission, the preventive measures revolve around avoiding droplet transfer.

6.5.1 General Preventive and Control Measures of COVID-19

- *Wash hands frequently*: Wash hands with a hand sanitizer, soap and running water or disposable alcoholic sanitizer. This kills viruses present on hands. In daily life, the general public will often wash their hands, and therefore gloves are not required. However, health professionals, close contacts, nurses and staff working in crowded environments will have to wear gloves to reduce the possibility of transmitting through communication. Wearing gloves, however, is no substitute for washing your face (Web MD 2020).
- *Restrict travelling*: In order to contain the spread of COVID-19 pandemic, international travel of passengers has been prohibited under MHA's (Ministry of Home Affairs) orders related to lockdown measures (Web MD 2020).

- *Practise social distancing*: Stay home as much as possible, as one can get and spread the infection without realizing it. Six-feet distance must be kept from everyone if one decides to go out (Web MD 2020).
- *Cover your mouth and nose when in public*: Wearing a mask protects one from COVID-19 especially when you encounter people, go to public places, enter crowded or enclosed spaces, take public transportation, etc. There is no need of wearing a mask when alone or at home in an open environment. If one has COVID-19, even if they do not feel sick, they will spread it. Wearing a mask of fabric can shield others. This is not a substitution for distancing from society (Web MD 2020).
- *Cover your mouth and nose with elbows or tissues*: Never place hands over your mouth and nose while coughing or sneezing. If your nose and mouth are covered with your elbows, the viruses will remain in clothing without contaminating other objects' surfaces (Web MD 2020).
- *Don't touch your face*: Coronaviruses may live several hours on surfaces that we touch. They can get into the body if they come onto the hands and then into the eyes, nose or mouth when touched with those hands (Web MD 2020).
- *Clean and disinfect*: Using soap and water, first clean but also disinfect objects that are in constant reach, such as chairs, doorknobs, light switches, toilets, faucets and sinks using a combination of household bleach and water (1/3 cup of bleach per gallon of water or 4 teaspoons of bleach per quarter of water) or a home cleaner certified to treat SARS-CoV-2. Wear gloves while cleaning/ disinfecting and throw them away when you're done. There is no evidence that herbal therapies and tea can prevent infection (Web MD 2020).
- *Home quarantine*: The aim of home quarantine is to prevent transmission of virus from person-to-person contacts, thereby preventing the development of cases of second and third generation. When there are a large number of asymptomatic near contacts or potential patients, home quarantine should be an effective choice for solving the problems which medical institutions cannot solve. If there are any suspicious symptoms, seek guidance from the medical personnel. Home quarantine must be suggested for the following people: people who have travelled or lived in countries or regions where local cases begin to rise and individuals with close contact with suspects and confirmed cases (Wenhong Zhang 2020).
- *Isolation*: Keeping people who are ill away from healthy people like, where possible, using a separate 'ill' bedroom and bathroom. A report published by the WHO on 9th July also stated that COVID-19 airborne transmission cannot be ruled out entirely. Rare situations like surgical procedures and noisy, enclosed spaces raise the possibility of airborne transmission. They also mentioned that when it comes to researching the airborne transmission of the virus, 'more studies are desperately needed', now that transmission by contact and respiratory droplets have been concluded to their best understanding. The latest protection measures would now have to provide adequate and efficient ventilation in public buildings, office settings, schools, hospitals and nursing homes with these new possibilities. Ventilated spaces must now be supplemented with methods for managing airborne pathogens, such as local exhausts, highly efficient air filters and ultraviolet

germicidal lights mounted far away to minimize exposure to the skin and eyes (Wenhong Zhang 2020).

- *Overcrowding, as previously observed, must be avoided at all costs*: Safe physical distance maintenance, while not the ultimate method for prohibiting transmission, may lead to lower chances of infection. This must be followed with strict measures in public transport and buildings particularly. These steps are easy to execute and are also relatively inexpensive. Some, like distance maintenance, may not entail money but a strict rule-and-punishment program; though it might sound extreme, it's the only way to control the virus spread and stop the pandemic as we know it (Wenhong Zhang 2020).

