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Herd Immunity Play in Covid-19 Pandemic

¹N Rakesh, ¹Sujatha S Reddy, ¹L Fabina Sharma, ¹T Pavan Kumar, ¹Shwetha V.

¹Department of Oral Medicine, Diagnosis and Radiology, Faculty of dental sciences, M S Ramaiah University of applied sciences, MSRIT Post, New BEL Road, Bangalore, Karnataka, India

Corresponding Author: Fabina Sharma Laipubam, Faculty of Dental Sciences, M S Ramaiah University of Applied Sciences, Gnanagangothri Campus, MSR Nagar, M.S.R.I.T Post, Bengaluru - 560 054, Karnataka, India

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Abstract

The world today mourns every day for the people who have succumbed to the pandemic caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2). After a strict restriction of movement of the population to hold off further spread of the virus, while experts figure out a solution to this infection, economy deteriorated in various countries. While looking for a new strategy to hold off the virus and also avoid succumbing to further economic crisis, an idea started running around in every corner of the world which is HERD IMMUNITY. Even though Herd Immunity is an old topic, the risks of it have not been accessed fully while trying to achieve it today. Till now, vaccination was the only way it was obtained, but with this pandemic, the alternate strategy of obtaining it by natural infection and recovery of the healthy individuals is now a burning debate across the world.

Keywords: SARS-CoV-2, coronavirus, Covid-19, pandemic, herd immunity, vaccine

Introduction

The world came to its knees with the report of 27 cases of pneumonia of unknown etiology in Wuhan, China on 31st December, 2019 [1]. On further investigation of the causative agent by the Chinese Centre for Disease Control and Prevention (CCDC), it was named as Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) on 7th January, 2020. After the spread of the infection like wild fire globally, World Health Organization (WHO) named the disease COVID-19 on 11th February, 2020 and its outbreak a pandemic on 11th March, 2020. Complete lockdown was imposed in about a third of the world and policy makers were increasingly pressed for new strategies and to articulate their rationales in order to move out of lockdown because of the impact it had on the economy of the countries. The way to fight a pandemic is through mass vaccination that will help prevent further spread of the infection crippling every country physically, mentally and economically. A vaccine that will be specific for this virus requires research on the exact mechanism of

animal-to-human and human-to-human transmission and constant surveillances and on-going monitoring for tracking and potential predicting of its host adaptation, transmissibility, evolution and pathogenicity. Only then, a prognosis and mortality rates can be determined [2]. The role that a vaccine will play is not just for individual protection but also to achieve "herd immunity" which is nothing but mass immunization to protect the immunocompromised and unvaccinated part of the population by keeping the susceptible number of individuals below the threshold level of transmission, like in the case of small pox where >80% of immunization globally led to the eradication of the virus [3]. Another way herd immunity is achieved is by direct infection, but it is practically a suicide mission, considering this current infection as we all know by now that it is not just another flu. It has claimed lives of many people targeting the most weak and vulnerable individuals especially the elderly and with the rate it is spreading and infecting thousands per day, not all people who are infected are able to receive the full treatment due to lack of hospital facilities and staffs.

COVID-19 vaccines in development have more than 100 candidates that need to be scrutinized and then assessed for immunogenicity and safety. It takes years to develop vaccines (though it's discovery is being reportedly quicken considering the present situation) and the delivery of efficacious vaccines is not a competition, but rather, a considered evaluation of a potent, safe global response [4]. The efficacy and safety of a vaccine is not an overnight job, and takes time from few months to years to assess it. With urgency driving the use of the vaccine, once it is developed, one should not forget incidents of mishaps in the past of vaccination of other diseases. For example, after the approval in 2006 for the first vaccine against Human Papilloma Virus named Gardasil, it was used to vaccinate 10-14 years old girls in North India as part of a study, but it was soon halted by the government after an activist group opposed the trials pointing towards unsafe trials and ethical violations following the deaths of 7 girls who had received the vaccination. Even if an internal Government inquiry in 2011 concluded that the deaths were unrelated to the vaccines and no ethical infringing was done, the controversy led to the suspension of the HPV vaccination in India that time [5]. But, yes, few years after that, the government did make efforts again to launch HPV vaccination in New Delhi, India as a public health programme in schools [6].

Even if a sure vaccine was far from its discovery, taking into consideration the deteriorating economy of various countries, some areas started to re-emerge cautiously like Austria, Denmark, Switzerland, Wuhan and in some states of the US [7]. There were a lot of debates going on especially in European countries such as Italy, Spain, Germany, France and the UK on how to handle the pandemic, whether lockdown was the only strategy they should be following, or an alternative strategy of increasing herd immunity by letting the causal virus (SARS-CoV-2) to spread, but at the same time protecting the elderly and those with multiple comorbidities, who are the most vulnerable to this virus [8]. The countries that followed the alternative strategy let to a sudden spike in the infection rate. Our country India has also partially lifted the lockdown and the start of the essential works systematically to restore some of the economy with everyone mindset focused on one thing, "we have to learn to live with it" and it has been a disaster, to be brutally honest. With the rise in the reported cases everyday and the hospital beds and medical work force getting the worst hit, trying to achieve herd immunity at this rate will likely leave us with an enormous amount of unnecessary death. Cases that could have been handled in an orderly manner if it was in a reasonable number are now leading to more

serious complications with not enough medical management and this is one of the most important impact the release of people freely in the streets is causing. Whether it is an intentional measure taken up behind closed curtains to see who come out surviving is still a thought that often comes to our mind.

