PSYCHONEUROIMMUNOLOGY

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As published in Pain Management: A practical Guide for Clinicians - Sixth Edition, R. Weiner (Ed.) Chapter 64 ,pp 807 - 816, CRC Press, 2002

Historically, the study of the mind/body interaction can be traced to early Greek physicians. Indeed, when one begins a search of its earliest origins, one is inevitably lead to Hippocrates and Galen of ancient Greece. To the ancient Greeks, emotions were seen to play a significant role in the progress and maintenance of diseases. What today is known as tuberculosis was described symptomologicaly by Hippocrates and prescribed to have its etiology in stress. However, the importance of the role of the mind in maintaining health has passed through many significant perceptions since that time. Until recently, post Descartian thinking resulted in the role of the mind in immune functioning being allocated to the periphery of medicine.

Masek, et.al. (2000), pointed out that PNI was first comprehensively described only as recently as 20 years ago. They go on to define PNI as the bidirectional communication between the central nervous system, neuro-endocrine system and immune system. With the return to the examining of the interactive role of the central nervous system, endocrine and immune system came a new field currently labeled psychoneuroimmunology (PNI). Many definitions of PNI are present, depending on the emphasis or direction of the pathways particular fields of researchers choose to emphasize. One definition offered by Paul Martin in 1998 is “the field of scientific research that is concerned with the complex interrelationship between the psychological and emotional factors, the brain, hormones and immunity and disease.” The purpose of the chapter will be to offer three things: First: a basic understanding of precisely what are the pathways being considered in PNI. For example, what are the biological immune responses (cortisol levels, cytokines levels, natural killer cell levels, etc.) which are affected by environmental and internally mediated stress. Secondly, to restate the question often raised by clinicians which is, “Does statistical significance (i.e., changes in hormone levels) assume clinical relevance (i.e., a clinical change in the immune system’s protective potential)”. Thirdly, if we accept that stressors experienced through conscious awareness and judgment impact the immune system, what can be done to reduce those stressors?

A discussion of treatment modalities is offered, and finally, hope for a united direction for future research unifying the basic sciences (statistical analyses) and the applied sciences (clinical relevance). What then do we know about the integrative reaction of the CNS and the immune response?

Stress, via bidirectional interactions between the central nervous system, endocrine system and immune system, impacts the hypothalamic, pituitary, adrenal (HPA) and the sympathetic adrenal medullary (SAM) axes, can induce modulation of the immune system and thereby defense against infectious agents and health (Yang, 2000).

In a review of research articles, Sali (1997) notes that stress increases the risk of viral infection. Stress and depression can depress immunity, whereas stress reduction enhances immunity. Sali points to outcome data on improved cancer prognosis via enhanced immunity resulting from stress reduction. Spiegel (1999) found increased survival rates in breast cancer patients who attended stress reduction groups or programs. Further, Vander Pompe (1986) suggested the importance of psychotherapy and psychological resiliency in breast cancer survival. Utilizing a twin study model (124 normal adult twin pairs, Hickie Bennet, et. al. 1999), found a positive genetic relationship between psychological distress and immunity. They concluded that genotype may play a significant role in the reactivity of our immune system to stress. Garssen (1999) suggests that some evidence has been found that a low level of social support and tendency toward helplessness and repression of negative emotions are factors that promote cancer progression but not cancer initiation. These same factors are also symptoms commonly associated with depression. Further, Christiansen et. al (1996) found that immuno-suppression (NKC activity) could be positively impacted by self-declosure of traumatic or stressful experiences.
A question is then raised: "Does the correlation between depression, suppressed immunological functioning and the elevation of underlying disease processes to a level above threshold (i.e., the symptomatic expression of herpes or the increase in joint counts in rheumatoid arthritic patient) exist?" Research continues to support the concept that stress plays a significant role in exacerbating pathophysiology. Berin (1997) notes that reported stress often precedes relapses in patients with inflammatory bowel disease or irritable bowel syndrome and that CNS and immune mediated pathophysiology as expressed by changes in the epithelium may exist.

