

# Conjoint Citizen Participation of Pro-vaxxers and Vaccine Deniers to Eradicate Vaccination Conflicts: Illuminating a Novel Win-Win Pathway

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## ABSTRACT

Conflicts among pro-vaxxers and vaccine deniers will remain endless if both these groups fail to view vaccination through an unusual lens agreeable to both. Citizen participation encourages people to get involved in decision-making processes to build a better society or nation. Pro-vaxxers and vaccine deniers might be correct from their health activism and citizen participation standpoint but lack effective basis towards scientific precision. Under such circumstances, it is important to scrutinize if any aspect of the science remains neglected to facilitate resolving persistent conflicts. Lack of immunological tests to objectively measure the natural and adaptive immunity could have been instrumental in vaccination disputes. Epidemiological findings and publications should not be solely trusted to devise public health strategies. Affordable and precise immunological tests to prove the necessity and efficacy of vaccination on an individual level should be discovered to equally benefit pro-vaxxers and vaccine deniers. Perhaps, such immunological tests should be made disease-specific and vaccine-specific, and also enable development of an immunological classification system with gradations for immunocompetent and immunodeficient individuals. If disease-specific immunological tests are unavailable or cannot be discovered, tests based on homeostasis could be the best alternative but the relationship between homeostasis and immunity is surprisingly neither well established nor widely discussed, thus, immunity may be often seen as an 'isolated', 'vaccine-dependent' department in the human body. Any prophylactic intervention or treatment should

upbring measurable changes in homeostasis of an individual to prove its scientific credibility. Ideally, both pro-vaxxers and vaccine deniers should be labeled as 'defeated' in their meaningless tug-of-war for being ignorant about "objective immunoassays". As citizens, the pro-vaxxers and vaccine deniers have important onus to eradicate vaccination disputes by exploring what is equally relevant and beneficial to both of them to evaluate and regulate their immunity to ensure satisfactory personal health and community health, without any obligation to be sacrificial to justify the authenticity of their citizen participation. A scope for pro-vaxxers and vaccine deniers to work together (conjoint citizen participation) to eradicate vaccination conflicts is possible only based on 'affordable and reliable immunological test' to clinically examine themselves and clearly interpret if they are genuinely contributing to herd immunity or sabotaging herd immunity through their personal immune status. Even a single individual could contribute to massive scientific transformations through his or her discoveries, or just through critically questioning established scientific practices, and this is how naturally science evolves as a marvelous product of intellectual humility. Pseudoscience evolves as a malevolent product of intellectual arrogance.

**Keywords:** Citizen Participation, Vaccination, Immunology, Pro-vaxxers, Vaccine deniers, Herd immunity, Antibodies, Innate immunity, Adaptive immunity, Immunological memory

## INTRODUCTION

It is widely known that before and after administration of a treatment or

prophylactic intervention to any individual, elaborate objective diagnosis sets a suitable foundation. Meticulous diagnosis determines the extent of healing or anticipated health outcomes. In contrast to pseudoscience, whenever a treatment or prophylactic approach is implemented, it is quite natural that its effectiveness can be proved only through suitable diagnostic technique(s). At times, discovery of a new treatment or prophylactic approach naturally accompanies discovery of suitable diagnostic methods also. In the absence of such diagnostic methods, the favorable health benefits or unintended harmful outcomes (Iatrogenesis) caused by the healthcare technologies cannot be proved to every recipient separately. For vaccinations, the diagnosis part is inherently absolutely eliminated, which has created a perspective that regardless of the health status, microorganisms have equal chance of infecting all, hence, vaccines should be administered to all to achieve herd immunity. Various relevant questions regarding the methodology and purpose of all types of vaccinations remain unquestioned or unheard. If we have scientific explanations to all these questions, that would be beneficial to both pro-vaxxers and vaccine deniers. Not all the pro-vaxxers and vaccine deniers are immunocompetent or immunocompromised which means immune-diversity may be extensive among pro-vaxxers and vaccine deniers because homeostasis is highly individual-specific. Homeostatic competence is accompanied by health, immunocompetence and healthy aging whilst impaired homeostasis is accompanied by co-morbidities, immunodeficiency and unhealthy aging. It is also quite perplexing to see a very large percentage of people supporting compulsory vaccinations to save everyone but seldom integrate to influence the government to curb the risk factors that cause excruciating co-morbidities. Nevertheless, as citizens, the pro-vaxxers and vaccine deniers have important onus to eradicate vaccination disputes by exploring what is equally

relevant and beneficial to both of them to evaluate and regulate their immunity to ensure satisfactory personal health and community health, without any obligation to be sacrificial to justify the authenticity of their citizen participation. A scope for pro-vaxxers and vaccine deniers to work together (conjoint citizen participation) to eradicate vaccination conflicts is possible only based on 'affordable and reliable immunological test' to clinically examine themselves and clearly interpret if they are genuinely contributing to herd immunity or sabotaging herd immunity through their personal immune status and homeostasis. Pro-vaxxers and vaccine deniers might find several literature excerpts and insights discussed in this article as new information, probably illuminating a novel win-win pathway to eliminate their erroneous standpoints and contradictions. Vaccination entered modern medical practice in the 1800s with the smallpox vaccine developed by Edward Jenner.<sup>[1]</sup> "Achieving herd immunity through infection relies on enough people being infected with the disease and recovering from it, during which they develop antibodies against future infection. In addition, antibodies from a prior infection may only provide protection for a limited duration. People who do not have immunity to a disease may still contract an infectious disease and have severe consequences of that disease even when herd immunity is very high".<sup>[2]</sup> "The immune system possesses immense individual-to-individual diversity. The extreme diversity of the human immune system, forged and maintained throughout evolutionary history, provides a potent defense against opportunistic pathogens. Genetic variation is an important driver of immune variation. The evolution of immunity has not halted with modernity. Understanding variation in response to environmental factors in particular, such as diet, microbiome, and environmental exposure, holds the promise of using simple environmental manipulations in a targeted manner to reroute an individual's immune

