# EFFICACY OF SOLITARY AND CONJOINT GUIDED IMAGERY WITH BREAST CANCER PATIENTS

By

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ABSTRACT

EFFICACY OF SOLITARY AND CONJOINT GUIDED IMAGERY WITH BREAST CANCER PATIENTS

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The purpose of this research was to study the effects of imagery and active spousal support on blood counts in women with diagnosed premenopausal breast cancer who had followed a standard course of treatment. For each participating couple a 15-day protocol was followed. In the initial session a baseline blood draw preceded a fifteen-minute immune system videotaped presentation (Bioimagery, 1993). In the two succeeding weeks pre-and post-treatment blood samples were obtained. The subjects utilized guided immunoimagery, alone and with their spouse, to ascertain whether imaging with a partner affects the desired increments in the assayed numerosities following imagery. For thirty minutes after each imagery session, prior to venipuncture, the woman or couple was asked to draw the cancer and their corresponding immunoimages. The pictorial accounts were assessed relative to the patient's and spouse's attitudes about the virulence of the cancer, and the power of the patient's immune system. The drawings were rated according to the IMAGE-CA developed by Achterberg and Lawlis (1984); the relative strength and vividness of the depicted cancer cells and immune system cells were related to blood count changes for white blood cells,

absolute lymphocytes, total T-cells, helper/inducer T-cells, suppressor/cytotoxic T-cells, and segmented neutrophils. The couples' satisfaction and adjustment within the marital relationship (DAS scores/Spanier, 1976) was an intervening variable for both the solitary and conjoint imagery and the subsequent blood assays.

In only 8 of 72 instances did blood counts increase by more than 10% over the course of an imagery session; in slightly more than half the cases blood counts decreased by more than 10%. There was no significant two-week learning effect nor was there statistical support for the notion that conjoint imagery has an incrementing effect on blood count numerosity over a two-week time span. For all of the blood measures except segmented neutrophils, the probability that blood counts will stay the same or increase following the guided imagery was inversely related to the IMAGE-CA Score. There was no relationship between marital satisfaction and adjustment and changes in blood counts.

The uniform decreases in lymphocyte counts following imagery measured in this investigation (although generally within measurement error) are consistent with results in the few published studies evaluating short term blood cell changes following behavioral treatment. Clearly, a longer term study is indicated.

Achterberg, J. and G. F. Lawlis (1984). Imagery and disease. Champaign, IL: Institute for Personality and Ability Testing, Inc.

Bioimagery (1993). The science of immuno-imagery. Irvine, CA: Bioimagery.

Spanier, G. B. (1976). "Measuring dyadic adjustment: New scales for assessing the quality of marriage and similar dyads." Journal of Marriage and the Family, **38**: 15-28.

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# CHAPTER I

# PROLOGUE

## Introduction

Many people with health problems use therapies that do not conform with the standards of the medical community. Although most physicians are unaware of its popularity, alternative medicine is being used world-wide (Murray & Rubel, 1992). There is strong evidence that people in every social, economic, and educational class seek and use alternative care (Murray & Rubel, 1992). In a recent survey, thirty-four percent of the respondents reported using at least one unconventional therapy during the past year, and seventy-two percent of those did not inform their medical doctor about the use of these therapies (Eisenberg et al., 1993). The types of alternative therapy sought were relaxation techniques, chiropractic, massage, imagery, spiritual healing, commercial weight-loss programs, macrobiotics, herbal medicine, megavitamin therapy, self-help groups, energy healing, biofeedback, hypnosis, homeopathy, acupuncture, folk remedies, exercise, and prayer. It was discovered that, in particular, unconventional treatment is sought by cancer patients (Eisenberg et al., 1993). Of those who used unconventional therapies, thirteen percent used relaxation techniques, twenty-five percent prayer, four percent imagery, one percent biofeedback and one percent hypnosis. The authors concluded that unconventional medicine has an enormous presence in health care delivery in the United States. The number of visits made to providers of unconventional therapy was greater than the number of visits to primary care medical doctors nationwide (Eisenberg et al., 1993). Recently, the United States Department of Health

and Human Services has recognized the need for scientific understanding of these phenomena by establishing in the National Institutes of Health a new Office of Alternative Medicine.

Imagery is one form of an alternative and usually adjunctive approach in the treatment of cancer. The possibility of influencing the course of cancer through imagery as well as other behavioral interventions is an exciting notion which is receiving attention in the psychoneuroimmunology literature (Gruber et al., 1993; Kennedy, Kiecolt-Glaser, & Glaser, 1988; Kiecolt-Glaser & Glaser, 1995; Ratliff-Crain, Temoshok, Kiecolt-Glaser & Tamarkin, 1989; Zachariae et al., 1994).

A preliminary study to assess the efficacy of conjoint (spousal) imagery versus individual imagery by breast cancer patients is described in this dissertation. The research involved a volunteer group of premenopausal women who have had surgical intervention and completed a standard protocol of chemotherapy (and, in one case radiation therapy in addition) for breast cancer, as well as their husbands. At the first meeting of each couple with the experimenter, blood was drawn from the woman (to establish baseline blood counts), a medical history of the patient was obtained, and the partners independently completed the Dyadic Adjustment Scale (Spanier, 1976) questionnaire (which was later used to evaluate the marital relationship). The wife and husband then watched a fifteen minute educational video (Bioimagery, 1993) about the body's immune system. At this session the researcher informed the couple that she was particularly interested in T-cells. Later the participant was on two occasions guided in immune system imagery, once alone and once with her co-imaging spouse. Blood was drawn from the female participant before and thirty minutes after (Achterberg, 1993) each of the two succeeding weekly imagery sessions, for the purpose of

comparing the blood assays. The participants drew on paper their imagery experience in the intervening thirty minutes following the immunoimagery. After venipuncture of the woman, they were interviewed about their drawings, according to the IMAGE-CA protocol (Achterberg, 1985). The pre- and post-treatment blood counts for each imagery session were compared, as were the baseline and pre-imagery numerosities and the post-treatment levels. The relative vividness and strength of the pictorial representations of the cancer and the white blood cells were assessed independently by two raters, according to the IMAGE-CA scale (Achterberg, 1985).

**Background**

"Imagery is the thought process that invokes and uses the senses; visual, auditory, smell, taste, the sense of movement, position, and touch. It is the communication mechanism between perception, emotion and bodily change." (Achterberg, 1985) Imagery techniques allow a person to experience an imaginative transformation that carries with it the energy to induce change. A most remarkable feature of imagery work is that it can be accompanied by physiological changes. This has been quite powerfully noted in the professional literature by numerous practitioners (Achterberg, 1985; Benson, 1975; Dossey, 1989; Epstein, 1989; Siegel, 1986; Siegel, 1989; Simonton, Matthews-Simonton & Creighton, 1978). This connection is astonishing only in the context of the past three hundred years of Western medicine. In ancient societies health practitioners assumed the mind and body to be intimately intertwined (Achterberg, 1985). Recently, the field of psychoneuroimmunology has begun to explore the connections between the mind and the workings of the immune system. Convincing evidence exists that the mind

and body are one unified system (Pelletier & Herzing, 1988; Pert, 1997; Rossi, 1993; ).

Rossi (1993) writes: "Mind and body are not separate phenomena, one being somehow spirit and the other matter. Mind and body are both aspects of one information system. Life is an information system. Biology is a process of information transduction. *Mind* and *body* are two facets or two ways of conceptualizing this *single information system.*" Rossi goes on to describe that the two fundamental processes of mind-body communication and healing to be mind-body information transduction and state dependent memory, learning and behavior, with the limbic-hypothalamic system being the major transducer. He believes state-dependent memory, learning and behavior phenomena to be the "missing link" in all previous theories of mind-body relationships. Following Selye, Rossi regards stress to be an important consideration in this model. Figure 1 illustrates Rossi's view of the entire process of mind-body information transduction. Figure 2 depicts some of the cells in immune system that are responsive to stress and psychosocial cues (Rossi 1993).

Our persona is multifaceted. We not only have minds that can affect our bodies, but bodies that respond to drugs, surgery, radiation, and other medical treatments. It is important to recognize the complementarity of the roles of the treatment of the mind (emotions, attitudes, feelings, and perceived meanings) and physical treatment of human illness. We need a balanced approach that considers the mental and physical aspects of human nature when illness arises.

Figure 1. Schematic representation of the role of the limbic-hypothalamic system on the autonomic, endocrine and immune systems. [Reproduced with permission from: "The Psychobiology of Mind-Body Healing" by E. L. Rossi (1993) W. W. Norton & Co., New York, p. 29.]

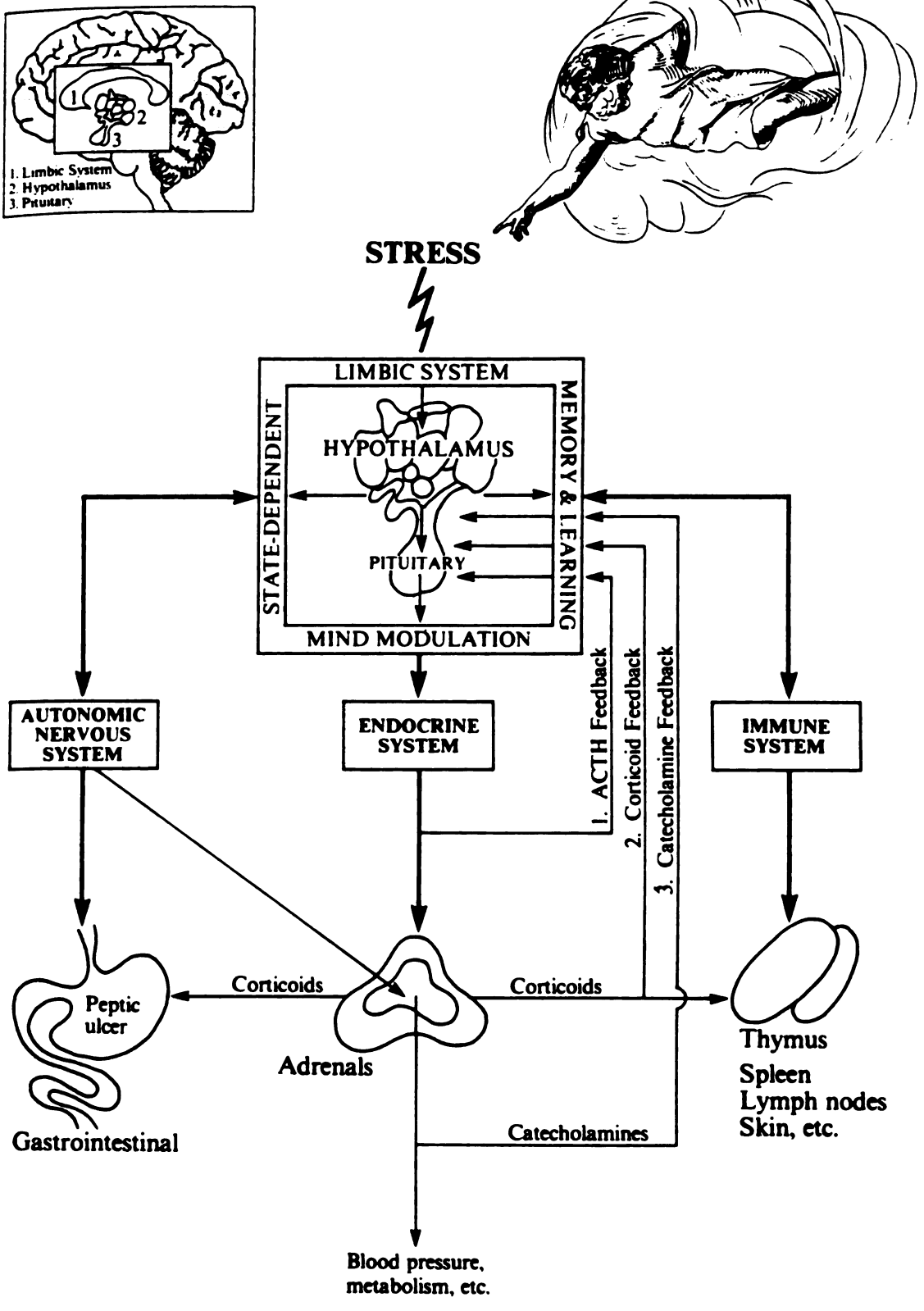
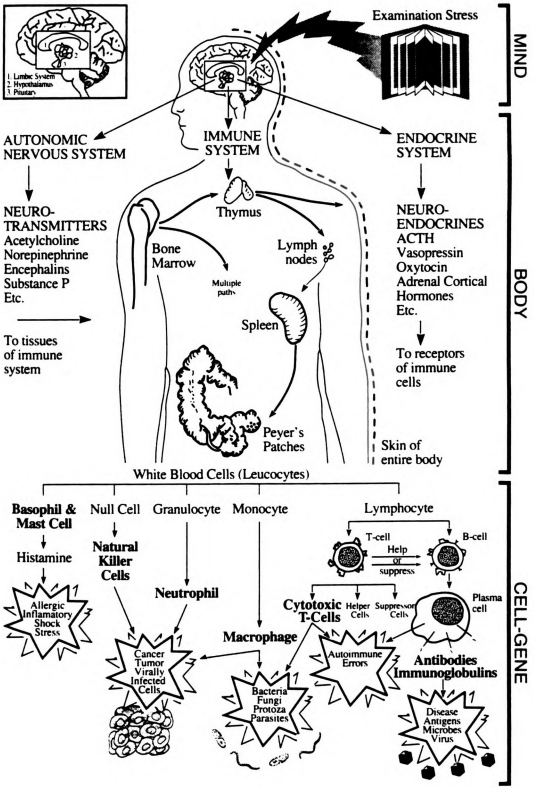

1. Limbic System
2. Hypothalamus
3. Pituitary
STRESS
LIMBIC SYSTEM
STATE-DEPENDENT
MEMORY & LEARNING
HYPOTHALAMUS
PITUITARY
MIND MODULATION
AUTONOMIC NERVOUS SYSTEM
ENDOCRINE SYSTEM
IMMUNE SYSTEM
1. ACTH Feedback
2. Corticoid Feedback
3. Catecholamine Feedback
Corticoids
Corticoids
Peptic ulcer
Gastrointestinal
Adrenals
Thymus
Spleen
Lymph nodes
Skin, etc.
Catecholamines
Blood pressure, metabolism, etc.

Figure 2. Major communication paths between the mind-brain and the interacting networks of the immune system.
[Reproduced with permission from: "The Psychobiology of Mind-Body Healing" by E. L. Rossi (1993) W. W. Norton & Co., New York, p. 219.]


MIND
BODY
CELL-GENE
Examination Stress
1. Limbic System
2. Hypothalamus
3. Pituitary
AUTONOMIC NERVOUS SYSTEM
IMMUNE SYSTEM
ENDOCRINE SYSTEM
NEURO-TRANSMITTERS
Acetylcholine
Norepinephrine
Encephalins
Substance P
Etc.
To tissues of immune system
Thymus
Bone Marrow
Lymph nodes
Multiple paths
Spleen
Peyer's Patches
Skin of entire body
NEURO-ENDOCRINES
ACTH
Vasopressin
Oxytocin
Adrenal Cortical Hormones
Etc.
To receptors of immune cells
White Blood Cells (Leucocytes)
Basophil & Mast Cell
Histamine
Allergic Inflamatory Shock Stress
Null Cell
Natural Killer Cells
Granulocyte
Neutrophil
Monocyte
Macrophage
Lymphocyte
T-cell
B-cell
Help or suppress
Cytotoxic T-Cells
Helper Cells
Suppressor Cells
Plasma cell
Autoimmune Errors
Antibodies Immunoglobulins
Cancer Tumor Virally Infected Cells
Bacteria Fungi Protoza Parasites
Disease Antigens Microbes Virus

In 1988 researchers studied ten adults with metastatic cancer for one year, drawing monthly samples of blood (Gruber, Hall, Hersh & Dubois, 1988). The subjects were at the same time regularly engaged in relaxation and guided imagery. Several measures of immune system function, including T-cells, were found to be significantly elevated in the direction of enhanced activity in a fifteen month time span. It was concluded that relaxation and imagery can measurably affect immune responsiveness. Several weeks to months elapsed for immune system changes to reach statistical significance. The authors suggest that measures of T-lymphocytes may be more reliable outcome measures than other indices (Gruber et al., 1988).

Immunological responses of thirteen women with Stage I breast cancer (lymph node negative) who were healthy at the time of training were studied over a period of eighteen months (Gruber et al., 1993). The researchers found T-cell measures to be very responsive to behavioral interventions over time, and suggest that the efficacy is cumulative. Their results show statistically significant effects, primarily on T-cell and natural killer (NK) cell populations. Although behavioral interventions correlated with immune system measures, no significant psychological changes were detected except a reduction in anxiety (Gruber et al., 1993).

Investigations have also revealed that stress hormones, such as cortisol and the catecholamines (epinephrine and norepinephrine), decrease after relaxation (Jemmott & Locke, 1984). Because our immune defenses tend to weaken when we generate stress hormones, relaxation exercises may be one way to maintain healthy resistance. Stressed medical students (Kiecolt-Glaser et al., 1984) had decreased levels of helper T-cells on the day of examinations. When half the subjects were taught relaxation exercises, their T-

cells increased in number. The percentage increase of T-helper cells could be predicted by how frequently the students practiced relaxation.

Cacioppo and his colleagues (1995) evaluated the effects of brief psychological stressors in older women. They noted heightened autonomic activation, elevated sympathetic adrenomedullary activity and an effect on cellular immune response as evidenced by increased circulation of NK cells, increased NK cell lysis, and a decreased blastonogenic response to the mitogen Con A, and increased CD8 cell numbers.

Equally strong evidence of the connection between coping style and immune suppression comes from studies involving natural killer cells, which kill cancer cells that are trying to spread through the bloodstream. For example, breast cancer patients who appeared "adjusted" to their illness -- passive, fatigued, apathetic -- and who were lacking in social support were found to have more cancerous lymph nodes and weaker NK cells than those who complained more, had difficulties accepting their prognosis and had stronger social support (Levy, Lippman, & Terry, 1980; Levy, Herberman, Maluish, Schlien, & Lippman, 1985).

In a longitudinal study of 280 men and women, those who presented a pessimistic style of thinking had significantly lower immune function in both T-lymphocytes and NK cells (Seligman, 1986). Locke and co-workers reported lower levels of immune function, including NK activity, among depressed or anxious persons (Locke et al., 1984). Both depression and reduced NK activity have been associated with cancer (Levy et al., 1985; Shekelle et al., 1981).

Research on the effects of social support and the prognosis for women with breast cancer indicates consistently positive correlations. Supportive friends and a strong social support network clearly contribute to length of

survival. Conversely, social isolation and lack of social support (in addition to apathy and unhappiness) were predictive of a lowering of the natural killer cells and a poor prognosis in early stage breast cancer (Levy, Herberman, Lippman, & d'Angelo, 1987; Levy et al., 1985; Reynolds & Kaplan, 1986). Cohen et al. (1997) found more diverse social networks to be associated with greater resistance to upper respiratory illness. They found the number of social connections to be much less important than gathering support from a *variety* of sources (Cohen, Doyle, Skoner, Rabin, & Gwaltney, 1997).

David Spiegel and his colleagues have done a carefully controlled longitudinal study of support group intervention with women who have metastatic breast cancer (Spiegel, Bloom, Kraemer, & Gottheil, 1989). They found the pain experiences between the treatment and the control groups to be significantly different. The sensation of pain increased over time in the control group and decreased in the treatment group. Retrospectively, the authors examined the state death records on the 86 patients who had participated in the study and found that after 48 months all the control patients were dead while a third of the treatment patients were still alive. When the mean differences in survival time of the two groups were compared, the investigators found the treatment group lived twice as long as the control group (Spiegel et al., 1989).

The immediate and long-term effects of immune function were evaluated for participants in a six-week structured psychiatric group intervention for patients with malignant melanoma (Fawzy et al., 1990). The results suggested that short-term psychiatric group intervention was associated with longer-term changes in affective state, coping, and the natural killer lymphoid cell system (Fawzy et al., 1990).

Levy and her colleagues found that a significant amount of natural killer activity variance in Stage I and II breast cancer patients could be explained by five variables (Levy et al., 1990). Higher NK activity could be predicted by the perception of high-quality emotional support from a spouse or significant other, perceived social support from the patient's physician, estrogen receptor-negative tumor status, having an excisional biopsy as surgical treatment, and actively seeking social support as a major coping strategy (Levy et al., 1990). The most important predictor was the perception of emotional support from a spouse or significant other.

Esterling, Kiecolt-Glaser and Glaser (1996) explored the cellular and psychological mechanisms that might explain the observed changes in natural killer cell cytotoxicity associated with chronic stress. Former and current spousal caregivers of patients with Alzheimer's disease showed higher enriched natural killer cell responses to two cytokines when heightened levels of positive emotional and tangible social support were present.

Stress and social support have been found to modulate biological responses in normal healthy adults (Glaser et al., 1992). Both stress and social support were related to medical students' ability to generate an antibody response to the hepatitis B inoculation. Students who were more anxious and more stressed showed a delay in seroconversion. Those who reported less social support had a poorer immune response to the HBsAg as shown in the combined measure for antibody titers and the T-cell response.

In women, the immune system seems to be sensitive to the social support that comes from a good marriage. In a study of 38 married women, researchers found that marital quality was significantly associated with immune functioning, including percentage of helper T-cells and ratio of helper to suppressor lymphocytes. The women who perceived their marriages

as satisfying and supportive had less depression and loneliness, as well as better immune defenses. The quality of a person's marriage as perceived by the subject was a more powerful predictor of happiness than work satisfaction or relationships with friends (Kiecolt-Glaser, Fisher, et al., 1987). Relatively few marriages (7%) end in divorce after a diagnosis of breast cancer. It is possible that women react less intensely and less pessimistically to stressful events if they know they have someone to share them with who will support and help them. However, it is difficult to know whether those in a satisfying marital relationship are less prone to depression and loneliness or whether the absence of loneliness and depression in marital partners makes the marriage more satisfying or whether a separate third factor is involved.

Research over the years has suggested that when we mentally picture our bodies doing something, internal changes occur accordingly (Achterberg, 1985). If one rehearses a strenuous dance routine mentally, s/he evokes muscular changes, increased blood pressure, altered brain waves, and activation of sweat glands. MSU researchers have demonstrated the effect of imagery on neutrophils, which are white scavenger blood cells that are important in keeping us free from infection (Schneider, Smith, & Whitcher, 1983). They concluded people who are ill need to know some specifics about their illness and the body's natural defenses and convert the knowledge into some type of image in order to have an impact on cellular activity and function. They determined that relaxation training is a factor in making the imagery effective. In a separate study, they also found educating subjects about lymphocyte function and relaxation, and training them to do guided imagery, may have influenced changes in numerosity of T-helper and T-suppressor lymphocytes (Schneider, Smith, Mining, Whitcher, & Hermanson, 1990).