Stress and pain have also been demonstrated to have an adverse effect on endocrine and immune function in regard to postsurgical wound healing, with greater fear or distress prior to surgery being associated with slower and more complicated postoperative recovery (Kiecolt et. al., 1998) and to small punch biopsy wound healing in caregivers as demonstrated by increased healing time and lower cytokines (IL–1) levels (Glasser, 1996). In regard to posttraumatic patients, Klapheke, (2000), suggested that depression in their psychological state should be seen as a contributory factor to the net state of immunosuppression in transplant patients
Psychoneuroimmunology and Pain: The impact of pain on immune functioning has been studied extensively in animals, but more recently the role of various types of pain on immune function have been examined. Kremer (1999) notes that surgery negatively affects immune function, and that pain has a deleterious effect on immune function. Via neuroendocrine pathways, depression, stress and pain can be viewed as psychoneurological phenomena. He suggests that treatment of postoperative pain must be included in the recovery process due to its psychoneural immunological impact on the patient.

In a study to assess acute pain impact on immune levels in ten HIV+ and ten HIV- patients, Eller (1998) found no significant difference between groups. However, significant changes in state anxiety, systolic blood pressure, diastolic blood pressure and CD4+, lymphocyte numbers were associated with levels of perceived pain intensity to a cold pressor test.

In extreme situations where physical trauma and pain are severe, the body releases endogenous opioids which reduce the perception of pain and have pain-relieving actions. However, as a result, the immune activity of natural killer cells and lymphocytes is reduced.

This raises the issues of placebos and other treatments which work by altering the individual's perception of pain without actually providing an external source of analgesia. If, in fact, they operate as some believe by triggering pain-relieving opioids, do they then represent a two-edge sword which offers pain relief and thus diminishing the immunosuppressant levels of IL-6 and cortisol while possibly decreasing tumor suppression by lowering NKC and certain lymphocyte activities?

Another issue about pain is its controllability. Laudenslager (1983) found that lack of control versus control over pain induced by electric shock determined lymphocyte responsiveness of rats. This may also explain the more recent findings of researchers that depression (learned helplessness) with regard to pain may be significantly related to dysfunctional reciprocal relations between neuroendocrine and immune function (Geiss, 1997).
The patient's perception of the controllability of pain and level of optimism may also play a significant role on the impact that pain has on immune functioning. In examination of pain, patients suffering with temporomandibular pain and dysfunction syndrome, immune functioning was not impacted compared to controls. However, patients who scored high on measures of "demoralization" (low self-esteem and perceptions of helplessness and hopelessness) demonstrated significant decreases on measures (Marbach, 1990).

In a review article, Paige and Ben Eliyahoo (1997) note that the immune system plays a role in controlling the spread of cancer and that perio-operative pain relief improves immune status and health outcomes. They suggest that sufficient evidence exists to view pain as a pathogen in and of itself capable of facilitating the progression of metastatic disease, via immuno-suppression.

Along similar lines, a study by Parker, et. al. (1992) utilizing the Beck Depression Inventory, the Arthritis Helplessness Index, and the Arthritis Impact Measurement Scales (AIMS) pain score in conjunction with immunophenotypic analyses of peripheral blood lymphocytes found that the percentage of HLA-DR+ cells in the peripheral blood and helplessness related to joint count in rheumatoid arthritis (RA) patients. Further, joint count had an effect upon depression and depression upon the perception of pain, demonstrating the interrelationship among psychological factors, immunologic activation

and disease activity in RA. Zautra, et. al. (1997) also found that interpersonal stressors were associated with increased disease activity in a study of 41 rheumatoid arthritic women.

Affleck, et. al. (1997) examined sedimentation rates, an indication of systemic inflammation and soluble interleukin-II receptors (a marker of immune system activation known to correlate with the RA disease activity). For RA patients, they found that daily events stressors were associated with increased joint pain (regardless of mood) and decreased joint inflammation (reduced levels of soluble interleukin-II receptors).

Another issue which often is raised is the impact of acute stressors on individuals who are experiencing chronic life stressors. It would seem that individuals who are experiencing chronic life stress might be more vulnerable to the impact of acute stressors. The importance of this is apparent when we look at disease onset rates in more vulnerable populations, such as the infirmed, ill, or impoverished, which may be experiencing higher levels of chronic life stress. Indeed, Pike (1997) found that individuals experiencing chronic life stress demonstrated greater subjective stress, higher peak levels of epinephrine, lower peak levels of beta endorphin and of NK cell lysis and NK cell distribution to a mild acute stressor than did controls. These changes persisted beyond termination of the stressor and sympathomedullary recovery. It reinforces the concept that those already suffering often the case in chronic illness or injury patients are most vulnerable to further immunosuppression from acute stressors. In the case of traumatic injury, Schrader (1996) suggests that the individual's psychologic and physiologic state may alter the immune system and decrease the immunity as measured by serum cortisol levels; and further, that the perception of diminished control and subjective stress may contribute to immune changes when combined with the immunosuppressive effects noted with regard to pain, suggesting that state of significantly decreased immunity needs to be addressed from a psychological, controlled coping skill, and pain management approach.