system toward a less pathogenic configuration. Although the advantages of personalized immune modification are manifold, they first require a baseline knowledge of the source of our individual differences. The confounding interaction of many of these variables currently makes it difficult to assign definitive contributions to human immune diversity”.<sup>[3]</sup> Physiological homeostasis is the tendency of the body to maintain critical physiological parameters (like blood glucose, blood salinity, blood pressure, core body temperature) of its internal environment within a narrow range of critical values that may not be identical from one instance to the next.<sup>[4]</sup> “Innate immunity is the first immunological mechanism for fighting against an intruding pathogen. It is a rapid immune response, initiated within minutes or hours after aggression, that has no immunologic memory. Adaptive immunity is antigen-dependent and antigen-specific with capacity to memorize the antigen and mount a rapid and efficient immune response upon subsequent exposure to the antigen. Innate immunity and adaptive immunity are not mutually exclusive mechanisms of host defense, but rather are complementary, with defects in either system resulting in host vulnerability or inappropriate responses”.<sup>[5]</sup> The traditional definition of natural antibodies (Nabs) states that these antibodies are present prior to the body encountering cognate antigen, providing a first line of defense against infection thereby, allowing time for a specific antibody response to be mounted.<sup>[6]</sup> “In contrast to adaptive antibodies, natural antibodies are present in a non-immunised organism from birth. Though natural antibodies were discovered nearly half a century ago, there is still a lot that we do not know about them, we are still discovering their varieties and functions in the human body. Their basic property is the protection of our body after birth. They ensure specific homeostasis by reacting to self-antigens and neo-determinants that are formed during mechanism like apoptosis and oxidation.

About 80% of all natural antibodies circulating in the human body are natural IgMs (which are best known immunoglobulins). IgA and IgG together with IgM are formed mainly by B1 lymphocytes and lymphocytes of the marginal zone of the spleen”.<sup>[7]</sup> “Natural antibodies (nAbs) are most commonly defined as immunoglobulins present in the absence of pathological conditions or deliberate immunizations. These nAbs provide immediate protection against infection while the adaptive arm of the immune system mounts a specific and long-term response. Beyond immediate protection from infection, nAbs have been shown to play various functional roles in the immune system, which include clearance of apoptotic debris, suppression of autoimmune and inflammatory responses, regulation of B cell responses/repertoires. The notion that an antibody must be of high affinity in order to be biologically relevant originates primarily from the analysis of the requirements for an efficient immune response against pathogens. This concept does not necessarily apply to natural antibodies, because polyreactive property of natural antibodies does not suggest lack of specificity.”<sup>[8]</sup> “Since their discovery in the early 1960s, natural antibodies were neglected or denied within the immunological society because of their apparent contradiction with established immunological dogmas. Furthermore, the properties of natural antibodies could be perceived as redundant because high-affinity binding and mono-specificity are regarded as key characteristics of relevant and effective immunoglobulins. Immunoglobulins in the absence of known immunization or vaccination against foreign antigens are persistently found in many species and have been isolated from various sources, including serum, milk, saliva, mucus, eggs, and feces”.<sup>[9]</sup> “Unlike the adaptive immune system, the innate immune system has classically been characterized as being devoid of memory functions. However, recent research shows that innate

myeloid and lymphoid cells have the ability to retain memory of prior pathogen exposure and become primed to elicit a robust, broad-spectrum response to subsequent infection. This phenomenon has been termed innate immune memory or trained immunity<sup>[10]</sup> “Trained immunity - a concept recently proposed by Cassone, that challenges the dogma of immunologic memory being attributed solely to the adaptive immune system. Trained immunity proves to be an indispensable element of host defense. This de facto innate immune memory is elicited by distinctive epigenetic and metabolic programs. Trained immunity is not restricted to innate immune cells, and evidence is accumulating that long-term adaptation can develop following brief stimulation of various nonimmune cells including vascular endothelial cells, vascular smooth muscle cells, fibroblasts, epithelial stem cells, and microglia<sup>[11]</sup> “A vaccine is different from immunoglobulin in that the vaccines help in developing protective antibodies in the body of the individuals (vaccine recipients), and protection is available after a lag period of a few weeks to several months. However, immunoglobulin provides immediate protection. When a person who has been fully vaccinated develops the disease against which he/she has been vaccinated, it is referred to as vaccine failure. When the vaccine recipient does not produce enough antibodies when first vaccinated, it is called as primary vaccine failure, and infection can therefore occur at any time post vaccination. Secondary vaccine failure occurs when adequate protective levels of antibodies are produced immediately after the vaccination, but the levels fall over time, hence, the incidence of secondary vaccine failure increases with time after the initial vaccination<sup>[12]</sup> “Vaccine-associated deaths clearly do fall within the scope of protection. Since the primary aim of vaccination programs is to protect the individual concerning as well as the population as a whole, these are technically to be regarded as unintentional killings, for

which the state is additionally required to have breached its obligation to take ‘appropriate steps to safeguard life’ to be liable. A prerequisite for the states to ensure compliance with the positive obligation to protect lives is, that an individual examination has been made to rule out the existence of contraindications. As long as sufficient precautionary measures in place, compulsory vaccination is therefore not an interference with the right to life<sup>[13]</sup> “Since vaccines are mainly administered to healthy and young people, even non-serious adverse events are often deemed unacceptable by vaccinees or their parents/relatives. Hence, the adverse events following immunization (AEFIs) must be evaluated carefully and very seriously<sup>[14]</sup> “The CDC and FDA established The Vaccine Adverse Event Reporting System (VAERS) in 1990 to detect possible signals of adverse events associated with vaccines. About 30,000 events are reported each year to VAERS. Between 10% and 15% of these reports describe serious medical events that lead to hospitalization, life-threatening illness, disability or death. VAERS is a voluntary reporting system. Anyone such as a parent, a health care provider, or friend of the patient, who suspects an association between a vaccination and an adverse event may report that event and information about it to VAERS<sup>[15]</sup> Understanding the predictors of both negative and positive attitudes towards vaccination is therefore extremely important both from a purely scientific and applied perspective<sup>[16]</sup> “Generalization in medical profession should solely depend on invariable facts but lack of critical thinking leads to development of faulty evidences or fabricated evidences or unproductive anecdotal evidences. In medical profession, rendering unbiased evidence-based support to the scientific facts is not possible without experimentations using similar methodologies. Though the greatest achievement of any medical invention (diagnosis, treatment procedure, prophylaxis, public health measure) is its

