INA-RESPOND

INDONESIA RESEARCH PARTNERSHIP ON INFECTIOUS DISEASE

KEMENTERIAN KESEHATAN REPUBLIK INDONESIA

NEWSLETTER

October 2023

Comic Corner

"Charting the Path Forward in Global Health: Nkengasong's Five P's of Pandemic Preparedness"

Sports & Lifestyle

Why Whey?

Science Corner

Cross-Reactivity in The Immune System: Sin or Virtue?

Free Writing

Demystifying Mental Health: Understanding the Spectrum, Causes, and Stigma

HEALTH POLICY AGENCY

MINISTRY OF HEALTH REPUBLIC OF INDONESIA

2023

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content

October 2023 Edition | issue #121

FEATURES

INA-RESPOND Newsletter

InVITE & PROACTIVE Study Updates

By: Eka Windari R., I Wayan Adi Pranata, Lois E. Bang, Melinda Setiyaningrum, Nur Latifa Hanum, Retna Mustika Indah, Restu Amalia, Riza Danu Dewantara

InVITE

As of October 6, 2023, a total of 700 participants were enrolled in the study. Among these participants, 512 individuals (73.14%) have completed their participation, while 188 individuals (26.86%) are currently still engaged in the study. The research is being carried out at three separate locations, each of which is presently prioritizing visits 4 and 5. Table 1 presents a detailed breakdown of the visits per site.

The study had certain difficulties pertaining to participant retention during its duration. Among the cohort of 512 participants that fulfilled their involvement, a majority of 450 individuals (equivalent to 64.29%) successfully concluded the study. A smaller subset of 45 participants (accounting for 6.43%) chose to withdraw from the study due to personal decisions, personal reasons, or loss of interest. Furthermore, it should be noted that a small subset of participants failed to adhere to the recommended immunization schedule within the designated 12-month timeframe following enrollment. Consequently, this resulted in the exclusion of three individuals, accounting for a mere 0.43% of the total patients involved in the study. Two participants, accounting for 0.29% of the total sample, were excluded from further participation in the study based on considerations of their best interest. Additionally, one person, representing 0.14% of the sample, demonstrated non-compliance with the prescribed study procedures. Regrettably, the study experienced a mortality rate of 0.14%, resulting in the unfortunate demise of one person. Additionally, 10 subjects, accounting for 1.43% of the total, discontinued their participation due to various other causes.

Furthermore, the study has been monitoring symptomatic visits among participants. Table 2 provides details of these visits as of Oct 6, 2023. It is important to clarify that while some participants have reported COVID-19 symptoms, this does not necessarily indicate that they have contracted the disease.

The shipment of specimens using the credo box from Site 02 (TC Hillers Hospital) and Site 03 (dr. Ansari Saleh Hospital) has been completed.

Site	Symptomatic Visit		
	# of visit	Positive	Negative
01	104	61	43
02	14	6	8
03	2	1	1
Total	120	68	52

Table 2. Symptomatic Visit Details per Oct 6, 2023

Site	Screening / Visit 1	Enrollment Failure	Enrolled	Ongoing	Add. Visit 1	Visit 2	Add. Visit 2	Add. Visit 3	Visit 3	Agree Ext.	Not Agree Ext.	Ext. Visit 4	Ext. Visit 5
01	345	2	343	104	88	326	314	306	315	285	30	277	178
02	228	1	227	32	97	214	191	188	195	151	44	151	117
03	130	0	130	52		130			129	95	35	95	43
Total	703	3	700	188	185	670	505	494	639	531	109	523	338

Table 1. Details of Visits per site per Oct 6, 2023

INA104

In connection with the subject visit activities that were completed at all sites, on October 4-6, 2023, site 680 completed the study close-out visit activities, making it the last site to complete a series of PROACTIVE study site closure processes. Information about site close-out visit activities until Oct 2023 can be seen in Table 1.

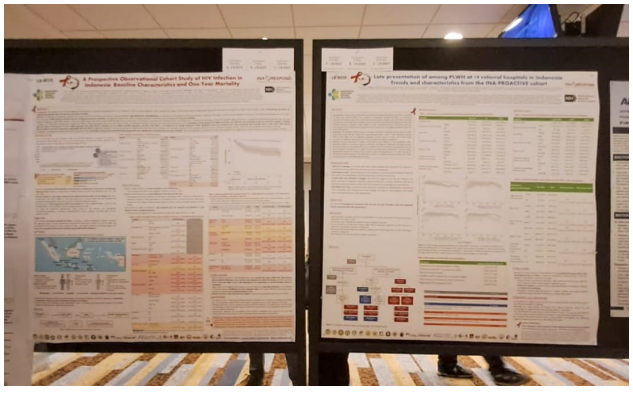
Following the site close-out activities, the site will then complete pending items and the document archiving process, which is expected to be completed by the end of October 2023. On the other hand, the data management team is currently conducting general cleaning related to data that has been entered post-quality assurance across all sites. the Data Management team targets the general data cleaning to complete at the end of October.

In parallel, the study team is also in the process of preparing a final study report for submission to both the central and local ethics commissions, as well as preparing a study manuscript. The final report of this study is being prepared on a provisional basis as an attachment for the purpose of notifying the Central Ethics Committee (FK-UI RSCM Ethics Committee) and the Director/ Education and Research department of the site (if necessary) of the site closure this year, while the final research report with data results will be submitted to both central and local Ethics Committee.

Regarding manuscript preparation, there are three main manuscripts being developed by the secretariat, study core team, NIAID team, and will also involve the PI and Co-PI from each site. The first manuscript, concerning baseline characteristics and predictors for all cases of death within one year (Baseline Characteristics and One-Year Mortality), has been distributed/circulated to all teams targeted for publication in the Journal of the International AIDS Society.

The other two main manuscript concepts are the initial analysis of all cases of death within three years (Early Analysis of Three-Years Mortality in People Living with HIV) and the concept of virological, immunological, disease, and clinical progression (Clinical, Immunological, and Virological Responses of HIV-infected People with Anti-Retroviral Therapy in Nationwide Indonesian Cohort). These two concepts are currently being developed, along with determining the writing team and their specific responsibilities in the writing process. The composition of the writing team for each concept was determined by considering the concept plan previously submitted, as well as the enthusiasm from the study sites.

In addition, there are three main ideas for additional manuscripts that discuss late presenters, resistance-phylogenetic analysis, and analysis of pediatric subjects. Apart from the Baseline Characteristics and One-Year Mortality manuscripts, the late presenter manuscript takes priority in the process. Previously, abstracts for these two concepts had been submitted to The American Society of Tropical Medicine and Hygiene (ASTMH) and were accepted, with presentations in poster form at the ASTMH Annual Meeting at the Hyatt Regency Chicago, Chicago, IL, USA, held on October 18-22, 2023. For other concepts, the concept plan will be discussed further with NIAID for refinement once the description of the writing aspects has been agreed upon by the writing team.