Interestingly, research suggests when the stress is consistent with the stressor (perhaps demonstrating better coping skills by the individual), immunological changes are less severe than when the stress experienced is greater than expected from the trauma. Solomon (1997) found that earthquake survivors who manifested acute psychological reactions to a realistic degree of the life-stress experienced the least disruption of an aspect of immunity (lymphocyte subsets – total T[CD3+] helper T[CD4+] cytotoxic T[CD3+ and CD8+] 19+) and natural killer cell (NK; CD3-, CD16+ sign CD56+) as well as lymphoid cell mitogenesis (PHA and DWM) and NK cell cytotoxicity, than those who had more severe reactions or those who repressed their stress reactions

Adaption to stress and its impact on the immune system may be somewhat more complicated. Kelly, et. al. (1997) have suggested that PNI measures may act as markers to adaption to socioeconomic and psychosocial stressors.

There appears significant evidence that psychological stress contributes to immunological suppression (Biondi 1997). However, there is less compelling evidence suggesting that immunosuppression may result in mental disease. However recent research identifies the

hypersecretion of IL-2 in schizophrenia and IL-6 in depression. Muller (1997) suggests that cytokine changes resulting from stress impacting the immune system may play a role in psychiatric disorders.
Further, Dabkowska and Rabakowski (1994) suggest that the immune system may play a role in increasing the vulnerability to psychiatric disorders.

Given the interactive nature of PNI, it is evident that a relationship exists between emotional disorders such as depression and alterations in the response of the immune system. However, as Kay, et. al. (2000) points out, the associations and relevance of these alterations with regard to health and illness are not yet fully determined.
Anyone who has spent a night in pain or stressed knows the impact that either can have on sleep. Hall et.al. (1998) report that sleep has been demonstrated to be a significant factor in the stress/immune relationship of NKC number and functions.

Severity of pain was also a factor. This suggests that clinicians must be aware of patient's mental state and take into account immunological susceptibilities in those patients who present with significant levels of emotional demoralization (chronic pain syndrome) when invasive potentially immunosuppressant interventions are considered.

In fact, an optimistic outlook may protect the immune system from the negative impact of stress. First year law students evaluated at the onset of the semester who were found to manifest a more optimistic attitude, had more helper T-cells (T-cell increased 13%) and higher natural killer cell cytotoxicity mid semester than their pessimistic peers (T-cell dropped 3%). This led to the suggestion that the optimist's attitude protected their immune functioning (Segerstrom 1998).

Another important question often asked is, Does stress impact sufficiently enough on the immune system to create a health risk? Glasser (1996) found that by looking at antibody responses to flu-vaccinated Alzheimer's disease caregivers and to Hepatitis B vaccinated medical students, the findings indicated that psychological stress may be able to alter a person's response to a vaccine; and therefore by implication, their risk to infection by a live virus. Koenker (2000) states that psychological stress impacts the immune system sufficiently to raise catecholamine and CD9 levels and increases the risk of viral infection-released histamines which then triggers severe bronchoconstriction in asthmatics. It also alters insulin needs increasing the risk for diabetes mellitus, alters acid concentrations in the stomach contributing to peptic and stress-ulcers and ulcerative colitis; plaque buildup in arteries increasing the risk of angina and heart attack. (Elliott, Eisdorfer 1982, Lieberman 1974).

As we continue to understand the complex PNI interaction our views of the forms of intervention and pharmocotherapies may significantly change. Masket et. Al. (2000) points out that the data strongly suggest that in the very near future we will not only better understand a very complex communication between mind and body, but also completely new types of compounds might become available.

Although the question raised by Vedhara, Fox and Way (1999) as to whether in vitro statistically significant results equate to in vivo immune outcomes is not yet

completely answered, significant " in vivo" research is present as evidenced by the plethora of treatment outcome studies represented in the literature.

