

THE ROLE OF PSYCHOLOGICAL WELL-BEING IN BOOSTING IMMUNE RESPONSE:  
AN OPTIMAL EFFORT FOR TACKLING INFECTION

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**Abstract**

**Background:** Many attempts have been made to improve human body resistance towards infection. These attempts were exemplified by promotion of hygiene and the use of antiseptic ingredients, pharmaceutical compounds, and vaccines. To prove an aspect which intentionally less explored was attempt to boosting the host immune responses by creating a psychological balance, which was important aspect of psychological well-being.

**Material and Method:** These article reviews searched and compiled using database Google Scholar, from 1995 to latest. Search keywords were: immune response, psychological well-being, psychological ill-being.

**Results:** Based on literature our findings showed that psychological well-being was proven could increase human body immune response. The evidenced were by improvements of several indicators in saliva, blood and plasma. In other way, psychological ill-being was associated with decreased immune responses. Numerous studies compiled and discussed in review also suggested that improving immune response through psychological well-being could increase living comfort.

**Conclusion:** The psychological well-being could improve the human body immune responses, enhance resistance towards diseases (including infectious diseases), and create a spiritually and physically more prosperous life.

**Keywords:** Resistance to Infection, Immune Response, Psychological Well-Being, Psychological Ill-Being, Living Comfort.

**Introduction**

Humans have been trying and are always aiming to get their life more prosperous. One of the considerably important burden factors making life less prosperous was occurrence of infectious diseases. Infectious diseases have been scouring the world for a long time. Infectious diseases impair quality of life and caused the morbidity which was often lead to mortality (Pappas, et al, 2009). Individual susceptibility to infectious diseases was known to be influenced by host immune responses. Immune responses were the reaction of cells and fluids towards the presence of an entity that was typically not recognized as a constituent of body. The ability of immune response to tackle infectious diseases was thought to be influenced by the psychological status (Cohen, 1996)

Moreover, many attempts have been made to increase the body resilience towards infection. These attempts were exemplified by the promotion of hygiene and the use of antiseptic ingredients, pharmaceutical compounds, and vaccines. One thing that was proposed to be effective and efficient as an effort to improve body immune response was strengthening psychological balance in context of psychological well-being.

Whereas, from the literature review, Cohen et al, (2001) obtained information about correlation of psychological stress and antibody response, included in immunization process. Lutgendorf & Costanzo (2003) conducted a psychological intervention that based on the premise that psychological status could affect the immune response. They were intervened medical psychology to modulate the immune response. Those interventions towards good behavior in the field of health and health of individual teaching methods was more adaptive in interpreting life's challenges, as well as the method of handling the problem was more effectively.

Redwine et al, (2004) found an interesting difference immune response among patients with Alzheimer's who accompanied and Alzheimer patients who did not use the companion. The differences occurred due to changes in their psychological status. Barak (2006) collected data from literature and supports hypothesis that individual was described as having negative affective style, bad they recruit immune cells, and might be at risk to disease far more than those with positive affective style. Freitas et al, (2015a) provides some evidence that inflammatory bowel disease was associated with a change in the sense of coherence, psychological balance and quality of life.

## **Materials and Methods**

These articles review searched and compiled using database Google Scholar, from 1995 to latest conducted using SALSA framework (Search, Appraisal, Synthesis, and Analysis). Search keywords were: immune response, psychological well-being, psychological ill-being.

There are very much literatures. After the selection of 105 literatures, selected 39 literatures is up to date and most appropriate to intent these articles review. Furthermore, a critical study of these 39 literatures was conducted.