Poster presentation at ASTMH Annual Meeting 2023

Site	Site Name	First Patient First Enrolled	Last Patient Last Enrolled	Schedule SCV Ver 17 Feb 2023	Actual SCV
510	RS Hasan Sadikin, Bandung	Feb-2019	Dec-2019	Jun-23	15-16 Jun 2023
520	RSUP Sanglah, Denpasar	Sep-2019	Jun-2020	Sep-23	23-24 Aug 2023
530	RS Cipto Mangunkusumo, Jakarta	May-2018	Aug-2019	Jul-23	31 Jul – 1 Aug 2023
540	RS Sulianti Saroso, Jakarta	Feb-2019	Dec-2019	Sep-23	14 Sep 2023
550	RS Wahidin Sudirohusodo, Makassar	Mar-2018	Aug-2019	May-23	24-15 May 2023
560	RS Kariadi, Semarang	Aug-2018	Aug-2019	Mar-23	30-31 Mar 2023
570	RS Soetomo, Surabaya	Apr-2018	Aug-2019	Apr-23	13-14 Apr 2023
580	RS Sardjito, Yogyakarta	Sep-2018	Sep-2019	Apr-23	20-21 Apr 2023
590	RS Persahabatan, Jakarta	Jul-2018	Aug-2019	Jun-23	14-15 Jun 2023
600	RS Adam Malik, Medan	Mar-2018	Aug-2019	Jun-23	21-23 Jun 2023
610	RSU Kab Tangerang, Banten	Jan-2018	Aug-2019	Mar-23	08-09 Mar 2023
630	RSUD M. Ansari Saleh, Banjarmasin	Jul-2018	Aug-2019	Apr-23	05-06 Apr 2023
640	RS St. Carolus, Jakarta	Aug-2018	Sep-2019	Jun-23	05-06 Jun 2023
650	RS Budi Kemuliaan, Batam	Aug-2018	Aug-2019	Jun-23	07-08 Jun 2023
660	RSU Wahab Sjahranie, Samarinda	Aug-2018	Sep-2019	Jul-23	12-14 Jul 2023
670	RSUD dr. Zainoel Abidin Banda Aceh	May-2019	Dec-2019	Jul-23	12-13 Jul 2023
680	RSUD dr. Soedarso, Pontianak	Jul-2019	Dec-2019	Sep-23	04-06 Oct 2023
690	Abepura	Jul-2019	Jun-2020	Jul-23	1-2 Aug 2023
700	RSUD Dr. TC Hillers Maumere	May-2019	Jun-2020	Aug-23	9-10 Aug 2023

Table 1: Study Activities - Close-out Visit (PROACTIVE Study)

INA-RESPOND Newsletter

SCIENCE CORNER

CROSS-REACTIVITY IN THE IMMUNE SYSTEM: SIN OR VIRTUE?

By: Adhella Menur

How the adaptive immune response memorized the pathogen attack

The human immune system resembles a top-tier orchestra, capable of playing anything from the simple "Twinkle-Twinkle Little Star" to the challenging Beethoven's "Symphony No. 9, also known as The Choral Symphony." Each instrument plays its role harmoniously to deliver an optimal performance. Even a similar symphony played by this orchestra deserves a standing ovation.

In the human immune system, every immune cell plays a significant role in collectively defending against various pathogens. This complex mechanism can be simplified into having two "lines of defense": innate immunity and adaptive immunity. Innate immunity serves as the first line of defense against pathogens, consisting of four types of defensive barriers: anatomical (skin and mucous membranes), physiological (temperature, low pH, and chemical mediators), endocytic and phagocytic, and inflammatory responses. It provides immediate, non-specific defense responses, involving cells of both hematopoietic and non-

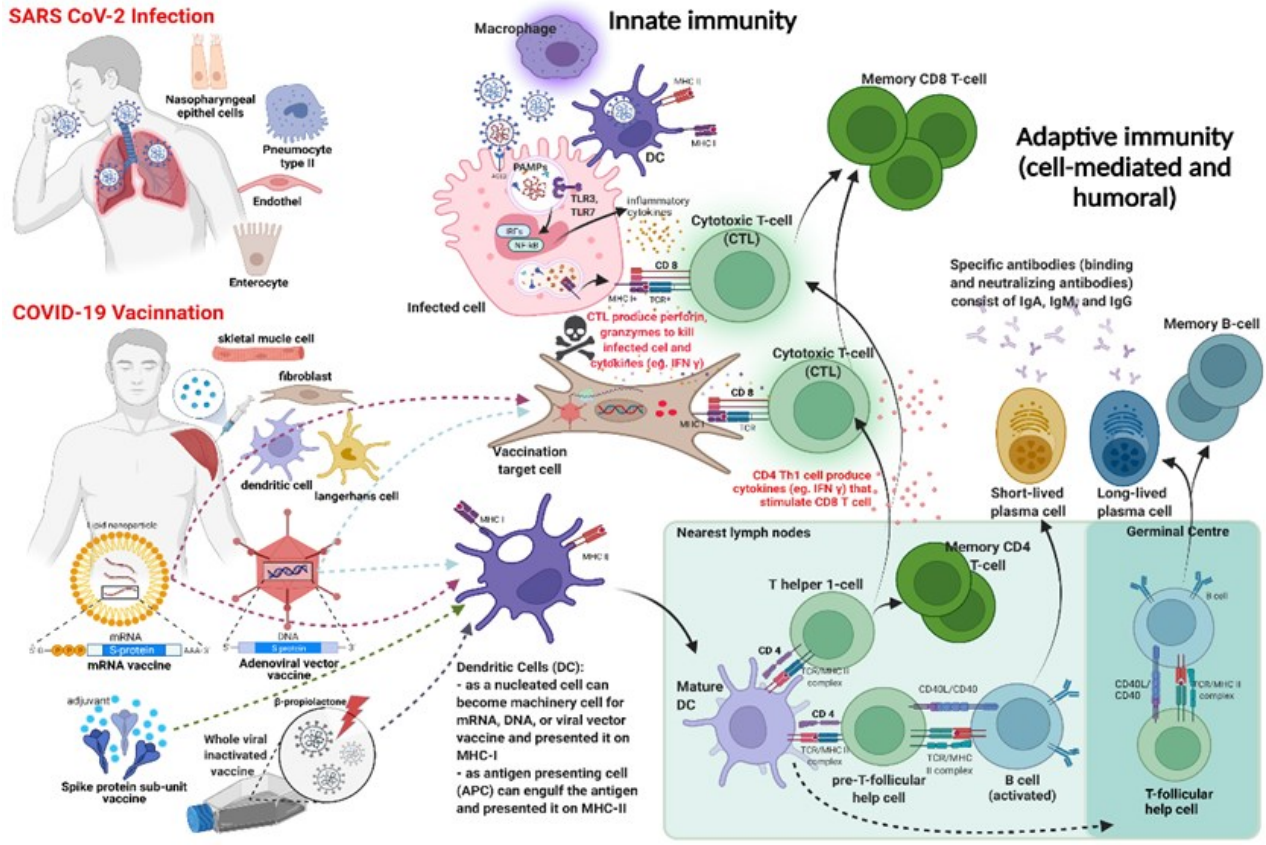


Figure 1. How infection and vaccine generate immune responses (SARS-CoV-2 and COVID-19 vaccines as examples). Inspired by Azkur et al, 2020, doi: 10.1111/all.14364 and Teijaro et al, 2021, doi: 10.1038/s41577-021-00526-x. Created by Biorender.com.