6.5.2 Scope of Nanotechnology in Prevention and Control of COVID-19

The outbreak of COVID-19 puts a global pressure on modern societies and particularly the infrastructure related to health care. Nanotechnology offers fresh opportunities for developing inexpensive and scalable methods of detection, secure equipment for personal safety and more successful medical solutions of COVID-19 (Chan 2020). Recently a nano-filter was developed which is believed to retain filtering efficiency through the use of nanofibers, even after hand washing. A reusable, nano-filtered face mask could help ease the pressures of face mask supply shortages. For years now, researchers have developed the potential nanoparticles to treat bacterial and viral infections (Statnano 2020). For example, gold nanoparticles are designed to specific viruses such as Ebola and influenza. These nanoparticles can break the structure of the viruses by heating the particles with infrared wavelength of light. Nanoparticles can also be used for drug delivery.

Nanotechnology approaches should reduce acute and chronic effects of the COVID-19 pandemic from the perspective of identification, safety and treatment. Nanotechnology contributions may include but are not limited to the following topics and their application to address the challenges of COVID-19.

Different applications have been found in medical field, such as Ag NPs, which can be used for biosensors, as they have a wide antiviral spectrum; the suppression of viruses can be expected. The silver nanoparticles are having a strong and broad-spectrum microbicidal activity (Prasad 2014). Ag NPs produce reactive oxygen species resulting in oxidative stress and generation of free silver ions; therefore, healthcare workers can be protected from the risk of acquiring infection by the use of these nanoparticles (Aziz et al. 2014, 2015, 2016; Joshi et al. 2018). Usually healthcare workers use primary protection equipment like clothing to avoid contact with infected individuals. Research is being carried out to develop protective clothing using Ag NPs which are absorbed on a polymer sheet with a nanoscale fibre like structure (Nanoshel 2020).

There are numerous nanotechnology products available for equipping people to battle COVID-19. While enhanced respiratory masks and gloves are used to reduce the infection and people are exposed to external environment, soaps, sanitizers, disinfectants, shampoos and detergents, made up of antiviral and antibacterial non-materials, are used internally to counter the disease. Graphene, nano-diamond, polymer nanofibers (e.g. polyacrylonitrile) and nanoparticles such as platinum, titanium dioxide and copper oxide are generally included in these product groups which add to their expertise (Statnano 2020).

Below are the latest updates on COVID-19 nano-products:

6.5.3 Nano-based Vaccines

(i). RNA- Based Vaccine

A type of candidate vaccine: LNP-encapsulated mRNA

(ii). Viral Vector-Based Vaccine

A type of candidate vaccine: Adenovirus type 5 vector
Nanotechnology part: Designing a nanoscale viral vector to deliver vaccine agent

(iii). Protein Subunit-Based Vaccine

A type of candidate vaccine: Recombinant protein nanoparticle vaccine
Nanotechnology part: Designing the recombinant F-proteins to self-assemble into nanoparticle constructs that approximate the size of the RSV virus

(iv). DNA-Based Vaccine

A type of candidate vaccine: Proteo-lipid vehicle (PLV)
Nanotechnology part: Using a neutral lipid formulation (liposome-based) with the high efficacy of the fusogenic protein-mediated delivery technology (Statnano 2020)

6.5.4 Respiratory Masks

(i) Nanofibers Membrane Technology

Queensland University of Technology (QUT) researchers have constructed and examined a highly breathable nanofiber-based cellulose material which is able to remove virus-size nanoparticles. This nanoparticle-removing new material is developed to be used as a disposable filter cartridge in biodegradable, anti-pollution masks. This is an important factor for people who have to wear masks for long

periods or those with existing respiratory conditions. The higher the breathability, the greater the comfort and reduction in fatigue (Statnano 2020).

(ii) Air Filtration Systems

Clean air filtration systems are designed by Mack Antonoff HVAC to counter COVID-19 (coronavirus), mould, mildew and pet dander. Installed in your existing ductwork, the five HEPA, PECO, and nano-filters with UV light are important for families with allergies, asthma, bronchitis and other health problems. Turn-Key Environmental Consultants sells HealthPro® Compact Air Purifiers which capture up to 0.003 microns of 99.5% of particles (e.g. viruses and bacteria). The exclusive IQAir HyperHEPA® filtration technology lies at the core of this revolutionary system. A thick nanofiber network effectively traps particles of all sizes (Statnano 2020).