## **Dichotomy of Individual Psychological Status, Psychological Well-Being (PWB) and Contrary Psychological Ill-Being (PIB).**

According to Ryff and Keyes (1995), the structure of PWB were:

1. Autonomy,  
i.e. I have a high confidence towards my opinion, even if that belief was not in accordance with public opinion.
2. Environmental Mastery,  
i.e. In general, I was personally had a responsibility towards my environment.
3. Personal Growth,  
Which I should feel continue to grow and evolve with experience and new understanding of world. New ideas emerge in tune with passage of time and age.
4. Positive Relationships towards Others,  
Namely being a person who always cast a positive benefit for others, giving, helping and forgiving and praying for others.
5. The Purpose in Life,  
Namely know him and know which direction to go through, how through it in order to reach the goal.
6. Self-Acceptance  
After He realized and knew what needs to be optimized, a point of uniqueness himself and know what should be improved as a point of weakness.

According to Wilt et al, (2016), religiosity and spirituality were the unique variance in well-being (higher satisfaction of life and better self-esteem, less depression and anxiety), while PIB was the contrary.

## **Many Studies Show That PWB Could Boost Immune Responses**

Ryff and Singer (2013) recommend that the PWB could have a positive impact on health. PWB enhance the immune response. Increased immune response be known by measuring the increase in cortisol response and cortisol awakening response (CAR). Rickard et al, (2016) put forward the thesis that CAR totally reliable as an indicator of increasing the immune response in healthy adolescents. Fredrickson et al, (2015) using the conserved transcriptional response to adversity (CTRA) and to see the expression of gene transcription, where the both of it were increase the regulation of pro-inflammatory-gene nor were down-regulated interferon type I also who linked the antibody to detect presence of PWB impact in enhancing immune response.

Anderson et al. (2010), using indicators of natural killer cell cytotoxicity and multiply of T cells for knowing evidence that PWB has a role to improve the immune response. Zhao et al, (2016) using other indicators. He was using CD3 +, CD4 +, CD8 +, CD4 + / CD8 + ratio and free cortisol levels in serum to find the impact of PWB in enhancing immune response. Another researcher, Wu and Gau (2010), studied the levels of phagocytes. As we know, phagocytes did the first response on inflammatory reaction. Later on, much more of phagocytes could accelerate wound healing. As a result, the time needed for a hospital stay becomes shorter at preschool-age child development. Teaching the primary caregiver was another adequate way to induce PWB. Teaching the primary caregiver adequate at-home wound dressing skills reduced re-admission rates for children with low immunity suffering from the phagocyte deficiency.

Next, Bakke et al, (2002), use natural killer (NK) cells and their number of activities to prove that psychological treatments could positively alter the immune system. Religious coping and social support as an effort towards PWB showed to boost the immune responses in people living with HIV/AIDS (Dalmida et al, 2013). They used CD4 + cell count to prove their findings. Then, the effort to PWB via religious coping was definitely associated with reduced psychological distress, increased health-related quality of life (HRQoL), and better medication adherence (8-item Morisky Medication Adherence

Scale) in inflammatory bowel disease (IBD) (Freitas et al, 2015b). They found that religious coping could decrease the relapse of IBD also, meditation could use as an effort to PWB. Long-term practice of meditation might cut stress reactivity and could be therapeutic benefit in chronic inflammatory conditions that characterized by neurogenic inflammation (Rosenkranz et al, 2016). They used cortisol and alpha amylase levels to quantify size of inflammatory and stress response.

Manczak et al, (2016) found attitude of parents like empathy, provide psychosocial impact and physical impact was very good for children's health. Health improvement is indicated by increasing immune response. Increasing body's immune response identified using blood samples. Blood samples are known to decrease signs of systemic inflammation by measuring the amount of interleukin 1-ra, interleukin 6 and C-reactive protein. The effects of empathy from parents to teens could make the better of emotion regulation. The effect of empathy for parents was parents get a higher self-esteem, also get to know the purpose of his life. These findings show importance of mutual solidarity, mutual understanding, to make conditions of psychosocial and physical condition better. In fact, empathy was also very good when develop to principles medical services and for anyone who involve in medical services