The main requirement of re-emerging from the lockdown that was imposed in order to prevent further spread of the infection, is having the best possible data and understanding of this infection, for the policy makers in all affected countries to balance between socioeconomic costs and further disease spread[7]. This sensible thought followed by various countries on opening their gates again was, keeping taps on contact tracing, possibility of returnto-works permits based on immunity status [9], new or repurposed therapeutics [10] and vaccination[11,12], as the key for a strategic move out of lockdown, but the various representatives have disregarded the complexity of immunology in molecular medicine regarding COVID-19. Till now there is still some uncertainty regarding antiviral protection and the proportion of population immunity required against this virus and so confirmation of immunity can never be solidified for any individual. For example, the discussion of addressing the notion of determining who is immune by scaled up antibody testing, thereby indicating the extend of herd immunity and confirming the re-entrance of workforce[7]. Then there is the question of accuracy and practicability of laboratory based vs. home use assays [13], and along with this how much can one be sure that the presence of antibodies spike protein equals functional protection[7]. When patients with flu symptoms arrived with the worry of the second wave of this pandemic, a study was conducted in Japan for antibody test of covid-19 in community level, and

concluded that it was beneficial to understand the spread

of infection on a community level, but there are issues of

the reliability of the test, selection bias of positive ratio interpretation and the biological meaning of existence of the antibody regarding second infection [14].

Herd immunity: Origin, History, Successful Cases, How To Achieve And How Are We Doing So Far With Covid-19?

An important concept in epidemic theory to prevent transmission of infection is "HERD IMMUNITY", which is the existence of immunity in adequate proportion in the population to prevent materialization of an outbreak if the pathogen is introduced by an infected person since the contact of the diseased to the susceptible individuals are reduced [15]. To understand it further, factors like infected dynamic, modes of transmission and acquisition of immunity is required [16].

History of Herd Immunity

"The spread of bacterial infection: the problem of herd immunity", a paper published by Topley ad Wilson in 1923 was the first time the term "HERD IMMUNITY" was published, which was one of the studies of various epidemic causing infections conducted in closely monitored lab mice [17]. Later on, Wilson recalled that this term was picked up by Major Greenwood during a conversation who had used it in a textbook named, "Epidemics and Crowd Diseases" [18], but the authors of the book didn't clearly distinguish the achievement of the immunity directly or indirectly from vaccination. Soon, other authors and researchers picked up the term and started using it to define herd immunity as an achievement of indirect protection against an infection by the presence and in proximity to immune individuals.

The benefit of vaccine and vaccination can be dated back to two important figures namely Jenner [19] and Pasteur [20] but neither of them explained about the herd effects [21].

Currently, in every corner of the world there is a continuous attempt to find a solution to this pandemic, a global crisis. The first ever attempted global eradication by World Health Organization of a disease was none other than "malaria" after a powerful argument made by Ross on "mosquito theorem", which stems the field of vaccination and herd immunity [21].

Three separate theories to derive measures of Herd Immunity were converged into a general theory called, "The Mass Action Principle". Hamer in the year 1906 introduced the theoretical basis of herd immunity concerning the dynamics of measles [21], where he stated that the function of the number of susceptibles in a population was the "ability to infect" per measles case and also for successive changes over time, the number of susceptibles is recalculated for each new time period. This led to the epidemiologic "law of mass action" which is the function of the product of current prevalence times current number susceptible. Kermack and McKendrick in 1927 formalized from Hamer's relation the "threshold theorem" which states that epidemic threshold is like a critical mass (density per some area), and if they exceed the susceptibility limit, there will be an explosive increase in the number of people infected when a new infection is introduced. Hamer and other authors soon picked up this logic to explain infection dynamics like about time required for susceptibles to reach epidemic threshold, interepidemic interval relation, susceptibles persistence when an epidemic ends and also about cyclical epidemics [22-24].

So How Far Are We Doing With This Pandemic And Herd Immunity?

The dynamics of infection considers the individual of its state of infectiousness, that is, if the animal is infected or not, or even whether the disease ever clinically manifests, more than in which disease process stage it is in [25]. One

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should remember that being infected does not necessarily mean being infectious. Being infectious means the capability of the host to be able to transmit the pathogen to others. This is why quarantine of the infectious person and the mass lockdown was done globally in different countries to minimize further infecting of healthy individuals. Another point to be noted is that absence of clinical signs doesn't necessarily mean they are not infectious. It has been found that many asymptomatic patients were tested positive for Covid-19, and hence presence of clinical signs and infectiousness is a poor correlation.