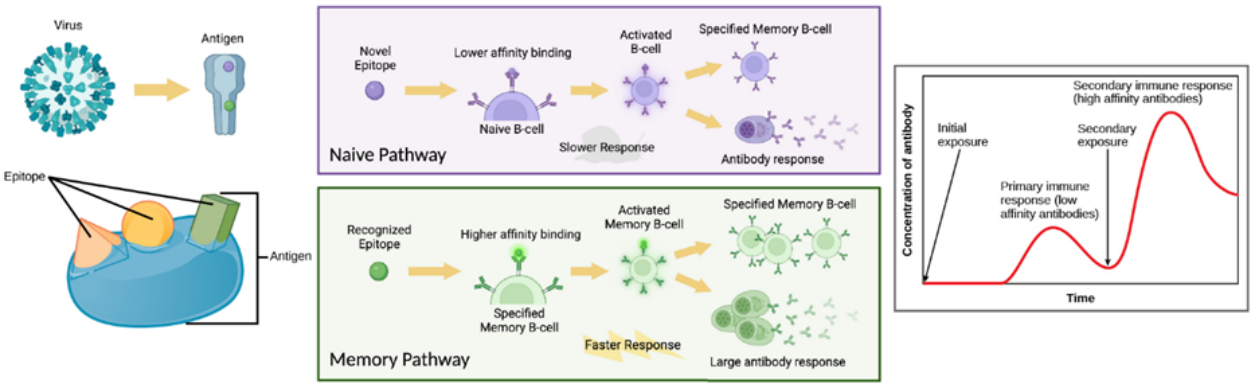


Figure 2. The benefit of memory B-cell responses when re-encounter the same pathogen. Adapted from https://opentextbc.ca/biology/chapter/23-2-adaptive-immune-response/ and King SM et al, 2023, https://doi.org/10.3390/pathogens12020169.

hematopoietic origins, relying on pattern recognition receptors (PRRs) to detect pathogen-associated molecular patterns (PAMPs). Hematopoietic cells involved in innate immune responses include phagocytes (macrophages and neutrophils), eosinophils, basophils, dendritic cells, mast cells, natural killer (NK) cells, and NK T-cells. Upon encountering pathogens, innate immune cells rapidly migrate to infection sites and promote inflammation by producing cytokines and chemokines for clearance. Phagocytes engulf pathogens and activate the adaptive immune response by mobilizing and activating antigen-presenting cells (APCs).

Subsequently, the innate immune system aids the action of the adaptive immune system, mainly when innate immunity is ineffective in eliminating pathogens. The adaptive immune system is based on the clonal selection of lymphocytes with antigen receptors: effector T-cells (cytotoxic T-cells and helper T-cells) which are the cornerstone of cell-mediated immunity and B-cells, which involve in humoral-mediated immunity via differentiation into plasma cells to produce antibodies. T and-B cells are activated when they recognize small components of antigens, called epitopes, presented by APCs. Then, they develop a special feature of adaptive immunity, immunologic memory, to record and store their experiences with various pathogens. After the activated T-cells undergo expansion and contraction and initiate the memory pool, 90-95% undergo apoptosis, and the remaining 5-10% differentiate into memory T-cells. Then, memory T-cells form central memory T-cells (Tcm), effector memory T-cells (Tem), tissue-resident memory T-cells (Trm), regulatory T-cells (mTreg), and stem memory T-cells (Tscm). They circulate in the blood and persist in secondary lymphoid organs, like the spleen and lymph nodes. Memory B-cells can be formed in two T-cell-dependent mechanisms: they differentiate into short-lived plasma cells, and in the second, they are formed and differentiated in dependent or independent germinal centers (GCs) of peripheral lymphoid organs. They reside mainly in secondary lymphoid organs and undergo affinity maturation, where their antibodies acquire increased specificity and affinity for the particular pathogen. This enables the immune system to mount efficient and swift responses when re-encounters the same or similar pathogens. Vaccination relies on the principle that introducing known antigens pathogens triggers a primary immune response. While the vaccinee may not experience this response as an illness, it still confers immune memory.

Cross-reactivity in the immune system: The Sin

In our daily lives, we encounter various pathogens and survive thanks to the remarkable features of the adaptive immune system, which recognizes and memorizes diverse antigens, thus generating specific immunities. However, the picture becomes incomplete when we consider cross-reactivity in the immune system. Cross-reactivity is expected in both T and B-cells due to the presence of many overlapping epitopes on antigen surfaces and the limited diversity of unique human B-cell receptor (BCR) and T-cell receptor (TCR) clonotypes needed to maintain immunity against various pathogens. Cross-reactivity occurs when two distinct epitopes share structural similarities and are recognized by immune memory cells. This phenomenon has significant consequences for both hosts and pathogens in terms of host health, antigenic variation, and epidemiological dynamics. It can provide cross-protection, preventing immune escape and aiding vaccine strategies. However, it can also have detrimental effects by inducing or amplifying disease pathogenesis and immunopathology. The question remains: Is cross-reactivity a strategy to combat pathogens across antigenic space, or is it an unintended consequence of the immune system's work in the vast ocean of antigenic variation—sin or virtue?

When discussing cross-reactivity as a sin, we encounter the term "original antigenic sin" (OAS). This term was proposed by Thomas Francis Jr. in 1960, referring to the original sin committed by Adam and Eve in the Bible. The original sin is a Christian view that arose from Adam and Eve's transgression in Eden, the sin of disobedience in eating the forbidden fruit from the tree of the knowledge of good and evil. The sin is then imprinted and is passed on to all future generations. In Francis Jr.'s observation, he noticed that influ-