Moreover, the cancer patients were accepted therapy music, especially singing. Music could produce better therapeutic effect. Fancourt et al, (2016a) conducted a study on the three populations of cancer patients. They were examined the impact of singing on mood, stress and immune responses in cancer patients, family of patient and nurses. They used indicator; cortisol, beta-endorphin, oxytocin and ten cytokines, they earn from saliva. Their research proved singing could boosting the mood, also singing was modulate immune component's system. Music could evoke positive mood on acute stress (Koelsch et al, 2016). Then, the music could evoke the PWB. Intervened music in therapy base on discovery of several indicators: serum levels of several immune function mediators (IL-6, TNF- $\alpha$ , leptin and somatostatin), as well as noradrenaline, and two hypothalamic-pituitary-adrenal axis hormones (ACTH and cortisol). Other types of music intervention were group drumming. Researchers found an increased immune response through various indicators obtained through saliva samples such as: cortisol, cytokines and interleukin (IL) -4, IL-6, IL-17, tumor necrosis factor-alpha (TNF- $\alpha$ ), and monocyte protein chemoattractant (MCP) -1 (Fancourt et al., 2016b). This study shows the psychological benefits of group drumming and shows the underlying biological effects, supporting the therapeutic potential for mental health.

Whereas, traditional the mind-body method was integrates the roommates slow body movements, breathing, and meditation have a positive impact physically and mentally. One of them was Qigong. Qigong could improve the body's immune response. Indicators obtained from a blood sample for quantification of immune parameters (number and percentage of monocytes, neutrophils, eosinophils, and number of lymphocytes, B lymphocytes, and NK cells). They found statistically significant differences between the experimental and control groups, which experimental group showed a higher value number and percentage of B lymphocytes ( $p = 0.006$  and  $0.04$ , respectively), as well as the values that were lower in percentage of NK cells ( $p = 0.05$ ), compared to controls. Thus, Qigong was an effort towards PWB capable of delivering immunomodulatory effects on components of innate as well as adaptive immune response (Vera et al., 2016).

Other PWB part was affective arousal. Affective arousal also modulates the immune response. Moreno et al. (2016) had evidence through research. They assessed plasma markers of inflammation, including soluble tumor necrosis factor receptor type II (sTNF-RII), C-reactive protein (CRP), and interleukin-1 receptor antagonist. They found that affective arousal has a positive effect on inflammatory process on body. Affective arousal affects the inflammatory activities process on body of breast cancer survivor's.

Kitayama et al, (2016) found an association between meaning of life as sociocultural determinants and PWB using CTRA gene expression. They did study on 106 male workers at a large Japanese information technology firm. They used CTRA gene expression as a marker to detect the role of PWB could enhance immune response, thorough improving regulation process of inflammation and viral resistance. Resume of PWB increase immune response list was in Table 1.