Biofeedback research has shown if we imagine hot scenes (sun, beach, desert) we can increase blood flow and warmth of our hands and other parts of the body (Schwartz, 1984).

The evidence suggests that people may also be able to alter their immune systems and disease states by what they imagine and visualize. In other words, people may be able to activate self-healing systems. Researchers have found that how a group of cancer patients pictured their malignant cells and their immune systems was the most powerful predictor of their disease status two months later (Achterberg, et al., 1977). Those with the best outcome visualized their white blood cells as being like Vikings or other legendary figures who fought for God and country. Those with poor outcomes pictured their immune cells as weak or soft, like snowflakes or clouds.

Trestman (1981) analyzed the color of cancer patients' images of their cancer. Thirteen of the fourteen people with "good" status imagined their cancer as red or black, while eight out of eleven with relatively poorer status described their cancers as lighter colors.

Thus there is a growing body of research that documents the interrelationship between mind and immune system function, the importance of social support to breast cancer patients, and the impact of imagery upon personal health. Imagery techniques are rarely credited as being essential to the practice of technological medicine, but they are considered useful to the psychological well-being of patients. Imagery's beauty is multifaceted: it is affordable by the masses, and indeed it has been used in folk healing for centuries; it is a tool whose power has been documented throughout history. Imagery is a powerful, non-invasive, self-controlled, inexpensive method of healing. In order for imagery to move from an adjunctive role to an essential factor in

healing, a solid, convincing body of research must be conducted to support the role of imagery in total health.

**Problem Statement**

The purpose of this research was to study the effects of imagery and active spousal support on blood counts in women with diagnosed premenopausal breast cancer who had followed a standard course of treatment. The subjects utilized guided immunoimagery, alone and with their spouse, to help the researcher ascertain whether imaging with a partner results in more salutary effects. For thirty minutes after each imagery session, prior to venipuncture, the woman or the couple was asked to draw a picture of the cancer and their corresponding immunoimages. The pictorial accounts were assessed relative to the patient's and spouse's attitudes about the virulence of the cancer, and the power of the patient's immune system. The drawings were rated according to the IMAGE-CA developed by Achterberg and Lawlis (1984); the relative strength and vividness of the depicted cancer cells and immune system cells were related to the efficacy of the blood count changes. The couples' satisfaction and adjustment within the marital relationship (DAS scores) was an intervening variable for both the solitary and conjoint imagery and the subsequent blood assays.

# CHAPTER II

# REVIEW OF THE LITERATURE

Imagery is a multisensory representation of an experience. Some think of imagery as a waking dream or similar to daydreaming. It is produced by imagination. Individuals generally utilize one or two senses as primary sources for experiencing their world. For example, musicians frequently are very aware of the presence or absence of sound in their environment; they are often keenly aware of auditory change.

Imagery can be guided or spontaneous. Therapeutic guided imagery includes an induction, a phase of involvement or disassociation, and a reversal. Either purposefully guided or spontaneously experienced, imagery is embedded in a sensory environment: visual, auditory, tactile, olfactory, taste, or kinesthetic. It is limitless and can embrace the *impossible* -- flying, living in a different time and space, communicating with animals or inanimate objects. Although many people associate imagery with memory representations of physical objects, non-physical processes, such as mathematical problems and logical relationships, can also be represented in imagery.

Imagery is often used to *distract* (escape from pain, stress, or problems) or to *focus* (explore an issue in depth for the purpose of understanding or changing it) (Schneider, 1987-1991). *Distraction* allows an individual to avoid pain and anxiety for a time. It provides short-term relief and is often used in pain management. *Focusing* is a technique described by Gendlin (1978) that facilitates the development of a *felt sense* -- a contact with a special kind of internal body awareness. A *felt sense* is body and mind before they are split

apart, the body's *knowing* what a person's problems feel like. Gendlin (1978) believes that the body finds its own way in providing answers to many problems. Focusing is being studied in relation to issues such as spirituality, business, problem-solving, creative writing and dreams.

*End result imagery* occurs when the objective of induced imaging is the individual seeing the desired result as having already occurred; the method is utilized by Simonton, Matthews-Simonton, and Creighton (1978) in Getting Well Again. *Process imagery* occurs when the individual images a specific desired effect; it is illustrated by Bernie Siegel's (Siegel, 1986) healing imageries in Love, Medicine & Miracles.

Dendinger and Trop (1979) purport imagery to flow out of movement and movement to flow out of imagery. "The body's motional usages of and emotional attitudes toward space, time, energy and rhythm can engender in the imagination deep images. The way we move within ourselves, gesture, posture, touch, or the way we move and are moved in relationship to another person contains the non-verbal movement history of our way of being in the world."

Mental imagery is non-logical. Epstein (1989) defines mental imagery as the mind thinking in pictures, and terms it the thinking used for making contact with our inner subjective reality. According to Achterberg (1985), "Imagery is the thought process that invokes and uses the senses; visual, auditory, smell, taste, the sense of movement, position, and touch. It is the communication mechanism between perception, emotion and bodily change. A major cause of both health and sickness, the image is the world's oldest and greatest healing source."

In ancient societies the mind and body were believed to be interconnected. In the realm of shamanism, nothing exists in isolation; shamanism

speaks to the unity of all things and all beings (Kalweit, 1988). Epstein notes that no medical system in the history of the world, including Western medicine prior to the seventeenth century, has distinguished the mind as separate from the body (Epstein, 1989). The emerging field of Behavioral Medicine (psychoneuroimmunology) is exploring the connections of the mind and body (Achterberg, 1985; Achterberg, Lawlis, Simonton, & Simonton, 1977; Holden, 1978; Palmbad, 1981; Rogers, Dubey, & Reich, 1979; Schneider et al., 1990; Sklar & Anisman, 1979; Solomon, 1985; Solomon & Amkraut, 1981).

Locality has become a premise in modern medicine; healers must be by the bedside or in the operating room. Yet acknowledgment of the role of mind expansion and spirituality in the healing process is powerfully present in the scientific literature. Spiritual beliefs and faith often are connected to the concept of a Higher Being in the role of a spiritual guide. Prayer is directed to an imaged entity *who has not been confined to a specific place* and the prayer is often an image of the process or result desired by the praying individual.

Dossey (1989) advances the concept of nonlocality in healing. He regards the body as a local entity that can be treated with physically based approaches anchored in the present, and the mind as nonlocal (infinite in time and space) and also capable of bringing about profound changes in the body. Dossey regards the best therapeutic reality as one that combines both approaches.

Guided imagery encourages the user(s) to let go of extraneous, distracting thoughts and to focus exclusively on the desired purpose of the imagery. It is similar to the meditative state utilized in prayer. Transpersonal imagery, where one's purpose is to affect another, closely parallels praying for

another's healing. Despite objections from both scientists and religionists, researchers have sought evidence for prayer's power for more than a century.

According to healers who employ prayer routinely, it is more effective for some problems than others. Therapies should be judged according to the effects that occur in the conditions to which they are applied, and prayer is not an exception. More than one hundred experiments, many conducted under stringently controlled laboratory conditions, are reported in the scientific literature, over half showing that prayer engenders significant changes in both animals and human beings (Dossey, 1993). The effects of prayer were not dependent on the praying person being physically proximate to the organism being prayed for. Even when an object was placed in a lead-lined room or in a cage that shielded it from all known forms of electromagnetic energy, the treatment effect still occurred (Dossey, 1993).

Descartes equated the mind with the brain, and Western thought expects the mind to have locality, specifically in the brain. However, scientific evidence is beginning to support the nonlocality of the mind. Brainlike tissue is found throughout the body; chemical endorphin receptors have been discovered outside the brain, in white blood cells and in the gastrointestinal tract. Healers who employ a more holistic conceptualization would say mind, body and world are one. Via computer-controlled experiments, minds have communicated complex messages over long distances (Jahn & Dunn, 1987). There was no difference whether the subjects were separated by one block or by thousands of miles. If minds are not confined to time or space, they are unbounded.

Throughout the body, the systems most important to our health -- the brain, the glands, and the immune system -- connect and communicate via messenger molecules that are sensitive to our cognition (Pert, Ruff, Weber, &

Herkenham, 1985). Pert sees the "body as the outward manifestation of the mind" and body and mind as inseparable (Pert, 1986). For Pert, evidence of that inseparability came from the discovery that a number of the chemical messengers in the body are the same as the ones in the brain. Among these "communication molecules" are neuropeptides that regulate our moods and emotions. Because some can be found in the intestines as well as in the limbic system (our *feeling* brain), Pert says, "the emotions are not just in the brain, they're in the body."

In Who Gets Sick: How Beliefs, Moods, and Thoughts Affect Your Health, Justice explores the key role of recently discovered neurotransmitters, brain hormones, and other chemical messengers in the functioning of the body and some of the ways by which these powerful molecules play a part in illness and disease (Justice, 1987). How the chemical messengers are affected by our attitudes and reactions to stress is examined. Justice traces the pioneering work on "giving up" as a major factor that precipitates illness, and looks at how some people postpone their deaths until after some special occasion. He suggests positive attitudes and beliefs can protect and restore our health by turning on self-healing systems.

The biopsychosocial risk-factor concept of disease differs from germ/virus theory, the traditional medical model that suggests that pathology is mostly caused by foreign forces that attack our bodies (Engel, 1960). Mechanisms of disease are connected with the brain and seem to be influenced by our mental processes. Messages sent by brain cells in the form of neurotransmitters, hormones and neuropetides are received by cells that have receptors all over their surface membranes. Our thoughts and perceptions direct the chemical messages the brain sends.

Kendall (1981) reports that the mentally retarded and emotionally disturbed population has a selective protection from cancer and autoimmune disorders such as rheumatoid arthritis. The percentage of deaths from cancer for the mentally handicapped is approximately 4%, in contrast to a 15-18% incidence among the general population. As the mentally handicapped subjects approach normal intelligence their cancer rate also increases (Kendall, 1981). Achterberg (1985) notes that the criminally insane also seem to have a low incidence of cancer, despite heavy smoking. She speculates that there is a relationship between the diverse mental conditions of mental retardation and emotional disturbance, both of which indicate a lack of awareness of information from the environment. Is stress managed in a way that does not inhibit the immune system in these populations?

Hope and belief in becoming well stir the imagination into action. There are countless anecdotal accounts of an individual's images contributing to a premature death or to a prolonged life despite the presence of grave health issues. Achterberg (1985) describes the murderous power of images of a woman diagnosed with early stages of breast cancer, who died within hours, apparently from the workings of her imagination. Another such example is the woman who was brought to a hospital comatose, paralyzed and diagnosed with a massive brain tumor (Achterberg, 1985). A surgeon removed as much of the tumor as safely possible, and since the patient was close to death, neither radiation nor chemotherapy was attempted. The word *tumor* did not imply a deadly cancer to the woman; her images were of recovery, not death, and she defied the odds.

In the introduction to Normal Cousins' book, The Healing Heart (1983), Bernard Lown describes a critically ill patient whose cardiac muscle was irreparably compromised and for whom no further treatment was known.

During rounds Dr. Lown mentioned to the accompanying staff that the patient had a "wholesome gallop" (indicative of a failing heart). Several months later the patient, who had made a remarkable recovery, told Dr. Lown that he knew when he heard that his heart had a *wholesome gallop* that he must have a lot of kick left in his heart and therefore could not be dying. He reported that he knew instantly that he would recover. The words, wholesome gallop, conveyed to the patient an image of a horse that was full of life, and this image was credited by his physician as being responsible for his new state of health.

Several investigators have ingeniously attempted to measure mystical elements in healing. Prayer has long been held by most religions to contain powerful healing properties and throughout time it has often been used as a form of intervention in illness.

Experiments have been carried out to address such questions as: Is spiritual healing real? Does prayer work? Is there an effect that can be measured and reproduced? In one study, the effects of prayer on patients in a coronary care unit were followed by Randolf Byrd (1988) in a randomized double blind experiment over a ten-month period. Neither the patients, the nurses, nor the doctors knew which group a given patient was in. Roman Catholic and Protestant prayer groups were recruited around the country to pray for the 192 members in the designated group; 201 patients in the control group were not prayed for. Members of prayer groups were given the names of the patients, told something about their condition and instructed to pray for them, but were not told how to pray. Each person prayed for many different patients, and each patient in the experimental group had five to seven people praying for him or her. The prayed-for patients were five times less likely to need antibiotics than the control group; they were three times less

likely to develop pulmonary edema; none required endotracheal intubation; and few patients in the prayed-for group died (although that difference was not statistically significant). The geographical distance between the patient and the person praying did not seem to matter; prayer groups around the corner from the hospital were not found to be more effective than ones hundreds of miles away.

A careful set of experiments involving the survival and growth of seeds, known as the Spindrift project, also sought to answer the question: Is prayer more powerful if a specific goal is prayed for or if the person praying simply asks: "Thy will be done"? Although both approaches worked, nondirected prayer was found to be quantitatively much more productive (Dossey, 1989). Dossey writes: "Thus, after many years of research, the Spindrift researchers have formulated the *law of the conceptual whole:* So long as the practitioner can hold in his mind an overall concept of the system involved, the effect of prayer is constant over all components." Seemingly in contrast, researchers and practitioners who employ imagery as a tool for healing have observed more powerful effects when the patient had knowledge about the disease and the healing process (Achterberg, 1985; Schneider et al., 1990).

Hemolysis is the process of putting red blood cells in a dilute solution where they are stressed and gradually swell and burst, thereby leaking their hemoglobin into the solution. Hemolysis can be measured with extreme accuracy with a spectrophotometer. William Braud (1990) used hemolysis to investigate whether ordinary people could mentally protect red blood cells from seriously stressful influences. Further, he wondered if mental protection could be done at a distance and whether it works better on a subject's own red blood cells or if it equally protects the cells of others. Thirty-two untrained subjects (17 female, 15 male) mentally attempted to keep red blood

cells from dissolving when the cells were placed in a dilute solution in a test tube in a distant room. In a double blind design, about half were trying to protect their own cells and the other half were protecting cells of another person. A session consisted of two control and two protect periods, each fifteen minutes long. When asked to protect the blood cells, the subjects were shown a color slide projection of healthy red blood cells. In the control period the subject was asked to think about matters not connected with the experiment. The technician performing the post-measure did not know if the blood originated from the subject or someone else, or whether the session was the treatment or control condition. The author concluded from this study that the subjects could affect rate of hemolysis. He also found healing thoughts could function at a distance and that they seem to occur regardless of whether they are directed at oneself or another. Although the overall effect was unselfish, there also appear to be individuals whose healing thoughts may be more potent for themselves than for others (Braud, 1990).

Braud and Schlitz (1983) studied the ability of 62 people with no special characteristics to influence the physiology of 271 subjects who were isolated from the influencers. Of the 271 subjects, the only participants especially recruited were a group of those in need of a "calming" influence on their physiology. These subjects had evidence of greater than usual sympathetic autonomic activation, as evidenced by stress-related complaints, excessive emotionality, excessive activity, tension headaches, high blood pressure, ulcers, or mental or physical hyperactivity. These special subjects were screened and it was confirmed that they indeed exhibited greater than average arousal of the sympathetic nervous system. There were thirteen experiments in all.

The subjects were attached to sensitive instruments that measured their electrodermal activity (the ability of the skin to conduct an electrical current, which is an indicator of activity of the sympathetic part of the autonomic nervous system). At a given signal, the influencer would try to exert a calming or activating influence on the distant subject, who was unaware of when the attempt was made. During influence periods the influencer used mental imagery and self-regulation techniques to induce relaxation or activation in him or herself, while imagining an intended corresponding change in the distant subject. Then the influencer would imagine the desired pen tracings of the polygraph.

The effect was consistent, reliable and robust. In some experiments the subjects reported spontaneously receiving the exact image of the influencer. Braud and Schlitz (1983) concluded the transpersonal imagery effect compared favorably with the magnitude of the influence on one's own physiology; that the ability is widespread in the population; that transpersonal imagery can occur at distances of 20 meters (greater distances were not tested); that subjects for whom the influence would be beneficial were more susceptible; and that this effect can occur without the subject's knowledge.

Most physicians respect the patient's *will to live* and realize their treatments are far more effective if their patients *believe* in them (Schneider, et al., 1990). Achterberg and Lawlis attempted to quantify beliefs and attitudes about cancer with "disease imagery" ratings objectively obtained from patients (Achterberg & Lawlis, 1978). They investigated the potential of imagery as a predictor of survival time in critically ill cancer patients. A projective instrument has been developed, called the IMAGE-CA (Achterberg & Lawlis, 1979) to assess patients' attitudes about their disease and treatment, as well as the belief that they may have innate ability to overcome the

illness. While developing their measure of disease imagery, Achterberg and Lawlis (1979) administered a battery of psychological tests and obtained informal disease imagery ratings for 126 cancer patients who had a five percent chance of five-year survival. The results indicated that disease imagery was a far better predictor than any standard psychological instrument or blood chemistry for predicting disease status. In a validation study of the IMAGE-CA with three separate groups of cancer patients having a total number of about 200, Achterberg (1985) reported that the instrument predicted with 93% certainty who would be in remission, and forecast an unfavorable prognosis (death or significant deterioration within a two-month time period) with 100% accuracy.

Lydia Temoshok and Henry Dreher (1992) speculate that living in a state of chronic emotional repression may contribute to physiological illness. They identify a Type C personality, "nice" people who do not express anger or fear about their own well-being. For these people, emotional pain seems to be entirely repressed. Type Cs appear patient, unassertive and cooperative. The authors hypothesize that the chronic emotional repression may overtax the brain, weaken the immune system and leave one more vulnerable to disease. They suggest that since Type Cs neither fight nor flee when faced with stress; they may overproduce opiates and adrenaline, both of which can suppress the immune system. Temoshok's research on melanoma patients revealed that patients who expressed their emotions more openly had more cancer-fighting immune cells gathering around their tumors. Conversely, patients who repressed their emotions had far fewer localized cancer-fighters (Temoshok & Dreher, 1992).

The following immune system information has been summarized from Jeanne Achterberg's description (1985):

*The hypothalamus serves as an important regulator in the immune system and it is intimately connected to the parts of the brain that are involved in emotion (i.e., the limbic system). The limbic system forms a connecting network with the frontal lobes, which are the most evolved part of the cortex itself and believed to be critical for imagery and for planning for the future.*

*Neutrophils are white blood cells that are given life in the bone marrow, and constitute about 65% of the total white blood cell (WBC) population. They are chiefly responsible for fighting infections. They circulate, daily, looking for bacteria that don't belong in the body. Neutrophils respond to chemicals that are released at the injury site and prepare to attack by changing into a shape that can more easily pass through blood vessel walls. They adhere to capillary walls that have become sticky, and extend a small foot (pseudopod) through any gap and slither out of the blood steam. Neutrophils then move toward the offender and begin the process of destroying the intruders, which is called phagocytosis. The engulfment and digestion are accomplished when the neutrophil sends its cytoplasm flowing around the foreign particle, and then isolates it in a sac (phagosome). Enzymes are then shot into the sac, and the intruder is destroyed. Neutrophils are the first line of defense and are followed by other specialized attackers.*

*B-cells and T-cells are WBCs called lymphocytes, because they circulate through the lymph fluid. Both respond only to certain microorganisms, and both are given their life in the embryonic bone marrow. The T-cells migrate to the thymus, where they are energized for action. There are at least three kinds of T-cells: the* ***killers****, whose specialty is killing viruses and foreign tissue with potent chemicals; the* ***helpers****, which assist the B-cells in going after*

*their highly specific targets; and the* ***suppressors****, which serve a regulatory function, perhaps keeping the immune system from going wild and attacking self as well as nonself. The killer T-cells are known to be involved in the defense against cancer, the suppressor Ts in the prevention of autoimmune breakdown. The B-cells create proteins called antibodies that can identify a specific invader and start the complicated process of destruction.*

*The white blood cells, the chief representatives of the immune system, have an uncanny ability to sort out friend from foe. Immunization through vaccination is based upon the natural ability of the body to learn to defend itself. When the skills of the white blood cells go awry, autoimmune disease, such as rheumatoid arthritis and multiple sclerosis, as well as infectious disease and cancer, are possible. What the immune system doesn't already know or hasn't learned from vaccination, it may be able to learn in another way. All the biochemical changes that happen during the real-life exposure may occur during fantasy.*

*Cancer can be viewed as a disease of the immune system. Particular white blood cells, T-cells, identify and destroy the cancer cells they meet in the body. Following the destruction of cancer cells, the macrophages join the scene and digest any remaining pieces.*

*The surveillance theory of cancer suggests that just as our bodies often house the potential for strep and staph infections, they also have malignant cells that are held in check by the T-cells and macrophages. According to this theory, when these cells fail to recognize and kill the malignant cells, the cancer cells multiply and become a tumor.*

*The numerous accounts of spontaneous remission (the disease goes away in the absence of medical treatment) support the idea that the body has an ability to heal itself.*

*With most autoimmune disorders, as well as with cancer, cytotoxins (cell poisons) are sometimes a successful treatment. They are believed to stop the multiplication of the offensive cells, which seem to be more susceptible to the poison than healthy cells. It is conceivable that chemotherapy could be paired with a neutral substance and the immune system could be conditioned to respond to the administration of the neutral substance alone as it did when it was paired with the cytotoxin, thereby eliminating some of the toxic effects of the drug.*

It has been noted that alpha-endorphins and other opioid peptides, secreted under inescapable stress, suppress the function of T-cells in the immune system and reduce the effectiveness of natural killer cells (Shavit, Lewis, Terman, Gale, & Liebeskind, 1984). [Natural killer (NK) cells are other lymphocytes that do not require sensitization to express the killer function (Berkow, 1992).] A 1988 study of 312 patients revealed that those who were repressing emotion had increased levels of opiates in their brains and bodies (Jamner, Schwartz, & Leigh, 1988). These patients also possessed far fewer white blood cells in their immune systems. The excess opiates, the authors concluded, were a result of negative coping under stress and helped suppress patients' white blood cells.

In a paper reviewing hypnosis as it relates to the body's immune system, Hall hypothesizes that it should be possible to raise immune functioning under controlled laboratory conditions and that hypnotizability may be related to one's ability to enhance immune system functioning (Hall, 1982-1983). Voluntary self-regulation of immune responses through relaxation and imagery resulted in a statistically significant increase in one mitogen measure and a marginally significant increase in one of the blood count measures. Age, hypnotizability, and their interaction significantly predicted

changes in the set of blood count measures, but not in the set of mitogen blood measures (Hall, Mumma, Longo, & Dixon, 1992).