TREATMENT

Having reviewed the mechanisms and correlations between the psyche (mind), neuro (brain/endocrine), and immune system and seeing that a bidirectional relationship exists, we should next review what forms of intervention have been applied in treating various conditions. One might feel initially tempted simply to try to correlate treatments with conditions/diseases, but this would undermine the very essence of the psychoneuroimmunological model which seeks to approach immunosuppression from a more holistic framework. Perhaps the best title for all interventions which utilize this model is the one proposed by Biondi and Zammino (1997) who refer to such interventions as psychoimmunotherapy, namely the application of conjoint psychological intervention in pathologies such as tuberculosis, herpes simplex virus, HIV. Coyle (1996) offers a similar concept of psychoneuroimmunology in the treatment of multiple sclerosis.

An important issue which rises, however, in the point of intervention, Hiramoto, et. al. (1999) state, "Psychoimmunology has been credited with using the mind as a way to alter immunity. The problem with this concept is that many of the current psychoimmunology techniques in use are aimed at alleviating stress effects on the immune system rather than at direct augmentation of immunity by the brain. They raise the question as to whether the mind can, via conditioning, be trained to remember an output pathway to raise immunity." If so then it lends increased credibility to the mind control components in promoted in eastern philosophies and healing arts.

Further, as we break down the concept of training pathways, one is again presented with a crossroad of to what extent is the conditioning behaviorally mediated via the build up of neural pathways or unconsciously mediated via imagery-based internal experiences.

To begin, let us first examine the different modalities that have been utilized and presented in the literature concerning stress reduction as a means of enhancing immune function. Stress management represents a broadly defined treatment orientation encompassing a huge variety of treatments. The singular underlying common goal is to bring about either objectively or subjectively reported changes in the patient's experience of stress. However, as has been frequently noted in the literature from Selye (1956,1976) to the present, not all stress is negative and that although general stress values have been numerically quantified (Holmes and Reyhe 1967), not all events maintain equal stress values for all individuals. In addition, factors such as controllability of the stressors (Schrader 1996; Kiecolt, et. al. 1998, Kay, et. al. 2000, Laudenslager 1983), support systems (Spiegel 1999), chronicity of the stressor (Pike, et. al. 1997), and adaptation to the stressors (Kelly, et. al. 1997), may play a significant role in the impact of stress on immunological functioning and responsiveness to treatment.

Some of the treatments which have sought to address the effects of stress include biofeedback, hypnosis, cognitive behavioral, behavioral approaches, exercise, nutrition,

physical manipulation, yoga and a host of other techniques including laughter therapy, dance and the arts. What almost all of these approaches have in common is they seek to change the patient's (assuming that they are ill at this point) appraisal of stressors which preceded the influence of immunodepression, the stressors associated with their appraisal of their illness and treatment. This typically includes the ability to control their pain and the degree to which they are limited or disabled by their illness or pain, as well as the stressors associated with their appraisal of future functioning and/or mortality.

In essence stress combined with a stress-prone personality leads to physiological and hormonal consequences which deplete the immune system. This opens the door for possibly increased susceptibility to or maintenance of illness. Ultimately, the presence and impact of that consequent illness, especially if pain is concomitant, can easily become a stressor unto itself and further mitigate stress-induced immunosuppression. In this model then, a downward spiral of health requiring significant multimodal intervention is required if we are to reverse its direction.

BASIC STRATEGIES OF CHANGE

Biofeedback: Biofeedback as a form of intervention provides the patient with an increased sense of control over physiological responsivity to stressors. Through monitoring their EMG, their EEG, and/or thermal responsiveness to covert and/or overt stimuli, patients can learn to significantly reduce physiological reactivity. Biofeedback can be especially useful in reducing arousal responses to conditioned stressors such as finger sticks, nausea associated with chemotherapy, and stress-induced cervical headaches associated with environmental queues (i.e., entering a hospital).

In addition, by experiencing feedback on their physiological functioning, patients who have been educated to the concept of PNI can gain an increased sense of control (previously noted as extremely important) over their physiological responsiveness and thereby over their environmental stressors. It provides a generally positively perceived concept of "learning and master" to be placed back into the patient's hands. For example, even patients who feel little control over their illness and/or pain, can gain some emotional and/or pain relief by focusing on minor "successes" in controlling physiological changes during biofeedback. Immediate biological biofeedback may be especially helpful with patients who evidence "low to moderate levels" of hypnotizability, whereas "high hypnotizable" patients appear to benefit more from "delayed biological feedback". In delayed biofeedback information is provided after severeal minutes of self-hypnosis training in order to shape and confirm the efficacy of the self hypnosis training (Wickramasekera 1999).