(iii) Photoelectrochemical Oxidation Technology

In March 2020, a newly designed air purification device called Molekule is set to be tested against a virus that serves as a substitute for coronavirus, which effectively killed air pollutants such as bacteria, mould spores and viruses, according to the University of South Florida. The device uses photoelectrochemical oxidation (PECO), a process that uses UV-A light to trigger a catalyst in the filter covered by nanoparticles of Molekule to produce free radicals which oxidize air pollutants (Statnano 2020).

6.6 Treatment of COVID-19

To date, there is still no specific approved treatment for COVID-19 and no cure for an infection though treatments and vaccines are under investigation and will be tested through clinical trials. Instead, treatment focuses on symptom management as the virus continues its course (Cascella et al. 2020).

Types of treatments practised for COVID-19 include:

- Antiviral and/or retroviral drugs
- Breathing helps, including mechanical ventilation
- Steroids to reduce inflammation in the lungs
- Transfusion of plasma into the blood

The FDA has not licensed any medications or biologics for the prevention or treatment of COVID-19. On 1st May 2020, remdesivir obtained an FDA Emergency Use Authorization (EUA), based on preliminary data showing a quicker recovery period for hospitalized patients with serious illness (Cascella et al. 2020).

(i) O_2 Fast Challenge

For a patient with $SpO_2 < 93–94\%$ ($< 88–90\%$ if COPD) or respiratory rate $> 28–30$ min or dyspnoea, 40% of Venturi mask administration of oxygen is needed.

After a reassessment of 5 to 10 minutes, if the clinical and instrumental image has improved, the patient will continue the treatment and undergo a re-evaluation within 6 hours. In case of failure improvement or new worsening, the patient undergoes a noninvasive treatment, if not contraindicated (Cascella et al. 2020).

(ii) HFNO and Noninvasive Ventilation

As for HFNO or NIV, the panel of experts point out that such approaches carried out by devices with good interface fitting do not produce widespread dispersion of exhaled air, and their use can be regarded at low risk of airborne transmission (Cascella et al. 2020).

6.6.1   Other Therapies

(i) Corticosteroids

Among other therapeutic approaches, while systemic corticosteroids were not prescribed for treating viral pneumonia or acute respiratory distress syndrome (ARDS), these medications are typically used in extreme CARDS (e.g. methylprednisolone 1 mg/Kg/day). Of note, a recent large-size RCT (the RECOVERY trial) has shown that dexamethasone decreases deaths in critically ill COVID-19 patients by one-third. In the intervention group, 2,100 patients received dexamethasone (6 mg/day for 10 days), while patients in the control group ($n = 4,300$) received the disease standard treatment (Ledford 2020).

A medication named dexamethasone is the talk of the hour despite recent reports that in patients with extreme types of COVID-19, it may reduce mortality by one-third. The allegations emerged in a press release from the University of Oxford released by scientists participating in the RECOVERY (short for 'COVID-19 Therapy Randomized Evaluation') trial. They said the test data suggest that dexamethasone in patients with ventilator support cuts the risk of death by one-third and one-fifth in patients requiring oxygen support. Dexamethasone is not something of a novel drug. It is a steroid often used with potent anti-inflammatory properties. Dexamethasone falls within a broader drug class called corticosteroids for COVID-19 patients; when it is too aggressive to control by any means, dexamethasone helps to dampen the body's immune response (Healthworld 2020).

(ii) Antiviral Agents

Although no antiviral therapies have been approved, several approaches such as lopinavir/ritonavir have been suggested (orally 400/100 mg per 12 hours) (Bimonte et al. 2020). Preclinical studies have indicated that remdesivir (GS5734)—an RNA polymerase inhibitor with in vitro activity against multiple RNA viruses, including Ebola—may be useful for both prophylaxis and HCoV infection therapy (Gordon et al. 2020). This drug has been tested positively in a rhesus macaque model of MERS-CoV infection and recently in SARS-CoV-2-infected macaques. Alpha

interferon (e.g. 5 million units by aerosol inhalation twice per day) was also used (De Wit et al. 2020; Williamson et al. 2020).

Several anti-flu drugs such as oseltamivir were used to treat COVID-19 patients (Chen et al. 2020). Another anti-flu medication, favipiravir, has shown some in vitro effect against SARS-CoV-2. A retrospective analysis found once again that the broad-spectrum antiviral arbidol would increase the rate of discharge and decrease the rate of COVID-19 patient's mortality (Wang et al. 2020c).