Researchers studied 108 undergraduates who received immunizations for swine flu (Locke, 1982). They found students who coped poorly with stress had a significantly impaired immune response as measured by decreased natural killer cells; the students with high stress and good coping ability had the highest level of NK cell activity. In a later study, Locke noted that when anxiety and depression were high, activity of natural killer cells was low, suggesting possible lowered immunity (Locke et al., 1984).

Zachariae and his colleagues at the University of Denmark (1990) measured the effects of relaxation and guided imagery on cellular immune function on ten healthy subjects. When the subjects were instructed to imagine their immune systems becoming very effective, a significant rise in natural killer function resulted. The study does not indicate whether the rise in NK activity is due to the relaxation, mental imagery, or both. No significant differences could be detected for numerosity of mature T-cells, T-helper cells, T-suppressor cells, B cells or monocytes. One hour following the imagery most T-cell counts decreased from the baseline value. Since NK cells may be a defense for newly formed neoplasias, these authors suggest relaxation and imagery might be beneficial for cancer patients with minimal residual disease (Zachariae et al., 1990).

Another group of researchers led by Zachariae (1994) compared an imagery group and a relaxation group to controls and found a decrease in blood counts following the intervention in both the imagery and relaxation groups, and no differences in pre and post blood draws in the control group. No differences in natural killer cell activity were found between the imagery, relaxation and control groups (Zachariae et al., 1994).

The literature that examines the impact of stress on immune system measures in humans yields conflicting results, illustrating the complexities encountered when researchers try to isolate variables and to control for the myriad of influences (some positive, some negative, some long term, some short term) on immune system functioning.

A study of first year medical students found that the stress of exams caused a drop in both the number and activity of natural killer cells. Also, extremely lonely students had the least active natural killer cells and weaker immune systems (Kiecolt-Glaser et al., 1984). A reduction of interferon, an important protein produced in the body that stimulates NK activity, was also found in medical students during final examinations.

In a more recent study, students who were more anxious or more stressed showed a delay in seroconversion to the Hepatitis B vaccine. Following seroconversion, the students who reported less social support also showed a poorer immune response to the vaccine, as measured by antibody titers and T-cell response (Glaser et al., 1992).

A Canadian research group tested the effects of stress on medical students on three occasions: one month prior to an exam (during a time of low academic stress); immediately following an exam; and ten days following the same exam (Dobbin, Harth, McCain, Martin, & Cousin, 1991). Lymphocytes decreased significantly after the exam, and at the ten day post-exam measurement they had not returned to baseline levels. Interferon-g (IFNg) is mainly produced by T-lymphocytes (Benjamini, Sunshine, & Leskowitz, 1996); therefore, the IFNg decrease noted in this study was consistent with the decrease in lymphocytes. Interleukin-1 (IL-1) is a cytokine that has a proliferative effect on T- and B-cells. IFNg and IL-1 impact the immune response in an integrated fashion (Benjamini et al., 1996). Thus, the

significantly higher IL-1 levels measured after the exam were unanticipated by the researchers, who concluded that this divergence between IFNg and IL-1 production suggests that stress affects the IL-1 producing cells (*e.g.*, monocytes) in a very different way than it affects IFNg producing lymphocytes (Dobbin et al., 1991).

Psychological stress may not suppress cellular immune function in all individuals. T-suppressor/cytotoxic lymphocytes increased in number and T-cell response to stimulation by phytohemagglutinin decreased after subjects were exposed to a twenty minute laboratory stressor, but only for persons who also showed elevated catecholamine and cardiovascular reactions to stress (Manuck, Cohen, Rabin, Muldoon, & Bachen, 1991)

An experimental group of healthy subjects who were trained in biofeedback techniques exhibited significant increases in blastogenesis (a method used to assess lymphocyte competence), most notably the interaction of a 100 ml suspension that contained $10^6$ lymphocyte cells/ml with 100 mg of phytohemagglutinin (PHA), when compared to untrained controls (McGrady et al., 1992). Contrary to the documented suppression of immune function by stress (noted earlier), biofeedback in this study increased responsiveness of the lymphocytes to mitogenic stimulation.

Caregivers for close relatives with Alzheimer's disease who for years put aside their own needs for the benefit of others suffered marked loss of immune strength (Kiecolt-Glaser, Dura, Speicher, Trask, & Glaser, 1991). Lymphocyte suppression during bereavement has been documented to occur as early as one month following a death (Schleifer, Keller, Camerino, Thornton, & Stein, 1983). Natural killer cell activity is much reduced in grieving spouses (Irwin, Daniels, Smith, Bloom, & Weiner, 1987). Kiecolt-Glaser and Glaser (1992) in their review stated: "The weight of the evidence

to date suggests that chronic stressors are associated with continued down-regulation of immune function rather than adaptation." (Kiecolt-Glaser & Glaser, 1992)

On the other hand, the ability to love and care about others seems to result in lower levels of the stress hormone norepinephrine and a higher ratio of helper/suppressor T-cells, an important balance in a healthy immune system (McClelland, 1985). McClelland professes that the evidence strongly suggests that love aids the lymphocytes and improves immune function. People who are in love suffer fewer colds and have white blood cells that more actively fight infections. Lovers were reported to have lower levels of lactic acid in their blood, which means they are less likely to get tired, and higher levels of endorphins, which may contribute to a sense of euphoria and a reduction of pain (Siegel, 1986).

The interdependence of happiness and health was found to predict longevity better than any health or physical activity factor in 268 subjects who were controlled for effects of age, work satisfaction and happiness (Palmore, 1969). Palmore also found marital satisfaction to be highly associated with both the level of immune functioning and psychological well-being. A significant association between perceptions of life satisfaction and health was also reported among different groups of men and women whose illnesses were charted for more than twenty years (Hinkle, 1961). Ten thousand men in Israel showed nearly two times lower risk for development of angina pectoris if they answered "yes" to the question: "Does your wife show you her love?" (Medalie & Goldbourt, 1976).

Some research has explained how immunity is impacted by our thoughts, beliefs, and attitudes as well as by the social support we perceive (Plaut & Friedman, 1985). In one example, Maddi and Kobasa (1984) found

that executives who were high in hardiness and low in illness used "transformational coping" to deal with problems. They describe transformational coping as the process of "altering the events so they are less stressful." The hardy executives thought about problems in optimistic terms and acted decisively.

Support affects T-cells when a person is under stress. Kemeny (1984) found lack of support to be related to a reduction of suppressor T-cells and associated with recurrence of herpes simplex, Type II. When social contact is increased or loneliness is reduced, the immune system seems to strengthen. A group of thirty elderly people in retirement homes showed increased immune function in terms of both NK cells and antibodies when they were visited three times per week for one month (Kiecolt-Glaser et al., 1985).

Berkman and Syme tracked the health of people in Alameda County, CA for nine years. They found those people with social ties -- married, having friends, contact with relatives, participating in church affairs and belonging to other groups -- had significantly lower mortality rates (Berkman & Syme, 1978). In another study, Reynolds and Kaplan studied 6848 Alameda County residents over a period of seventeen years. Women who were socially isolated and felt socially unsupported were found to be at a significantly higher risk of getting cancer, and of dying from the disease. Social ties did not seem to affect whether men got cancer. However, among men who got cancer, the socially isolated ones died much sooner than those with social ties (Reynolds & Kaplan, 1986). In a very recent publication the diversity of kinds of social support as opposed to the numbers of supporters was found to be important in resistance to upper respiratory disease (Cohen et al., 1997).

Thus, the notion that guided imagery can have a salutary effect for women who have had breast cancer, and the hypothesis that conjoint imagery

with a supportive spouse can enhance the benefits, are well grounded in the literature. A preliminary study of this proposition is described in this dissertation.

# CHAPTER III

# RESEARCH METHODOLOGY

## Conceptual Model

Modern medical treatment is depicted by evolutionary complexity. Intricate cancer protocols can be stressful for patients and their families. There may be biopsies, blood chemistries, X-rays, surgery, radiation, and chemotherapy. These procedures may be protracted, frightening, painful, and difficult to endure. The breast cancer patient also has to deal with her illness as well as with her altered roles as a career woman, wife, mother, and sexual partner. She may be confronting her mortality for the first time. There may be financial and psychological stresses on the family as its members individually and collectively face the multilayers of change and loss that occur with the diagnosis of breast cancer.

Engel speaks of the powerful influence of paradigms upon what scientists select to study and how they pursue questions (Engel, 1992a). He further points out that reliance on reductionistic thinking and Newtonian and Descartes dualism automatically excludes that which is distinctively human from the realm of science (Engel, 1992a). He acknowledges that science is a *human* activity, and notes that what the scientist does cannot be separated from the research question because every observation is predicated on the scientist's decisions as to what s/he observes and how.

The biomedical model that has been prevalent in the Western culture for the past 300 years accounts for disease by its biochemical factors without considering social or psychological dimensions. The patient complains, at

times, that the disease is being treated rather than the person. The biomedical model separates mind from body. Reductionistic medical thinking is particularly neglectful when the impact of non biological circumstances upon biological processes is ignored.

In Medical Family Therapy (McDaniel, Hepworth, & Doherty, 1992), a new paradigm for the biopsychosoical treatment of patients and their families who are dealing with health issues is proposed. Systems concepts are applied to patient care for a broad range of medical concerns. The concepts underlying this new paradigm are derived from the work of George Engel (Engel, 1960; Engel, 1977; Engel, 1980a; Engel, 1992).

In 1977 Engel proposed a biopsychosocial model for organizing and delivering medical care; this classic article was reprinted in *Family Systems Medicine* in 1992 (Engel, 1992b). Engel attributes medicine's crisis to adherence to a model of disease no longer adequate for the scientific tasks and social responsibilities of medicine. He contends that the biomedical model does not include the human dimension and that the systems biopsychosocial model successfully resolves this problem (Engel, 1980; Engel, 1985).

Rooted in general systems theory principles attributed to von Bertalanffy, the biopsychosocial model acknowledges the hierarchical, interdependent relationships of biological, psychological, individual, family, and community systems. Within the framework of this model one can see how multiple levels of systems are affected simultaneously. Any change in a part of the organism impacts the whole person within the context of his family and culture. All human problems are biopsychosocial systems problems: psychosocial problems have biological features and biomedical problems have psychosocial features (Engel, 1992b). Engel advocates the inclusion of psychosocial systemic awareness without sacrificing the enormous advan-

tages of the biomedical approach and cautions the medical community that absence of psychosocial awareness distorts perspective and interferes with patient care (Engel, 1992b). He writes "psychophysiologic responses to life change may interact with existing somatic factors to alter susceptibility and thereby influence the time of onset, the severity, and the course of the disease" (Engel, 1992b).

Engel presented the biopsychosocial model schematically by vertical stacking to illustrate the hierarchy (see Figure 3) and by a nest of squares to emphasize the continuum (see Figure 4) (Engel, 1980b). Engel notes the individual person as the highest level of the organismic hierarchy and simultaneously the lowest level of the social hierarchy (Engel, 1980b):

Consideration of the hierarchy as a continuum reveals another obvious fact. *Each system is at the same time a component of higher systems* (Figure 4). System *cell* is a component of systems *tissue* and *organ* and *person*. *Person* and *two-person* are components of *family* and *community*. *In the continuity of natural systems every unit is at the very same time both a whole and a part. Person* (or individual) represents at the same time the highest level of the organismic hierarchy and the lowest level of the social hierarchy. Each system as a whole has its own unique characteristics and dynamics; as a part it is a component of a higher-level system. The designation "system" bespeaks the existence of a stable configuration in time and space, a configuration that is maintained not only by the coordination of component parts in

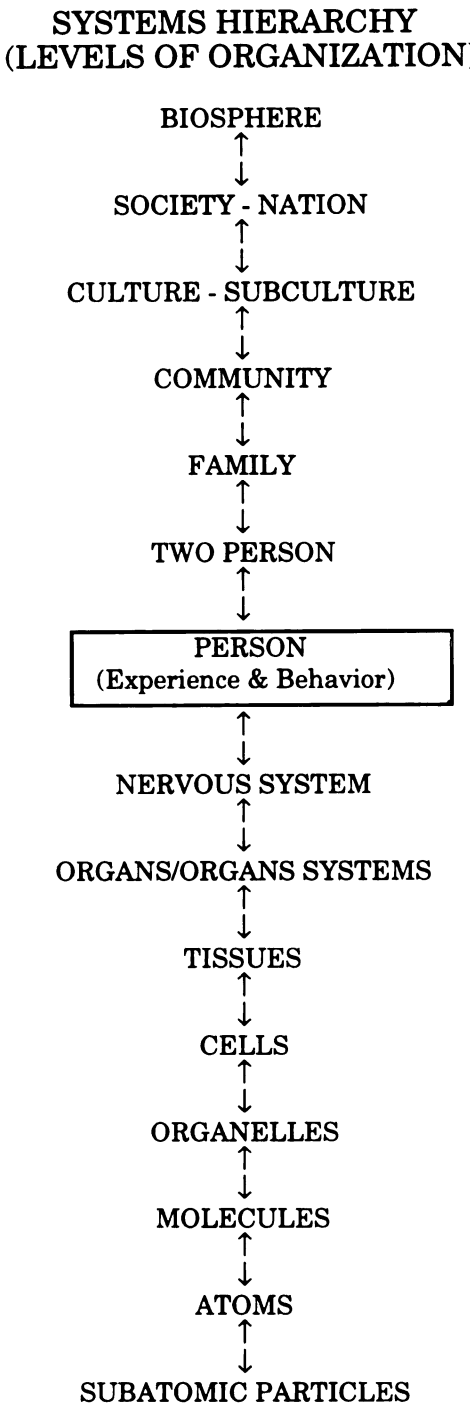



Figure 3. Hierarchy of Natural Systems [Reproduced with permission from: "The Clinical Application of the Biopsychosocial Model" by G. L. Engel,1980, The American Journal of Psychiatry, 137, p. 537.]

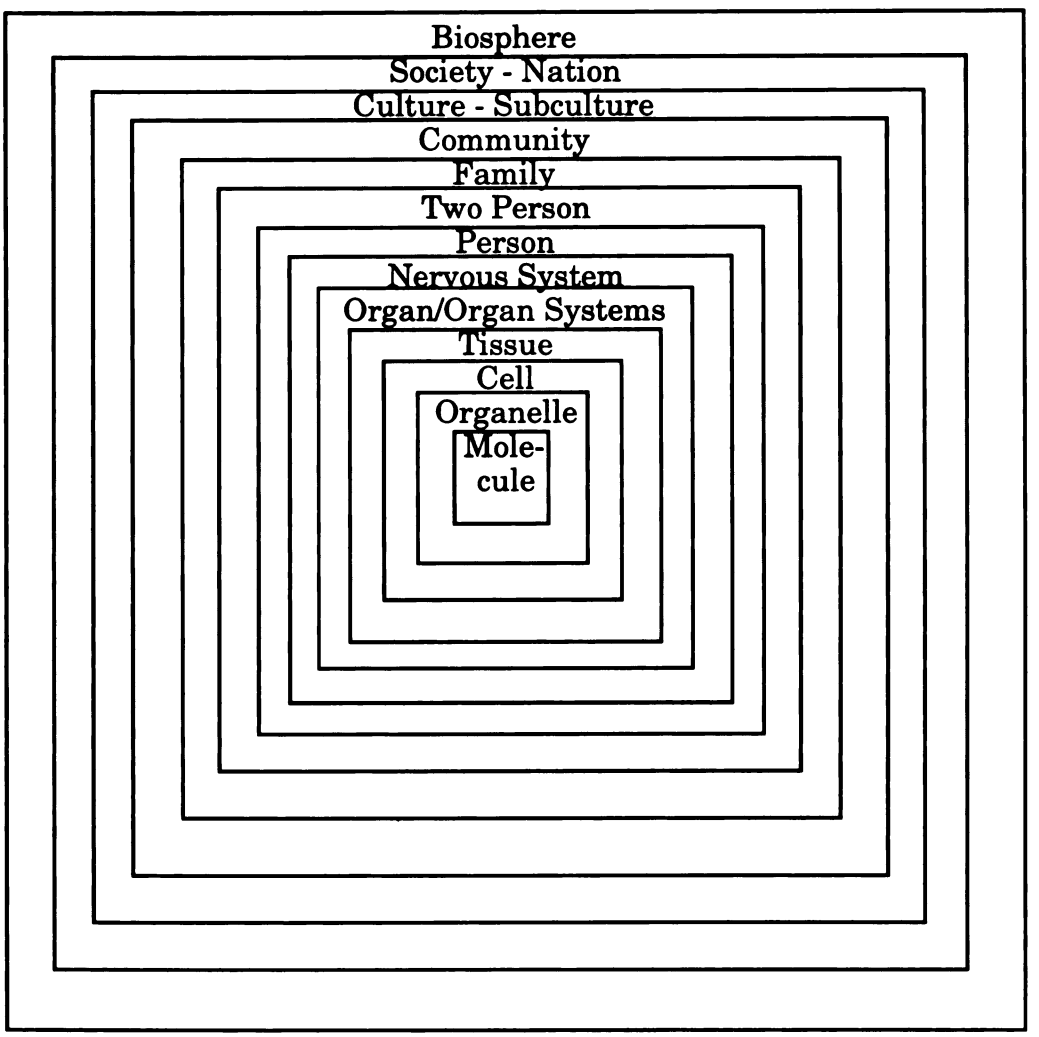



Figure 4. Continuum of Natural Systems
[Reproduced with permission from: "The Clinical Application of the Biopsychosocial Model" by G. L. Engel, 1980, The American Journal of Psychiatry, 137, p. 537.]

some kind of internal dynamic network but also by the characteristics of the larger system of which it is a component part. Stable configuration also implies the existence of boundaries between organized systems across which material and information flow.

Nothing exists in isolation. Whether a cell or a person, every system is influenced by the configuration of the systems of which each is a part, that is, by its environment. More precisely, neither the cell nor the person can be fully characterized as a dynamic system without characterizing the larger system(s) (environment) of which it is a part. This is implicit in the labels used. The designation "red blood cell" identifies directly and by implication the larger systems without which the red blood cell has no existence. The term "patient" characterizes an individual in terms of a larger social system. Identification of the patient by name, age, sex, marital status, occupation, and residence identifies other systems of which that patient is a component and which in turn are part of his or her environment. Thus, one may consider the possibility that the healing of breast cancer can be enhanced by conjoint imaging with a supportive spouse.

In another article, Engel traces the foundation of his model (Engel, 1992b): Arguing the need for a more fundamental reorientation in scientific perspectives in order to open the way to holistic approaches more amenable to scientific inquiry and conceptualization, von Bertalanffy developed general systems theory. This approach, by treating sets of related events collectively as systems manifesting functions and properties on the specific level of the whole, has made possible recognition of isomorphies across different levels of organization, as molecules, cells, organs, the organism, the person, the family, the society, or the biosphere. From such isomorphies can be developed fundamental laws and principles that operate commonly at all

levels of organization, as compared to those which are unique for each. Since systems theory holds that all levels of reorganization are linked to each other in a hierarchical relationship so that change in one affects change in the others, its adoption as a scientific approach should do much to mitigate the holist-reductionist dichotomy and improve communication across scientific disciplines. For medicine, systems theory provides a conceptual approach suitable not only for the proposed biopsychosocial concept of disease, but also for studying disease and medical care as interrelated processes.

**Research Objectives**

The purpose of this research was to study six premenopausal women volunteers who have followed a standard course of treatment for breast cancer to determine whether a change in blood assays is present following immunoimagery, and whether this change is greater when she images conjointly with her husband or when immunoimaging alone. Information about the woman's treatment course, stage designation at the time of surgery, the type of surgical procedure(s), the number of lymph nodes involved, and the presence and extent of metastasis was gathered.

Six blood count measures were obtained for each of the wife participants: White Blood Cell (WBC) counts, Absolute Lymphocyte (Abs Lymphs) counts, total T-cell counts (CD3), helper/inducer T-cell counts (CD4), suppressor/cytotoxic T-cell counts (CD8), and Segmented Neutrophils (Segs), generally reported as percentage of the WBCs. These measures were selected owing to their merit in reflecting immune system efficacy.

WBCs are the chief representatives of the immune system; they have the ability to identify foreign invaders in the body. Lymphocytes (including B-cells and T-cells) are white blood cells having a variety of functions that

circulate in lymph fluid; their numbers are reflected by the Abs Lymphs counts. T-cells are a type of lymphocyte that are responsible for cellular immunity. T-cells are derived from bone marrow and stored in the thymus. There are many different types of T-cells and their total count is represented by Cluster Designation 3 (CD3). Approximately 90% of CD3 cells are helper/ inducer T-cells (CD4) and suppressor/cytotoxic T-cells (CD8). Helper T-cells (CD4) cooperatively interact with B-cells. Suppressor T-cells (a component of CD8) monitor cellular activity and are instrumental in reducing the activity of parts of the immune system when those parts are no longer needed. Cytotoxic or killer T-cells (another component of CD8) are T-cells that migrate to the site of a foreign invader. They attach themselves to the non-self substance and secrete a chemical that destroys the antigen. Segmented neutrophils (Segs) are mainly responsible for fighting infections. They continually circulate in the body, looking for bacteria that do not belong. Segs are the first line of defense. They react quickly to engulf and digest foreign matter. Neutrophils comprise 50% - 65% of WBCs.

The total white blood cell count is the enumeration of all nucleated cells in the sample. The differential white blood cell count gives the proportions of different cell types that comprise the total number of white blood cells. The normal ranges for these blood measures for adults are as follows: WBC--4000-12000; Abs Lymphs--1000-4800; CD3--1120-2580; CD4--660-1500; CD8--360-850; and Segs--2500-6500.

Marital adjustment, as measured by the Dyadic Adjustment Scale (Spanier, 1976), was administered to husband and wife and the scores were compared with the changes in blood cell numerosity in each condition. Further, husbands and wives were asked to depict the cancer and the wife's immune system forces (white blood cells, specifically T-cells) through draw-

ings following the imagery. The drawings were scored by two independent evaluators in accordance with the standardized IMAGE-CA (Achterberg & Lawlis, 1984), and were related to the post-treatment blood count measurements.