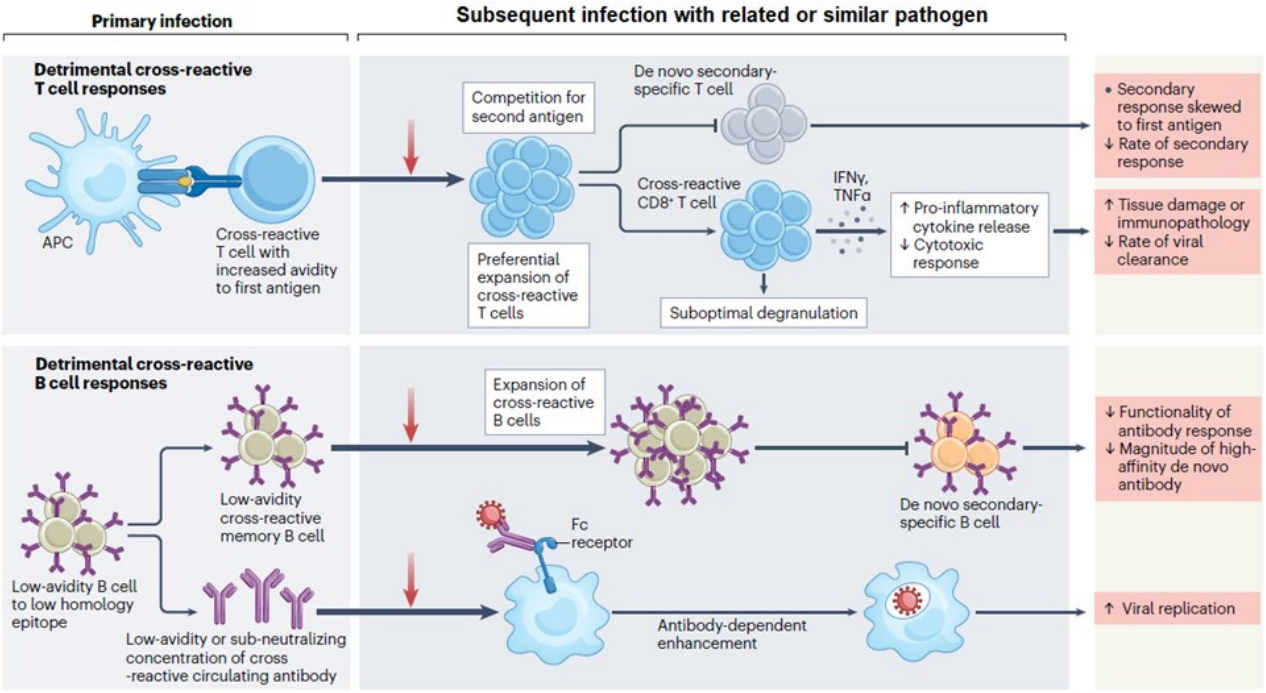


Figure 3. Cross-reactivity in the immune system: the sin. Adapted from Murray SM et al, 2023, https://doi.org/10.1038/s41577-022-00809-x.

enza antibody titers, as determined in the hemagglutination inhibition (HI) assay, were highest against those influenza strains to which specific age cohorts had first been exposed. For example, people infected with H1N1 influenza viruses during childhood (and thus imprinted with that set of epitopes) were protected later in life against infections with a related virus such as H5N1 but not infections with more distantly related H3N2. The basis for the original antigenic sin thus is imprinting: the phenomenon where the first exposure to an antigen shapes the immune response to subsequent exposures to related antigens that have a mixture of shared previously encountered and new epitopes.

The mechanism of OAS occurs when the body is re-exposed to a slightly evolved or different pathogen during a subsequent exposure but has similar epitopes from the first exposure. Still, the immune memory cells process it based on their memory storage with a focus on the imprinted antigen. As a result of the cross-reactivity, the immune system is thus able to respond to the intrusion more robustly and quickly. However, the problem arises when the new antigen is sufficiently different from the imprinted antigen, and the response to the new antigen is not quite precise, leading to a less effective response and possibly failure to clear the pathogen. In such a scenario, not only can the memory response be ineffective, but it can also hinder naïve activated immune cells from differentiating and neutralizing in responding to new epitopes.

The detrimental impact of cross-reactivity in the immune system is when the response toward the original or primary antigen by immune memory cells dominates and disrupts the production of high-avidity de novo immune cell responses. Cross-reactive T-cells may bind with lower affinity to epitopes from the subsequent pathogen compared with the first. Low-affinity epitope binding by cross-reactive CD8+ T cells may lead to immunopathology and reduce viral clearance. Low-avidity cross-reactive antibodies or low levels of high-avidity cross-reactive antibodies that cannot neutralize a subsequent pathogen may even aid the pathogen entry into cells through Fc-receptor -mediated endocytosis, known as antibody-dependent enhancement (ADE).

The OAS resulting in ADE phenomenon is well recognized in the secondary dengue virus (DENV) infection with different serotypes. Antigen-specific antibodies provide long-lasting protection against re-infection with the same DENV serotype but are not protecting enough against other serotypes. In that case, previous DENV serotype antibodies occupy most of the immune response due to immunological memory, thus preventing the development of a new response to different serotypes. Unable to neutralize the virus, the cross-reactive antibodies facilitate viral uptake to cells and enhance viral replication associated with severe DENV infection. Due to its high similarity with DENV, it is also probable that in previously DENV-infected individuals, Zika virus (ZIKV) infection will trigger the production of non-neutralizing antibodies or ineffective T-cell responses. OAS also had been the cause of a significant setback for the first Respiratory Syncytial Virus (RSV) vaccine development in 1960. When the vaccine was administered to RSV-naive newborns who later became naturally infected with RSV, a high proportion had severe respiratory disease, with fatal outcomes in some cases. Another example of OAS is that pre-existing immune responses to other microorganisms might have skewed anti-

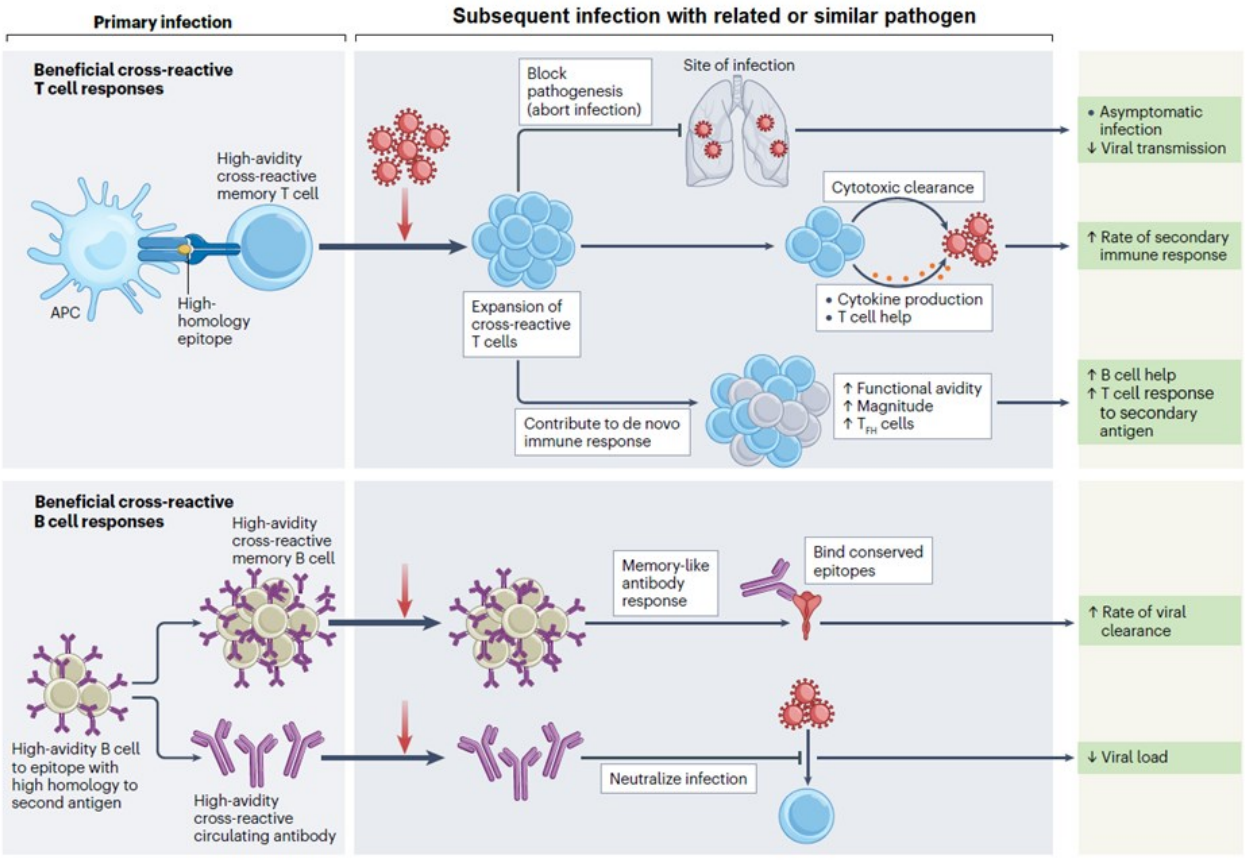


Figure 4. Cross-reactivity in the immune system: the virtue. Adapted from Murray SM et al, 2023, https://doi.org/10.1038/s41577-022-00809-x.