The possibility of getting infected after exposure to the virus depends on the dose, agent and host. The likelihood of getting infected increases with the increase in the number of organisms. Thus, personal hygiene, washing and cleaning of surfaces with disinfectant, wearing protective masks will reduce the number of organisms or the vectors that will transmit the infection. Host factors (to be taken into consideration) are the vaccination against the pathogen or prior infection. Regarding this pandemic, with no vaccine in hand, prior infection is the only way a person is holding the immunity card against the virus. But how long will the immunity last is also a question still unanswered with this virus and if they will wane over time with immunosuppressant like malnutrition, chemotherapy or viral infection like Bovine viral diarrhoea (BVDV). Another host factor is the ability of the host to be able to defend or clear off microorganisms, like in case of individuals with diseases pulmonary or immunocompromised, they are more likely to get infected than the healthy ones [25]. Super spreading happens during super shedding of the pathogen [26], and since SARS CoV-2 is a respiratory disease, the chances of transmission increases manifold while a person coughs or sneezes. There has been report of SARS-CoV-2 presence

in stools and wastewater and needs further research if faecal-oral transmission is possible. If so, safe water and adequate sanitation has to be added to the current strategies of COVID-19 pandemic control [27].

If a person is infected with a pathogen, there are three outcomes: resolution, persistence or death of the host. These also will determine the duration of the infection. It is like a see-saw ride with the host on one end and the pathogen on the other. Highly virulent virus will reduce duration of infection by killing the host quickly. Host immunity, pathogenicity and related therapy are the factors that the resolution of infection will depend upon. There are also pathogens that will infect the host at multiple periods, like the herpes virus with recurrent periods of infectiousness and latent periods [25].

There are still uncertainties about the COVID-19 pathophysiology and its spread mechanism, so current knowledge is based on the similar coronaviruses that are transmitted by respiratory fomites from human-to-human [28], especially during the symptomatic phase. But, now there are various evidences that suggest that the virus can be transmitted during the asymptomatic incubation period that is estimated between 2-10 days [28–30]. Hence, the lockdown was imposed in various countries, including eluding of travel to high risk areas, contacting with symptomatic individuals, consumption of meat from areas with known COVID-19 cases and personal hygiene like frequent washing of hands and using PPE was given utmost importance [2].

Secondary attack rate needs to be identified to quantify contagions in a population which is the infection probability of susceptibles coming in contact with diseased that can be determined by knowing the infectiousness and transmission given infectiousness [25]. Reproductive number or R_0 , is another similar concept to secondary attack rate, and can simply be put as, if

$R_o > 1$, then there will be an outbreak,

$R_o < 1$, unlikely for an outbreak, or of low magnitude

Thus, R_0 is used to model the potential size of an outbreak and also form the base to achieve herd immunity. But, it has many factors affecting it, ranging from contact rates, seasonality change, population density or social organization[31]. Another value of importance, similar in concept to R_0 is Reproductive ratio, R [32], which is the average number of infected transmissions from the diseased [25]. The difference between R_o and R is that R varies over time with the change in population immunity, and hence is a population-based data, while R_o refers to susceptible contagions in a population. Thus, R will increase if susceptible individuals are added to the population and it will decrease if immuned individuals from exposure or vaccination are added. In case R becomes less than 1 or more than 1 with the change in the immunity of the population, the transmission of infection will wane or an epidemic will occur respectively [25,32]. There are various studies conducted to find the R_o value and the general knowledge now is a value of about 2.2 [29], that means a minimum of 60% of the population needs to be infected if there are no vaccines are available to achieve the herd immunity[33]. It should be kept in mind that we still are unaware of the accurate value as it can change with the various factors like seasonality, contact rates, population density and social organization. If R₀ has been underestimated, this percentage increases[7].

Mathematically defined by Kendall's pandemic threshold theorem, threshold level is another value to be kept in mind that would cause an outbreak or prevent one. This is the calculation of minimum density of susceptibles according to the geographical distribution, incorporating transmission dynamics effects. Simply put, if the infected individual has a value greater than the threshold density, it

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further will infect more than one individual and thus cause an outbreak [34]. This is of great importance to prevent a similar pandemic again in the future.

The first cases of the virus that has the world on its knees were linked to Wuhan's Huanan Seafood Wholesale Market, which trades in varieties of fishes and live animal species, bats, poultry, marmots and snakes [1]. This brings us to another value called dissemination rate that describes movement of pathogen from one area to another, thus spreading the infection further in a large area. This can be controlled by behavioural changes and awareness among the individuals handling the infected animals by preventing mixing with other animals in the market. An advice on preventing further spread of COVID-19 has been issued by the WHO and US Centers for Disease Control and Prevention (CDC). Avoiding the consumption of meat from regions with known COVID-19 outbreak is one among the various recommendations [2,28]

Immune senescence is something that should be alerted to the masses which is the progressive loss of the immunity against a pathogen due to decreased antibody titer or cellular response. A lesson learnt from the past in 20th century is the "near" eradication of measles in China, Korea and United States because of vaccination as early as they could and proper booster delivery. However, as time passed, the antibody titers decreased in the aged individuals and soon a "wild-type" measles virus got reintroduced in the community, bringing back the infection from its "near death". This should be taken into consideration after the development of immunity against the virus through infection or vaccination. [35]. Studies on COVID-19 have shown that there is little or no detectable antibody in about 10-20% of symptomatically infected person [36]. Recovered individuals of SARS-CoV-2 infection with negative report on RT-PCR may nevertheless be harboring persisting viruses and therefore,

anecdotal report of reinfection from some Asian countries should be cautiously regarded[7]. Weakening of immunity gained, might be related with immunosuppression (as stated before) due to chemotherapy, malnutrition, or some other infections [25] and need studies of viral sequencing to understand the factors behind the reinfection[7].