generalizability, the tendency of the health care professionals to generalize a finding of someone or themselves without repeated applications in real-life situations has been an impediment. Critical thinking is the precursor for evidence-based practices in medical profession”.<sup>[17]</sup> “Epidemiology, also referred to as “population medicine”, is used to estimate the individual risk of disease and the chances of avoiding it from group experience averages. Such information is crucial to planning interventions and allocating resources. Bias, confounding and chance are the threats to validity that can distort the results of epidemiological studies”.<sup>[18]</sup> There is a serious risk that some epidemiological publications reach misleading conclusions.<sup>[19]</sup> “All sciences and scientists make mistakes, and epidemiology and epidemiologists are no exception. Epidemiological mistakes may maim and kill, and sometimes the toll can be massive. Populations differ by place, their characteristics and time. The results may not generalize easily between population, within subgroups of the same population, or within the same population at different times. This applies particularly to the burden of disease and risk factors, but also to causal understanding”.<sup>[20]</sup> Vast majority of social and medical science research aggregates across subjects, but conclusions drawn from aggregated data may be worryingly imprecise.<sup>[21]</sup> Much of the published medical research is apparently flawed, cannot be replicated and/or has limited or no utility.<sup>[22]</sup> “Statistical malpractice is an insidious, and indeed prestige-laden and grant-rewarded, activity. Brilliantly clever, but fundamentally wrong-headed, number-crunchers are encouraged to devise inappropriate applications of mathematical methods to health problems. This species of misdirected zealot has so far been immune from criticism. The seeking of algorithms for scientific decision-making is an offence best described as statistical malpractice. Medicine has been deluged with uninterpretable answers generated by heavy statistics operating on big databases of

dubious validity”.<sup>[23]</sup> “The medical-political complex tends towards suppression of science to aggrandise and enrich those in power. And, as the powerful become more successful, richer, and further intoxicated with power, the inconvenient truths of science are suppressed. When good science is suppressed, people die. When good science is suppressed by the medical-political complex, people die”.<sup>[24]</sup> “Psychology of pseudoscience explores what makes people vulnerable to misbeliefs. We must ask not just about how individuals hold mistaken beliefs but how misbeliefs spread from one mind to the next. This propagation of misinformation is how pseudoscience becomes a cultural phenomenon. People might come to accept counterintuitive pseudoscientific claims because they trust the source, are convinced by reasons offered, or are helped by these beliefs to reduce their stress and anxiety”.<sup>[25]</sup> “The advancement of medical knowledge follows a process resulting in a ‘spectrum of evidence’. The development of evidence is a process that has to be supported at all levels. In addition, most of the decisions in medical care are made on the basis of evidence that has not progressed to the level of randomized trials because randomized trials are remarkably expensive, and the level of evidence is sometimes so strong that mounting a trial is considered unethical. It is important to both understand how a question advances to ever-higher levels of evidence, and how most medical hypotheses/decisions are made at lower levels of evidence”.<sup>[26]</sup> “Intellectual humility has been identified as a character virtue that allows individuals to recognize their own potential fallibility when forming and revising attitudes. Intellectual humility is therefore essential for avoiding confirmation biases when reasoning about evidence and evaluating beliefs. In an era of polarization, fake news, and the wide spread of misinformation, there is a strong public need for an understanding of how citizens can inoculate themselves against deception and inaccurate information. The capacity to

critically evaluate information in nonbiased ways requires *intellectual humility* – the understanding of one's limitations and biases when making evidence-based decisions. Intellectual humility allows us to avoid psychological tendencies to overlook evidence and confirm prior beliefs. Identifying and cultivating the cognitive factors shaping intellectual humility may be a key endeavour in building more evidence-based, tolerant, and effective discussions about the contested issues that divide and polarize our societies today".<sup>[27]</sup> India too should ensure that robust systems are in place to monitor adverse events and fatal outcomes as a result of vaccination and ensure transparency in making this data available at local level, so that the communities are able to take informed decisions.<sup>[28]</sup> "Public participation is a democratic process and to be classified as public involvement genuinely, it needs the redistribution of power. It includes the following eight steps namely citizen control, delegation, partnerships, placation, consultation, informing, therapy, and manipulation. Therapy and manipulation belong to 'non-participation', informing, consultation and placation belong to 'degrees of tokenism', and, partnership, delegated power and citizen control belong to 'degrees of citizen power'. Negotiations between citizens and public officials can also result in citizens achieving dominant decision-making authority over a particular plan or program – 'Delegated power'. Partnership can work most effectively when there is an organized power-base in the community to have some genuine bargaining influence over the outcome of the plan as long as the community and powerholders find it useful to maintain the partnership".<sup>[29]</sup>

### **Uncertainties in antibody assays and efficacy of vaccinations**

"Antibody testing becomes particularly important when a sufficiently large proportion of the population is unaware of its immunity. Antibody testing is another