Plasmodium-specific T-cell repertoire to a non-specific and non-protective response against malaria.

Cross-reactivity in the immune system: The Virtue

In reality, cross-reactivity in the immune system has two sides: it can be detrimental when the response to a non-protective epitope dominates, as explained earlier, or it can be desirable when the response to shared epitopes results in successful neutralization. Under certain circumstances, cross-reactivity in the immune system can simultaneously protect the host against a diverse range of pathogens. Beneficial cross-reactive T-cells can be generated through the priming of T-cells by high-homology epitopes. These T-cells can then cross-react with high avidity during a subsequent infection with a related or similar pathogen, potentially aborting the infection or expediting pathogen clearance by forming a 'secondary-like' memory immune response with an increased magnitude of B-cell and T-cell responses. Beneficial cross-reactive memory B-cells and antibodies can be generated against epitopes with high similarity between a primary and a new subsequent infection. Cross-reactive B cells specific to highly conserved epitopes may produce an expedited and highly functional memory-like response to heterologous infection, including the production of cross-neutralizing antibodies.

The most famous example of the virtue of cross-reactivity is the discovery by Edward Jenner in 1796 that inoculation with cowpox protected individuals from the related but deadly smallpox virus

Disease target	Vaccine	Vaccine content	Cross-reactivity/protection
Tuberculosis	BCG	*Mycobacterium bovis*	*M. leprae* (leprosy)
Invasive pneumococcal disease (IPD)	PCV-7	4, 6B, 9V, 14, 18C, 19F, 23F	6A
	PhiD-CV	As PCV-7 plus 1, 5, 7F	6A; 19A
	PPSV-23	As PHiD-CV plus 2, 3, 8, 9N, 10A, 11A, 12F, 15B, 17F, 19A, 20, 22F, 33F	6A, 6C, 6D
HPV-associated genital and anal lesions	Gardasil	HPV-6/11/16/18	High-risk HPV-31
Rotavirus (gastroenteritis)	Rotarix	G1P[8]	G2P[4], G3P[8], G4P[8], G8P[4], G9P[8]
Meningococcal (meningitis)	MenB-4C	MenB	MenC, MenW, MenX, MenY
	MenB	MenB	*Neisseria gonorrhoeae*
Seasonal influenza	Various adjuvanted trivalent vaccines	Two influenza A types and one influenza B type	Related strains
Pandemic influenza H5N1	Prepandrix	A/H5N1/Vietnam/1194/2004 strain	A/H5N1/Indonesia/5/2005; A/H5N1/turkey/Turkey/1/2005; A/H5N1/Anhui/1/2005

Table 1. Examples of the virtue of cross-reactivity in the vaccine field (Vojtek I, et al, 2019, https://doi.org/10.1016/j.vaccine.2018.12.005)

— leading to the eventual eradication of smallpox and the foundation of the field of vaccinology. Another example includes cross-reactive antibodies from a person infected with Plasmodium vivax, which can inhibit the growth of Plasmodium falciparum in vitro. Moreover, cross-reactive antibodies benefit people living in endemic areas of multi-strain malaria transmission. Additionally, the Japanese encephalitis (JE) vaccination has been shown to induce cross-reactive antibodies to West Nile virus in humans. Vaccinologists aim to achieve the virtue of cross-reactivity in the form of ''cross-protection", which implies clinically significant protection against infection or disease due to an immune response elicited against a related pathogen.

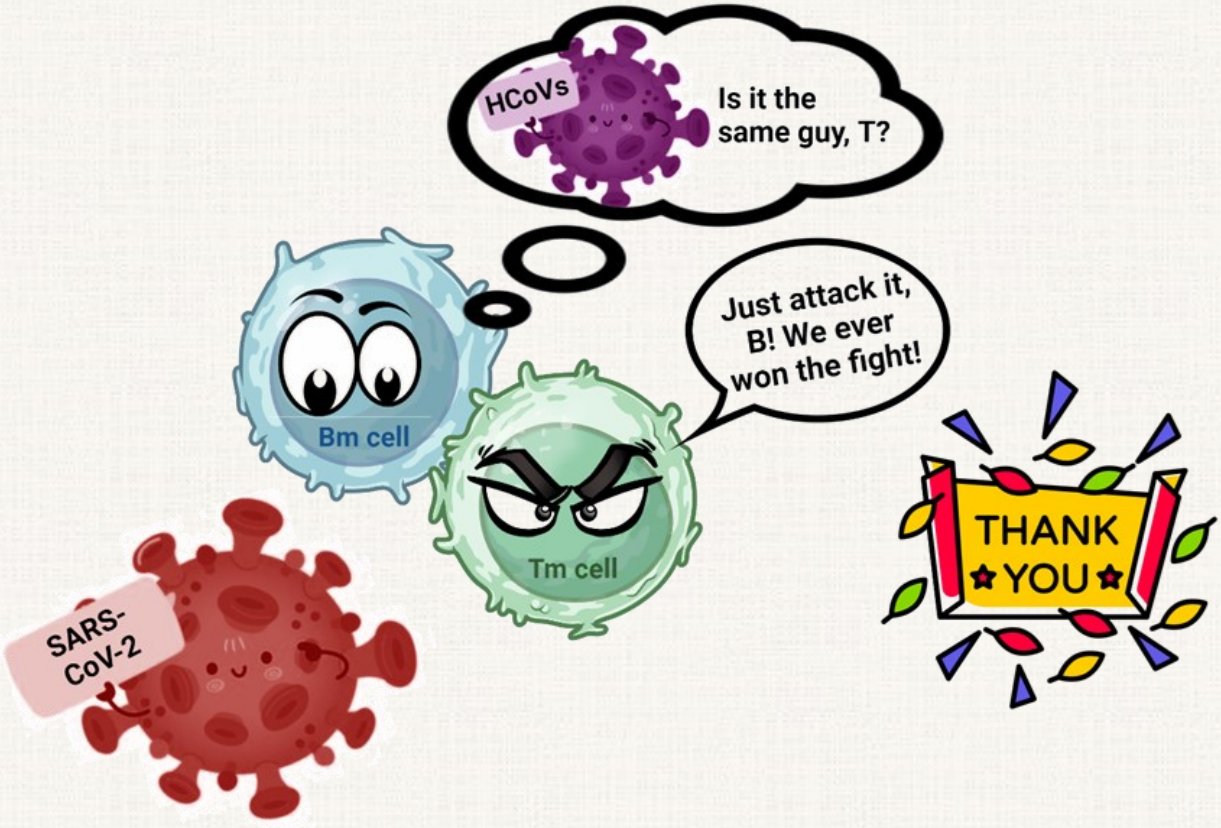
There is an intriguing yet debatable hypothesis regarding the role of cross-reactivity in SARS-CoV-2 infection and COVID-19 vaccines in relation to other pathogens. Since the beginning of the COVID-19 pandemic, pre-existing serum antibodies and B and T-cell responses capable of recognizing SARS-CoV-2 have been detected in naive, unvaccinated individuals. These responses may be shaped by prior infections with SARS-CoV-1, seasonal human coronaviruses (HCoVs), paramyxoviruses, and even certain endemic pathogens such as DENV and Plasmodium spp. There is a complex and dynamic interplay of cross-reactivity of those pathogens with SARS-CoV-2 infection and COVID-19 vaccines due to sequence homology, especially in the Spike region, which may have positive clinical and epidemiological impacts.