As mentioned before, immunology is complex and even if all factors are checked off and achieved, there is also the issue of breadth and length duration of herd immunity that depends on the interaction of the virus with the immune system. Covid-19 belong to a large family of a singlestranded RNA viruses (+ssRNA), coronaviruses [37]. Antigenic diversity can happen easily in RNA viruses giving rise to different strains due to antigenic drift, antigenic shift, and recombination. For example, norovirus has >30 genotypes, and so even after maintaining 93.9% amino acid sequence homology between the earliest and latest strains, there is still no control over it and hence a pandemic burst occur every 2-5 years approximately. With the postulation of the virus reservoirs being the young children and immune-weak population, the virus constantly emerge and escape neutralization by mutation [35].

If we take the example of Dengue that has four serotypes, infection with one serotype will introduce cross-reactive and serotype-specific neutralizing antibodies. Hence, when a second infection occurs from a different serotype, the original memory immune response will get triggered but due to variability in the antigenicity of the new serotype, it will not be able to neutralize the virus effectively thus resulting in immune evasion (a strategy used by pathogenic organisms and tumors to evade a host's immune response to maximize their probability of being transmitted to a fresh host or to continue growing, respectively [38]) through immune imprinting. This will result in secondary infection causing severe disease [39].

Similarly, in influenza A and norovirus, consequent infection by different serotypes results in weaker response due to the memory antibody response [40,41]. A mismatch of the vaccine or in case of re-infection by a different variant of the virus will all help in making the virus adapt and mutate making all efforts go to waste.

Now that we have registered the ability of RNA virus being able to mutate over time causing weak defense against a secondary infection from a different variant of the virus, introducing immunity by vaccine or infection in the community will depend on age and pre-exposure history. It carries high risk to predict future epidemic strains even if a strict global surveillance is done like the mismatching of Influenza vaccine both in 2014-15 and 2017-18 [42].

There are still ongoing research on cross-reactive antibody titers and chimeric serotype attenuated viruses to provide broad immunity through vaccination [43,44] and this would help us enormously in this pandemic by a virus which we have still don't know fully yet. There are still many studies going to understand this virus. One study was conducted for variant analysis on Covid-19 genomes where they identified that the most common clade was the D614G variant, and that its location being at a highly immunodominant region in a B cell epitope, may affect the effectiveness of vaccine. Further it mentioned that a resistive strains may emerge quickly against the antivirals like remdesivir and favipiravir due to the susceptibility of mutation in the target protein, summarizing that a meticulous study of the virus is required for therapy design and development, weighing on the evolving nature of the SARS-CoV-2 genome [45].

Success And Failure Cases Of Herd Immunity

The eradication of small pox was the spark that lit the fire of the concept of "Herd Immunity" and it came with the resolution from World Health Organization stating that small pox eradication in an endemic area can be achieved with the successful vaccination or re-vaccination of the 80% of the population within a period of 4-5years. A note to be taken is the use of the word, "revaccination" suggesting that waning of the vaccine induced immunity was an obstacle towards achieving Herd Immunity.

We, right now, focus so much on the concept of herd immunity which is nothing less than trying to shoot a target blindfolded from all the risks and collateral damage it brings. A bit history can probably open our eyes on how effective the quarantine and all the other strategies that countries have been following from the last few months are. Back in 1970, it was found that rather than relying entirely on herd immunity, variola virus was eradicated from a population by just active case detection, proper quarantining of cases, contact tracing and breaking the transmission chain[46]. Ever since 1967 the target to eliminate Measles has been going on with vaccinations and hence ultimately to establish Herd Immunity. Different estimates have been made over the years for measles Herd Immunity threshold, and many nations have made it a policy to achieve that. But then, reports of sporadic outbreaks in immunized community have broken all faiths that were placed on herd immunity [15,47]. This incident highlights the fact that heterogenicity within a population does play an important role and is an obstacle in achieving herd immunity.

Rubella has a similar basic transmission dynamics with measles, but is less transmissible comparatively and is usually incorporated with measles vaccine. This is done with the belief that rubella will also disappear with measles eradication, thus proving the R_o levels of Rubella and herd immunity effectiveness and also avoiding the additional effort of outbreak containments, which are usually followed for measles outbreak in US [21].