## Conceptual and Operational Definitions

Husband's and wife's perceptions of marital adjustment:

| | |
|---|---|
| Conceptual: | The husband's and wife's individual contentment with the spouse and the marital relationship. |
| Operational: | The husband's and wife's score on the Dyadic Adjustment Scale. |

Husband's and wife's perception of the strength of the cancer and the strength of the wife's immune system:

| | |
|---|---|
| Conceptual: | The husband's and wife's individual drawn illustrations and oral descriptions the cancer cells and the immune system's cancer-fighting cells. |
| Operational: | The husband's and wife's scores on the IMAGE-CA. |

## Research Assumptions and Conditions

1. Human beings are capable of imaging to some degree.

2. Human mental and physical functions are inter-dependent.

3. The human mind, through imagery, is capable of effecting physiological changes within the body to some degree.

4. Laboratory blood analyses can be demonstrably accurate and reliable.

5. Certain cellular changes can represent the body's healing processes.

6. Beliefs, attitudes and stress affect the immune system.

7. Breast cancer patients and their husbands are motivated to participate in guided imagery to the best of their ability.

8. Volunteering to participate in this study is an indication of the husband's supportiveness for his wife.

**Research Questions**

Can the imagination exert a positive influence on immunology, and on cancer? Will conscious manipulation of the immune system through imagery be related to increased blood counts? Will the strength and vividness of the images drawn by husband and wife be related to the changes revealed by the blood analysis? Further, will any salutary effects upon the immune system increase when a woman in a satisfying marriage images with her husband?

**Research Hypotheses**

*Null Hypothesis 1:* There will be no difference between the white blood cell (WBC), absolute lymphocyte (Lymphs), total (CD3), helper/inducer (CD4), suppressor/killer (CD8) T-cell, and segmented neutrophil (Segs) counts between the baseline measure and the subsequent pre- and post-treatment measures.

*Working Hypothesis 1a:* There will be differences white blood cell (WBC), absolute lymphocyte (Lymphs), total (CD3), helper/inducer (CD4), suppressor/killer (CD8) T-cell, and segmented neutrophil (Segs) counts in the pre- and post-treatment measures relative to the baseline measure.

*Null Hypothesis 2:* There will be no differences between the white blood cell (WBC), absolute lymphocyte (Lymphs), total (CD3), helper/inducer (CD4), suppressor/killer (CD8) T-cell, and segmented neutrophil (Segs) counts between the pre-imagery blood draws and the post-imagery blood draws.

*Working Hypothesis 2a:* There will be differences in the white blood cell (WBC), absolute lymphocyte (Lymphs), total (CD3), helper/inducer (CD4), suppressor/killer (CD8) T-cell, and segmented neutrophil (Segs) counts following the solitary and conjoint imagery sessions relative to the pre-session values.

*Null Hypothesis 3:* There will be no differences between the changes in white blood cell (WBC), absolute lymphocyte (Lymphs), total (CD3), helper/inducer (CD4), suppressor/killer (CD8) T-cell, and

segmented neutrophil (Segs) counts measured under the solitary and conjoint imaging conditions.

*Working Hypothesis 3a:* There will be differences in the changes in white blood cell (WBC), absolute lymphocyte (Lymphs), total (CD3), helper/inducer (CD4), suppressor/killer (CD8) T-cell, and segmented neutrophil (Segs) counts following the conjoint imagery condition with respect to those measured under the solitary imagery condition.

*Null Hypothesis 4:* There will be no relationship between the strength and vividness of the wife's imagery (measured by the IMAGE-CA) and her post-imagery white blood cell (WBC), absolute lymphocyte (Lymphs), total (CD3), helper/inducer (CD4), suppressor/killer (CD8) T-cell, and segmented neutrophil (Segs) count changes.

*Working Hypothesis 4a:* The stronger and more vivid the imagery (higher IMAGE-CA score), the greater the change in white blood cell (WBC), absolute lymphocyte (Lymphs), total (CD3), helper/inducer (CD4), suppressor/killer (CD8) T-cell, and segmented neutrophil (Segs) counts following the solitary and conjoint imagery sessions.

*Null Hypothesis 5:* There will be no relationship between DAS scores and the differences in the white blood cell (WBC), absolute lymphocyte (Lymphs), total (CD3), helper/inducer (CD4), suppressor/killer (CD8) T-cell, and segmented neutrophil (Segs) counts between the solitary and conjoint imagery conditions.

*Working Hypothesis 5a:* The higher the wife's and husband's DAS scores, the greater the change in the white blood cell (WBC), absolute lymphocyte (Lymphs), total (CD3), helper/inducer (CD4), suppressor/killer (CD8) T-cell, and segmented neutrophil (Segs) counts between the solitary and conjoint conditions.

**Research Design**

An exploratory double-blind quasi-experimental design was employed to achieve the objectives of this study. The unit of analysis is comparative white blood counts, T-cell counts, and neutrophil counts on blood drawn from the breast cancer patient before the training session and prior to and following each of the two guided imagery sessions. Ethical and financial considerations required this investigation to be conducted in a natural setting with a convenience sample (premenopausal married women with breast cancer who had completed a standard course of surgical and systemic treatment, and who along with their husbands chose to participate in this study). The women were randomly assigned to two groups (image alone first; image with husband first). Subjects were recruited as volunteers from physicians and nurses in the Lansing/Grand Rapids area who specialize in the treatment of women with breast cancer. Physicians did not refer any patient for whom five blood draws in fifteen days was contraindicated. The women and their husbands volunteered for this study after learning about the imagery component, and the commitment to three sessions spaced one week apart, with blood draws at each session. No patient or insurance company was asked for reimbursement for the blood chemistry connected with this study. Prior to

the training session, both husband and wife completed the Dyadic Adjustment Scale (Spanier, 1976, Appendix A).

There was a sample group of six women who imaged alone and with their husbands. The subjects served as their own control, with three of the women first imaging with their husbands, and the remaining three imaging alone first. A baseline white blood count, T-Cell count (CD3, CD4, CD8), and neutrophil count was established prior to educating the couples about the immune system and guiding them to focus on blood cell increments, especially cytotoxic T-cells. It is possible that learning about the immune system and how it fights disease could alter blood cell scores even prior to the treatment. Further, these subjects were assumed to be highly motivated as a result of a potentially life-threatening diagnosis and they may have begun thinking about (*i.e.*, rehearsing) the imagery process or immune system function for a period of time prior to the pre-treatment blood draws, which could affect white blood cell numerosity in the pre-treatment blood samples. Therefore, recruitment of couples was accomplished by presenting in only general terms the goal of promoting well-being through the use of imagery, and promising the volunteers a closure meeting following completion of the project, when the hypotheses and results could be more fully described.

For each subject, all blood samples were drawn within ninety minutes of the same time of day, to control for ultradian effects. The blood samples consisted of 12.5 $cm^3$ of blood drawn from the patient's arm (contralateral to the mastectomized side) into pre-sealed vacuum tubes. Venipuncture was performed by a registered nurse, and if the nurse predicted any difficulty in obtaining a successful draw, another experienced nurse from the IV team performed the draw. All lymphocyte assays were carried out on fresh cells within twenty-four hours after the blood was drawn. A comprehensive proce-

dural description for the Complete Blood Count (CBC) and the T-cell Absolutes (CD3, CD4, CD8) is contained in Appendix B.

During the first session, the baseline blood draw preceded each woman's completion of a medical history form and demographic questionnaire. Both husband and wife then completed the Dyadic Adjustment Scale and were instructed not to communicate with one another during the administration of the measure. Immune system education consisted of the couple watching a fifteen minute film (Bioimagery, 1993) about immune system function (Appendix C). The couple was assured that it would not be necessary for them to remember in detail the information provided by the film, but rather that they obtain a general overview of how the immune system functions, paying particular attention to the information about T-cells. After viewing the video, each couple had the opportunity to share their reactions about the experience for five to ten minutes and the video was shown a second time.

In the second and third sessions the imagery exercise began with a tape recorded (the experimenter's voice with background music) induction of deep relaxation (6 minutes). The focusing phase (30 minutes) began with the suggestion that the subjects place themselves in a safe and relaxed setting where all things are possible. They were then given general guidelines regarding the immune system and health-promoting cellular processes. Subjects were asked to get a sense of the T-cells and their activities of multiplication, surveillance, and destruction of any malignant cells in the woman's body. No specific images were suggested, although the participants were encouraged to introduce an element of playfulness in their images. A six minute reversal of the deep relaxation concluded the tape recording. (The immunoimagery audiotape script is reproduced in Appendix D.)

For thirty minutes following the guided imagery, and prior to the venipuncture, the subjects were asked to draw their imagery experience on white 11" x 14" drawing paper. It was suggested that these drawings include the participant's image of any malignant cells in the body, the woman's white blood cells including the T-cells, the woman's external resources including medical treatment, and how the white blood cells including T-cells interacted with the malignant cells. These drawings were scored according to the standardized IMAGE-CA (Appendix E).

Since it is important to learn about any factors that might affect the female participant's immune system, the woman was asked to document all medications taken during the month prior to the first session (thereafter, medications used during the weekly intervals), and to describe medical treatment, any acute illness, and interpersonal or other changes that had occurred since the previous interview.

A flow chart summary of the research protocol is provided in Table 1.

**Instrumentation and Measurement Procedures**

Marital contentment and satisfaction were measured by asking each breast cancer patient who met the selection qualifications and her husband, who volunteered for this study, to complete the Dyadic Adjustment Scale (DAS) [Appendix A]. The DAS is a 32 item self-report Likert-style questionnaire instrument with 5-, 6-, and 7-point response formats ranging from either *always agree* to *always disagree* or *all the time* to *never* (Spanier, 1976). Of the more than 1000 reported studies that utilized the DAS, 90% have involved married couples (Touliatos, Perlmutter, & Straus, 1990). Factor analysis identified four areas: dyadic satisfaction, dyadic cohesion, dyadic consensus, and affectional expression (Spanier, 1976). Cronbach's alpha = .96

Table 1. Research Protocol

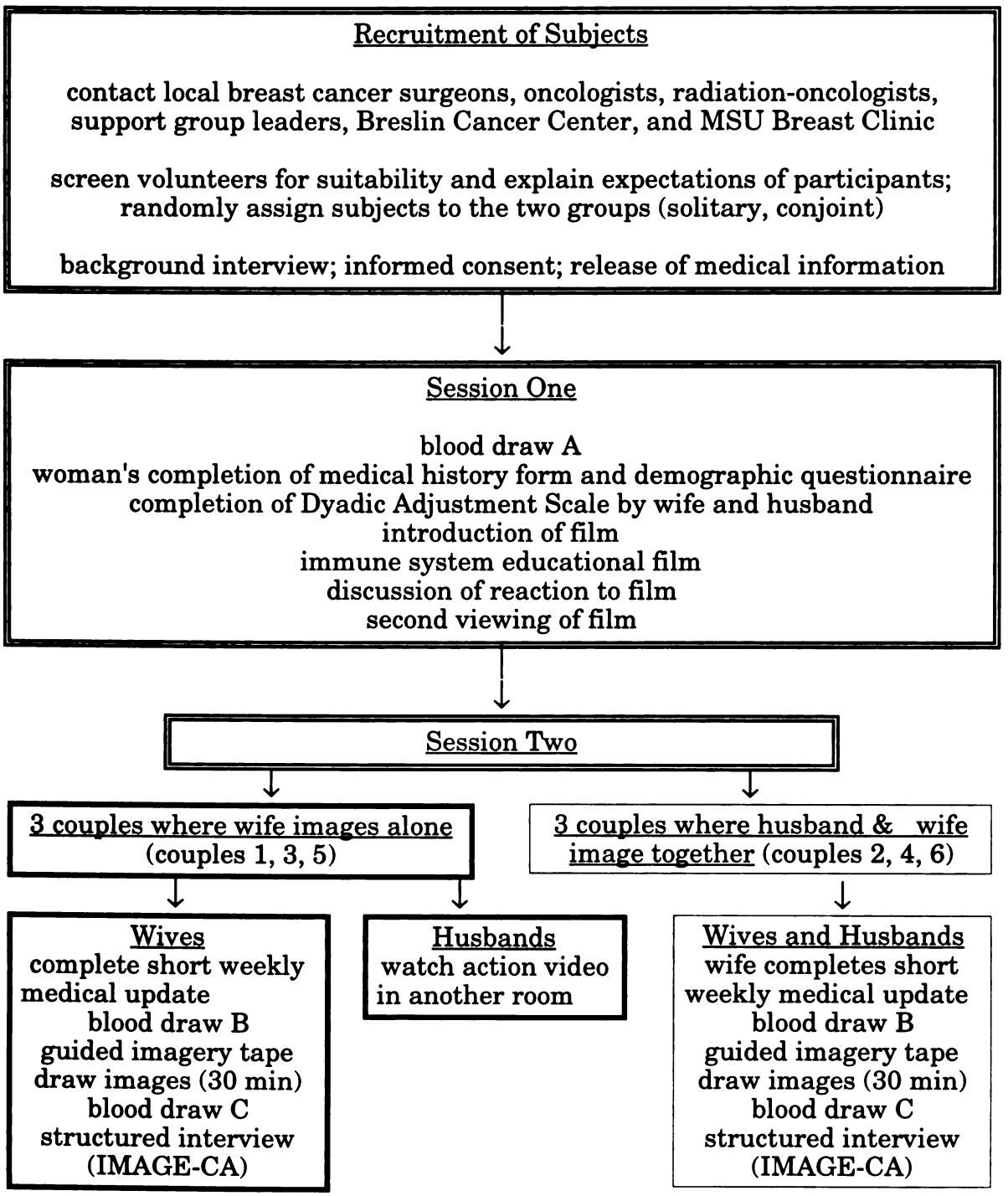
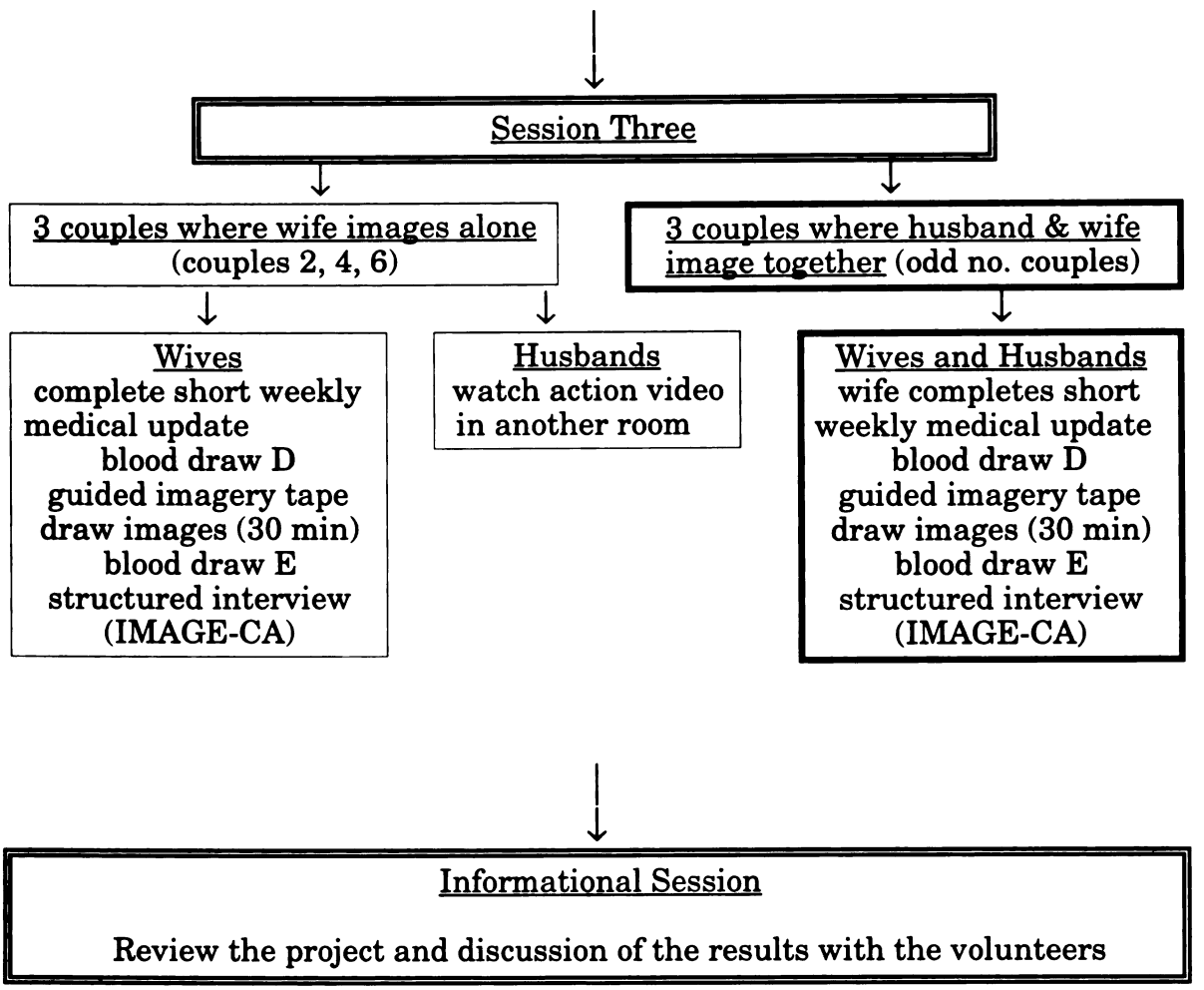


Table 1
Research Protocol
(continued)



for the entire scale, and ranges from .73 to .94 for the subscales (Sabatelli, 1988). Sabatelli (1988) reports that the validity of the scale is supported by the consensus of judges on the relevance of the scale's content and that the scale has been successfully used retrospectively when respondents were asked to recall the last months of their marriages. In addition, there is a high correlation (r = .88) between the DAS and Locke-Wallace Short Marital Adjustment Test (LWMAT) (Sabatelli, 1988).

Complete procedural descriptions of the CBC and T-cell Absolute blood assays have been provided by the Sparrow Hospital Laboratory where the blood was analyzed within twenty-four hours after each draw. They are reproduced in Appendix B.

Two modes of communication were used in completing the IMAGE-CA: a personalized drawing of the disease and internal and external resources, and a structured interview. The reliability of the IMAGE-CA has been assessed by both interdimensional correlation and interrater correlation. The correlations for the dimensions applicable to this project range from .27 (vividness of the cancer cell) to .93 (overall imagery strength). Interrater reliability correlations between two independent raters were all statistically significant and range from .60 (strength of cancer cells) to .87 (symbolism) for the dimensions applicable to this study. The measurements also were analyzed to determine whether the raters were in agreement about absolute levels, and one hundred percent agreement was found (Achterberg & Lawlis, 1984).

The combined dimensions of the IMAGE-CA have been used to predict current health status and to project health status in two months. Health status was categorized as death, evidence of new tumor growth and degenerative disease, stabilized condition, evidence of reduction of existing tumor(s)

and positive process, evidence of complete absence of tumor(s) or disease. Ninety-three percent prediction was obtained for favorable prognosis and one hundred percent prediction was obtained for unfavorable prognosis (Achterberg & Lawlis, 1984). Reliability and validity coefficients remained similar for a sample of twenty-one patients (racially mixed group) from low income and educational levels.

In this study, after the woman or couple was guided through relaxation and imagery, focusing on the disease and the white blood cells (T-cells in particular) and external resources including medical treatment, the subject(s) was(were) asked to draw the images with crayons (64 color assortment). A structured interview followed to clarify and objectify the meanings underlying the drawings. The drawings and interviews were scored on the following dimensions using a 5-point scale: vividness of the cancer cell, activity of the cancer cell, strength of the cancer cell, vividness of the white blood cell (T-cell), activity of the white blood cell (T-cell), relative comparison of numbers of cancer cells to white blood cells (T-cells), relative comparison of size of cancer cells to white blood cells (T-cells), strength of the white blood cells (T-cells), concreteness versus symbolism, and overall strength of the imagery (Achterberg & Lawlis, 1984). The interviews were both video and audio tape recorded and evaluated along with the drawings by two independent, trained raters and their ratings are compared and reported.

**Sampling Methods and Data Collection Procedures**

The men and women who agreed to participate were studied over a 15 day period of time. The woman had been diagnosed with premenopausal breast cancer, had followed a standard course of surgical and systemic treatment, and was judged by her physician capable of sustaining five blood draws

over a fifteen day period without compromising her health status. The couples included in this study were all married and living together. Each couple member was able to read, write, and speak English. Each respondent gave written and verbal informed consent [Appendix F], and made an initial commitment to participate in this study consisting of three one- to two-hour sessions spaced one week apart, accompanied by blood draws. Each woman had to obtain her physician's written approval in order to participate in this study. Further, it was made clear to each participant that this study was a preliminary investigation that in no way condoned the use of imagery as a substitute for conventional medical treatment, nor promised any salutary effects as a result of its use [Appendix G].

The sample group was collected from those couples meeting the above selection criteria who agreed to participate in this investigation and who lived within a seventy-mile radius of Lansing, Michigan. Permission for the study was requested and granted from the Michigan State University Committee On Research Involving Human Subjects (UCRIHS) [Appendix H]. Physicians specializing in the treatment of women with breast cancer, oncology or radiological oncology and nurses who conduct breast cancer support groups were asked to identify a woman's potential suitability for inclusion in the study. Information about the project and the researcher's name and telephone number was disseminated to potential subjects by mail or at support groups. If a couple was interested, they contacted the researcher.

Consent of the couple was obtained by personal interview after verbal interest has been indicated and satisfaction of selection criteria was ascertained. Many people have either heard or read about imagery and its use with cancer patients. Some of the participants believed in its possible efficacy and volunteered to learn more about it; others were more circumspect, yet

open to the possibility of its helpfulness. After hearing a general description of the project and giving verbal and written informed consent [Appendix F], the couple was scheduled for three successive weekly sessions, to occur at the same time each week. (T-Cell Absolutes are less variable when the blood is drawn at similar times of the day.) If participation by otherwise interested and suitable volunteers was precluded by transportation difficulties, it was determined that rides would be offered to and from the research site. All volunteers had their own transportation. The forms used to obtain physician consent, to establish demographic and medical data, and to collect recent information about the participants, are reproduced in Appendix I.

At the first session the woman's blood was drawn; the couple filled out the DAS; they watched a 15 minute educational video (Bioimagery, 1993), discussed their reactions to the video and then watched it a second time. A phone call was made the day before the second session to remind the couple of the importance of being on time for the successive blood draw. Husband and wife each had a couch to rest on during the imagery sessions; the pre-and post-treatment blood draws were conducted while the woman sat on a couch. Following venipuncture, the second session for half the couples consisted of imaging the woman's cancer, then imaging the body's response to the cancer, in particular the T-cell response, and to imagine the woman's external resources (family, friends, prayer, medical treatment, community) guided by the researcher's voice on a tape cassette; of drawing the imagery experience for up to thirty minutes post imagery; and completing the post-treatment blood draw at thirty minutes post imagery. Only then did the couple move from the couches they occupied during the imagery and drawing process. (On several occasions a participant used the restroom prior to venipuncture.)