Non-Pharmaceutical Intervention (NPI) – not recognized so far in the literature – that reduces contagion. The point is that susceptible and asymptomatic agents that are unaware whether they are immune are socially active than those who are sure of not being immune. By revealing that susceptible and asymptomatic individuals are not immune or by increasing the number of people who are sure of not being immune, antibody testing saves lives and increases welfare by reducing their social activity".<sup>[30]</sup> Inherent accuracy of all serological tests for antibodies is a big difficulty that may inevitably lead to misclassifications even when the best methodologies, most reliable reagents, and stringent internal and external quality controls are used.<sup>[31]</sup> "As the pandemic unfolded, the concept of an immunity passport based on having antibodies did not pan out. As the antibody assay's usefulness for individual patients became less clear and testing for active infections expanded, the public's clamor for antibody testing waned. But for some, the arrival of COVID-19 vaccines revived their interest in serology. Could a simple blood test reveal whether the vaccine was working or, later, if it was time for a booster shot? Doria-Rose noted that measuring neutralizing antibodies requires a complex test that is run in only few laboratories and has not been scaled up for diagnostic use. Doria-Rose wrote, 'it is not a simple relationship - there is no clear titer at which you can say whether a particular person is protected, thus different neutralizing antibody thresholds and different immune responses may correlate with protection against asymptomatic, symptomatic, or severe disease'. Theel found although antibody levels were associated with protection, the researchers were unable to pinpoint a threshold. None of the cases were severe, but antibodies obviously were not foolproof against the virus. Theel also said 'Individuals can have neutralizing antibodies and still get infected. We know that higher antibody levels, specifically higher neutralizing antibody

levels, are better. But we do not know how high is high enough'. Offit pointed out the impracticality of using periodic boosters to keep neutralizing antibodies high and he also said 'You can have a robust or high level of virus neutralizing antibodies in your circulation. That is not going to prevent the virus from attaching to your nose and beginning to reproduce itself. That is an asymptomatic infection.'<sup>[32]</sup> In the field of antibody assays, focusing on absolute thresholds or reference values does not look feasible and efforts shall be better aimed to establish assay-independent ranges of antibody response that shall characterize different infection stages or satisfy clinical needs, such as establishing an adequate response to vaccination or the antibody levels that may trigger a medical intervention e.g., start or stop of a specific treatment or switch to a different schedule or drug combination.<sup>[33]</sup> "Although numerous immunoassays have been reported for diagnosing COVID-19, many of them either showed an unsatisfactory diagnostic performance or lacked stringent evaluation for their performance in the real world based on enough samples. False negatives of antibody immunoassays may result from poor sensitivity or inadequate antibody levels in the specimen. False positives of antibody immunoassay mainly involve cross-reactivity from other viruses, and possibly autoimmune diseases such as rheumatoid factor. One of the foci on current technological innovations of immunoassays is to improve sensitivity to reduce the false negatives and to improve specificity to decrease the false positives".<sup>[34]</sup> "There is high consumer demand for antibody tests to detect past infection with severe SARS-CoV-2 but there is a great deal of uncertainty about what a positive test means immunologically. Uneven test accuracy and statistical challenges, especially in areas of low disease prevalence, further complicate use of antibody tests for individual decision making. At the population level, antibody tests are needed to support sero-surveillance

studies, determine case fatality rate, track increases or decreases in incidence and prevalence, but currently they are of limited utility for individuals. Seropositive antibody test results should not be used to avoid appropriate physical distancing or mask wearing".<sup>[35]</sup> "George Kassiotis believes that the correlation between the activity of antibodies against the virus in lab tests and the real-world immunity they provide is not clear enough to allow us to determine cut-offs above or below which an individual is protected or not. In time, perhaps we will have a better understanding of the relationship between neutralizing antibodies and immunity to the virus, but until then, tests need to come with a better explanation of what they can – and cannot – tell us about our risk of contracting, or transmitting infections. How useful quantitative antibody tests are is also complicated by the intricacies of the immune response to vaccine".<sup>[36]</sup> "If a person has been tested positive for and recovered from COVID-19, becoming immune to it, he or she cannot be considered a hazard to public health and, therefore, the curtailment of his or her fundamental rights (eg, the right to freedom of movement) is not legitimate. If a person does not pose a threat to public health because he or she cannot spread the infection, then his or her right to freedom of movement should be respected, regardless of how he or she acquired that immunity. If we accept that the vaccine produces some form of immunity, it will be because we have been able to establish some test that will allow us to certify that immunity. If such a test exists, it would be logical to respect the right to freedom of movement for all persons who satisfy that test, regardless of how they have acquired that immunity. If a person is able to show clinical evidence that she meets the standard immunity requirements, on what grounds could she be denied further enjoyment of his or her right to freedom of movement? It will be necessary to differentiate, even if it seems discriminatory, between people who are immune and not immune to COVID-19

for public health reasons. So, there will be indeed be two different types of citizens till vaccines become available to large masses of people within an acceptable timeframe. However, a further pressing problem may arise: those who do not want to be vaccinated will probably form a separate group or get discriminated”.[37]

### **Immuno-diversity and the relevance of Immunological classification system**

Development of immunological classification system should be given the highest priority to identify the immunologic status of all the individuals at any time, and such classification system also looks feasible if all the variables linked to homeostasis, immunity (innate and adaptive) and medical history are meticulously diagnosed. “Diversity of immunologic fitness among people could widely range from immunocompetent to immunodeficiency. It is imperative to objectively estimate, classify and grade the immunologic diversity of the individuals both directly (Antibodies, White blood cell count) and indirectly (homeostatic factors like Temperature, pH, Blood pressure, Body composition, Blood glucose, Blood cholesterol, Hemoglobin, etc.) to further advance immunology”.[38] “The human immune system is highly variable between individuals but relatively stable over time within a given person. Human immune systems vary as a consequence of heritable and non-heritable influences, but symbiotic and pathogenic microbes and other non-heritable influences explain most of this variation. Understanding when and how such influences shape the human immune system is key for defining metrics of immunological health and understanding the risk of immune-mediated and infectious diseases. If the composition of cells and proteins that make up individual’s immune system is referred to as the individual’s ‘immunotype’, it is interesting to study whether such immunotypes are distributed as discrete groups or as a continuum. Such a global understanding of human immune