**Table 1: PWB increases immune response.**

<b>Reference</b>	<b>Type of Study</b>	<b>Outcome (indicators for the body's immune response against infectious diseases)</b>
Ryff and Singer (2008) Rickard et al (2015)	Measurement of cortisol response/ cortisol awakening response (CAR)	Positive impact of PWB on health, CAR as a reliable indicator of immune response in healthy adolescents.
Fredrickson et al (2015)	Conserved transcriptional response to adversity (CTRA) for expression of gene transcription	Increase the regulation of pro-inflammatory interferon type I as well as antibody, reflecting PWB enhanced immune response.
Anderson et al (2010)	Measurement of NK cell cytotoxicity and multiplicity of T cells	PWB has a role to improve immune response.
Zhao et al (2016)	Measurement of CD3 +, CD4 +, CD8 +, CD4 + / CD8 + ratio and free cortisol levels in serum	PWB enhances the immune response.
Wu and Gau (2010)	Assessment on the levels of phagocytes	PWB can increase number of phagocytes in preschoolers which was associated with accelerated wound healing and shorter hospitalization time.
Bakke et al (2002)	Measurement of NK cells and their number of activities	Psychological treatments can positively alter the immune system. Religious coping and social boosted immune responses in people living with HIV/AIDS
Dalmida et al (2013)	Measurement of CD4 + cell count	Religious coping and social support showed to boost immune responses in people living with HIV/AIDS
Rosenkranz et al (2016)	Measurement of cortisol and alpha amylase levels	Long-term practice of meditation may cut stress reactivity and could be therapeutic benefit in chronic inflammatory conditions characterized by neurogenic inflammation
Manczak et al (2016)	Measurement of interleukin 1-ra, interleukin 6 and C-reactive protein	The attitude of the parents in the form of empathy, provide psychosocial impact very good for children's health. Health improvement shown by the immune response
Fancourt <sup>(a)</sup> et al (2016)	Measurement of cortisol, beta-endorphin, oxytocin and ten cytokines	Singing can boost immune response in cancer patients, the family of the patient and the nurses.
Koelsch et al (2016)	Measurement of IL-6, TNF- $\alpha$ , leptin and somatostatin, noradrenaline, ACTH and cortisol	The music can evoke the PWB. PWB boost immune response.
Fancourt <sup>(b)</sup> et al (2016)	Measurement of cortisol, cytokines and interleukin (IL) -4, IL-6, IL-17, tumor necrosis factor-alpha (TNF- $\alpha$ ), and monocyte protein chemoattractant (MCP) -1	Group drumming as kind of music intervention can increase immune responses
Vera et al (2016)	Measurement number and percentage of monocytes, neutrophils, eosinophils, B lymphocytes, and NK cells	Qigong can improve the body's immune response
Moreno et al (2016)	Measurement of soluble tumor necrosis factor receptor type II	Affective arousal modulates the immune response

**Table 2: PWB decreases immune response**

Reference	Type of Study	Outcome (indicators for the body's immune response against infectious diseases)
Kudoh et al (2001)	Measurement of plasma IL-6, IL-8, and TNF- $\alpha$	The pro-inflammatory cytokine responses decreased in abdominal surgery on patients with schizophrenia
Cohen et al (2001)	Measurement of immunoglobulin A	A secondary antibody response was lower among patients with chronic high-stress levels
Burleson et al (2002)	Measurement subset of leukocytes, mitogen-induced proliferation of lymphocytes, NK cell activity and Epstein-Barr virus (EBV) antibody titer	The effects of stress in reducing the immune response in the first year
Kiecolt-Glasera and Glaserb (2002)	Measurements of healing time of infection and process of wound healing, as happened in burns	Depression can directly decline production of pro-inflammatory cytokines
Salleh (2008)	Measurement of tumor growth factor and NK cells	Chronic stress lowers the immune response.
Salim (2016)	oxidative stress	The mechanisms proposed to explain why PIB lowered immune response
Martin-Suberoa et al. (2016)	Measurement of IL-1 and TNF- $\alpha$ , IL-6 trans-signaling; Th-1 and Th-17-like responses; neopterin and soluble IL-2 receptor levels; haptoglobin and C-reactive protein; albumin, transferrin, zinc; IL-10, transforming growth factor- $\beta$	The mechanisms proposed to explain why PIB lowered immune response thorough the way of oxidative, and nitrosative stress. Both seem as co-morbidity and as a contributor
Britvi'c et al. (2015)	The diagnostic of cardiovascular, dermatological, musculoskeletal, pulmonary and metabolic diseases	Posttraumatic Stress Disorder (PTSD) increase suffering somatic diseases
Loewa (2014)	Visual Stress Syndrome (VS)+CFS larger than VS without CFS	PIB, Chronic Fatigue Syndrome (CFS) can increase the body's susceptibility to disease
Riis et al. (2016)	Measurement of IL-1 $\beta$ , IL-6, IL-8, TNF- $\alpha$ and activity of cortisol	Stress can alter the function of neuroendocrine-immune (NEI) in children, stress increases the risk of disease

### Some Studies Show How PIB Lower the Body's Immune Response

Many of the previous studies have shown that PWB improve the immune response, where PIB was contrary also, PIB lowered the immune response. Again, Baum and Posluszny (1999) reminded us that psychological status making an impact on immune response. Cohen et al, (2016) stating the stages of disease model starting from the stress as a trigger of disturbance to equilibrium of body. Stages of disease start from stress, it will stimulate the body's response biologically and behaviorally. Stress also makes people more susceptible to disease.