Another disease vaccination incorporated with Measles, is Mumps which also has a lower R_0 . The effort placed on measles eradication by routine administration of the vaccine will thus also help in mumps eradication, and in case it does not, it will reveal the population heterogenicity role in the mump virus transmission. Pertussis is a disease that has cost lives of many and even if vaccination programs for it were started since 1940s, till now global prediction of herd immunity for this disease is not possible. This is due to the fact that it has very high population herd immunity requirement (estimated to be about 93% like measles, and if vaccine waning is absent, it still is about 88%), the vaccine efficacy is still controversial and wanes over time (hence childhood vaccination is not enough) and additionally it has been reported that the adults also take part in the transmission of the disease without any disease manifestations.

A success story of public health is diphtheria, but even if herd immunity played a role in it, this story opens up more of the complexity of herd immunity. Vaccinations against Diphtheria were done using Diphtheria toxoid in the form of three doses at different age groups. However, researchers started to question the efficacy of the vaccine the toxoid is not a normal constituent of as Corynebacterium diphtheria. Studies soon confirmed this [48] and a paradox was created as there were extremely low rates of diphtheria cases since the vaccination programs. The resolution to the paradox probably could only be related to that the vaccine merely provided protection against infection transmission and not against getting the infection in the first place [49]. Since the cases have now clearly declined over the years, more studies to understand what exactly happened is impossible with only questions left with us.

Another vaccination program that was conducted was for tetanus in 1940s. Herd Immunity clearly can't play a role in this since it is not communicable between hosts, but still vaccination provides some sort of protection in the community and is thus conducted to mothers to provide protection against neonatal disease [50].

Herd Immunity in Polio has been debated for decades and it rotates around the controversy of use of two different forms of vaccines- killed, inactivated polio vaccine and live oral polio vaccine. Claims had been made that live oral polio vaccine provides better immunity than killed inactivated polio vaccine[51,52] by two points, viz., live oral polio vaccine impart greater intestinal (local, immunoglobulin A-mediated) immunity, and also herd immunity induction is more because of its sufficient excretion in feces and the oropharynx, thus transmitting it to unvaccinated individuals. But still the benefit or the efficacy of inactivated polio vaccine could be seen in countries (e.g., Sweden, Finland, and the Netherlands) that only used killed inactivated polio vaccine and had no reports for wild polio virus infection for a long period of time. However, in Finland, an outbreak of 10 cases in 1984-85 occurred which attributed to a type 3 virus that was not included in the vaccine [53]. While in Netherland, outbreaks were restricted in the population due to a religious community who were against vaccination, but there were no reports of transmission even if at least 400,000 unvaccinated individuals were present[54]. Since polio outbreak can't be contained due to its spread through sewage, water, and foodstuffs, it relies a lot on herd immunity. And, thus the flooding of the environment with mass live oral polio vaccine campaigns started in Cuba and then to Brazil and so on, thus providing protection against it directly or indirectly to the population. But this was inapplicable in Africa and Asia because of logistic difficulties and less efficacy of live oral polio vaccine

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compared to the rest of the world[55,56]. Thus, a proposal of a combination of both live oral polio and killed, inactivated polio vaccine was suggested.

Another infection where herd immunity has been tried often, but due to its genetic liability where there is frequent major (shift) and minor (drift) antigenic changes of their hemagglutinin (H) and neuraminidase (N) antigens, is Influenza. Also there is persistence in different vertebrates which just adds to the burden and prevents it from getting it eradicated ever. There has been claims that HERD IMMUNITY might actually be the reason behind the frequent change of the virus profile and its subsequent disappearance [21], due to cross protection between the subtypes leading to spread of new antigenic variants, and hence, giving us no proper hold over it. This was further dug in after an increase in reports of cocirculation of subtypes after 1977 in the same population unlike before where there usually were reports of only a single major virus (shift) subtype circulation [57]. This has been claimed to be either of two reasons, either the virus changed and hence, there is less cross subtype protection or the population has changed like increase population, increase in number of susceptibles per year, and in worldwide communication, thus persisting in the population until the threshold of susceptibles is reached to support transmission. If this is the case of population change, then we have bigger problems to worry about, as such changes are only a matter of time for other infectious agents too. One can wonder if Covid-19 can be one of those changes. On one hand, the reason behind it may simply be because the immunity one gains against influenza is less durable comparatively with other viruses and the unpredictable nature of its antigenic changes. Even if eradication is impossible for Influenza, trials for herd immunity through vaccination of children have been proposed and positive results were achieved, and in Japan[58], this has been a national policy for years. But, a different strategy is followed in US where they focus on direct protection of the susceptible instead of indirect protection through vaccination of children [59]

BCG vaccine has been the most widely received vaccine by the masses alive today which is against tuberculosis, yet herd immunity is not discussed much about it since the knowledge about the immunity obtained either by natural infection or vaccine is very little till now [21]. Usually the transmission of this infection is from loss of immunity against it in older long infected individuals, and not because of failure of achieving prior immunity. BCG vaccine still now has no evidence of prolonging protection against it or even convincing evidence of protection against risk of infection from tubercle bacillus in any population [60].