system variation could help identify individuals with outlier immunotypes and immunotypes associated with increased risk of severe infections or immune-mediated disease. The idea of personalized therapy or precision medicine stems from the realization that individual patients vary with respect to their disease mechanisms and requirements for successful treatment, and this principle should also take into account of human immune system variation (to analyze and manage immune system both during health and disease). In the more long-term perspective, understanding when and how an individual’s stable immune system state is established might help us promote the long-term immunological health for all populations through the optimization of modifiable environmental conditions”.[39] “The number of patients with immunosuppressed states is increasing. The background and characteristics of the immunosuppressed states differ between different patient groups. Vaccination of immunocompromised patients is challenging both regarding efficacy and safety. Patients who are most at risk for infectious morbidity and mortality as a result of their severely immunocompromised state are also those least likely to respond to vaccination”.[40] Seroconversion rates after covid-19 vaccination were significantly lower in immunocompromised patients, especially organ transplant recipients.[41] “Many people who are immunocompromised with severe immunosuppression are likely to remain susceptible to COVID-19 even after an additional dose. Cumulative antibody response rates after the additional dose in people who are immunocompromised typically fall some way short of the response rates observed in people who are not immunocompromised”.[42] “Healthy people can also clear a virus through their nonspecific innate immunity: this immunity is not known to be assessed, and in these people no trace of their encounter with the virus may be readily detectable. In Covid, natural infection begins in the mucous



membranes of the nasopharynx, which are an immune sanctuary, and such innate immunity at this level may be sufficient to eliminate viruses without significant intervention of adaptive immunity, thus without significant production of specific antibodies. Moreover, the infection can be fought by the cross-immunity already acquired against common cold coronaviruses. Serology (measurement of the level of specific antibodies) gives heterogeneous results depending on the individual, the time elapsed since infection, the severity of the symptoms observed at the time of infection, the reagent used and the laboratory performing the analysis. According to recent publications, the level of antibodies depends on the severity of the disease. Symptomatic adults showed three times higher antibody levels than asymptomatic adults.<sup>[43]</sup> “If the basic mechanism behind herd immunity is blocking the transmission routes that sustain a pathogen in the host population, then researchers need to know how well vaccines prevent even asymptomatic infections as well as transmission by those who do get infected. ‘That’s a totally different kind of study’, Corey says. ‘You vaccinate people and swab their nose every day, and if they become positive, do contact tracing to see if they are transmitting it’. Herd immunity is a slippery concept, but if herd immunity is too slippery, then what is the best way to convey how the pandemic ends? One key point is that the ‘end’ of the pandemic likely will not mean the end of the virus. After infections reach a pinnacle, eventually the case numbers begin to fall during a refractory period when a large proportion of the population is presumed to be immune and this would be the point when the population crosses the herd immunity threshold and there are no longer enough susceptible individuals to support long viral transmission chains— says, Lavine. But if the virus keeps evolving or immunity fades over time after infection or vaccination, then as people become vulnerable to reinfection, transmission chains will start up again and

the conditions of herd immunity would no longer be met – ‘transient herd immunity’. With so little certainty about what is required to even reach herd immunity and what that would accomplish, and how long it would last, the only thing seems clear is that the idea itself may have become something of a mirage. Researchers and public health officials might need a different way to describe an end to the pandemic”.<sup>[44]</sup> “Asymptomatic infection is a tricky and uncharted territory for infectious disease immunologists and clinicians. Our natural territory is understanding the mechanism underlying severe infection and protection against it. By contrast, relatively few studies have investigated potential differences in innate immune responses in individuals with symptomatic or asymptomatic infection. An initial question was whether some people become infected but are able to rapidly control the virus through innate immune pathways and therefore do not become ill.”<sup>[45]</sup> “On which groups of citizens should we build this herd immunity? Given the fact that young people face a mortality rate which is at least a thousand times smaller than people aged 70 years and more, there is a simple rationale to build it on these younger generations while the elders remain confined as long as this herd immunity has not been attained by the younger generations. This would be a potent demonstration of intergenerational solidarity towards the most vulnerable people in our community. But transferring the mortality risk to less vulnerable people is ethically questionable, and may not be socially desirable if society values the lives of these less vulnerable more. However, given the huge differences in mortality risk across age classes, this herd immunity should be built by deconfining the younger generations first”.<sup>[46]</sup> “Today the two arms of antigen-specific acquired and antigen-nonspecific innate immunity are best viewed as a yin-yang concept, with highly intertwined, partly overlapping, and mutually beneficial activities. Perspectives on immunology progressed from a dichotomy between

cellular-unspecific innate immunity and humoral-specific acquired immunity, toward the concept of complementary binarity”.[47] “It is high time to search noninvasive objective immunity tools to assess individual immunity status. Till time medical science is talking about the measurement of specific immunity for a specific disease. There is not much discussion on the role of general health on immunity status. It is time to explore the relationship between general health and immunity. Currently, there is no scientific tool available to measure health. It is high time to develop such tool. Researchers should work on developing such self-assessment tool with scientific evidence. Such a tool will be great help to the family physician and primary care practitioners to guide the community and build community immunity. If you are fit means your body immunity is working at an optimum level”.[48] “Individual-specific longitudinal evaluation of the overall homeostatic efficiency of healthy and unhealthy individuals on the basis of exercise performance still remains as an under-developed domain in medical profession. A single objective measure of homeostasis based on exercise tolerance will suffice to understand a person’s immunocompetence, resistance to diseases, prospective ageing trajectory, recovery from any illness, etc.”[49] “Based on physical efficiency, individuals can be categorized as Non-athlete, Borderline athlete, Average athlete and Above-average athlete. Three primary differences between unhealthy and healthy individuals are simple to understand by evaluating their exercise performance. Less

work capacity in a given time period, low resistance to fatigue and slower recovery from fatigue become the foundations of homeostatic instability and unsuccessful aging. More work capacity in a given time period, high resistance to fatigue and quicker recovery from fatigue become the foundations of homeostatic stability and successful aging”.[50] “In view of the aggravating uncertainties created by asymptomatic and symptomatic transmission of infections, an immunological classification system (preferably based on ‘Exercise Tolerance Diversity’) should be discovered as it becomes necessary to quantitatively measure the immunologic strengths of humans in all the phases of life cycle. Homeostatic apoptosis enables perfect homeostasis (pH) without unnecessary loss of cells and organ mass. Allostatic apoptosis could disturb the homeostatic stability probably leading to diseases almost equally among sedentary individuals and exercisers due to morbidity-exacerbating lifestyle behaviors. If the universal goal is to ensure only homeostatic apoptosis to function in the human body in the all the phases of the human life cycle, the medical profession as a whole along with the political machinery should shift its orientation towards salutogenesis”.[51] Thus, construction of immunological classification systems should take into account of multiple variables (especially measurable variables using reliable diagnostic methods and instruments) to perform in-depth explorations to get versatile advantages in public health (Table 1 and Table 2).