Kudoh et al, (2001) got results that pro-inflammatory cytokine responses decreased in abdominal surgery on patients with schizophrenia. They took measurements of several indicators: plasma IL-6, IL-8, and TNF- $\alpha$  as a variable. Other evidence was supported a link between psychological stress and suppression of humoral antibody, as happened in immunization action (Cohen et al, 2001). There was evidence that secondary antibody response was lower among patients with chronic high-stress levels (a problem that lasts longer and severe or very negative attitude to life). These responses were found most consistent among adults who have an older age. The moderate response was found in people who were influenced by acute stress or negativity personality. The study was only done by measuring antibody secretory immunoglobulin A that correlated with psychological status. Antibodies immunoglobulin A strongly associated with psychological status if counted at same time. Moreover, the literature supports the association between psychological stress and antibody responses to immunizations. Researchers have some data of antibody reaction for secondary response. The effect of stress on immune response lasts stable. Burleson et al, (2002) examined the effects of stress in reducing immune response at first year. They were measured the several parameters, including a subset of leukocytes, mitogen-induced proliferation of lymphocytes, natural killer cell activity and Epstein-Barr virus (EBV) antibody titer.

In another hand, through literature study, Kiecolt-Glasera and Glaserb (2002) obtaining scientific information that depression could directly decline the production of pro-inflammatory cytokines that affect the spectrum of conditions associated with aging, including cardiovascular disease, osteoporosis, arthritis, type 2 diabetes, certain cancers, diseases of periodontal, weakness and functional decline. In addition, they obtain scientific information that depression might be decrease cellular immune response, causing some consequences which include, prolonged healing time of infection and prolonged process of wound healing, as happened in burns.

Chronic stress was one type of PIB that has an important role in lowering immune system. This role will emerge the diseases as prolonged stress, old to be able to suppress catecholamine and suppressor T-cells. These two roles resulted in suppression of immune system. Decreased immune system would allow the body more susceptible to viral infections. On the other hand, prolonged stress resulting histamine release in large quantities. Histamine excessive the amounts that lead bronchus narrowed, especially in asthmatics. Prolonged stress easier to made people suffering from diabetes mellitus. Diabetes mellitus more likely occur in people who have more weight. Psychological stress could disturb body's insulin balance. It was already well known that long stress could make the concentration of gastric acid change. The changes concentration of gastric acid could cause the stomach ulcers. Even, long stress could cause stress also changed the concentration of acid in stomach, which might cause ulcerative colitis. In blood vessels, long stress had a negative impact. Long stress could cause plaque buildup in arteries (atherosclerosis). Plaque could be increased in people who received a high-fat diet but a higher risk was found in those who had a behavior change. Later on, it was found a stronger correlation between the events of a life filled with stress and mental illness, compared to a correlation of stress and diseases related to the physical. The relationship of stress with mental illness was more powerful in neurosis. They also obtained a strong relationship between stress and depression, as well as schizophrenia, the strongest links were with neurosis (Salleh, 2008). Furthermore, thorough appropriate literature study, he found evidence of link between stress, tumor growth and suppression of NK cells, which were actively involved in preventing metastasis and destroying metastasis which was still in its early stages. Chronic stress lowers the immune response.