Again, a prior day's phone call reminder stressed the importance of being on time for the fourth blood draw, which began the third session. The procedure for the same three couples consisted of the identical process as described in Session Two, but this time for the woman only. The husband was in a separate room watching a distracting, action-filled video in an attempt to control for supportive husbands who may be thinking about their wife's participation in the study and her immune system response, thereby reducing a potential confounding variable. The husbands were not asked *not to image* their wife's immune response, because the suggestion may actually increase the impulse; instead, the action-filled video was provided in an effort to circumvent his empathic focus on bolstering her T-cells. The procedures described for the second and third sessions were reversed for the other half of the volunteer group.

This study utilized a purposive nonprobability sample, and its findings describe six marital dyads in which the husband's participation was supportive of the wife and in which the female has been diagnosed with premenopausal breast cancer and followed a standard course of surgical and systemic treatments.

**Data Analysis**

This was a pilot investigation, circumscribed by the limited funding procurable for the expensive blood analyses; moreover, because the female participants were required to satisfy certain medical criteria and were asked to submit to five blood draws, there was great difficulty in recruiting volunteer subjects. Therefore, this was more of a preliminary study than one from which the findings can be statistically generalized. If the results suggested

an imagery effect or a solitary/conjoint imagery effect, then the expense of a larger scale investigation could be justified.

This investigation involved a single subject design, where the results from individual subjects were examined, and each subject served as her own control. The use of single subject experimental design is well established in clinical research and the design efficacy and legitimacy is well documented (Barlow & Hersen, 1984; Kazdin, 1982; Kratochwill, 1978). The results for each subject are displayed in the following chapter, in tables that list the pre- and post-treatment blood analyses, imagery ratings, and marital satisfaction scores.

Logistic regression, employing several explanatory variables (solitary/conjoint imagery, imagery sequence, imagery ratings, marital satisfaction and adjustment) was utilized to characterize the dependent variable (changes in blood assays). The statistical method of logistic regression is becoming more frequently used in the health research literature because it can treat a binary response variable (*e.g.*, success or failure of a given treatment, coded as 1 or 0) as a function of a mixture of continuous or nominal independent variables (Hirsch & Riegelman, 1991). In the conventional, multiple linear regression model, a continuous, normally distributed response variable (Y) is fitted to a linear combination of several predictor variables (X): $Y = b_0 + b_1*X_1 + b_2*X_2 + ... + b_k*X_k$.

In the linear logistic model it is assumed that for each set of values of the X variables there is a probability p that success occurs. The odds of success are therefore [p/(1-p)], and can range from zero to positive infinity. In logistic regression the natural logarithm of the odds ratio is taken as the independent variable, so that the range is from minus to plus infinity, with zero reflecting equal probability of success or failure. The "logit transforma-

tion" of the probability is formed, such that Y in the above equation is replaced by ln[p/(1-p)]. The $b_j$ constants are then fitted by multiple linear regression. [Several good introductions to logistic regression are available. See for example Hosmer & Lemeshow, and Kleinbaum (Hosmer & Lemeshow, 1989; Kleinbaum, 1994)].

Logistic regression can be applied successfully to sparse and imbalanced data sets. Nonetheless, despite the use of a multivariate model, the external validity of this study is threatened as the result of the small sample size, and generalizability is limited.

**Limitations of the Research**

Marital satisfaction and marital adjustment were assessed retrospectively through husband's and wife's own perceptions. There may be biases resulting from the naturalistic selection of respondents, the small sample size and the absence of separate control and placebo groups (which were eliminated due to the difficulty in recruiting subjects and the costly blood chemistry analyses). The sample of couples all resided within seventy miles of Lansing, Michigan, which may further limit the generalizability of the research results.

# CHAPTER IV

# RESULTS AND DISCUSSION

The protocol was designed to examine whether imaging alone or as a couple affects blood cell measures, specifically changes in white blood cell (WBC), lymphocyte (Lymphs), T-cell (CD3, CD4, CD8), and segmented neutrophil (Segs) numerosity. The blood count changes were related to raters' assessments of each subject's imagery, and the couples' marital satisfaction. The study is limited by the small sample size and the impossibility of controlling all confounding variables. These factors restrict the statistical methods that can be employed.

## Demographic Information

Six volunteer breast cancer patients who met the prescribed criteria, and their husbands, participated in this study. All of the volunteers were Caucasian and of middle socioeconomic status. All of the women had experienced premenopausal onset, at a mean age of 44.3 years (range: 33 years, 4 months to 56 years, 1 month). Their mean age at the time the study was conducted was 47.5 years (range: 34 years, 6 months to 59 years, 1 month). All six were surgically treated; five had unilateral mastectomies and one had a bilateral mastectomy. Two had surgical breast reconstruction as well. All participants received chemotherapy as part of their treatment protocols, ranging from four to eleven treatments. One was treated with radiation, as well. Three of the participants were receiving hormonal therapy in the form of Tamoxifen. The subjects had no, one or two lymph nodes that were malig-

nant; none had metastasis. All participants had Stage 1 or 2 cancer classification. Three of the participants were estrogen receptor positive, one both estrogen and progesterone receptor positive, and two were estrogen receptor negative. Three reported consulting a mental health professional in relation to the cancer diagnosis (one of the three was currently involved in marital therapy) and two reported being in cancer support groups. In addition to breast cancer, one of the participants had heart disease treated by quadruple bypass surgery, fibromyalgia, systemic lupus, and a thyroid condition treated by oral medication. Four of the participants volunteered that they had tried alternative treatments including massage, imagery, polarity therapy, reflexology, prayer, and exercise, along with standard medical treatment.

It was not possible to control for diseases, stressors and pharmaceuticals that could affect the participants' immune systems. In order to identify such potential confounding issues, each subject was asked to fill out a questionnaire about illness, drugs, and interpersonal stressors before each session. During the course of the study each participant noted information that could have impacted her immune system. The following items were reported by the participants in the course of their 15-day observation periods: colds, allergies, fusarian, depression, sore throat, sick and injured pets, body aches, abnormal digestion, nausea, runny nose, possible cancer recurrence, serious illness of family members, family members involved in a car accident, marital problems, death of a close family member, and the attempted suicide of a close family member. Although three of the participants were taking twelve prescriptive drugs, none of these were known to be immunosuppressants. All the volunteers denied ingesting any non-prescribed drugs.

**Laboratory Results and Primary Data**

The results of the laboratory analyses of the blood drawn from the volunteer subjects at the designated times (Draws A through E), as well as the imagery ratings (IMAGE-CA Scores) and the couples' Dyadic Adjustment Scale scores, are presented in Tables 2 - 9. Photocopied reductions of the wives' drawings following each imagery session are collected in Appendix J. It should be noted that the segmented neutrophils were reported by the laboratory in percentages of the white blood cell count. The percentages were transformed into the absolute numbers shown in Table 7 by multiplying the reported white blood counts by the reported percentage segmented neutrophils. Also, owing to accidental hemolysis of the sample in one instance, the third session for Couple Four had to be repeated, two weeks after the original date. Data for the later, repeated session are entered as Draw D and Draw E, in lieu of the original values.

**Interpretation**

For each blood variable analyzed, there are three distinct trend possibilities in each the Sequence condition (first session/second session) and in the Alone/Together condition. Blood counts could decrease in numerosity following the guided imagery, blood counts could remain the same (within the measurement error) with respect to the pre-imagery values, or blood counts could increase in numerosity following the guided imagery. Figure 5 illustrates the trend possibilities.

Table 2. White blood cell counts (cells/mL) relative to sequence and to solitary vs. conjoint imagery.

| Sequence | Baseline | Session One | | Session Two | |
|---|---|---|---|---|---|
| | Draw A | Draw B | Draw C | Draw D | Draw E |
| Couple 1 | 4200 | 5300 | 4700 | 4400 | 4000 |
| Couple 2 | 4700 | 4700 | 4200 | 4100 | 3900 |
| Couple 3 | 5700 | 6100 | 4800 | 5200 | 5000 |
| Couple 4 | 4900 | 4500 | 4300 | 5200 | 4800 |
| Couple 5 | 8100 | 7500 | 6800 | 6800 | 7400 |
| Couple 6 | 3900 | 4300 | 3600 | 4100 | 3200 |

| Alone/ Together | Baseline | Wife Alone | | Couple Together | |
|---|---|---|---|---|---|
| | Draw A | Pre | Post | Pre | Post |
| Couple 1 | 4200 | 5300 | 4700 | 4400 | 4000 |
| Couple 2 | 4700 | 4100 | 3900 | 4700 | 4200 |
| Couple 3 | 5700 | 6100 | 4800 | 5200 | 5000 |
| Couple 4 | 4900 | 5200 | 4800 | 4500 | 4300 |
| Couple 5 | 8100 | 7500 | 6800 | 6800 | 7400 |
| Couple 6 | 3900 | 4100 | 3200 | 4300 | 3600 |

Table 3. Absolute lymphocyte counts (cells/mL) relative to sequence and to solitary vs. conjoint imagery.

| Sequence | Baseline | Session One | | Session Two | |
|---|---|---|---|---|---|
| | Draw A | Draw B | Draw C | Draw D | Draw E |
| Couple 1 | 1344 | 1330 | 1344 | 1505 | 1468 |
| Couple 2 | 1800 | 1598 | 1420 | 1304 | 1119 |
| Couple 3 | 1693 | 2001 | 1723 | 1586 | 1520 |
| Couple 4 | 715 | 891 | 937 | 1076 | 1032 |
| Couple 5 | 2066 | 2018 | 1863 | 1815 | 2131 |
| Couple 6 | 998 | 1058 | 896 | 1066 | 826 |

| Alone/ Together | Baseline | Wife Alone | | Couple Together | |
|---|---|---|---|---|---|
| | Draw A | Pre | Post | Pre | Post |
| Couple 1 | 1344 | 1330 | 1344 | 1505 | 1468 |
| Couple 2 | 1800 | 1304 | 1119 | 1598 | 1420 |
| Couple 3 | 1693 | 2001 | 1723 | 1586 | 1520 |
| Couple 4 | 715 | 1076 | 1032 | 891 | 937 |
| Couple 5 | 2066 | 2018 | 1863 | 1815 | 2131 |
| Couple 6 | 998 | 1066 | 826 | 1058 | 896 |

Table 4. CD3 counts (cells/mL) relative to sequence and to solitary vs. conjoint imagery.

| Sequence | Baseline | Session One | | Session Two | |
|---|---|---|---|---|---|
| | Draw A | Draw B | Draw C | Draw D | Draw E |
| Couple 1 | 766 | 665 | 659 | 856 | 749 |
| Couple 2 | 1386 | 1230 | 1093 | 1082 | 884 |
| Couple 3 | 1185 | 1401 | 1206 | 1142 | 1125 |
| Couple 4 | 472 | 499 | 619 | 427 | 699 |
| Couple 5 | 1756 | 1634 | 1490 | 1470 | 1716 |
| Couple 6 | 699 | 762 | 609 | 800 | 595 |

| Alone/ Together | Baseline | Wife Alone | | Couple Together | |
|---|---|---|---|---|---|
| | Draw A | Pre | Post | Pre | Post |
| Couple 1 | 766 | 665 | 659 | 856 | 749 |
| Couple 2 | 1386 | 1082 | 884 | 1230 | 1093 |
| Couple 3 | 1185 | 1401 | 1206 | 1142 | 1125 |
| Couple 4 | 472 | 427 | 699 | 499 | 619 |
| Couple 5 | 1756 | 1634 | 1490 | 1470 | 1716 |
| Couple 6 | 699 | 800 | 595 | 762 | 609 |

Table 5. CD4 counts (cells/mL) relative to sequence and to solitary vs. conjoint imagery.

| Sequence | Baseline | Session One | | Session Two | |
|---|---|---|---|---|---|
| | Draw A | Draw B | Draw C | Draw D | Draw E |
| Couple 1 | 430 | 372 | 363 | 452 | 440 |
| Couple 2 | 648 | 623 | 540 | 535 | 425 |
| Couple 3 | 609 | 720 | 638 | 571 | 562 |
| Couple 4 | 293 | 267 | 328 | 430 | 402 |
| Couple 5 | 950 | 908 | 820 | 835 | 895 |
| Couple 6 | 529 | 561 | 448 | 597 | 438 |

| Alone/ Together | Baseline | Wife Alone | | Couple Together | |
|---|---|---|---|---|---|
| | Draw A | Pre | Post | Pre | Post |
| Couple 1 | 430 | 372 | 363 | 452 | 440 |
| Couple 2 | 648 | 535 | 425 | 623 | 540 |
| Couple 3 | 609 | 720 | 638 | 571 | 562 |
| Couple 4 | 293 | 430 | 402 | 267 | 328 |
| Couple 5 | 950 | 908 | 820 | 835 | 895 |
| Couple 6 | 529 | 597 | 438 | 561 | 448 |

Table 6. CD8 counts (cells/mL) relative to sequence and to solitary vs. conjoint imagery.

| Sequence | Baseline | Session One | | Session Two | |
|---|---|---|---|---|---|
| | Draw A | Draw B | Draw C | Draw D | Draw E |
| Couple 1 | 323 | 279 | 282 | 376 | 294 |
| Couple 2 | 720 | 623 | 511 | 548 | 436 |
| Couple 3 | 559 | 660 | 534 | 476 | 441 |
| Couple 4 | 172 | 187 | 234 | 269 | 268 |
| Couple 5 | 744 | 706 | 689 | 635 | 789 |
| Couple 6 | 170 | 180 | 152 | 181 | 149 |

| Alone/ Together | Baseline | Wife Alone | | Couple Together | |
|---|---|---|---|---|---|
| | Draw A | Pre | Post | Pre | Post |
| Couple 1 | 323 | 279 | 282 | 376 | 294 |
| Couple 2 | 720 | 548 | 436 | 623 | 511 |
| Couple 3 | 559 | 660 | 534 | 476 | 441 |
| Couple 4 | 172 | 269 | 268 | 187 | 234 |
| Couple 5 | 744 | 706 | 689 | 635 | 789 |
| Couple 6 | 170 | 181 | 149 | 180 | 152 |

Table 7. Segmented neutrophil counts (cells/mL) relative to sequence and to solitary vs. conjoint imagery.

| Sequence | Baseline | Session One | | Session Two | |
|---|---|---|---|---|---|
| | Draw A | Draw B | Draw C | Draw D | Draw E |
| Couple 1 | 2066.4 | 3190.6 | 2730.7 | 2019.6 | 1820.0 |
| Couple 2 | 2411.1 | 2594.4 | 2419.2 | 2427.2 | 2390.7 |
| Couple 3 | 3243.3 | 3172.0 | 2553.6 | 2844.4 | 2770.5 |
| Couple 4 | 3895.5 | 3150.0 | 2906.8 | 3619.2 | 3336.0 |
| Couple 5 | 5281.5 | 4815.0 | 4256.8 | 4256.8 | 4417.8 |
| Couple 6 | 2457.0 | 2691.8 | 2217.6 | 2546.1 | 2009.6 |

| Alone/ Together | Baseline | Wife Alone | | Couple Together | |
|---|---|---|---|---|---|
| | Draw A | Pre | Post | Pre | Post |
| Couple 1 | 2066.4 | 3190.6 | 2730.7 | 2019.6 | 1820.0 |
| Couple 2 | 2411.1 | 2427.2 | 2390.7 | 2594.4 | 2419.2 |
| Couple 3 | 3243.3 | 3172.0 | 2553.6 | 2844.4 | 2770.5 |
| Couple 4 | 3895.5 | 3619.2 | 3336.0 | 3150.0 | 2906.8 |
| Couple 5 | 5281.5 | 4815.0 | 4256.8 | 4256.8 | 4417.8 |
| Couple 6 | 2457.0 | 2546.1 | 2009.6 | 2691.8 | 2217.6 |

Table 8. IMAGE-CA scores.

| | Wife Alone | | | | Wife Together | | | | Husband Together | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Rater 1 | | Rater 2 | | Rater 1 | | Rater 2 | | Rater 1 | | Rater 2 | |
| | Score | Sten | Score | Sten | Score | Sten | Score | Sten | Score | Sten | Score | Sten |
| Couple 1 | 196 | 7 | 206 | 7 | 163 | 5 | 143 | 3 | * | * | * | * |
| Couple 2 | 197 | 7 | 207 | 7 | 185 | 6 | 210 | 7 | 159 | 4 | 186 | 6 |
| Couple 3 | 185 | 6 | 215 | 8 | 82 | 1 | 133 | 3 | 114 | 2 | 149 | 4 |
| Couple 4 | 146 | 4 | 155 | 4 | 160 | 4 | 137 | 3 | 202 | 7 | 176 | 5 |
| Couple 5 | 168 | 5 | 176 | 5 | 133 | 3 | 137 | 3 | 189 | 6 | 131 | 3 |
| Couple 6 | 225 | 8 | 202 | 7 | 230 | 9 | 230 | 9 | 198 | 7 | 165 | 5 |

* Husband denied having imagery experience during session

Table 9. Dyadic Adjustment Scale scores (possible range: 0-151).

| | | Consensus | Satisfaction | Expression | Cohesion | Total DAS |
|---|---|---|---|---|---|---|
| Couple 1 | Husband | 56 | 39 | 12 | 16 | 123 |
| | Wife | 48 | 34 | 10 | 13 | 105 |
| Couple 2 | Husband | 46 | 32 | 5 | 15 | 98 |
| | Wife | 51 | 28 | 4 | 13 | 96 |
| Couple 3 | Husband | 57 | 40 | 10 | 17 | 124 |
| | Wife | 57 | 44 | 8 | 21 | 130 |
| Couple 4 | Husband | 55 | 34 | 11 | 12 | 112 |
| | Wife | 38 | 27 | 8 | 11 | 84 |
| Couple 5 | Husband | 44 | 37 | 7 | 12 | 100 |
| | Wife | 48 | 41 | 8 | 18 | 115 |
| Couple 6 | Husband | 51 | 45 | 9 | 11 | 116 |
| | Wife | 54 | 40 | 9 | 14 | 117 |

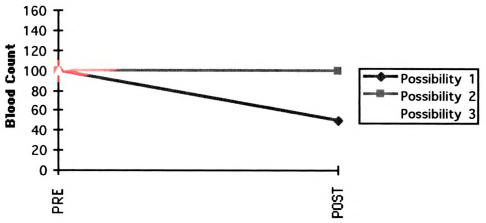



Figure 5. Trend Possibilities

The data were analyzed by subject and in the aggregate, for each of the blood measures. According to the Sparrow Hospital Laboratory Director, the assayed blood counts should be accurate within ± 10%. Changes in the *average* value of a particular pre- or post-imagery blood count, over time and whether imagery was solitary or conjoint, were generally small. As illustrated in Figures 6 and 7 for trends in the pre- and post-imagery segmented neutrophil counts, the averages mask larger, but sometimes opposite, changes measured for the specific subjects. Therefore, in the final analysis the data for each subject were treated separately.

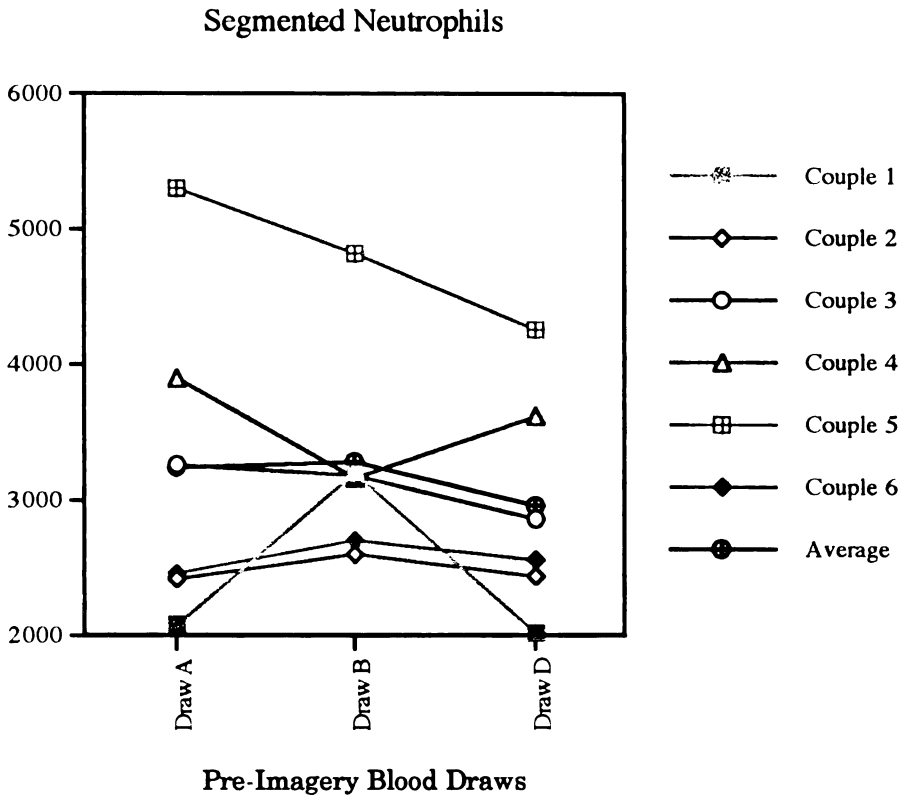



**Figure 6. Illustration of trends in individual data being obscured by averaging**

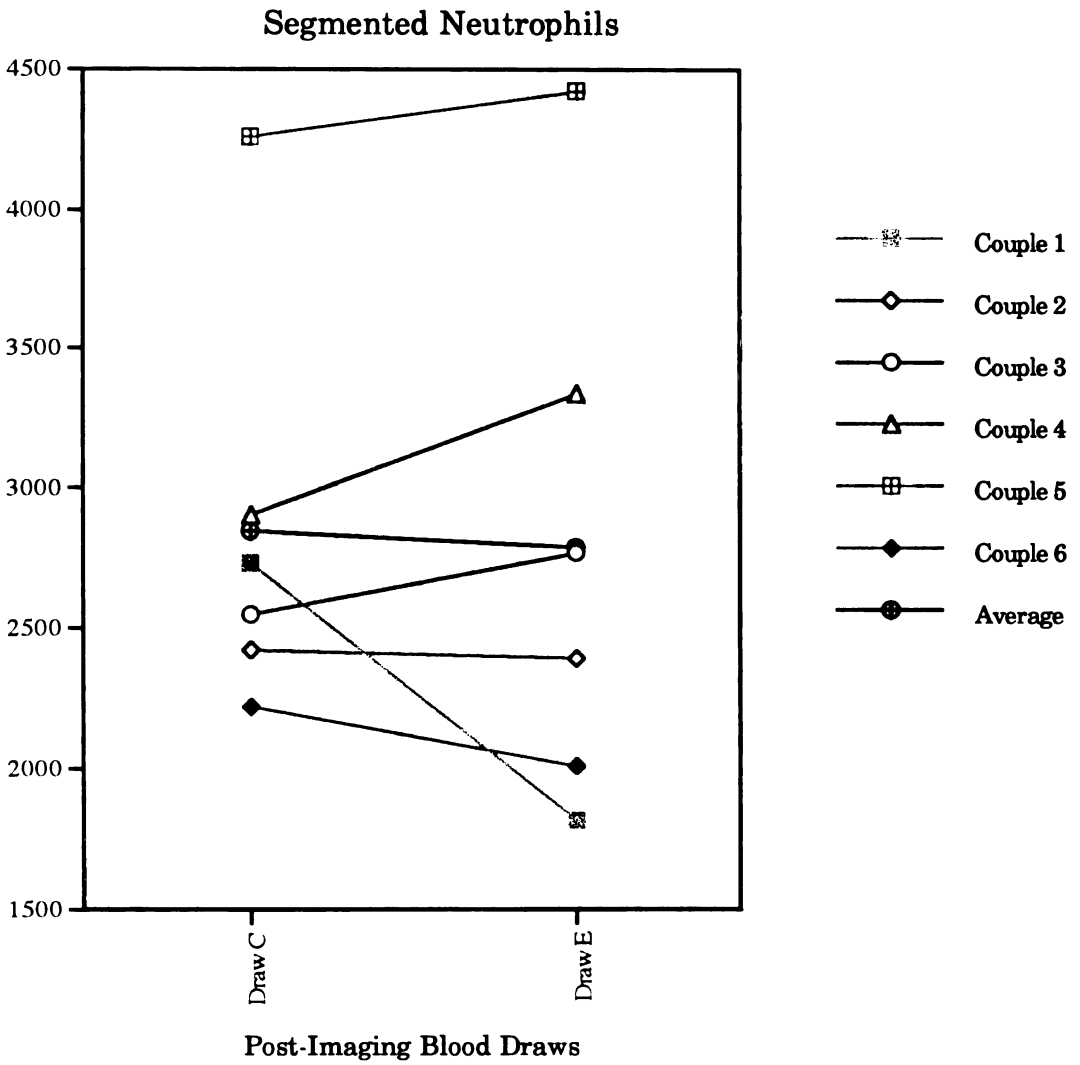



Figure 7. Example of how opposing trends are obscured by averaging

For those aspects measured, the span in blood count numerosities among the subjects range from more than a factor of two to almost a factor of five; see Tables 2 - 7. The ranges for the IMAGE-CA and DAS scores are much smaller; see Tables 8 and 9.