After three years of the COVID-19 pandemic with substantial circulating virus variants and rapid deployment of multiple vaccines, the worrying negative OAS effect, fortunately, has not been clearly observed. In the "Spotlight" section of Trends in Immunology Journal, Pillai S intrigued the readers with the title "SARS-CoV-2 vaccination washes away original antigenic sin". He discussed Röltgen et al. findings about Spike vaccination generating

greater antibody breadth than natural SARS-CoV-2 infection. Vaccination results in GCs B-cell responses and generates immunological breadth with antibodies that bind viral variants. In contrast, COVID-19 from SARS-CoV-2 infection disrupts GCs and sustains immune imprinting, resulting in limited immunological breadth. Interestingly, current evidence suggests that cross-reactive immunities form part of the immune response to SARS-CoV-2, alongside the de novo response. Data from B-cell fate-mapping experiments showed that secondary GCs are composed of over >90% of naïve B-cells; hence, there would be no competition for antigen between the higher affinity BCR of memory B-lymphocytes with the germline BCR on naïve B-lymphocytes. Kaku et al. assessed the Spike B-cell response in ancestral mRNA-vaccinated donors with Omicron breakthrough infection. Even though during the acute phase, antibodies had a bias towards recognition and neutralization of the ancestral SARS-CoV-2 strain (the OAS effect), the Omicron breakthrough infection then led to a shift in B-cell immunodominance in targeting the novel RBD. Therefore, although measurable immune responses may be negatively impacted by immune imprinting, this does not translate into diminished protection against infection.

Closing Thoughts

In the end, there is no definitive answer regarding whether cross-reactivity in the immune system is a sin or a virtue. Cross-reactivity may represent humans' adaptation to an unpredictable world of antigenic exposures. It is influenced by factors such as antigenic structures, kinetics (the speed and magnitude of memory versus naive B and T-cell responses), affinity and functionality of the



immune response, and the immunological breadth of the response at the time of exposure. If boosting imprinted memory against original antigens does not disrupt the immune response to novel epitopes, it is not a sin but a virtue.

Since 2012, a more neutral term that does not carry a negative biblical connotation has been introduced to describe cross-reactivity or boosted memory responses toward pathogens encountered earlier in life as "antigenic seniority." This term encompasses both the positive aspects (e.g., broad protection, back-boost) and the negative contributions of past exposures to the immune response toward new exposures (e.g., imprinting, antigenic interference).

Cross-reactivity may hold the key to developing vaccines against highly antigenically and genetically diverse pathogens and preparing for the next uninvited pandemic. Quantifying antigenic distances between pathogens of interest to predict the impact of cross-reactivity could provide insights into potential vaccine strategies. Continued and meticulous research in immunology remains an absolute necessity.

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INA-RESPOND Newsletter

WHY WHEY?

By: Monica Surjanto

Whey protein is a popular fitness and dietary supplement, widely used by both athletes and non-athletes alike. Whey is the liquid component of milk, which can be extracted and separated from casein or produced as a by-product during cheese manufacturing. There are three main forms of whey protein: concentrate, isolate, and hydrolyzed whey protein. Concentrate whey protein contains approximately 89% protein and 10% fat. Filtering this protein content further reduces carbohydrates, lactose, and fat, resulting in isolate whey protein with over 90% protein and less than 0.5% fat. Hydrolyzed whey protein is fractionated into small peptides with varying protein and fat content.[1] When compared to other protein sources, whey protein boasts superior bioavailability, solubility, and a higher concentration of branched-chain amino acids (BCAA), particularly leucine.[2]

Studies indicate that whey protein may assist athletes in recovering from exercise, building muscle, and gaining strength as part of a resistance training regimen. A recent meta-analysis of randomized controlled trials found that dietary protein supplementation during resistance training (lasting more than 6 weeks) resulted in greater gains in lean body mass and strength for both younger and older adults.[4] Additionally, some research suggests that whey protein may aid in weight loss efforts for individuals with overweight or obesity. Increased protein consumption can lead to a greater sense of fullness, potentially aiding in weight management. Whey protein is also considered a complete source of pro-

TYPES OF WHEY PROTEIN	PROTEIN CONCENTRATION	OTHER COMPONENTS	ALLERGENS
WHEY PROTEIN CONCENTRATE	25 TO 89% WHEY COMMERCIAL WHEY CONCENTRATES AVERAGE PROTEIN LEVELS ARE 80%	CONTAINS FATS, CARBS, LACTOSE AND OTHER MINERALS.	HIGH FOR LACTOSE INTOLERANCE AND MILK PROTEINS
WHEY PROTEIN ISOLATE	AVERAGE 90-95% WHEY PROTEIN	CONTAINS ONLY TRACE AMOUNTS OF FATS, CARBS, AND OTHER MINRELS.	LOW FOR LACTOSE INTOLERANCE AND HIGH FOR MILK PROTEINS
WHEY PROTEIN HYDROLYZED	80 TO 90% WHEY CONCENTRATION OF WHEY IS VARIABLE. BUT AN AVERAGE OF 80-90% IS FOUND	HIGHLY VARIABLE FROM BRAND TO BRAND	LOW FOR LACTOSE INTOLERANCE AND LOW FOR MILK PROTEINS

Types of whey protein[3]

tein, as it contains all the essential amino acids. Since our bodies cannot produce these essential amino acids, it is crucial to obtain them through our diet. For individuals struggling to meet their daily protein requirements, whey protein can be a helpful option.[5]

Timing of whey protein intake

Timing of whey protein intake following resistance training is also a crucial factor to consider. Consuming a protein supplement during the "anabolic window," which is within one hour before or after resistance training, is believed to be ideal for promoting muscle hypertrophy and strength gains. Several studies have demonstrated that when protein is consumed before and/or after resistance exercise, there are greater increases in muscle mass and strength/performance compared to a placebo, following a period of resistance training. However, not all trials have shown that protein intake during the peri-workout period directly influences muscle hypertrophy or strength in resistance training. Consequently, it appears that overall daily protein intake, rather than the timing of protein consumption, is the primary predictor of muscle hypertrophy following resistance exercise. Nonetheless, it is important to ensure sufficient protein intake throughout the day to support maximal muscle hypertrophy, which often naturally results in protein consumption before and/or after a resistance exercise session.[4]

How much whey protein should we consume?