There were several mechanisms proposed to explain why PIB lowered immune response. One such mechanism was oxidative stress (Salim, 2016). In other study, Martin-Subero et al, (2016) found spectrum disorders of immune-inflammatory, oxidative, and nitrosative stress (IO & NS) that converts depression, seem as co-morbidity and as a contributor, to process IO & NS. IO & NS interference pattern has same pattern with pathogenesis of IBD. Increased prevalence of depression in IBD associated with lower quality of life, was also associated with increased morbidity. Researchers highlighted the role of depression in modulating pathophysiology of IBD. They reviewed data covering wider and better explain conceptualization the high rates of IBD associated with depression. In general the underlying mechanism of IO & NS between the two disorders evidence increasing the levels of pro-inflammatory cytokines, for example, IL-1 and TNF- $\alpha$ , IL-6 trans-signaling; Th-1 and Th-17-like responses; neopterin and soluble IL-2 receptor levels; positive acute phase reactant (haptoglobin and C-reactive protein); lowering the level of negative acute phase reactant (albumin, transferrin, zinc) and anti-inflammatory cytokines (IL-10 and transforming growth factor- $\beta$ ); increased IO & NS with damage lipids, proteins and DNA; increased production of nitric oxide (NO) and inducible NO synthase; lowering elevated levels of plasma tryptophan but TRYCAT; autoimmune responses; and an increase bacterial translocation.

Britvi'c et al, (2015) through their study found evidence that Posttraumatic Stress Disorder (PTSD) trauma was as a result of ever doing battle on the battlefield that could increase likelihood of suffering somatic diseases. Their study of 1,558 subjects living in southern Croatia: 501 male veterans were exposed to war (PTSD) and the control group (825 males) were characterized by homogeneity that has PTSD but never exposed to the war. Veterans who have PTSD did not depend on how long they spent in war, more often suffer from cardiovascular, dermatological, musculoskeletal, pulmonary and metabolic diseases when compared to control subjects.

Symptoms Meares-Irlen/Visual Stress Syndrome (VS) in subjects diagnosed with chronic fatigue syndrome (CFS) was larger than VS without CFS-group (Loewa, 2014). The results of this study indicate that PIB, could increase the body's susceptibility to disease. CFS makes decreased immune response. Riis et al, (2016) found evidence that stress could alter the function of neuroendocrine-immune (NEI) in children, stress increases risk of disease. They did a research whether psychological distress was moderated by relationship child and mother. They came to conclusion that their findings indicate maternal stress associated with neuroendocrine-immune child relationship in saliva and could change the sensitivity of the inhibitory effects of cortisol on inflammatory process. This desensitization might increase the risk for children to get inflammatory diseases. Those researchers used data from laboratory-based studies of mothers and children of their five-year-old (n = 125 mother-child pairs) conducted from 2011 to 2013 in Baltimore, Maryland. They tested the saliva of children to acquire markers of immune function (i.e., cytokines: interleukin IL-1 $\beta$ , IL-6, IL-8, TNF- $\alpha$ ) and the activity of the hypothalamic-pituitary-adrenal (i.e., cortisol). Resume PIB decrease immune response list was in table 2.

### **PWB is Essential for Living Comfort**

PWB was a path to a happy life for each human being (Ryff & Singer, 2013). PWB has a positive effect towards comfort living even though in people suffering from illness, such as HIV / AIDS which is recognized as disease those has a very high mortality rate. PWB, as seen on good quality of social relationships can impact a better life (Mavandadi et al, 2009). Siegel (1988) in book titled "Love, Miracle, and Medicine" reported many cases of HIV / AIDS. People who suffered from HIV/AIDS and changed their living with love to universe (a kind of PWB), could recover completely, and turn to be good evangelist. PWB becomes a way of life to be comfortable, for who suffer from disease, more for healthy people.

## Conclusion

PWB boosts the human body immune response. Indicators showed the increasing immune response could observe objectively through many parameters in saliva, blood, and plasma. Increasing body immune response means improving its resistance towards infection. PWB could make the quality life of people be better. PWB made people prosperous, themselves, their families and communities. In addition, psychological well-being could improve the human body immune response, enhance resistance towards diseases (including infectious diseases), and make life more prosperous.

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