The focus of this investigation is the *change* in blood cell counts that occurs when a subject images alone or with her husband. These changes are illustrated for each couple in Figures 8 - 13. It should be noted that the blood assay changes are calculated by subtracting the post-imagery blood count from the pre-imagery value. Thus, a positive number reflects a *reduction* in blood count numerosity over the course of the imagery session. Figures 8 - 13 also include the wife's IMAGE-CA scores. For a given session, the IMAGE-CA score plotted is the average of the values determined by the two independent raters. The values are reported in Table 10.

Table 10. Interrater average IMAGE-CA scores for the wives.

| Couple | 1 | 2 | 3 | 4 | 5 | 6 |
|---|---|---|---|---|---|---|
| Alone | 201 | 202 | 200 | 150.5 | 172 | 213.5 |
| Together | 153 | 197.5 | 107.5 | 148.5 | 135 | 231 |

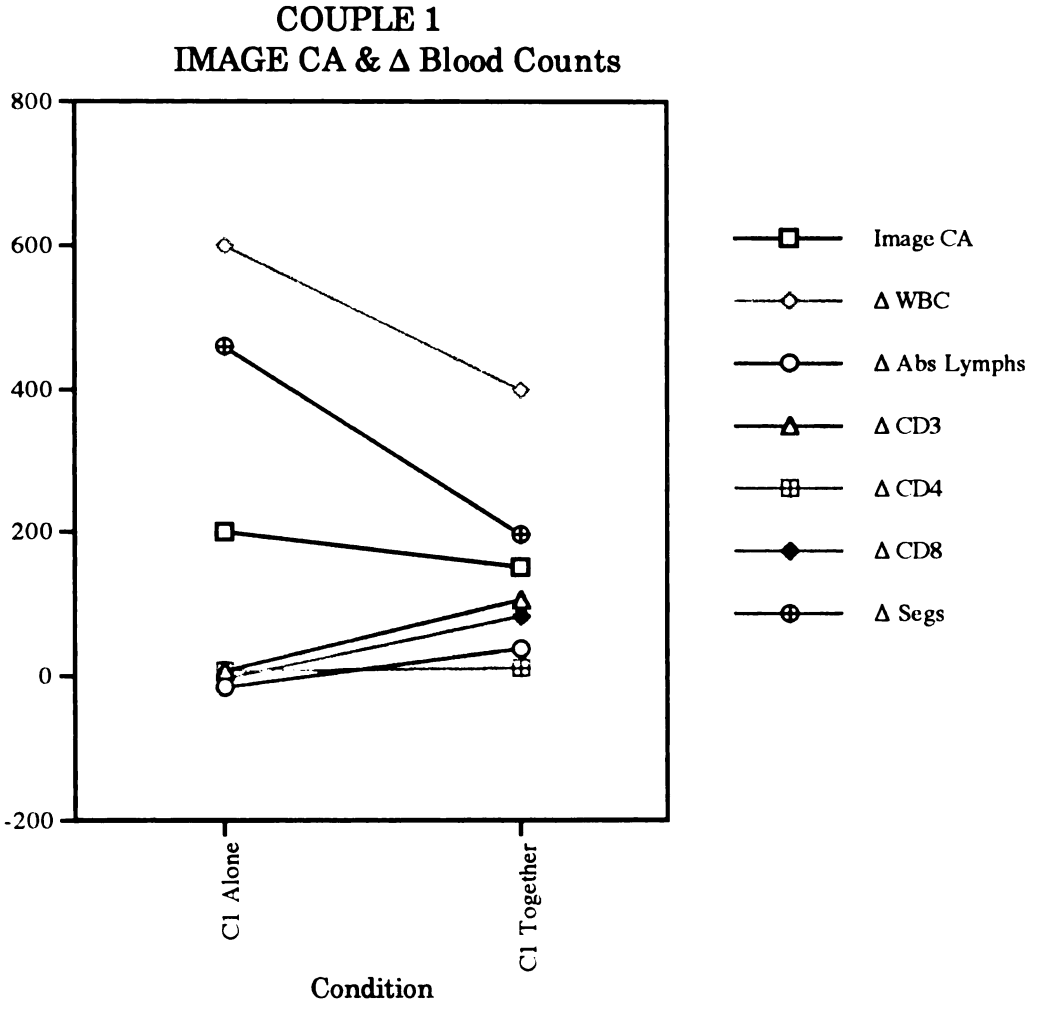



Figure 8. IMAGE-CA and blood count changes for Couple 1

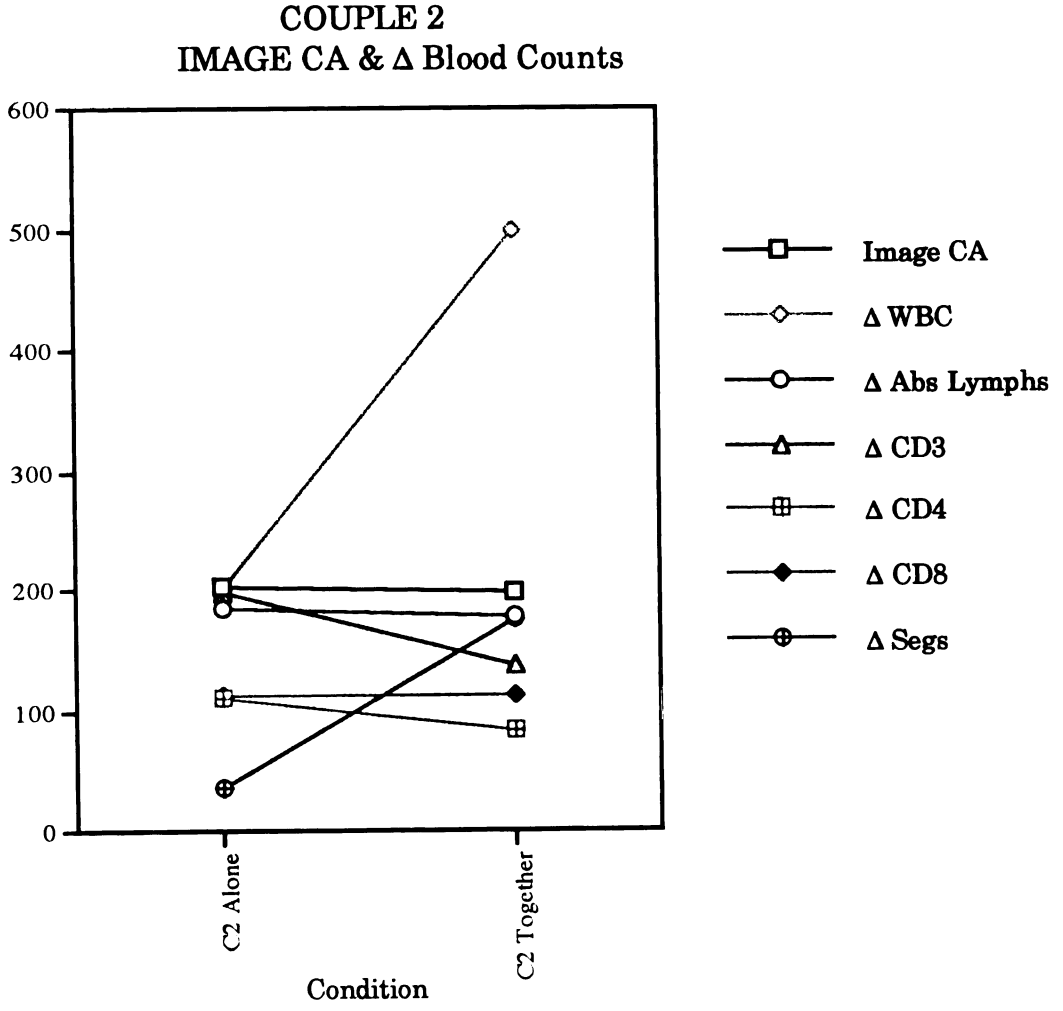



Figure 9. IMAGE-CA and blood count changes for Couple 2

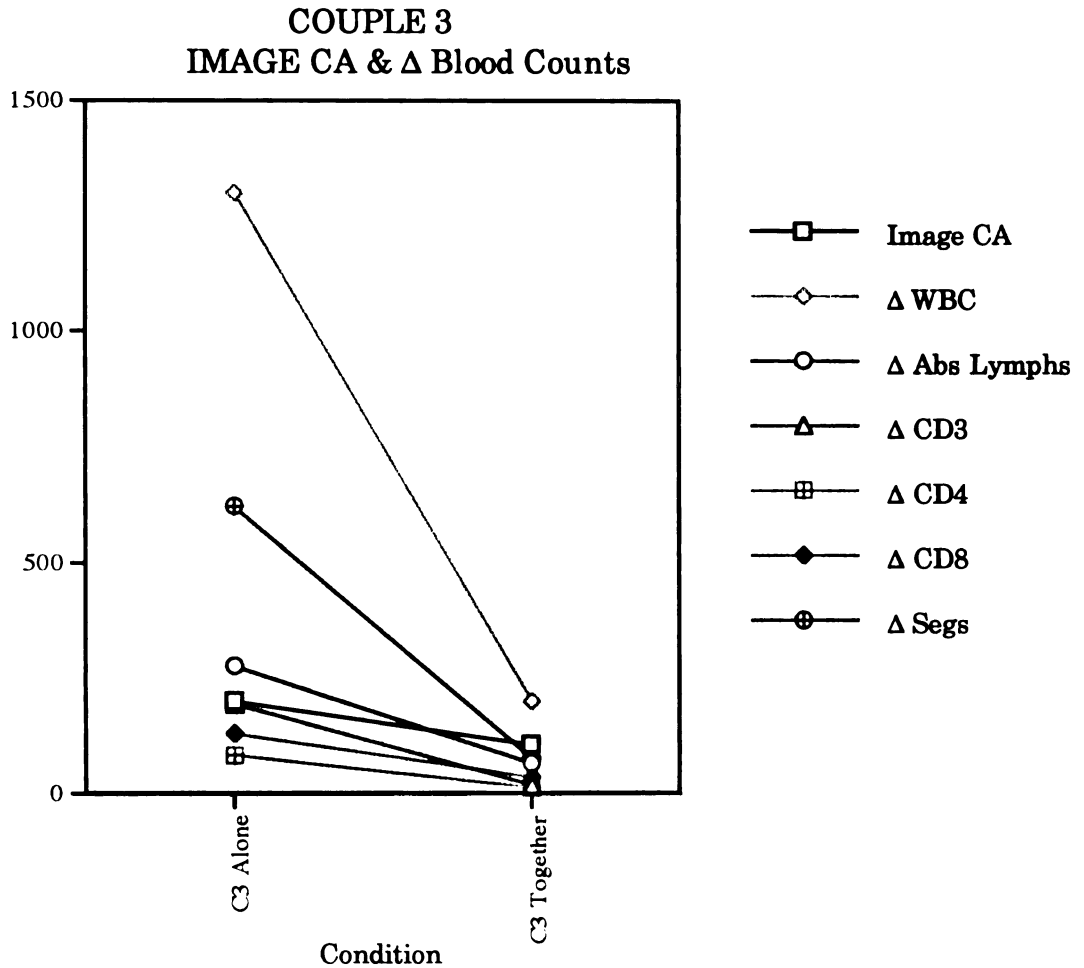



Figure 10. IMAGE-CA and blood count changes for Couple 3

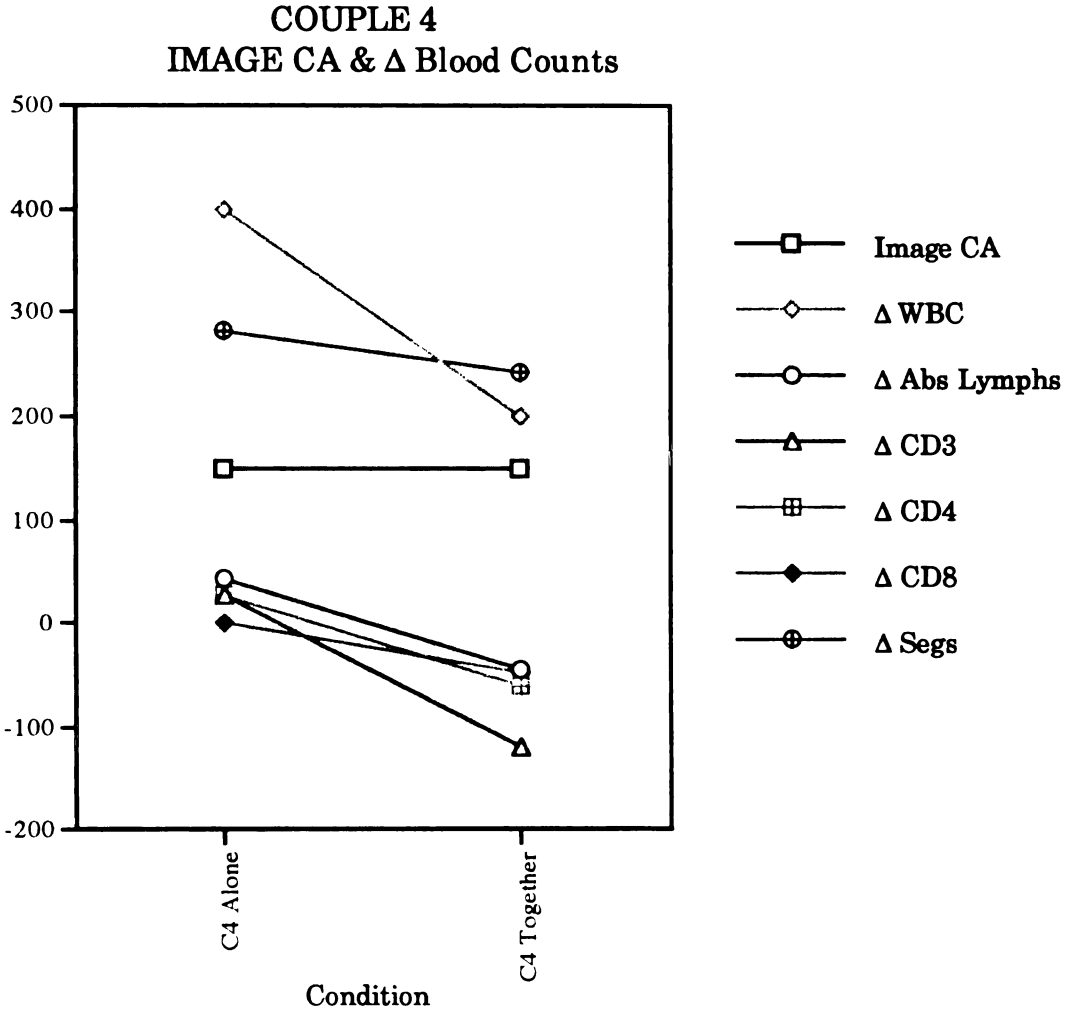



Figure 11. IMAGE-CA and blood count changes for Couple 4

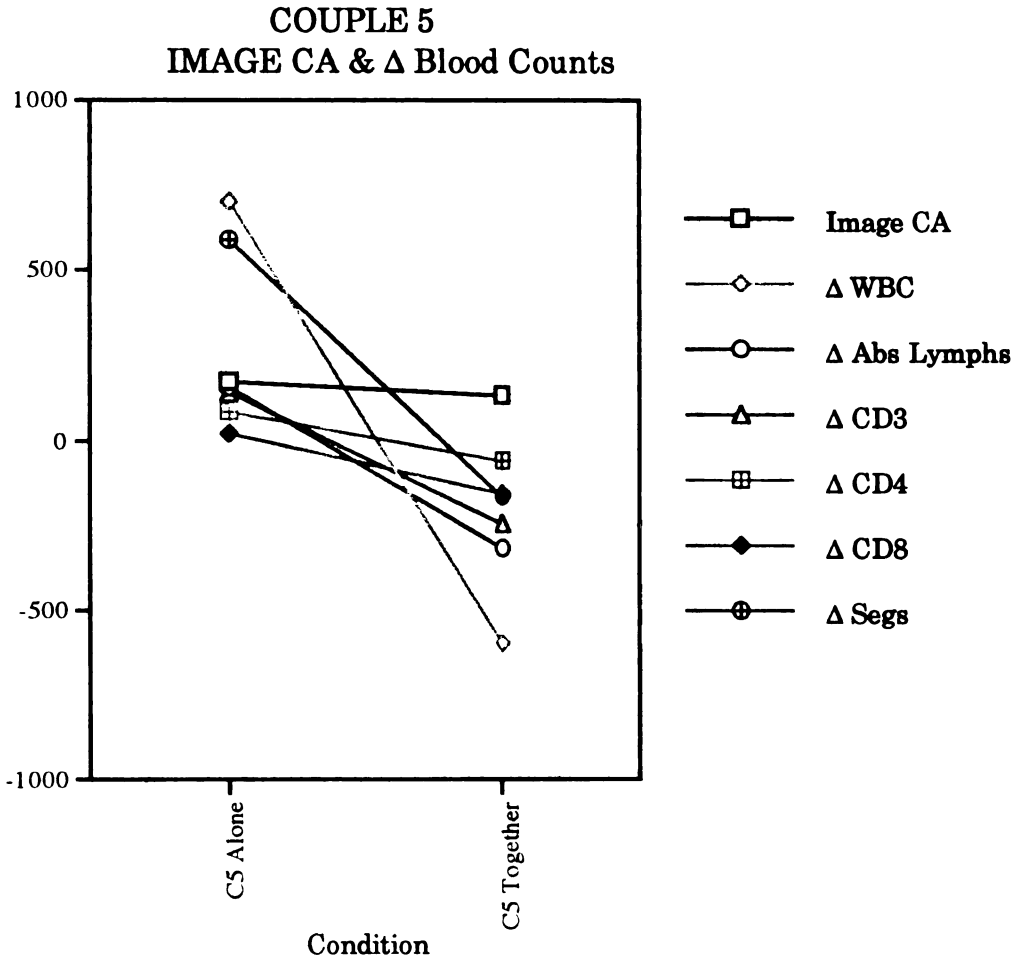



**Figure 12. IMAGE-CA and blood count changes for Couple 5**

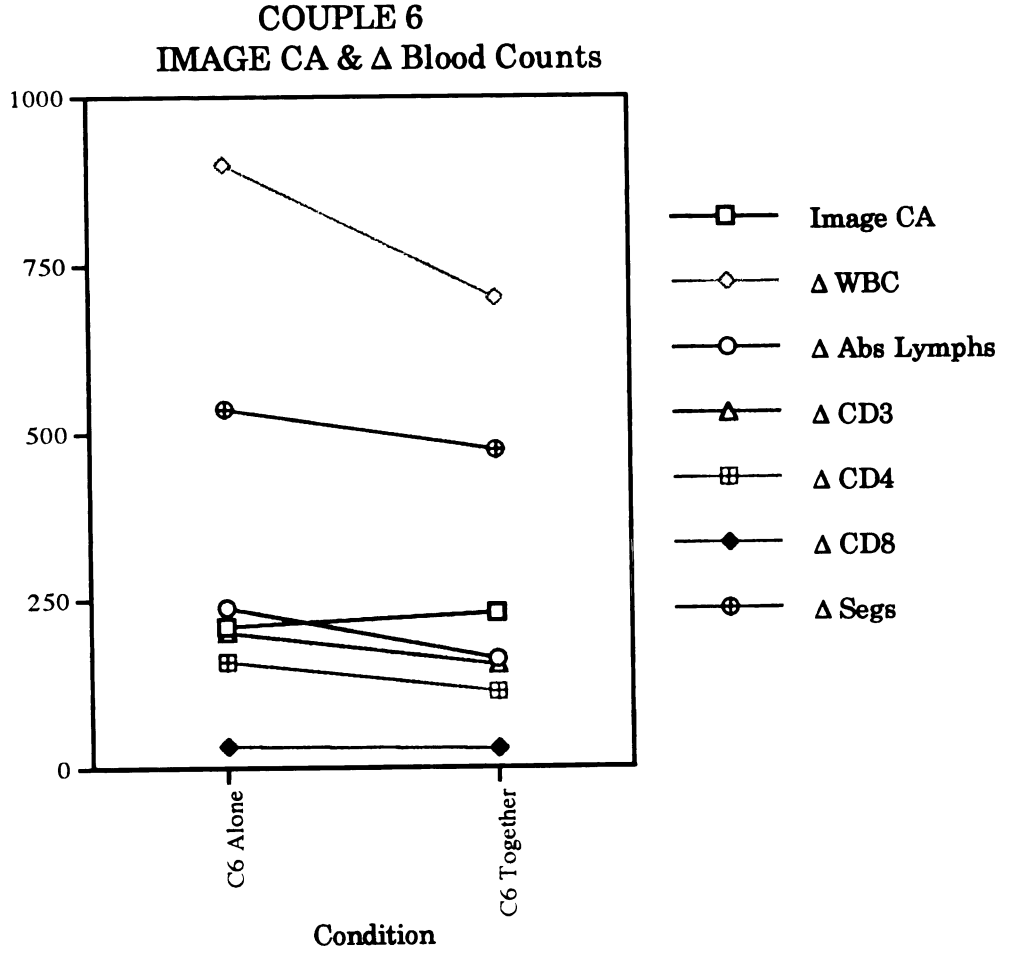



Figure 13. IMAGE-CA and blood count changes for Couple 6

As illustrated by the preceding figures, the changes in the wife's blood counts for Couples 3, 4, 5, and 6 decreased following the conjoint imagery sessions, with respect to the changes when she imaged alone; the differences are most dramatic for the White Blood Cell counts. For Couples 3 and 6 the change in numerosity was smaller when the wife imaged with her husband. For Couple 4 the absolute lymphocyte counts and the T-Cell absolutes improved (post-imagery values larger than pre-imagery values) following conjoint imagery. The Couple 4 wife indicated on the DAS (Score = 84) and verbally that she was dissatisfied with the marital relationship, and the couple was receiving weekly marital therapy at the time of this investigation. Following the conjoint imagery session and the wife's blood draw, the IMAGE-CA interview was conducted consistent with the research protocol. During his retrospective of the imagery experience, the husband described how supportive he had felt during his wife's cancer treatment process. His wife seemed to be witnessing his deep level of caring for the first time. This interaction occurred after the first imagery session, and the couple referred back to that debriefing during the course of their participation. It should be noted that the wife's blood was drawn prior to this discussion. Nonetheless, the Couple 4 wife was one of only two participants whose blood assays increased in the conjoint condition.