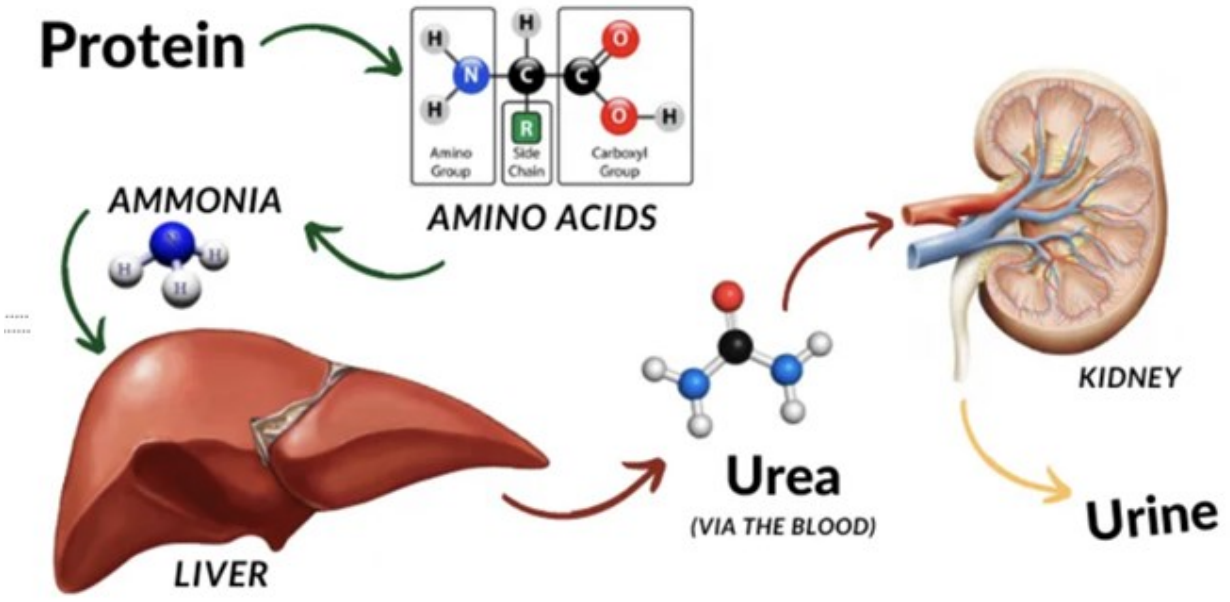
The Recommended Daily Allowance (RDA) for protein intake for the general population is 0.8 grams per kilogram of body weight per day. This amount is suitable for general fitness or light exercise intensity, but it can be increased to 1 gram per kilogram of body weight per day. Protein requirements rise with higher exercise intensity, with recommendations of 1.4 grams per kilogram of body weight per day for moderate exercise intensity and 1.7 grams per kilogram of body weight per day according to the International Society of Sports Nutrition (ISSN).[1] A common recommended dosage for whey protein is 1–2 scoops, which equates to around 25–50 grams, per day. It is advisable to follow the serving instructions provided on the packaging.

Health issues related to whey protein intake

Health concerns related to whey protein intake should also be addressed. Some individuals may experience digestive symptoms when consuming whey protein due to lactose intolerance. In such cases, it is recommended to opt for a whey protein isolate instead of whey protein concentrate. Additionally, some people may have allergies to whey protein, particularly if it originates from cow's milk, as individuals with a cow's milk allergy can be allergic to it.[5]

There are concerns about the potential impact of whey protein on kidney health. High-protein diets can increase the workload on the kidneys, as they must work harder to filter the blood. This can result in elevated levels of urea, albumin, calcium, and oxalate excretion, affecting Glomerular Filtration Rate (GFR). However, the evidence on this topic is mixed. Some studies suggest that the increased filtering work may not be harmful to healthy kidneys, as it is considered a normal adaptive response to physiological stimuli. Nevertheless, individuals with kidney disease may be at risk of further kidney damage when following a high-protein diet.[6]

Another concern is the potential for excessive protein intake to lead to liver damage. However, there is limited evidence to suggest that too much protein can harm the liver in healthy individuals. The liver utilizes some of the protein consumed to repair itself and convert fats into lipoproteins, which help remove fats from the liver. In a small study involving 11 obese females, the intake of 60 grams of whey protein supplementation over four weeks led to a reduction in liver fat by approximately 21%. Additionally, it contributed to a 15% decrease in blood triglyceride levels and a 7% decrease in cholesterol levels. Nonetheless, individuals with hepatic encephalopathy, a potential complication of severe liver



Protein metabolism and the elimination of ammonia.7

disease, should exercise caution when consuming a high-protein diet, as it may lead to elevated ammonia levels in the blood, potentially affecting brain function.[5]

Conclusion

In conclusion, the use of whey protein supplements should not be viewed in isolation as a strategy solely for increasing muscle mass or enhancing performance. Instead, it should be considered as a dietary option to optimize nutrition and support exercise-induced adaptations and outcomes. Whey protein is a popular supplement with purported benefits for muscle mass increase, enhanced recovery, and potential support for weight loss. However, research indicates both potential benefits and risks associated with whey protein and high-protein diets in general. Additional studies are required to gain a better understanding of the potential long-term effects of high protein intake, especially with regard to whey protein. It is advisable for individuals, particularly those with underlying health conditions such as liver or kidney issues, to consult with a healthcare professional before incorporating whey protein into their diet.

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INA-RESPOND Newsletter

DEMYSTIFYING MENTAL HEALTH: UNDERSTANDING THE SPECTRUM, CAUSES, AND STIGMA

By: Dedy Hidayat

Commemorating World Mental Health Day on October 10th, let us address and understand various aspects of mental health. Mental well-being is a vital component of a person's overall health, yet there remains a significant amount of misunderstanding and stigma surrounding it. In this article, we will explore key insights into mental health, aiming to dispel myths and provide accurate information.

The Mental Health Spectrum: A Broader Perspective

Mental health spans a vast range of sensations and feelings, and it is critical to understand the intricacies within this range. Individuals may experience optimal mental well-being at one end, defined by a sense of fulfillment, emotional resilience, and the ability to effectively cope with life's problems. Severe mental problems, on the other hand, can considerably impair a person's everyday functioning and quality of life. However, there is a wide range of experiences in between these two extremes.

Many persons in the middle of the spectrum may experience occasional tension, anxiety, or low mood without reaching the criteria for a recognized mental condition. These feelings are very normal and part of the human condition. It is critical to recognize that fluctuations in mental health are normal, and people may travel along the spectrum at different times in their lives.

Understanding the Complexity of Causative Factors

Mental health disorders are not the result of a single cause but rather arise from a complex interplay of factors. These factors interact in intricate ways, making it challenging to pinpoint one specific cause. Genetic predisposition can play a role, as certain individuals may be more susceptible to mental health conditions due to their family histo-

ry. Biological factors, such as brain injuries or chemical imbalances, can also contribute to the development of disorders.