Malaria is another infection that raises some issues in herd immunity even if it is not a vaccine-preventable disease. Before any infection, malaria was used to formulate eradication threshold and reproduction rate. And, R_o calculation of vector borne diseases is different from directly transmitted diseases. R_o was estimated to range from 5 to 100 in studies from different places which bring the herd immunity requirement of 80-99%, which is next to impossible to achieve [21]. But also, some studies have stated that there might be decrease in the R_0 calculation after it was found that different genotypes may cocirculate in same area. Another issue in Malaria vaccine is the different forms of them, viz, sporozoites or Merozoites providing protection like any other vaccines, but then there are vaccines against transmissible stages which have no protection of recipient from the infection, but just prevent him/her from transmitting it to others, causing ethical problems[61].

Conclusion

In our present scenario, understanding these values and concepts will play a huge role in achieving herd immunity (if one decides), which by any means is not less than any apocalypse movie. And with the lifting off the lockdown now in various places, we can already see a preview of the state we will be in to achieve herd immunity. A thought to be kept in mind about going ahead with the herd immunity is that, due to the ever changing statistics and constant unravelling of new researches, it carries a lot of potential risks [2]. The past cases of infections and their failures of achieving herd immunity should never be forgotten.

With the first official report case of Covid-19 and the declaration of pandemic, there has been many theories and predictions put forward by different researches and spread through social media, most of them without much of the hard proof evidence or only based on few cases to explain this new thing we are facing for the very first time. It is in human nature to find something and co-relate it with whatever problems they are facing. With the advancement of technology and lightning fast spread of an idea, confusions, panics and stress are created everywhere. Even if they have brought everyone to know about what exactly is happening every minute of the day in any parts of the world, there is also a clash of real facts of this virus with "almost true" ideas being dropped in by everyone who has read something off from a link, leading to various chaos theories. There is constantly a social pressure for answers to various questions to this pandemic, but a human being is immeasurably more complex than any other chaotic system that can be demonstrated, so the best that one can do is to assess probabilities which is happening everywhere now [62]. The idea of herd immunity, focusing on healthy young individuals gaining immunity through exposure and recovery, while the immune-weak and immunocompromised age groups stay

in quarantine sounds very promising. But even if the healthy young individuals make up for the minimum 60% of the population exposed to achieve herd immunity, the entire nation will be on a standstill due to the uncertainty of their recovery[33]. To top it all off, in a country like India, where there are apparent lack of Doctors and hospital beds, there is already a mass infection and lack of facilities to treat them. If this continues and everything goes downhill, there will be massive unnecessary death due to inability to receive basic treatments and we will left with be those immune-weak only and immunocompromised individuals who were never exposed to the virus, to function the country. With the economic crisis at hand, it has put all of us in a conundrum with the pandemic, and the debate of bringing balance in life on whether to go ahead with the full reemergence or wait out a little longer goes on.

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References

- Lu H, Stratton CW, Tang YW. Outbreak of pneumonia of unknown etiology in Wuhan, China: The mystery and the miracle. J. Med. Virol. 2020. doi:10.1002/jmv.25678
- Sohrabi C, Alsafi Z, O'Neill N, et al. World Health
 Organization declares global emergency: A review
 of the 2019 novel coronavirus (COVID-19). Int. J.
 Surg. 2020. doi:10.1016/j.ijsu.2020.02.034
- 3 Brilliant LB, Hodakevic LN. Certification of smallpox eradication. Bull World Health Organ 1978.
- 4 Thanh Le T, Andreadakis Z, Kumar A, et al. The COVID-19 vaccine development landscape. Nat

Rev Drug Discov Published Online First: 2020. doi:10.1038/d41573-020-00073-5

- Kumar S, Butler D. Calls in India for legal action against US charity. Nature Published Online First: 2013. doi:10.1038/nature.2013.13700
- Sankaranarayanan R, Bhatla N, Basu P. Current global status & impact of human papillomavirus vaccination: Implications for India. Indian J. Med. Res. 2016. doi:10.4103/0971-5916.195023
- Altmann DM, Douek DC, Boyton RJ. What policy makers need to know about COVID-19 protective immunity. Lancet. 2020. doi:10.1016/S0140-6736(20)30985-5
- Kwok KO, Lai F, Wei WI, et al. Herd immunity estimating the level required to halt the COVID-19 epidemics in affected countries. J. Infect. 2020. doi:10.1016/j.jinf.2020.03.027
- 9 Studdert DM, Hall MA. Disease Control, Civil Liberties, and Mass Testing — Calibrating Restrictions during the Covid-19 Pandemic. N Engl J Med Published Online First: 2020. doi:10.1056/nejmp2007637
- 10 Martinez MA. Compounds with therapeutic potential against novel respiratory 2019 coronavirus. Antimicrob Agents Chemother Published Online 2020. First: doi:10.1128/AAC.00399-20
- Amanat F, Krammer F. SARS-CoV-2 Vaccines: Status Report. Immunity. 2020. doi:10.1016/j.immuni.2020.03.007
- Thanh Le T, Andreadakis Z, Kumar A, et al. The COVID-19 vaccine development landscape. Nat. Rev. Drug Discov. 2020. doi:10.1038/d41573-020-00073-5
- 13 Adams ER, Anand R, Andersson MI, et al. Evaluation of antibody testing for SARS-Cov-2

using ELISA and lateral flow immunoassays. medRxiv Published Online First: 2020. doi:10.1101/2020.04.15.20066407