Each blood assay increased for Couple 5 in the conjoint condition. Thus one might have expected either very high IMAGE-CA or DAS scores for one or both couple members. However, the wife's IMAGE-CA score dropped 2 stens in the conjoint condition, and the husband's IMAGE-CA scores were disparate between the raters. Couple 5's DAS scores were not exceptional: 100 (husband) and 115 (wife). Further, the wife reported a number of serious health issues to be present in addition to the breast cancer (heart disease

requiring quadruple bypass surgery, systemic lupus, fibromyalgia and a thyroid condition) which could substantially impact her immune system; yet all of her baseline blood assays were in the normal range. The Couple 5 wife reported having a very large support network of friends, family, God, church, and professionals. This is consistent with Cohen's recent finding that more diverse social networks were associated with greater resistance to upper respiratory illness (Cohen, et al., 1997).

For Couple 1 the WBCs and Segs decreased less in the together condition, whereas the Lymphs and CD 3 and 8 decreased more in the together condition. The husband of Couple 1 was physically present during the imagery session, but denied listening to the tape or participating in the imagery experience. He reported that instead he had stared at the ceiling and assessed the quality of the paint job. (He was a professional painter.)

For Couple 2 the WBCs and Segs decreased more in the conjoint condition, whereas the Lymphs and T-cell measures decreased less or stayed the same when the couple imaged together. The wife reported on the day of conjoint imagery that she was experiencing much anger for her husband and the marital relationship during the month prior to participating in the study.

Since each subject served as her own control, the blood assay changes depicted in Figures 8 - 13 must be viewed with the knowledge that session order, and hence a possible learning effect, has not been considered. A meaningful statistical analysis must incorporate the order of the sessions (alone first vs. together first) when the effect of imaging alone or as a couple is evaluated. This problem is treated in detail in the section on statistical analysis.

Does guided imagery help effect an increase in blood count numerosity, as measured 30 minutes after the imagery session? Changes in six blood

measures, over two sessions, were obtained for each of six subjects. In only eight of 72 instances did the number increase more than 10%; in slightly more than half of the cases it decreased by more than 10%. Similar results have been reported by several other investigators (Fawzy, Fawzy, Hyun, Elashoff, Guthrie, Fahey, & Morton, 1993; Fawzy, et al., 1990; Gruber, et al., 1988; Gruber, et al., 1993; Hall, et al., 1992; Rider & Achterberg, 1989; Zachariae, et al., 1990)

Apparently, guided imagery and other relaxation techniques generally reduce T-cell numerosity and activity on a short time scale. In two studies, however, efficacious effects of imagery on T-cell activity have been measured over a period of several months to 18 months (Gruber et al., 1988; Gruber et al., 1993). In several other studies, group therapy and psychiatric intervention effects required 20 months to develop (Fawzy et al., 1993; Fawzy et al., 1990; Spiegel et al., 1989) In view of the published information, it is possible that long-term effects of behavioral interventions such as biofeedback, hypnosis, guided imagery or group therapy may be cumulative.

The results of this investigation, which spanned 15 days for all participants (except Couple 4, for whom the experimental phase spanned 29 days), support the observation that T-cells do not increase over the immediate course of an imagery session or over durations as short as 15 days. For each of the six blood variables measured, and for both sessions, the average post-imagery numerosities were lower than the average pre-imagery values.

Gruber et al. (1993) report that both muscle tension and autonomic activity reductions began within three weeks after initiation of relaxation and biofeedback training. These psychophysiological reductions occurred prior to immune system changes, but the actual cause of the immune system changes was not clear. Over 18 months, the authors found significant correlations

between indices of the immune system and behavioral interventions, leading them to conclude that the intervention might have the potential to modulate the immune system either directly or indirectly.

Zachariae et al. (1994) conjecture that the decreases in lymphocyte and neutrophil counts after guided imagery "could indicate that brief changes in cellular immune function may be related to changes in trafficking of leukocytes, which in turn may be influenced by autonomous nervous system activity." They suggest the possibility that other mediators such as norepinephrine or opioid peptides could underlie the observed immune function changes.

As noted earlier, Glaser et al. (1992) found that both stress and social support were related to medical students' abilities to produce an antibody response to the Hepatitis B vaccine. These authors report that convergent data from both human and animal studies support the idea that stress may delay the development of an immune response to a pathogen. Certainly the participants in the current study contended with stressors of considerable magnitude during the course of this investigation. They included death of a close family member, the attempted suicide of a close family member, the death of a pet, a possible recurrence of breast cancer, an auto accident involving immediate family, impending treatment of a lung fungus, a breast mass discovered in the daughter of a participant, breast cancer diagnosed in the sister of another participant, marital problems in the case of two participants, and serious other health issues for another woman. Therefore, if stress delays an increased immune response, it is not surprising that these women showed little immune system improvement during the course of this investigation. If the immune system of more severely stressed individuals delays or inhibits the synthesis of adequate protective agents, could these women be at

higher risk for infection or a recurrence of cancer than less stressed individuals?

The stress of the blood draws themselves may have impacted the post treatment blood counts. All of the women who participated in this study had experienced multiple necessary previous blood draws and chemotherapy. Venipuncture was difficult for these women; there were times that the regular nurse doing the venipuncture would summon a pediatric IV nurse to complete the draw. Some of the women gave voice to their apprehension and several of the particiants described the venipuncture as painful. Two of the women related stories about times during their treatment process when particlar blood draws or chemotherapy protocols were painful. Rossi (1993) discusses state-dependent learning as the experience of reverting back to a former emotional state when similar stimuli are introduced into the present. One potential participate for this study changed her mind one week later. She reported reliving the emotional experience of her cancer diagnosis and treatment that had occurred some years earlier. This woman said that the emotional upheaval that she experienced after volunteering was so intense and unsettling that she had decided not to participate.

The stressors on the subjects in this investigation were carefully noted; however, they could not be controlled or their effects measured. Moreover, blood assays are available over short time intervals, so the imagery effects can be monitored only over a limited temporal range. The focus of this study is the *change* that occurs when a subject images alone or with her husband. Therefore the blood analysis data were retabulated according to whether the specific blood measure increased, decreased, or remained the same (within 10%) following a particular imagery session. The results are presented in

Table 11, according to session sequence, and Table 12, according to whether the subject imaged alone or conjointly.

**Statistical Analysis**

The statistical method of logistic regression (Hosmer & Lemeshow, 1989; Kleinbaum, 1994) can be employed to analyze relatively small data sets involving binary random dependent variables, with either binary or continuous independent variables. It has been applied with success to a variety of clinical studies (Hirsch and Riegelman 1991; Colton et al., 1982-1996). Logistic regression was employed in this investigation to examine the relationship of the change in blood cell numerosity (the dependent variable, or "response") to the timing of the imagery session ("sequence"), or whether the session was solitary or conjoint ("alonetog"), with the wife's session average IMAGE-CA rating or her DAS score as covariates.

**Table 11. Post-imagery blood draw numerosities compared to the corresponding pre-imagery values, sorted by session sequence.**

| Measure | Session | Couple 1 | Couple 2 | Couple 3 | Couple 4 | Couple 5 | Couple 6 |
|---|---|---|---|---|---|---|---|
| WBC | 1 | **down** | **down** | **down** | same | **down** | **down** |
| | 2 | **down** | same | same | same | up | **down** |
| Lymphs | 1 | same | **down** | **down** | same | **down** | **down** |
| | 2 | same | **down** | same | same | up | **down** |
| CD 3 | 1 | same | **down** | **down** | up | **down** | **down** |
| | 2 | **down** | **down** | same | same | up | **down** |
| CD 4 | 1 | same | **down** | **down** | up | **down** | **down** |
| | 2 | same | **down** | same | same | up | **down** |
| CD 8 | 1 | same | **down** | **down** | up | same | **down** |
| | 2 | **down** | **down** | same | same | up | **down** |
| Segs | 1 | **down** | same | **down** | **down** | **down** | **down** |
| | 2 | same | same | same | **down** | same | **down** |

Table 12. Post-imagery blood draw numerosities compared to the corresponding pre-imagery values, sorted according to whether the wife imaged alone or together with her husband.

| Measure | Session | Couple 1 | Couple 2 | Couple 3 | Couple 4 | Couple 5 | Couple 6 |
|---|---|---|---|---|---|---|---|
| WBC | Alone | down | same | down | same | down | down |
| | Together | down | down | same | same | up | down |
| Lymphs | Alone | same | down | down | same | down | down |
| | Together | same | down | same | same | up | down |
| CD 3 | Alone | same | down | down | same | down | down |
| | Together | down | down | same | up | up | down |
| CD 4 | Alone | same | down | down | same | down | down |
| | Together | same | down | same | up | up | down |
| CD 8 | Alone | same | down | down | same | same | down |
| | Together | down | down | same | up | up | down |
| Segs | Alone | down | same | down | down | down | down |
| | Together | same | same | same | down | same | down |

The *LogXact-Turbo* computer program (1993, CYTEL Software Corporation, Cambridge, MA) performs unconditional maximum likelihood inference, conditional maximum likelihood inference, and conditional exact inference on the parameters of the logistic regression model. The software was used to fit the equation:

$$\ln[\pi_j/(1-\pi_j)] = \gamma + \beta_1 * \text{variable1}_j + \beta_2 * \text{variable2}_j$$

where $\pi_j$ is the probability that the j-th value of the dependent variable will be one, and $\gamma$ and the $\beta$s are constants. The null hypothesis tested is that there will be equal probabilities that the dependent variable will be zero or one, in which case the logarithmic term will be zero and thus all of the constants will be zero. The computer program also allows one to test whether each of the $\beta$ coefficients, or all of them together, are zero (*i.e.*, the constant term $\gamma$ is not treated).

If a particular blood assay numerosity following an imagery session remained the same within 10% of the pre-imagery value or increased by more than 10% (same and up in Tables 10 and 11), the response was assigned the binary value of 1. A decrease by more than 10% (down) was assigned the binary value 0. Logistic regression was employed to test whether the blood assay results were statistically dependent on the sequence of the imagery (binary variable: session 1 = 0, session 2 = 1) and the raters' average IMAGE-CA score (continuous variable). The same method was applied to test conjoint imagery (binary variable: alone = 0, together = 1) and the IMAGE-CA scores as the independent variables. The marital satisfaction index is used to encourage subjects with scores below a certain level to consider therapeutic intervention (Spanier, 1976). Therefore, the DAS score was also tested as a binary covariate. Total scores for the wives equal to or greater

than 100 were coded 1; 0 was assigned to lower DAS values. The analysis was repeated with the wife's DAS score considered as a continuous variable.

The *LogExact* data are collected in Appendix K. The parameters in the logit equation, g and the bs, are evaluated by the method of maximum likelihood, to give "maximum likelihood estimates" (MLE). In this method the observed data values are considered to be constants and the parameters to be evaluated as variables that are fitted using differentiation to find the values that maximize the likelihood function. Hypothesis tests arising from unconditional maximization are reported in terms of Likelihood Ratio, Wald and Scores statistics, with their corresponding p-values. Regression parameters estimated by this procedure are listed as asymptotic values, along with their standard errors, 95% confidence intervals, and p-values. When the values of these test statistics differ substantially, the asymptotic results may not be valid. Should this occur, another approach, exact hypothesis testing, is to evaluate the conditional maximum likelihood. This produces the Exact (Conditional Scores) statistic, exact p-value and mid-p-value (Barnard, 1990), as well as exact estimates of the logit equation parameters. The Exact hypothesis test is the preferred treatment for the data analyzed in this study.

Note that the program tests the null hypothesis that all of the linear regression constants are zero, or that the coefficients of the variables are individually or collectively zero. This is equivalent to saying the variables tested showed no relationship to each other. The significance level of a statistical test (often chosen as 0.05) is the pre-selected probability of rejecting the null hypothesis when it is in fact true. If the p-value is smaller than the significance level, *e.g.*, smaller than 0.05, the null hypothesis is

rejected. Here, if $p < 0.05$ then it is unlikely that the calculated parameter is zero. Larger values of p are often associated with high standard errors.

The DAS score, first as a binary and then as a continuous variable, was tested as a covariate with the Sequence of the imagery sessions and with the Alone/Together condition. For all four models, the null hypothesis cannot be statistically rejected (See Appendix K). Changes in blood cell numerosities are statistically independent of the marital satisfaction index rating as well as of the session sequence and whether the imagery was solitary or conjoint.

The IMAGE-CA score was also tested as a covariate with both the sequence of the imagery sessions and whether the wife imaged alone or together with her husband. The corresponding models are: Response = Sequence + IMAGE-CA, and Response = Alone/Together + IMAGE-CA. Exact tests were performed on both models on the combined variables and with each of the variables independently. In no instance could the null hypothesis be statistically rejected when only the Sequence or the Alone/Together variable was tested. Exact scores and p-values for the IMAGE-CA variable alone, except for the segmented neutrophil changes, suggested that the null hypothesis could be confidently rejected. Segmented neutrophils are inversely related to lymphocytes, so an incease in neutrophils is anticipated when lymphocytes decrease. Neutrophils may be observed to increase earlier than other measures because neutrophils elevate quickly to fight off bacterial and viral infection. The exact scores improved somewhat, but with moderately poorer p-values, when both variables were considered together.

For all six blood measures, the coefficient for the binary variable that describes Sequence cannot be confidently taken as non-zero. This suggests that there is no significant learning effect on the change in numerosity, measured on the short time scale surrounding the imagery sessions.

Likewise, the coefficient for the Alone/Together variable may satisfy the null hypothesis. Thus one cannot statistically support the notion that conjoint imagery has a positive effect on the change in blood cell numerosity, at least on the time scale of these measurements.

For segmented neutrophils, the coefficient for the continuous variable, IMAGE-CA score, may well be zero in both the alone/together and first vs. second conditions. However, logistic regression suggests that the IMAGE-CA coefficient is confidently non zero for the other five blood variables assayed, under both conditions. (The responses (binary-coded blood cell changes) for the limited subject group happen to be the same for lymphocytes and CD4 cells; therefore the *LogExact* output is identical for these two measures.) Moreover, the IMAGE-CA coefficient is negative, which implies that a higher IMAGE-CA score will more likely correspond to a *lower* probability that the blood cell numerosity will stay the same or increase following the imagery session. For white blood cells, lymphocytes, CD3 and CD4 cells, the coefficient is generally in the -0.04 to -0.06 range. For CD8 cells it is three times larger (-0.17) in the sequence condition, and ten times larger (-0.55) in the alone/together condition. Table 13 lists the exact scores and corresponding p-values, as well as the exact ß coefficients for the IMAGE-CA and their p-values, for the two models that included IMAGE-CA as a covariate.

One should view the statistical results from this small sample with caution. The inverse relationship between the magnitude of the IMAGE-CA score and the likelihood of blood cell numerosities remaining the same or improving over the corresponding imagery session (negative ß coefficient) may not hold for larger subject groups. In this study that relationship is most likely dominated by the observations for three couples. The Couple 6 wife had the highest IMAGE-CA scores in both sessions, yet her blood assay

Table 13. Exact hypothesis test results (conditional exact inference) for two models for changes in blood assay numerosities during imagery sessions, obtained with *LogXact* software. (The null hypothesis could not be rejected for the coefficients of Alone/Together or Sequence.)

Model: Response = Alone/Together + IMAGE-CA

| Assay | Exact Score | p-Value* | Exact ß(CA) | p-Value* |
|---|---|---|---|---|
| WBC | 4.7464 | 0.0682 | -0.0543 | 0.0200 |
| Lymphs | 6.2607 | 0.0173 | -0.0556 | 0.0133 |
| CD3 | 4.8194 | 0.0657 | -0.0555 | 0.0167 |
| CD4 | 6.2607 | 0.0173 | -0.0556 | 0.0133 |
| CD8 | 5.7431 | 0.0368 | -0.5523 | 0.0050 |
| Segs | 3.3672 | 0.2020 | -0.0136 | 0.2556 |

Model: Response = Sequence + IMAGE-CA

| Assay | Exact Score | p-Value* | Exact ß(CA) | p-Value* |
|---|---|---|---|---|
| WBC | 5.3064 | 0.0505 | -0.0358 | 0.0444 |
| Lymphs | 6.2440 | 0.0216 | -0.0555 | 0.0178 |
| CD3 | 4.9132 | 0.0682 | -0.0536 | 0.0233 |
| CD4 | 6.2440 | 0.0216 | -0.0555 | 0.0178 |
| CD8 | 6.0249 | 0.0390 | -0.1661 | 0.0100 |
| Segs | 3.2685 | 0.2083 | -0.0134 | 0.2333 |

* One-sided p-values are reported

counts decreased by more than 10% in each imagery session. The IMAGE-CA score for the Couple 3 wife was much lower in the Together condition than Alone, yet all of her blood cell numerosities dropped more than 10% in the Alone condition and none of them did when she imaged with her husband. Yet, except for the segmented neutrophil numerosities, the blood assays for wife 4 always remained the same or went up. Conversely, the Couple 2 wife had relatively high IMAGE-CA scores in both sessions; except for the Segs, most of her blood counts dropped more than 10% after imagery in both conditions. It is noteworthy that the IMAGE-CA regression coefficient for Segs was the only one for which the null hypothesis could not be rejected.

Moreover, the binary coding for the blood cell changes over an imagery session masks differences between same and up, and also situations where the numerosity decrements were different -- but both greater than 10% -- in the two conditions. In this respect the trends displayed in Figures 8 - 13 may be more revealing: most of the slopes are negative, which indicates that imaging in the Together condition led to smaller numerosity decrements, or greater improvements, with respect to the changes when the wife imaged alone. Thus there may be an effect of conjoint imagery -- perhaps a smaller numerosity *decrease* -- although the coefficient for this independent variable from the statisical analysis of the experimental data set could not be confidently ascribed a non-zero value. Clearly, larger sample populations would provide more reliable statistical results.

# CHAPTER V

# SUMMARY AND EPILOGUE

## Summary

Six breast cancer patients and their husbands participated in a 15-day study that included one solitary and one conjoint guided imagery session. A baseline blood count and two subsequent pre- and post-treatment blood analyses were used to measure changes in the wives' immune systems.

In only 8 of 72 instances did blood counts increase by more than 10% over the course of an imagery session; in slightly more than half the cases it decreased by more than 10%. There was no significant two-week learning effect nor was there statistical support for the notion that conjoint imagery has an incrementing effect on blood count numerosity over a two-week time span. For all of the blood measures except segmented neutrophils, the probability that blood counts will stay the same or increase following the guided imagery was inversely related to the IMAGE-CA score.

Four participants (wives 1, 2, 3 and 6) showed a decrease in blood counts, or changes only within 10% of the initial levels, following imagery in both the alone and conjoint conditions; two of the four showed a smaller drop in blood counts in the conjoint condition. For two participants (wives 4 and 5), several of the blood assay numerosities increased by more than 10%; this result was observed only in the conjoint imagery condition, in both cases. Although the wife of Couple 4 expressed dissatisfaction with the marital relationship (reflected also in her DAS score), blood counts increased on four of

the assays and showed less of a decrease on the other two measures in the conjoint condition.

The first null hypothesis, that there will be no difference between the baseline measure and the subsequent pre- and post-treatment measures was accepted. The average pre-imagery blood counts in weeks 2 and 3 were within 10% of the week 1 baseline measures. The post-imagery averages were consistently slightly lower, but still generally within 10%. However, there were opposing trends among subjects. The second null hypothesis, that there will be no differences between pre-treatment and post-treatment blood draws was also accepted. As just noted, the post-treatment values were lower, but on average within the measurement errors. The third null hypothesis, that there will be no differences between the changes in the blood counts in the solitary and the conjoint condition was also accepted. On average, blood counts decreased slightly following both treatment conditions, although the decrease was somewhat smaller in the conjoint condition. The fourth null hypothesis, that there will be no relationship between the IMAGE-CA score and blood count changes was rejected; for all the blood measures except the segmented neutrophils, higher IMAGE-CA scores were related to lower probability that blood counts stayed the same or increased following the imagery. The fifth null hypothesis, that there is no relationship between blood counts and DAS scores was accepted; no relationship was found between DAS scores of the wife and the blood count differences between the solitary and conjoint conditions.