**Table 1:** Prospective immunological classification system ranging from ‘Immunocompetent’ to ‘Severely Immunocompromised’. Further justifications and developments should be attempted through affordable and reliable immunological tests specific to the infectious diseases. Grade 3 population may not respond well to vaccinations. Grade 1 and Grade 2 population can resist or recover from infections without vaccinations. Hence, is there a possibility that Grade 1 and Grade 2 population could naturally contribute to ‘herd immunity’ even without the support of vaccines?

| Grade | Immunological characteristics of the individual   |
|-------|---|
| 1     | Asymptomatic. No 'infection-specific' antibodies formed because the pathogen could not harm the healthy individual. Highly efficient innate immunity associated with exemplary homeostatic competence. Should not be confused that they are immunocompromised because 'infection-specific' antibodies are absent in their body.   |
| 2     | Mild infection or risk of mild infection. Recovery from the mild infection is quicker even without pharmaceutical assistance. 'Infection-specific' Antibodies formed naturally and adequately. Highly efficient adaptive immunity. Innate immunity can be easily strengthened through lifestyle modifications after which the individual could acquire Grade 1 immunocompetence.  |
| 3     | Severe infection or risk of severe infection. Recovery from the severe infection is slower or even impossible. Inadequate or no 'infection-specific' antibodies formed despite multiple doses of vaccinations. Absolute inefficiency of Innate and Adaptive immunity due to multiple impairments in homeostasis associated with co-morbidities, polypharmacy, iatrogenic damages. |

**Table 2:** The status of innate and adaptive immunity (including infection-specific antibodies) of the symptomatic and asymptomatic individuals that belong to any of these four groups should be thoroughly investigated using at least one affordable diagnostic procedure.

|  |  |
|--|--|
| Group 1<br>NOT INFECTED, UNVACCINATED<br>Asymptomatic?<br>Symptomatic? | Group 2<br>NOT INFECTED, VACCINATED<br>Asymptomatic?<br>Symptomatic? |
| Group 3<br>INFECTED, UNVACCINATED<br>Asymptomatic?<br>Symptomatic?     | Group 4<br>INFECTED, VACCINATED<br>Asymptomatic?<br>Symptomatic?     |

### Conjoint citizen participation platform for Pro-vaxxers and Vaccine Deniers

Pro-vaxxers view an infectious disease as capable of killing healthy individuals too, and vaccine deniers view vaccines as capable of killing healthy individuals too, thus, both stand at opposite extremes with multiple conflicting perspectives. Both these groups should work together (health activism, transdisciplinarity, citizen participation) and question the fundamental doubts and problems in immunology and vaccinology, till satisfactory scientific clarity develops to benefit them equally. To objectively measure the immunity, which diagnosis is considered as must before and after availing any medical technology to enhance the immune status? Is there a classification system to categorize humans based on the magnitude of their immune status? How to objectively measure the strength of the natural immunity and adaptive immunity? What is the unit of measure of immunity? What level of natural immunity and adaptive immunity is considered "immunocompetent"? What level of natural immunity and adaptive immunity is considered "immunodeficient"? How to differentiate the vaccinated and

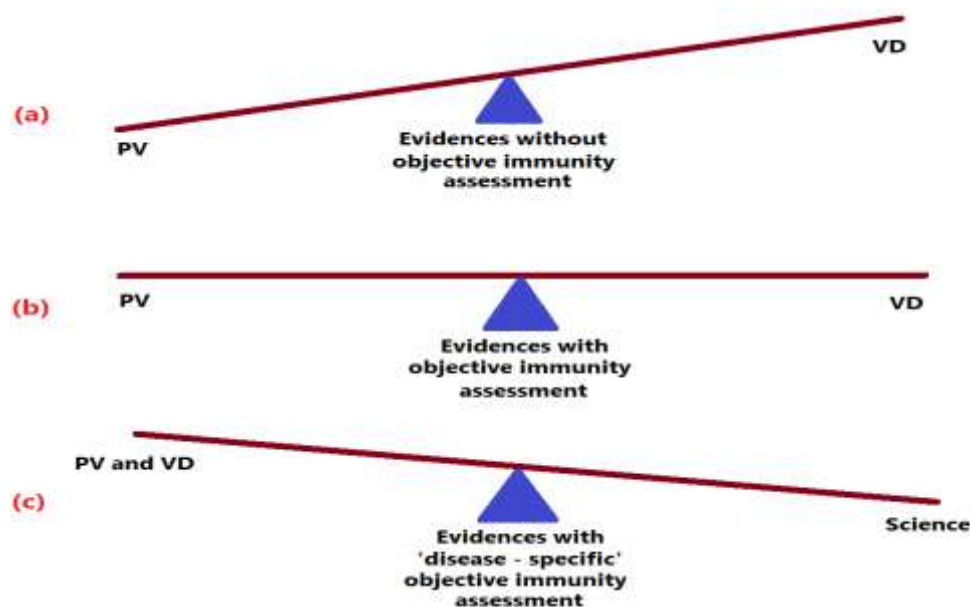
unvaccinated individuals based on the proofs of strengths of their natural and adaptive immunity? Is it possible to identify the individuals who are vaccinated and unvaccinated individuals solely based on their immune status (if the vaccination status is not revealed)? What are the mechanisms available in the human body in the absence of infection-specific antibodies to safeguard oneself from the infections? What level of immunocompetence exempts an individual from vaccinations? To what level an immunodeficient individual should raise his/her immune status? Is it possible for an immunodeficient individual to develop immunity through vaccinations in the presence of his/her co-morbidities? How to objectively measure the immunological memory? Is there an equal chance of transmission of infection from immunodeficient individuals to immunocompetent individuals and vice versa? If a diagnosis (like PCR test) shows negative for an asymptomatic unvaccinated individual, what would be his/her immune strength? If a diagnosis (like PCR test) shows negative for asymptomatic unvaccinated individuals and asymptomatic vaccinated individuals, will there be