(iii) Antiviral/Immunomodulatory Drugs

As immunomodulatory therapy, chloroquine (500 mg every 12 hours) and hydroxychloroquine (200 mg every 12 hours) were suggested. Of note, Gautret et al. (2020) found in a non-randomized trial that hydroxychloroquine was significantly correlated with viral load reduction before viral disappearance, and this effect was strengthened by the azithromycin macrolides (Gautret et al. 2020). Indeed, in vitro and in vivo studies have shown that macrolides can mitigate inflammation and modulate the immune system. In particular, these drugs can induce the downregulation of cell surface adhesion molecules, decrease the development of proinflammatory cytokines, stimulate phagocytosis by alveolar macrophages and inhibit neutrophil activation and mobilization (Zarogoulidis et al. 2012). Further studies are required to support the use of azithromycin, alone or combined with other medications, such as hydroxychloroquine, outside of any bacterial overlaps. Also, attention must be given to the concomitant usage of hydroxychloroquine with azithromycin as the interaction may result in a higher risk of prolongation of the QT period and cardiac arrhythmias. Chloroquine can also cause QT prolongation (Mercuro et al. 2020).

(iv) Serotherapy

Antibodies extracted from the healed individual's blood constitute a therapeutic choice currently under review. It is determined that the dosage of antibodies required to treat a single patient with SARS-CoV-2 demands that at least three patients recovered from the SARS-CoV-2 infection eliminate anticorps. A clinical trial for investigating an antibody cocktail for the prevention and treatment of COVID-19 has been initiated on 11th June 2020 (Cascella et al. 2020).

(v) Anticoagulant

Since COVID-19 patients have a higher risk of venous thromboembolism and the correlation of anticoagulant therapy with decreased ICU mortality, it is recommended that thromboprophylaxis should be offered to patients. In addition, complete therapeutic-intensity anticoagulation (e.g. enoxaparin 1 mg/kg twice daily) is indicated in the case of suspected thrombophilia or thrombosis (Kollias et al. 2020).

(vi) Inflammation Inhibitors

Throughout Italy, apart from traditional treatments, a major study led by the Istituto Nazionale Tumori, Fondazione Pascale di Napoli, focuses on the use of

tocilizumab. This is a humanized IgG1 monoclonal antibody, directed against the IL-6 receptor and widely used to treat rheumatoid arthritis, juvenile arthritis, giant cell arthritis and Castleman's syndrome and to mitigate toxicity due to inhibitors of the immune control level (Buonaguro et al. 2020). In addition, a randomized, double-blind, placebo-controlled, phase 2/3 research on sarilumab, which is another anti-IL-6 receptor antibody, is underway in the United States. Many specific approaches were put to the test. Anakinra is a recombinant antagonist of the IL-1 receptor used to treat auto-inflammatory disorders such as adult-onset still's disease, systemic-onset juvenile idiopathic arthritis and Mediterranean fever. The authors of a retrospective study found that the use of anakinra in patients with mild to extreme ARDS and hyper-inflammation (C-reactive protein in the range of 100 mg/L, ferritin in the range of 900 ng/mL or both) led to clinical improvement in 72% of patients (Cavalli et al. 2020). Acalabrutinib is a selective inhibitor of Bruton tyrosine kinase which regulates the signalling and activation of macrophages. Roschewski et al. (2020) tested this agent in a prospective off-label clinical trial on 19 patients hospitalized with severe COVID-19. They proved the medication increased oxygenation in most patients, enhancing inflammation indicators such as C-reactive protein and IL-6 (Roschewski et al. 2020).

Eli Lilly and Co may have a drug specifically developed to treat COVID-19 that is approved for use as early as September if all goes well with one of the two antibody therapies it is testing. The drugs belong to a class of synthetic medicines widely used to treat cancer, rheumatoid arthritis and many other disorders, called monoclonal antibodies. A monoclonal antibody drug developed against COVID-19 is expected to be more successful than currently being tested on repurposed drugs against the virus (Carl O'Donnell and Michael Erman 2020).

6.6.2   Nanotechnology in Treatment of COVID-19

Nanotechnology and nano-medicine have an excellent promise in solving a variety of specific health concerns, including viruses, which are considered a significant medical problem. Nano-biotechnology applications could represent a new avenue for virus treatment or disinfection. The possibilities of using non-materials effectively in this area as vaccines and nanosensors are also highlighted. Interesting and surprising properties of chemical compounds, especially nano-drugs, can contribute significantly not only to medicine and pharmaceuticals, but promising solutions to stop the deadly COVID-19 outbreak worldwide can also emerge.