Within the thermal biofeedback approach, one goal is to teach the patient to lower their sympathetic nervous system activity level through autogenic hand warming. Additionally, a quieting of the muscular armoring through EMG biofeedback,can benefit patients by reducing stress-induced pain as well as pain induced stress. The relaxing of the physiology and musculature is then enhanced with EEG biofeedback where patients can induce increased alpha and beta wave activity thereby seeking to incur a quieter mental and emotional state. Alterations of cognitions, beliefs and perceptions can be achieved via the association of altered physiological states with new concepts and coping thoughts. Bibliotherapy in conjunction with the biofeedback, which includes educating

the patient as to the benefits of controlling stress responses has upon their limbic system increasing NKC activity and possibly reducing mutagenic effects, gains the patient a tangible connection to intervening in their own treatment (Davis 1986).

Cranial Electrotherapy Stimulation (CES): With patients having difficulty acheiveing therapeutic levels of alpha states, even with biofeedback. Cranial electrotherapy can provide assistance by passing microcurrents through the cranial area via electrodes attached to the earlobes. CES stimulation has been shown to be helpful when utilized for emotional distress such as depression and anxiety by helping the patient achieve a relaxed, quieted but alert state. While CES hasn't been traditionally found to be useful in treating stress related disorders, recent studies have begun to demonstrate its effectiveness. Research has also demonstrated utility in pain management. By passing microcurrents through affected pain regions, patients report significant reductions at the site of their pain. By combining CES with microcurrent stimulation at pain sites patients can reduce emotional distress and physical discomfort, (Kirsh 1991) thereby positively impacting upon the pain and emotional components of the PNI triad. The pain relief associated with microcurrent stimulation may provide the patient with an increased sense of controllability over pain and a smoothing of EEG peaks (associated with pain) when both emotional and physical complaints are conjointly present (Hefferman, 1997).

Since this treatment can often be self administered by the patient, it further enhances their sense of self-efficacy. It has little or no documented negative interactions with other forms of treatment.

Visualization/ Imagery: Visualization/ Imagery has been conceived as the active process by which we voluntarily and intentionally instruct the body, whereas imagery is the spontaneously occurring "appearing in unconsciousness" modifier, qualifier, or belief emerging from the unconscious (Norris, 2000). Visualization represents how we ingest the world around us and what we then transfer to our unconscious or cognitive processing mind. Imagery represents then how we interpret that information from the perspective of our internal beliefs and knowledge base. It represents "What does that visualization mean to me?" Perhaps more succinctly stated, as clinicians, we can guide patients into varying visualizations but the imagery is the process within them, their "experience" of the visualization. Through the use of imagery patients can learn to change their outlook for the future, and the illness process. This has been shown to be tremendously helpful in improving clinical outcomes.

Pioneering work in the use of imagery in fighting cancer in works such as in the use as "Love, Medicine, and Miracles, (Siegel, 1986) helps patients develop a sense of personal efficacy in dealing with their illnesses, and enhancing the PNI triad. Visualization can help patients focus on the events that they are experiencing in the process of working through their illness.

An excellent example of the use of imagery applied to the treatment of severe and chronic illness, especially cancer, is the program developed by Mitchell Gaynor, M.D.. In his book, Healing E.S.S.E.N.C.E., he details the use of imagery throughout seven steps

toward healing; experiences, see, surrender empower, nurture, create, embody (Gaynor 1995). Even patients with no prior experience with imagery can develop a practical and useful means of controlling their illness and enhance their healing process.

Whatever the name, mental imagery (Moye, 1995), guided imagery (Giedt, 1997), relaxation imagery (Andrews and Paul, 1990), autogenic training (Benor, 1996), have been shown to be immuno-enhancing. In a somewhat more extreme example of drug induced imagery states, Roberts (1999) found that entheogen-induced mystical and peak experiences may boost the immune system.