Environmental influences should not be underestimated. Chronic stress, trauma, violence, or significant life changes can have a profound impact on mental health. Moreover, one's psychological makeup, including thought patterns, beliefs, and coping mechanisms, contributes significantly to mental well-being.

Socio-cultural factors are equally influential. Societal expectations, cultural norms, and social pressure can shape how individuals perceive their own mental health and whether they seek help when needed. Recognizing these multiple causative factors underscores the importance of a holistic approach to mental health.

The Hidden Struggles: Breaking the Stigma

The assumption that people suffering from mental illnesses must exhibit outward indications of pain can perpetuate stigma and dissuade people from seeking care. Many people who appear "fine" on the outside may be experiencing inner agony. It is critical to treat others with respect and compassion, acknowledging that mental health issues are not always visible on the outside.

Furthermore, while discussing mental health, language and vocabulary are important. Using inclusive and courteous language helps to minimize stigma and promotes open communication. The use of phrases such as "people with mental health conditions" rather than "mentally ill" emphasizes that people are not defined only by their disorders.

The Power of Prevention and Therapy

Prevention is essential for preserving excellent mental health. A balanced lifestyle that includes regular physical activity, a good diet, enough sleep, and social interactions can reduce the risk of mental health difficulties greatly. Learning excellent stress-coping techniques allows people to better navigate life's challenges.

Therapy, which is frequently regarded as a resource for persons suffering from mental illnesses, serves a broader function. It provides a safe area for people to explore their thoughts and feelings, gain insight into their actions, and develop personal growth and resilience techniques. Therapy aims to improve overall well-being as well as address mental illnesses.

Overcoming Stigma: A Collective Effort

One of the most significant challenges in tackling mental health concerns is the enduring social stigma associated with them. Stigma is a consequence of societal misconceptions and prejudices, and it can appear through discriminatory practices, prejudiced attitudes, and the exclusion of individuals from social contexts. The presence of stigma frequently acts as a barrier for individuals in accessing necessary assistance, resulting in the development of emotions such as shame and loneliness.

In order to address this prevailing social bias, it is imperative to prioritize educational initiatives and raise awareness. Promoting accurate information on mental health, mitigating prejudices, and cultivating empathy and comprehension are imperative endeavors. Promoting open dialogues regarding mental health within educational institutions, professional environments, and local communities can serve as a catalyst for fostering a culture that is more inclusive and supportive in nature.

Mental Health and Infectious Diseases

While infectious diseases predominantly influence physical health, they can also have a significant impact on mental health. Infectious diseases and


Source: Instagram @dungp13

mental health have a complex and bidirectional relationship. On the one hand, people who catch infectious diseases may experience heightened stress, worry, and sadness as a result of their illness's physical symptoms and uncertainties. Preexisting mental health issues, on the other hand, might impair the immune system, leaving people more susceptible to infections. Furthermore, the stigma associated with certain infectious diseases might increase the psychological suffering experienced by those who are infected. As a result, addressing mental health is not only important in and of itself, but also plays a role in individuals' general health and resilience in the setting of infectious diseases. We can better equip individuals to cope with the challenges provided by infectious diseases and work toward holistic well-being by breaking down stigma and developing a culture of understanding and support for mental health.

Conclusion

Mental health is a multifaceted aspect of our well-being that operates on a spectrum. Understanding the complexity of causative factors, acknowledging hidden struggles, and recognizing the value of prevention and therapy are all essential components of a comprehensive approach to mental health.

The battle against stigma is ongoing and requires collective effort. Let us strive to create a society where mental health is treated with the same importance as physical health. Fostering empathy and support for mental health issues directly impacts our overall well-being as individuals and as a society.

Together, we can break down barriers and support one another on the journey to better mental well-being.

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INA-RESPOND Newsletter

"CHARTING THE PATH FORWARD IN GLOBAL HEALTH: NKENGASONG'S FIVE P'S OF PANDEMIC PREPAREDNESS"

By: Aly Diana

COMIC CORNER

Source: https://www.inquirer.com/opinion/cartoons/coronavirus-world-leaders-spreading-epidemic-20200303.html

Recently, at the opening session of the American Society of Tropical Medicine & Hygiene Conference 2023, John Nkengasong shared invaluable insights from his hands-on experiences with two of the world's most pressing health challenges: HIV/AIDS and COVID-19. Nkengasong, a key figure in Africa's public health sector, has established a significant presence in global health, leveraging his deep experiences with these challenging pandemics. His path, from directing the Africa Centers for Disease Control and Prevention to adopting a crucial role in U.S. health diplomacy, has been defined by unwavering dedication and innovation amid health crises. Nkengasong's recent ascension to leadership in the U.S. Bureau of Global Health Security and Diplomacy, serving as the Global AIDS Coordinator and Special Representative for Health Diplomacy with the President's Emergency Plan for AIDS Relief (PEPFAR), paves the way for his ongoing impact on international health policies and initiatives.

John Nkengasong's insights from his vast experience with both the HIV/AIDS and COVID-19 pandemics underscore crucial elements in managing global health crises. His "five P's" framework—politics, population, policy, partnership, and pathogen—highlights the multifaceted nature of effective responses to such emergencies.

1. **Politics**: Nkengasong emphasizes that political will and action are pivotal in driving large-scale health initiatives. Without the support of governments and international bodies, scientific advances and healthcare strategies can't be effectively implemented. His example of President George W. Bush's role in PEPFAR underscores how political leadership can catalyze global efforts, facilitating resources like antiretroviral drugs that drastically reduced AIDS-related deaths in Africa.
2. **Policy**: The creation and enforcement of policies directly affect public health outcomes. Nkengasong points out that restrictive or punitive policies can hinder access to crucial health services for vulnerable populations, as seen with certain HIV policies in Africa. Progressive and inclusive policies are essential to ensure comprehensive healthcare access, especially during pandemics.
3. **Partnership**: Collaboration across countries, sectors, and industries is vital. Nkengasong's anecdotes about partnerships in both the HIV and COVID-19 responses illustrate that respectful, transparent collaboration can lead to innovative solutions, such as the Africa Medical Supplies Platform and improvements in HIV care for girls and young women in Tanzania.
4. **Population**: Understanding the demographics of those affected by a health crisis allows for targeted, efficient allocation of resources. Recognizing gaps in care or prevention among certain population groups, such as the high HIV infection rates in African youths, is essential for effective intervention strategies. This principle also extends to understanding public sentiments, like vaccine acceptance, to tailor communication and outreach efforts.
5. **Pathogen**: Scientific understanding of the disease-causing organism itself is fundamental. Research into the mechanisms of HIV and SARS-CoV-2 has led to life-saving drugs and vaccines. Continuous investment in scientific research is crucial for current and future interventions.

Nkengasong's optimism for future pandemics is highlighted in new initiatives like the Pandemic Fund, aimed at strengthening global preparedness and response, especially in less wealthy countries. His speech stresses that effective pandemic management needs a comprehensive approach, considering politics, science, and more. The "five P's" he presents are fundamental in guiding global health strategies, focusing on the importance of equity, cooperation, and understanding in addressing health emergencies now and in the future.

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