corresponding microorganisms in their body too? How to objectively prove the similarities or dissimilarities of the actions of vaccines in the body of healthy and unhealthy individuals? Immunological strength to defend an infection should be equal for all regardless of the age? If every human being should possess similar immunological strength to defend an infection, is it achievable? Which non-immunological test is the best alternative to understand an individual's immune strength in the absence of an immunological test? What is the contribution of innate immunity, natural antibodies and 'expanded trained immunity' to herd immunity?

"Citizen participation refers to citizen involvement in public decision making. Arguments for citizen participation variously emphasize benefits to individuals, communities, organizations, and the society, including increased knowledge, authority, power, and problem-solving ability. Some citizens, particularly the better educated and wealthier, generally have greater ability to participate than others. There are examples of citizen participation that has accomplished its purposes and solved problems, but empirical data are sketchy, and no systematic evaluation of citizen participation is possible at this time".<sup>[52]</sup> "Transdisciplinarity is generally defined by the inclusion of non-academic stakeholders in the process of knowledge production. Transdisciplinarity is a promising notion, but its ability to efficiently address the world's most pressing issues still requires improvement".<sup>[53]</sup> Transdisciplinarity today is characterized by its focus on "wicked problems" that need creative solutions, its reliance on stakeholder involvement, and engaged, socially responsible science.<sup>[54]</sup> "The key difference between participation and engagement is that citizen engagement requires an active, intentional dialogue between citizens and public decision makers whereas citizen participation can come from citizens only but both have same goal: Improving public service deliveries and

policy projects. Citizen engagement is a top-down initiative (formal process) and is instated by a governmental body. By contrast, citizen participation stems from the citizens themselves, thus a bottom-up initiative (informal process). Main challenges of citizen engagement are identifying what is important for citizens, convincing them to engage, and offering them all the necessary information to make well-founded decisions. Main challenges of citizen participation are mobilizing enough citizen support and targeting larger policy domains that require higher levels of inclusiveness and awareness".<sup>[55]</sup> "Informing citizens of their rights, responsibilities, and options can be the most important first step toward legitimate citizen participation. However, too frequently the emphasis is placed on a one-way flow of information – from officials to citizens – with no channel provided for feedback and no power for negotiation. Under these conditions, particularly when information is provided at a late stage in planning, people have little opportunity to influence the program designed 'for their benefit'. When powerholders restrict the input of citizens' ideas solely at the consultation level, the participation remains just a window-dressing ritual and people are primarily perceived as statistical abstractions".<sup>[29]</sup> Pro-vaxxers and vaccine deniers should conjointly demand affordable and reliable disease-specific objective immunity assessments to understand their immunological strengths in order to discover the exact truths about innate immunity, adaptive immunity, herd immunity and the efficacy of vaccines. In the presence of such disease-specific immunity assessments, both pro-vaxxers and vaccine deniers might be proved incorrect in many of their long-standing beliefs and standpoints but, in the current scenario, pro-vaxxers are enjoying reputation and vaccine deniers are facing oppression (Figure 1).

**Figure 1:** PV = Pro-vaxxers, VD = Vaccine deniers. (a) In the absence of evidences without objective immunity assessment (as in the current scenario), PV enjoy the benefits of the citizen engagement (being a part of top-down initiative of government) whilst VD faces oppression despite their citizen participation (being a part of bottom-up initiative of limited number of people in the community). (b) In the presence of evidences with objective immunity assessment, a win-win situation is possible for both PV and VD. (c) In the presence of evidences with ‘disease-specific’ objective immunity assessment, both PV and VD would be probably proved incorrect in many of their long-standing beliefs and standpoints whilst science becomes the ultimate saviour or winner.



## DISCUSSION

‘Herd immunity’ has been made labyrinthine by the science of immunology and vaccinology, absolutely ignoring the principles of homeostasis, eventually aggravating the miseries caused by stringent public health mandates. “Waning immunity and new variants mean that booster doses are increasingly likely to be regularly required, meaning that what constitutes being ‘fully vaccinated’ will be constantly shifting target. Daily rapid antigen testing is a viable alternative to a vaccine mandate that is non-coercive and fair. Given that vaccinated workers still pose a risk to patients and the issues associated with mandates, it is more equitable to require all health and social care workers, both vaccinated and unvaccinated, to undertake daily rapid antigen testing”.<sup>[56]</sup> “Many private-sector employers want their employees to be vaccinated against COVID-19 to prevent the spread of the virus,

reassure employees and customers that the premises are safe, avoid potential liability for transmission of the virus, and advance public health. A sound public health strategy for workplace-based vaccination should be predicated on prevention and persuasion grounded in science before resorting to compulsion”.<sup>[57]</sup> “Valid consent is often described as being morally transformative in the sense of enabling a subject to waive his or her right against the action in question. By providing valid consent, a research subject waives his or her right to bodily intrusion and permits the investigator to insert a needle in his arm for research purposes. To achieve this moral transformation, the individual must understand the action in question and must voluntarily agree to it. Yet, the prevailing emphasis on respect for individuals’ right and valid consent notwithstanding, some biomedical research, and a good deal of social and behavioral research, proceeds