Hypnosis: Hypnosis is arguably the most effective approach in unifying the different aspects of the PNI triad. In many ways, hypnosis may encompass many of the other approaches previously mentioned. Hypnosis can have a positive effect on illness by intervening at many levels including symptom alleviation, emotional stabilization, stress reduction, self-image enhancing, and self-efficacy empowering. It can also be employed in directly attempting to enhance endocrine responsiveness and CNS reactivity as well as pain control. Kalt (2000) states that "techniques which attempt to influence the mind fall into the theoretical categories of passive, active, or targeted approaches, each of which may carry varying degrees of importance in immuno-enhancement."

Hypnosis has often been segregated into three general orientations. These include direct, indirect and nondirective approaches. The following is a brief discription of each approach and it's utility in PNI intervention.

Traditional approaches of direct suggestion with formal induction: In these approaches, general trance depth is considered to be important in symptomological change or behavioral changes are given as a directive from the therapist. Although imagery may be employed, it is often the conceptualizations of the hypnotherapist which direct the patient's internal experience. Direct hypnotic approaches have been effectively used, especially in situations where patients either are strongly invested in turning over control to the therapist (i.e., pain management) or where the patient enters the therapeutic setting with significantly impaired feelings of self-empowerment or self-efficacy.

The need to feel that "the therapist is hypnotizing them" provides an initial sense of being taken care of, which may be critical to some patients, especially those deeply ingrained in the medical model. Issues of "suggestibility" and "susceptibility" are often raised when arguing the effectiveness of traditional hypnotherapeutic interventions .

With regard to pain management, significant support exists for the importance of "hypnotic suggestibility" of patients. Highly suggestible patients demonstrate significantly greater pain tolerance (Sandirini et al, 2000, Zachaviae etl al, 1998, De Pascalis et al 1999, Rainville et al 1999, Farthing et al, 1997) and post operative recovery than low suggestible patients (Mauer et al 1999, Defechereuz et al 1999). Other studies have demonstrated that hypnotizability may be less of a factor especially in emergency room settings where an increase in hypnotic susceptibility may be induced by the trauma (Pebbles-Kleiger, MJ 2000).

Indirect approaches: Currently, one of the most commonly utilized indirect hypnotic approaches is Ericksonian hypnosis. Ericksonian hypnosis promotes the idea of trusting in the patient's unconscious to deal with issues that arise. By its very nature, Ericksonian techniques employ a psychoimmunotherapeutic bent. Through the use of metaphor, storytelling techniques and indirect suggestion, the patient is asked to seek what internal images or associations arise while in a hypnotic state in order to bring about emotional and psychotherapeutic change (Erickson 1980). Distraction and dissociative suggestions have been utilized with pain patients within the Ericksonian model (Burte et al 1994). The therapist often acts in a reflective manner guiding the patient into deepening understanding of the spontaneously generated images applying metaphors or stories to relay the hypnotic suggestion while allowing the patient to integrate the message into their own schema. The therapist helps the patient to understand the nature and origin of their symptoms, whether emotional, physical or physiological. Ericksonian approaches have been extensively employed in the treatment of medical illness both symptomologically and etiologically (Erickson 1986).

Simonton (1992) utilizes hypnotic approaches in helping patients learn how to increase their ability to heal (enhance their PNI triad).Visualizing their bodies fighting illness by generating increased T-cells (i.e. little white Pac men eating the cancer) or visualizing bronchial dilation or shunting off blood flow to a tumor are examples of but a few of the plethora of indirect hypnotic applications patients can utilize.

Non-directive approaches: The New Hypnosis initially developed by Araoz (1985) presents a somewhat different model than either the traditional (direct suggestion) or Eriksonian model (indirect suggestion). The new hypnosis utilizes the symptoms brought to the session by the patient as the means of entering into the patient's “inner state”. A process of “observing” the patient's somatopsychic behaviors (i.e., hair twirling, fist clenching), psychosemantic expressions (i.e., he turns my stomach), within the framework of how these actions are manifested through the visual auditory olfactory/taste proprioceptive and kinesthetic senses is initiated. Patients are then “led” into their own inner “awarenesses” They are encouraged not to judge or critique what arises. Often the patient gains new insights into the process which affects their interpretation or reaction to stressors.

At this point, patients are given the opportunity to “visualize and introduce changes that promote greater well being.” Perhaps most critical in the PNI framework is the concept of negative self-hypnosis (NSH). Patients often find that they maintain negative self-hypnotic statements such as broad concepts of “I can never overcome this illness. It is going to kill me.” to more minute specific beliefs about their illness or stressors.