Theranostics is a newly emerging drug that involves the identification and neutralization of viruses using nano-drugs and nanomedicine, with an emphasis on diagnosis and treatment. Accordingly, there are studies of nanoparticles being used to combat pathogens that cause influenza and tuberculosis. Thanks to the potential surface modification and functionalization, nanoparticles have the ability to detect the pathogens and viruses with a huge amount of reports in the literature. Nanoparticles may be modified or functionalized to dissolve the virus' lipid

membrane or even bind to the spike proteins at S1 and/or penetrate into the envelope, encapsulating nucleocapsid and RNA. Nanoparticles can be modified/functionalized to target a specific virus, bacteria and other pathogens or a rage. Given their size, modified nanoparticles in the bloodstream can travel through the body without causing problems or affecting other functions, particularly those that participate in the human immune system and can remain in the body much longer to detect viruses (Nanografi 2020).

(i) Pharmaceuticals

(a) Novochizol™

Nanotechnology part: Chitosan-based nanoparticles aerosol formulation

Novochizol™ is a nanoparticle based on chitosan that is completely biocompatible and firmly adheres to the lung epithelial tissues and ensures continuous release without systemic dissemination. Extensive preclinical research, performed by academic collaborators at Bioavanta-Bosti, suggests that Novochizol™ is a safe and efficient technology for drug delivery (Statnano 2020).

(b) Peptide nanostructures against coronavirus' spike proteins

In the preclinical evaluation stage, researchers are engineering a new nanostructured therapy which could potentially disable the virus and prevent human cells from infecting it. The MIT team discovered a peptide molecule that binds directly and tightly to the spike protein of the coronavirus. The Simpson Querrey Institute (SQI) in Northwestern has been working on 'gluing' millions of peptides into a nanostructure that is the carrier of the precious drugs. The drug and carrier's identical chemistry helps scientists to develop nanostructures that shield the peptide medication as it circulates throughout the body until the disease's perpetrator, the novel coronavirus, is encountered. The nanostructures of the SQI carrier have water-filled channels which could keep and defend the antiviral therapies against destructive enzymes. The SQI team tested the idea using a possible Alzheimer's disease drug, and it was found that the general approach is highly successful in in vitro experiments (Statnano 2020).

6.7   Conclusions

The following are the main conclusions of this topic:

  (i) Coronavirus disease is a highly contagious pathogenic viral infectious disease which causes acute and mild infection of the upper respiratory tract.
 (ii) This epidemic resulted in more than 13 million cases worldwide and around 6 lakhs of deaths causing a global health crisis.
(iii) The primary transmission is by direct person-to-person contact. The infection also spreads through close contact via aerosol droplets. The rate of transmission of the virus has not yet been known as it differs based on different environmental factors.

(iv) Community transmission of infection resulted in rapid spike in the cases and deaths making it a global health emergency.

(v) Various methods have been developed for the diagnosis of COVID-19. Diagnosis is mainly done by chest CT examination. RT-PCR is routinely used in detection of acute respiratory infection. Apart from RT-PCR, antibody testing, antigen testing is also being used.

(vi) Different types of diagnostic detection kits are being developed using nano-technology for rapid and error-free testing. Magnetic levitation techniques and optical biosensor nanotechnology may provide useful insights for the detection of viruses.

(vii) the As there is no treatment available currently, preventing exposure is the only way to prevent the illness. Physical distancing, maintaining personal hygiene and self-isolation are the main important preventive measures to be followed.

(viii) Development of vaccines is a major preventive measure and nanotechnology-based protective equipment for efficient control of the infection.

(ix) The most serious part of this disease is that there is no definite treatment to cure the infection. Various drugs and vaccines are currently being studied as there is a severe necessity to develop drugs and vaccines to reduce the effect of COVID-19.

(x) This chapter also underlined the development of more efficient treatment methods by utilizing innovative techniques like nanotechnology by taking into consideration the cost of producing the clinical drugs.

(xi) As this pandemic is still in the spreading phase and not over yet, we are learning the new data about COVID-19 every day. There is a need to follow the updates in order to monitor the risk factors and also the therapy modalities to suppress the virus and the disease.

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