without valid consent”.<sup>[58]</sup> “Unvaccinated individuals will have to wait for the phasing out of the pandemic to return back their prior freedoms, for the sake of protecting society as a whole. Those who wish to be unvaccinated may freely make this choice, but bearing in mind that we all coexist in an organized society where it appears that it will continue to put at risk due to the emergence of various dangerous and infectious viruses and pandemics of various types and mutations. Refusing to become vaccinated which essentially equals refusal to fulfil the duty of social solidarity, may entail specific legal consequences”.<sup>[59]</sup> Although the Indian Government has a constitutional obligation under Article 47 of the Indian constitution to maintain and improve public health, it is of quintessence importance to comprehend that compulsory vaccination would only lead to social disorder and disunity, thereby leading to violation of Article 38 of the Indian constitution.<sup>[60]</sup> “In an effort to achieve total vaccine coverage, the government ends up forcing the vaccination without taking into account the objections raised by the populace. This leads to a reduction in the government’s accountability when faced with issues of adverse events following immunization (AEFI). Thus, while it is important that the government should provide for a better AEFI surveillance system and a vaccination data bank, stakeholder engagement has to be given due priority, in order to ensure that the programme functions with transparency and credibility”.<sup>[61]</sup> Implementing immunization programme cannot be segregated from the ‘knowledge-base’ in immunology. Globally, the practice of immunology has slowly become part of vaccinology, however, in India there is still limited focus on training in vaccinology and immunology.<sup>[62]</sup> Homeostasis is an underappreciated, far too often ignored central organizing principle of physiology and disruption of homeostatic mechanisms is what leads to disease, and effective therapy must be directed toward re-establishing these homeostatic

conditions.<sup>[63]</sup> “Science is the understanding of the mechanisms that govern our world, from the fundamental laws of the universe to the biological processes of the simplest living organisms to the complexity of the human body. Pseudoscience is a collection of beliefs or practices mistakenly regarded as being based on scientific method, characterized by unprovable claims, lack of openness to evaluation by other experts, absence of systematic practices when developing theories. Evidence is the available body of facts or information indicating whether a belief or proposition is true or valid. Post truth is a situation in which people are more likely to accept an argument based on their emotions and beliefs, rather than one based on facts, thus objective facts become less influential in shaping public opinion”.<sup>[64]</sup> “Science is the systematic description of phenomena. The term ‘phenomena’ with its implication of reproducibility and of common experience, separates the physical science from the arts, and from some aspects of psychical. The term ‘systematic’ serves to distinguish scientific statement based on empirical substantiation from merely causal expression of experience. Science is shown to be compounded of two types of thought, induction and deduction. Although the two methods of thought may be readily distinguished, they never occur separately in science. An inductive generalization always involves deduction in its expression”.<sup>[65]</sup> It is also high time to verify the science of immunology and vaccinology using the foundational knowledge of homeostasis because, when viewed from the principles of homeostasis, the ‘maintenance of health, and resistance to diseases’ in human body are always an integrated effort from all the systems. “Essentially all organs and tissues of the body perform functions that help maintain nearly constant conditions in the internal environment. Physiologists call this high level of internal bodily control homeostasis. Each cell benefits from homeostasis, and in turn, each cell contributes its share toward the maintenance

of homeostasis. This reciprocal interplay provides continuous automaticity of the body until one or more functional systems lose their ability to contribute their share of function. When this happens, all the cells of the body suffer. In disease states, functional balances are often seriously disturbed and homeostasis is impaired. Extreme dysfunction leads to death; moderate dysfunction leads to sickness. Thus, when even as single disturbance reaches a limit, the whole body can no longer live.”<sup>[66]</sup>

## **CONCLUSION**

‘Disease-free’ and ‘non-pharmaceutical’ life is an ultimate fitness competence, reputation, and freedom. Anticipating equal health benefits for all by introducing similar pharmaceutical product(s) in the body of all under coercion without regarding and rectifying individual-specific health status, disease status, socioeconomic conditions and lifestyle is a highly risky deviation from the ethics of medical science. Medicines and vaccines can never become common/applicable to all or can never be regularly consumed as fruits, vegetables, grains and our traditional foods. Politicians, Medical professionals, Officials and Professionals in all sectors, District magistrates, Police department, Armed forces, Employers, Education sector, Banks, Celebrities, Religious leaders, Jurisdiction, and vast majority of public, altogether develop a gigantic pro-vaxxer team. The number of people who belong to vaccine deniers’ team may be very limited but they might have genuine skepticisms and evidences to be valued. By readily complying to the vaccine mandates, pro-vaxxers enjoy powers of citizen engagement whilst vaccine deniers’ citizen participation is being viewed as antagonistic to the public health and welfare of the nation. If herd immunity must be accomplished, voluntarily accepting the recommended doses of vaccinations alone do not justify but every individual must honestly prove that they possess adequate and robust innate and adaptive immunity through objective

immunoassays. Developing an accredited immunological classification system to classify people based on objective immunological testing is not an act of discrimination because the medical system has been adapting several such classifications to differentiate normal from abnormal to understand health status and disease severity based on weight (BMI), blood pressure, heart rate, blood glucose, blood cholesterol, stages of cancer growth, functional ability etc., If disease-specific immunological tests are unavailable or cannot be discovered, tests based on homeostasis could be the best alternative but the relationship between homeostasis and immunity is surprisingly neither well established nor widely discussed, thus, immunity may be often seen as an ‘isolated’, ‘vaccine-dependent department’ in the human body. Absence of affordable objective immunoassays and immunological classification system to identify the immunocompetent and immunocompromised is a core problem that is still not noticed and questioned by pro-vaxxers and vaccine deniers. Microorganisms are invisible and achieving ‘herd immunity’ is the only target to eradicate any infectious disease but immunological status of the individuals are immeasurable – Science can never evolve and protect us through this way!! Science strives towards precision not vagueness. Health activism of pro-vaxxers and vaccine deniers has no effective basis towards scientific precision. Both pro-vaxxers and vaccine deniers should be labeled as ‘defeated’ in their meaningless tug-of-war for being ignorant about “objective immunoassays”. Even a single individual could contribute to massive scientific transformations through his or her discoveries or even through critically questioning established scientific practices, and this is how naturally science evolves as a marvelous product of intellectual humility.

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