- Takita M, Matsumura T, Yamamoto K, et al. Challenges of community point-of-care antibody testing for COVID-19 herd-immunity in Japan. QJM An Int J Med Published Online First: 2020. doi:10.1093/qjmed/hcaa182
- Fox JP. Herd immunity and measles. Rev Infect
 Dis Published Online First: 1983.
 doi:10.1093/clinids/5.3.463
- Smith DR. Herd Immunity. Vet. Clin. North Am. Food Anim. Pract. 2019. doi:10.1016/j.cvfa.2019.07.001
- Topley WWC, Wilson GS. The spread of bacterial infection. the problem of herd-immunity. J Hyg (Lond) Published Online First: 1923. doi:10.1017/S0022172400031478
- M. HW, Greenwood M. Epidemics and Crowd Diseases. J R Stat Soc Published Online First: 1935. doi:10.2307/2342310
- Riedel S. Edward Jenner and the History of Smallpox and Vaccination. Baylor Univ Med Cent Proc Published Online First: 2005. doi:10.1080/08998280.2005.11928028
- Rene, Dubos J. The White Plague. Tuberculosis, Man and Society. South Med J Published Online First: 1953. doi:10.1097/00007611-195308000-00035
- Fine PEM. Herd Immunity: History, Theory,
 Practice. Epidemiol Rev Published Online First:
 1993. doi:10.1093/oxfordjournals.epirev.a036121
- Koff RS. Infectious diseases of humans: Dynamics and control. By R.M. Anderson and R.M. May, 757 pp. Oxford: Oxford University Press, 1991.
 \$95.00. Hepatology Published Online First: 1992.

Page

doi:10.1002/hep.1840150131

- Soper HE. The Interpretation of Periodicity in
 Disease Prevalence. J R Stat Soc Published Online
 First: 1929. doi:10.2307/2341437
- Giles P, Bailey NTJ. The Mathematical Theory of Infectious Diseases and Its Applications. Oper Res Q Published Online First: 1977. doi:10.2307/3009004
- 25 Horsburgh CR, Mahon BE. Infectious disease epidemiology. In: Modern Epidemiology: Third Edition. 2011. doi:10.5005/jp/books/11410_16
- Naylor SW, Gally DL, Christopher Low J.
 Enterohaemorrhagic E. coli in veterinary medicine.
 Int. J. Med. Microbiol. 2005.
 doi:10.1016/j.ijmm.2005.07.010
- Heller L, Mota CR, Greco DB. COVID-19 faecaloral transmission: Are we asking the right questions? Sci Total Environ Published Online First: 2020. doi:10.1016/j.scitotenv.2020.138919
- 28 Centers for Disease Control and Prevention.
 Coronavirus Disease 2019 (COVID-19) Situation
 Summary. J Med Virol Published Online First:
 2020. doi:10.1002/jmv.25766
- 29 Li Q, Guan X, Wu P, et al. Early transmission dynamics in Wuhan, China, of novel coronavirusinfected pneumonia. N. Engl. J. Med. 2020. doi:10.1056/NEJMoa2001316
- 30 Rothe C, Schunk M, Sothmann P, et al. Transmission of 2019-NCOV infection from an asymptomatic contact in Germany. N. Engl. J. Med. 2020. doi:10.1056/NEJMc2001468
- Delamater PL, Street EJ, Leslie TF, et al. Complexity of the basic reproduction number (R0). Emerg Infect Dis Published Online First: 2019. doi:10.3201/eid2501.171901
- 32 De Jong MCM, Bouma A. Herd immunity after

vaccination: How to quantify it and how to use it to halt disease. In: Vaccine. 2001. doi:10.1016/S0264-410X(00)00509-0

- Guerra FM, Bolotin S, Lim G, et al. The basic reproduction number (R0) of measles: a systematic review. Lancet Infect. Dis. 2017. doi:10.1016/S1473-3099(17)30307-9
- 34 Thrusfield M. Veterinary Epidemiology, Third Edition. 2007. doi:10.1016/S0167-5877(03)001077
- 35 Mallory ML, Lindesmith LC, Baric RS. Vaccination-induced herd immunity: Successes and challenges. J. Allergy Clin. Immunol. 2018. doi:10.1016/j.jaci.2018.05.007
- Tan W, Lu Y, Zhang J, et al. Viral Kinetics and Antibody Responses in Patients with COVID-19.
 medRxiv Published Online First: 2020. doi:10.1101/2020.03.24.20042382
- Cascella M, Rajnik M, Cuomo A, et al. Features,
 Evaluation and Treatment Coronavirus (COVID-19). 2020.
- Foster TJ. Immune evasion by staphylococci. Nat.Rev. Microbiol. 2005. doi:10.1038/nrmicro1289
- 39 De Alwis R, Williams KL, Schmid MA, et al. Dengue Viruses Are Enhanced by Distinct Populations of Serotype Cross-Reactive Antibodies in Human Immune Sera. PLoS Pathog Published Online First: 2014. doi:10.1371/journal.ppat.1004386
- 40 Lessler J, Riley S, Read JM, et al. Evidence for antigenic seniority in influenza A (H3N2) antibody responses in southern China. PLoS Pathog Published Online First: 2012. doi:10.1371/journal.ppat.1002802
- 41 Lindesmith LC, Ferris MT, Mullan CW, et al.Broad Blockade Antibody Responses in Human