The goal in applying the New Hypnosis or any hypnotic intervention is to be able to intervene and exchange those negative self-hypnotic beliefs for positive self-hypnotic beliefs (PSH). This is best accomplished when, through the hypnotic experience, the patient “feels a change” and that it comes from changes in their “inner awareness” and belief system. For example, a patient who was experiencing chest pain of a non

organically based nature, he reported that in trance, he became aware of the pain as an image of his father's fist squeezing his heart due to unresolved issues between them. Upon imaging a conversation where he resolved these issues and could see his father's hand stroking his heart, the pain abated (Burte 1989).

In situations where pain or stress have a clear etiological basis, the new hypnosis has been employed in developing coping skills, visualizing analgesia, or promoting positive internal representation for change in biophysiology (Burte et al 1994).

EMDR: An interesting new approach, known as EMDR, has been employed with trauma patients. It demonstrates some promising results. Perhaps of most significance in PNI is when we consider the concept of repressed trauma as a possible precursor to immunosuppression.

Group Therapy: Extensive work has been conducted on the impact of group therapy and stress management on immunosuppression. David Speigel's (1999) work with breast cancer patients demonstrates the efficacy of group support as does the work of other researchers who have subsequently found that group therapy can enhance life expectancy and functioning of patients with HIV and other immunosuppressant disorders. It appears that group therapy, offers patients a sense of cohesiveness and an opportunity for them to express their negative emotions and beliefs while simultaneously helping them to develop a better mental attitude and better coping skills which in turn appears to enhance immune system functions.
Societal isolation and self imposed feelings of family isolation (at times when even under the best of supportive conditions) negatively impact upon the PNI triad in the chronic pain and chronically ill patient (Hitchcock 1998). The lack of family coherence at times present with severely ill patients emphasizes the importance of group therapy as an outlet for patients that they might not give to themselves (i.e. especially within their family or personal support networks). A review of the literature appears to suggest that a diverse range of therapeutic/support groups may be effective, and in fact it may be merely the intangible element of not facing adversity alone that enhances the immune functioning. Stress management, pain management, coping skills development, dance, acting ,'as if', group laughter, supportive nondirective groups, all appear to contribute positively to the patient's well being and demonstrate PNI enhancement.

Meditation, role play and dance: Another technique which has been found to impact the immuno system include meditation, which via the pineal gland influences melatonin levels which in turn have been shown to modulate the progression of breast and prostate tumors (Kochar, 1999). In addition to covert techniques such as meditation, the mere outward expression or "acting/modeling of happy behaviors have been found to stimulate endorphins and enhance immune system function" (Anderson, 1997). This may be especially helpful when it is difficult to convince patients of the impact of their negativistic thinking. At such times, perhaps we can encourage them to "act as if" they were happy in order to bring about immunological changes. Still other researchers have found that dance therapy (Hanna, 1995) may improve patients' immune functioning possibly by providing proprioceptive feedback, feelings of self-efficacy and physical self-

control during those times.

A variety of other modalities too far reaching to encompass in this brief chapter also deserve mentioning as they are represented in the PNI literature. Behavioral approaches (Cottrous, 1993; Caudell, 1996), diet and psychological health (Miller, 1996; Norris, 2000), healing energy (Wright and Sayre-Adams, 1999), laughter and music (Bitterman, 2000; Strickland, 1993), and exercise (La Pierriere, et. al., 1994) have been demonstrated to provide positive changes, though further investigation of their mechanism is necessary.

Physical manipulative techniques which directly effect the physiology and nerve transmission, massage therapy (Rich, et. al., 1999) which bring physical and restorative relief, direct pain control with or without opioides, are but a few ways which also promote healing via reducing stress, reducing pain or enhancing patient efficacy.
A word of caution is raised by Greer (1991) who notes that within the PNI model of intervention, one must be on guard that a "blaming the victim" mentality is not promulgated inadvertently. Emphasis should be on positive change, not responsibility for creating one's own impaired status. Any intervention which increases the individuals sense of controllability of their environment or pain level reduces stress, enhances optimism and self-efficacy, impacts the PNI triad proactively and may promote increased health by reducing immunosuppression (Burte, 2000).

"Goodbye" said the fox
"And now here is my secret, a very simple secret. It is only with the heart that one can see rightly. What is essential is invisible to the eye"
"What is essential is invisible to the eye" the little prince repeated so that he would be sure to remember. Antoine de Saint Exupery (1943)

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