Volunteers after Immunization with a Multivalent Norovirus VLP Candidate Vaccine: Immunological Analyses from a Phase I Clinical Trial. PLoS Med Published Online First: 2015. doi:10.1371/journal.pmed.1001807

- Wu NC, Zost SJ, Thompson AJ, et al. A structural explanation for the low effectiveness of the seasonal influenza H3N2 vaccine. PLoS Pathog Published Online First: 2017. doi:10.1371/journal.ppat.1006682
- Debbink K, Lindesmith LC, Ferris MT, et al.
 Within-Host Evolution Results in Antigenically
 Distinct GII.4 Noroviruses. J Virol Published
 Online First: 2014. doi:10.1128/jvi.00203-14
- Katzelnick LC, Montoya M, Gresh L, et al. Neutralizing antibody titers against dengue virus correlate with protection from symptomatic infection in a longitudinal cohort. Proc Natl Acad Sci U S A Published Online First: 2016. doi:10.1073/pnas.1522136113
- Koyama T, Platt DE, Parida L. Variant analysis of COVID-19 genomes. J Bull World Heal Organ Published Online First: 2020. doi:10.2471/BLT.20.253591
- 46 Henderson DA. Epidemiology in the global eradication of smallpox. Int J Epidemiol Published Online First: 1972. doi:10.1093/ije/1.1.25
- 47 Markowitz LE, Preblud SR, Orenstein WA, et al. Patterns of Transmission in Measles Outbreaks in the United States, 1985–1986. N Engl J Med Published Online First: 1989. doi:10.1056/NEJM198901123200202
- 48 Miller LW, Older JJ, Drake J, et al. Diphtheria
 Immunization: Effect Upon Carriers and the
 Control of Outbreaks. Am J Dis Child Published
 Online First: 1972.

doi:10.1001/archpedi.1972.02110090067004

- 49 Doull JA, Lara H. The epidemiological importance of diphtheria carriers. Am J Epidemiol Published Online First: 1925. doi:10.1093/oxfordjournals.aje.a119677
- 50 Newell KW, Dueñas Lehmann A, LeBlanc DR, et al. The use of toxoid for the prevention of tetanus neonatorum. Final report of a double-blind controlled field trial. Bull World Health Organ 1966.
- Fox JP. Eradication of poliomyelitis in the United States: a commentary on the Salk reviews. Rev. Infect. Dis. 1980. doi:10.1093/clinids/2.2.277
- 52 Melnick JL. Advantages and disadvantages of killed and live poliomyelitis vaccines. Bull World Health Organ 1978.
- Hovi T, Huovilainen A, Kuronen T, et al. 53 **OUTBREAK** OF PARALYTIC POLIOMYELITIS IN FINLAND: WIDESPREAD OF CIRCULATION ANTIGENICALLY ALTERED POLIOVIRUS TYPE 3 IN A VACCINATED POPULATION. Lancet Published Online First: 1986. doi:10.1016/S0140-6736(86)91566-7
- 54 Schaap GJ, Bijkerk H, Coutinho RA, et al. The spread of wild poliovirus in the well-vaccinated Netherlands in connection with the 1978 epidemic.
 Prog Med Virol 1984.
- Beale AJ. Polio vaccines: time for a change in immunisation policy? Lancet Published Online First: 1990. doi:10.1016/0140-6736(90)90945-2
- 56 Patriarca PA, Wright PF, John TJ. Factors affecting the immunogenicity of oral poliovirus vaccine in developing countries: Review. Rev. Infect. Dis. 1991. doi:10.1093/clinids/13.5.926
- 57 Thacker SB. The persistence of Influenza A in

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human populations. Epidemiol Rev Published Online First: 1986. doi:10.1093/oxfordjournals.epirev.a036291

- 58 Dowdle WR, Millar JD, Schonberger LB, et al. Influenza immunization policies and practices in Japan. J Infect Dis Published Online First: 1980. doi:10.1093/infdis/141.2.258
- 59 Prevention and control of influenza: Part I, Vaccines. Recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR Recomm Rep 1994.
- 60 Styblo K, Meijer J. Impact of BCG vaccination programmes in children and young adults on the tuberculosis problem. SELPAPNETHTBASS 1977.
- Halloran ME, Struchiner CJ, Spielman A.
 Modeling malaria vaccines II: Population effects of stage-specific malaria vaccines dependent on natural boosting. Math Biosci Published Online First: 1989. doi:10.1016/0025-5564(89)90074-6
- Firth WJ. Chaos Predicting the unpredictable. Br
 Med J Published Online First: 1991. doi:10.1136/bmj.303.6817.1565