This study supports the conclusion that blood counts do not increase over the immediate course of an imagery session or over the duration of 15 days. It is possible that the effects of behavioral intervention such as guided

immune system imagery occur over a longer time interval than the 15-day period employed in this investigation.

**Recommendations for Future Work**

The uniform decreases in lymphocyte counts following imagery measured in this investigation (although generally within measurement error) are consistent with results in the few published studies evaluating short term blood cell changes following behavioral treatment (Rider and Achterberg, 1989; Zachariae et al., 1990; McGrady et al., 1992; Hall et al., 1992; Zachariae et al., 1994). Behavioral studies of longer duration (6 weeks to several years) have shown increases in lymphocytes over time (Gruber, et al., 1988; Spiegel et al., 1989; Fawzy, et al., 1990; Fawzy, et al., 1993; Gruber, et al., 1993). Clearly, a longer-term study is indicated.

A pre- and post-treatment blood measurement design (with controls matched for age and gender) conducted over a 12 - 18 month period of time would yield both short- and long-term changes for both the solitary and conjoint conditions, for the participating subjects and their controls. Assessments of marital satisfaction, social support and depression could be made at intervals throughout the study. In addition, participants could be given the treatment audio tape and be encouraged to practice and record the number of rehearsals between sessions and blood assays. If adequate funding were available, a large number of subjects (forty in each group) would allow for more generalizable results. The possibility of cumulative effects of imagery in each treatment condition could be studied in this design.

Without exception, the cancer patients who volunteered to have their blood drawn for this study presented with veins damaged by prior necessary medical diagnostics and treatment, leading to considerable discomfort during

some of the venipunctures. Did the stress accompanying the anticipation and consummation of the blood draws impact the blood assays? A study that isolated the stress of venipuncture from a treatment condition in healthy and ill populations would yield useful information. If four groups of subjects (healthy subjects/alone, healthy subjects/with a spouse, cancer patients who had completed chemotherapy/alone, cancer patients who had completed chemotherapy/with a spouse) had two blood draws (the same time of day for each subject in each group), one hour apart with no intervening experimental treatment, variations in repeated venipuncture for healthy people and cancer patients, alone and with a spouse, could be measured.

There are numerous studies supporting the idea that stress impacts the immune system (Andrews & Tennant, 1978; Baker et al., 1984; Borysenko & Borysenko, 1982; Bowers & Kelly 1979; Glaser et al., 1992; Guillemin, Cohn, & Melnechuk, 1985; Kennedy, Kiecolt-Glaser, & Glaser, 1988; Kobasa 1982; Locke 1982; Locke et al., 1984; Manuck, Cohen, Rabin, Muldoon, & Bachen, 1991; Plaut & Friedman 1985; Sklar & Anisman 1979; Stein 1985). The relationship between stress and immunity needs careful study. Following stress, some immune system measures reportedly increase (Cacioppo et al., 1995; Sgoutas-Emch et al., 1994) while others decrease (Feng et al., 1991; Glaser et al., 1992; Jemmott & Locke, 1984; Kennedy, Kiecolt-Glaser, & Glaser, 1988; Kiecolt-Glaser, Glaser, et al., 1987; Kiecolt-Glaser & Glaser 1992; Kleinbaum, 1994; McKinnon, Weisse, Reynolds, Bowles, & Baum, 1989).

Manuck and his colleagues conducted correlational studies that found psychological stress to suppress cellular immune function in some individuals and not others (Manuck et al., 1991). Differences in types of stressors, variability in perceptions about that which is stressful, the variability in

immunologic responses to stress and the impact of acute stress versus prolonged chronic stress (as well as the immediate effects and the long term effects) all warrant further study.

Additional work in these areas will help clarify whether enhanced cell counts and activity are healthy processes or unhealthy processes. Perhaps the relative merit or liability of cellular changes is related to whether they are long or short term effects. Ultimately we need to learn how alterations in cellular immunity affect long term health.

The present investigation showed cellular response differences among individual subjects when the wife imaged alone and when she imaged with her husband. Blood measures following the conjoint condition, regardless of how one might interpret the relative merit of the imagery condition, increased for two participants and generally decreased less for the others.

Would cellular changes increase if a subject did the imagery with her whole family? Would the presence of the whole family impact the blood counts independent of the imagery condition? Would prayer for an immune system capable of maintaining health be more effective than specific immune system imagery? Would imagers unknown to the patient affect a woman's immune system in the same manner as the husband co-imager? Would experimentor-generated images known to be powerful have the same effect as participant-generated images (the method used in this study)?

The field of psychoneuroimmunology has been emerging over the past twenty years. It is now clear that the immune system does not operate autonomously, as once supposed. Further, the immune system is not a closed entity; behavioral and psychological processes impact immune function. The objective to understand the interactions between behavior and the immune

system offers many diverse and interesting future research projects in the realm of psychoneuroimmunology.

# APPENDICES

# APPENDIX A

## Dyadic Adjustment Scale

# APPENDIX A

## DYADIC ADJUSTMENT SCALE

Most persons have disagreements in their relationship. Please indicate below the approximate extent of agreement or disagreement between you and your partner for each item on the following list.

| | Always Agree | Almost Always Agree | Occasionally Disagree | Frequently Disagree | Almost Always Disagree | Always Disagree |
|---|---|---|---|---|---|---|
| 1. Handling family finances | | | | | | |
| 2. Matters of recreation | | | | | | |
| 3. Religious matters | | | | | | |
| 4. Demonstrations of affection | | | | | | |
| 5. Friends | | | | | | |
| 6. Sex relations | | | | | | |
| 7. Conventionality (correct or proper behavior) | | | | | | |
| 8. Philosophy of life | | | | | | |
| 9. Ways of dealing with parents or in-laws | | | | | | |
| 10. Aims, goals, and things believed important | | | | | | |
| 11. Amount of time spent together | | | | | | |
| 12. Making major decisions | | | | | | |
| 13. Household tasks | | | | | | |
| 14. Leisure time interests and activities | | | | | | |
| 15. Career decisions | | | | | | |

| | All the time | Most of the time | More often than not | Occasionally | Rarely | Never |
|---|---|---|---|---|---|---|
| 16. How often do you discuss or have you considered divorce, separation, or terminating your relationship? | | | | | | |
| 17. How often do you or your mate leave the house after a fight? | | | | | | |
| 18. In general, how often do you think that things between you and your partner are going well? | | | | | | |
| 19. Do you confide in your mate? | | | | | | |
| 20. Do you ever regret that you married (or lived together)? | | | | | | |
| 21. How often do you and your partner quarrel? | | | | | | |

| | | | | | | |
|---|---|---|---|---|---|---|
| 22. How often do you and your mate "get on each other's nerves"? | _____ | _____ | _____ | _____ | _____ | _____ |
| | | Every Day | Almost Every Day | Occa-sionally | Rarely | Never |
| 23. Do you kiss your mate? | | _____ | _____ | _____ | _____ | _____ |
| | | All of them | Most of them | Some of them | Very few of them | None of them |
| 24. Do you and your mate engage in outside interests together? | | _____ | _____ | _____ | _____ | _____ |

How often would you say the following events occur between you and your mate?

| | Never | Less than once a month | Once or twice a month | Once or twice a week | Once a day | More often |
|---|---|---|---|---|---|---|
| 25. Have a stimulating exchange of ideas | _____ | _____ | _____ | _____ | _____ | _____ |
| 26. Laugh together | _____ | _____ | _____ | _____ | _____ | _____ |
| 27. Calmly discuss something | _____ | _____ | _____ | _____ | _____ | _____ |
| 28. Work together on a project | _____ | _____ | _____ | _____ | _____ | _____ |

These are some things about which couples sometimes agree and sometimes disagree. Indicate if either item below caused differences of opinions or were problems in your relationship during the past few weeks. (Check yes or no.)

| | Yes | No |
|---|---|---|
| 29. Being too tired for sex | _____ | _____ |
| 30. Not showing love | _____ | _____ |

31. The dots on the following line represent different degrees of happiness in your relationship. The middle point, "happy", represents the degree of happiness of most relationships. Please circle the dot which best describes the degree of happiness, all things considered, of your relationship.

| • | • | • | • | • | • | • |
|---|---|---|---|---|---|---|
| Extremely Unhappy | Fairly Unhappy | A Little Unhappy | Happy | Very Happy | Extremely Happy | Perfect |

32. Which of the following statements best describes how you feel about the future of your relationship?

_____ I want desperately for my relationship to succeed, and *would go to almost any length* to see that it does.

_____ I want very much for my relationship to succeed, and *will do all I can* to see that it does.

_____ I want very much for my relationship to succeed, and *will do my fair share* to see that it does.

_____ It would be nice if my relationship succeeded, but *I can't do much more than I'm doing* now to help it succeed.

_____ It would be nice if it succeeded, but *I refuse to do any more than I am doing* now to keep the relationship going.

_____ My relationship can never succeed, and *there is no more that I can do* to keep the relationship going.

# APPENDIX B

## Laboratory Blood Test Procedures

# APPENDIX B

## Laboratory Blood Test Procedures



### WHOLE BLOOD PROCEDURE FOR DIRECT IMMUNOPHENOTYPING OF LEUKOCYTE SUSPENSIONS

I. PRINCIPLE:

Peripheral blood leukocytes can be divided into several distinguishable subpopulations: T cells (thymic - dependent), which are involved in cell-mediated immune responses; B cells (Bursa-dependent), which are involved in humoral immunity; Myeloid cells, granulocytic series; and Monocytic cells. Several of these populations of leukocytes are not easily distinguishable by morphology or by histochemical staining alone, but can be identified by antigenic markers associated with the plasma membrane. Monoclonal antibodies have been developed that react with antigens expressed on mature and immature lymphocytes, myeloid cells, and monocytes. Likewise, antibodies exist which can distinguish subpopulations of some of these cells such as the helper/inducer and suppressor/cytotoxic subpopulations of T-cells.

Enumeration and characterization of leukocytes by their surface membrane markers are useful in: 1) analysis of an increased number of, or phenotypically abnormal cells from peripheral blood, bone marrow aspirates, or lymph node biopsies, 2) the study of patients with a suspected primary immunodeficiency, and 3) the study of acute and chronic diseases associated with altered immune function including acute infection, allergy, leukemia, and lymphoma.

The reagents for direct staining the cells are already conjugated with FITC or Phycoerythrin (PE). These antibodies incubated with whole blood, the cells washed, lysed, and fixed with paraformaldehyde. Specimens may also be plated on microscope slides and evaluated using a fluorescent microscope.

II. SPECIMEN REQUIREMENTS:

1. Venous blood is collected by venipuncture into ACD or sodium heparinized tubes. One normal control must be tested with each batch of patients. Bone marrow specimens should be heparinized. Blood collected with other anticoagulants and clotted blood are unacceptable.

2. Bone marrow must be washed once with "Incomplete HBSS" and filtered through 37 micron mesh if fibrin strands or clots are present. A white count on the can be performed on the Smith-Kline ESKA Lab cell counter and the WBC concentration adjusted to 10-20 X $10^6$/ml using Incomplete HBSS.

3. Validate the name and time of collection of specimen by checking the specimen and paper work that accompanies it, if any discrepencies, notify Immunology supervisor immediately. Specimens must be shipped and stored at room temperature until used. Specimens older than 24 hours must have a viability test performed (see lymphocyte preparation and viability sections) to determine quality of specimen. Viabilities less than 85% must be interpreted with extreme caution.

III. REAGENTS - SPECIAL SUPPLIES AND EQUIPMENT:

Whole Blood Lysing Reagent Kit - Coulter Immunology, Hialeah, FL #6603152. This includes Coulter Clone Immuno-Lyse Concentrate and Coulter Clone Fixative. Immuno-Lyse must be stored at 2-8°C. Fixative must be stored at room temperature.

1X PBS-pH 7.4 Sigma, St. Louis, MO. Cat 1000-3.

Monoclonal Antibodies - Becton-Dickinson Immunocytometry Systems, Mountain View CA. Coulter Immunology, Hialeah, FL.

10% Na Azide - 10gm of Na Azide dissolved in 100ml of nanopure water. Store 2-8°C.

Hank's balanced Salt Solution ($Ca^{++}$ and $Mg^{++}$ free) - "Incomplete" Hank's, GIBCO, 310-4175. Shelf life one year. Use at room temperature.

IEC Clinical Centrifuge - Damon/IEC, Needham Hgts, MA.

Beckman Centrifuge Model TJ-6.

12 x 75mm plastic test tubes - Falcon, Oxnard, CA. Obtain through Sparrow Stores.

Micropipettors - Medical Laboratory Automation, Mount Vernon, NY.

Smith-Kline ESKALAB (CHS-3T) Smith-Kline Diagnostics, Inc.

Vortex Mixer, Scientific Products, S8223-1.

FACSCAN, Becton-Dickinson, Mountain View, CA.

Monoclonal Antibodies

| CLUSTER DESIGNATION | BECTON DICKINSON | COULTER | DISTRIBUTION |
|---|---|---|---|
| CD2 | Leu 5b | T11 | T cells, NK cells |
| CD3 | Leu 4 | T3 | T cells |
| CD4 | Leu 3a,b | T4 | Helper/Inducer, Monocytes |
| CD8 | Leu 2a,b | T8 | Suppressor/Cytotoxic, NK |
| CD10 | CALLA | J5 | Pre-B cells |
| CD13 | Leu M7 | MY7 | Monocytes, PMN's |
| CD14 | Leu M3 | Mo2,MY4 | Monocytes |
| CD15 | Leu M1 | | PMN's, Reed-Sternberg |
| CD16 | Leu 11a,b | | NK cells, PMN's |
| CD19 | Leu 12 | B4 | B cells |

| CLUSTER DESIGNATION | BECTON DICKINSON | COULTER | DISTRIBUTION |
|---|---|---|---|
| CD20 | Leu 16 | B1 | Early B cells |
| CD33 | Leu M9 | MY9 | Monocytes, PMN's |
| CD34 | HPCA-1 | | Progenitor cells |
| CD45 | HLE | KC56 | All Leukocytes |
| CD56 | Leu 19 | NKH-1 | NK cells, T subset |

Detailed monoclonal antibody specificity information can be found by reviewing Becton-Dickinson Monoclonal Source Book and the Coulter Clone Monoclonal Antibody Book.

Monoclonal antibody expiration dates are provided by the manufacturer. Monoclonal antibodies can be used past expiration date if normal control values fall with the normal ranges.

## IV. QUALITY CONTROL:

Normal peripheral blood from a co-worker that has been tested previously and showed to be normal for T & B cell populations is used with each analysis. Each individual monoclonal antibody that is being tested on a patient should also be tested with a normal control. Values should fall within established ranges for the particular antibody. If the values fall outside the normal ranges, notify Immunology supervisor or director. The staining of the patient will have to be repeated in parallel with a new normal control.

## V. PROCEDURE:

Reagent Preparation:

1. PBS-Azide - Prepare working solution of phosphate buffered saline (1X). Add 0.1% Na Azide (5ml of 10% Na Azide per 500ml PBS). Store at 2-8°C. Good for 6 months.

2. Immuno-Lyse working solution: One ml of Immunolyse working solution is required for each test tube. Prepare working solution of ImmunoLyse by adding ImmunoLyse to PBS Azide at a 1:25 dilution (40ul of Immuno-Lyse per 1ml of PBS Azide). See following panels to determine number of tubes to run, and therefore the number of mls of working solution that will be necessary.

Staining Procedure:

1. Label 12 X 75mm plastic test tubes for the appropriate panel. Make one line tape labels listing the initials of the person whose specimen will be in that tube (first name first) and the antibodies to be tested in that tube (green first, then red). If there is more than one type of specimen on one person, e.g. peripheral blood and bone marrow, also indicate on the label which specimen is being tested in which tube. For example, when testing John Smith's bone marrow with the CD3-Green and CD19-Red antibodies, the label would read: JS 3/19 BM.

2. Prepare working solutions of the monoclonal antibodies. The appropriate dilution is one test volume of antibody (generally 20ul) into 200ul of PBS-Azide. Make these dilutions in the 12 X 75mm tube in which the test is to be performed.

3. Add 100ul of the venous blood sample or diluted washed bone marrow to each tube.

4. Vortex vigorously. Always vortex with tubes covered or in the hood.

5. Incubate at room temperature for 30 minutes.

6. Wash with 3-4 ml of cold PBS-Azide in IEC Clinical or Beckman TJ-6 Centrifuge. IEC speed #3 for 3 min, Beckman 1200 rpm for 4-5 minutes. Aspirate supernatant carefully, and vortex vigorously. Repeat for a total of 2 washes.

7. **While vortexing,** add 1 ml of Immuno-Lyse working solution to each tube, allow tubes to sit no less than 30 seconds, and no longer than 1 minute before proceeding to step #8. (Stay as close to 30 seconds as possible, especially on leukemic specimens.).

8. **While vortexing,** add 250 ul of fixative.

9. Wash cells 3 times with PBS-Azide as in step 6. Aspirate supernatant.

10. Add 200 ul of PBS-Azide and vortex.

11. Store tubes, capped, in the refrigerator until flow cytometry analysis is performed.

## VI. FACSCAN SET-UP:

Please refer to the FACSCAN Set-Up/Maintainence manual for setting up the instrument using Calibrite Beads in the Autocompfunction.

## VII. CALCULATIONS:

The FACSCAN flow cytometer has a software switch which can make a quadrant correction when the percentage of lymphocytes within the analysis gate is less than 100%. This switch is only used when performing CD4/CD8 ratio analysis and absolute lymphocyte counts.

The calculation performed is:

$$\frac{\text{raw percent}}{\text{CD45\% - CD14\%}}$$

T & B Direct



VIII. REPORTING RESULTS:

Normal Ranges:

| Mab | Peripheral Blood | Bone Marrow | Lymph Nodes |
|---|---|---|---|
| CD2-CD3 | 52-90% | 5-50% | 50-80% |
| CD4 | 28-63% | 5-30% | 20-60% |
| CD8 | 8-38% | 5-20% | 8-40% |
| CD4-CD8 | 1-5 | — | — |
| HLA-DR | 2-20% | 5-30% | 5-30% |
| CD19 | 2-20% | 2-20% | 2-20% |
| CD13-CD33 | 2-20% | 5-40% | ND |

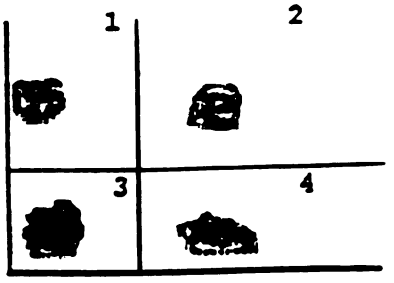
Using the antibody combinations CD3/CD4, CD3/CD8, and CD3/HLA-DR one can better interpret the data from the flow cytometer (See figures 1-3 below):

Figure 1

Use only quadrant 2 for CD4

Add quadrant 2 and 4 for CD3

CD3/CD4



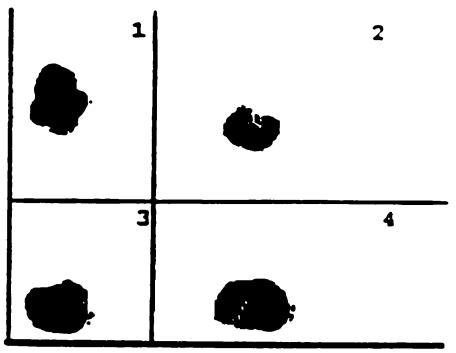

1=MONOCYTES
2=CD4+
3=B CELLS, ECT
4=CD8+

T & B Direct

Immunology Laboratory
Sparrow Hospital
Lansing, Michigan


Figure 2

CD3/CD8



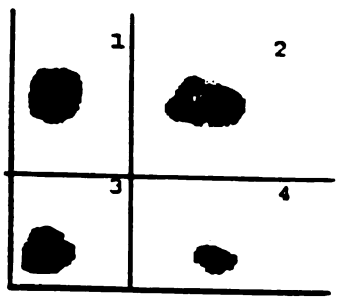

1=NK CELLS
2=CD8+
3=B CELLS, ETC
4=CD4+

Use only quadrant 2 for CD8

Add quadrant 2 and 4 for CD3

Figure 3

CD3/HLA-DR




1=B CELLS, ETC
2=ACTIVATED T CELLS
3=UNACTIVATED CELLS
4=UNACTIVATED T CELLS

Use quadrant 2 for activated T cells

Add quadrant 2 and 4 for total T cells

Add quadrant 1 and 2 for total activated cells

IX. REFERENCES:

Coulter Procedure for Indirect Immunofluorescence Cell Surface Staining with Coulter Clone Antibodies (Whole Blood Quick-Stain).

X. REVIEW AND UPDATE:

Prepared by: Faisal Rawas

| | | |
|---|---|---|
| Adopted | | |
| Reviewed | | |
| Reviewed | | |
| Reviewed | | |
| Revised | 9/15/92 | |

Supersedes:

I:\WP51\PRTCL\T&BDIREC

# APPENDIX C

## Immunoimagery Videotape Script

# APPENDIX C

## Immunoimagery Videotape Script
(16 minutes)

[Transcribed from: Bioimagery. (1993). The science of immuno-imagery. Irvine: Bioimagery.]

Science has shown that there is a direct link between the mind and the immune system. By using positive imaging techniques we can take an active role in strengthening our immune system to fight disease and promote good health and well-being. This science is called psychoneuroimmunology. The following information is an overview of the biological processes by which the mind, the nervous system and the immune system interact, and will provide you with excellent visuals for use in immunoimagery.

The wonder of life with its distinctive order and intelligence is as awesome as it is mysterious. Millions of years ago, perhaps by accident, perhaps by design, life itself was born from the smoldering embers left from violent explosions between dense gaseous clouds. All organisms, plants, and animals...all things living...can trace their ancestry back to the first single cell bacterial organism formed over three and one-half billion years ago. The genetic code of all living beings is composed of the same base elements. The same twenty amino acids build our proteins. The same combustion systems change food into energy. Scientists and philosophers alike have called this common denominator the blueprint of life. Through our creation nature has demonstrated a remarkable resiliency, a desire to survive and adapt to the changing environment. No life form on earth has demonstrated this resiliency, this adaptability, more than humankind.

The most complex manifestation of nature's creations is the human body. We are a living machine, more intricate and finely tuned than the most sophisticated computer. With an elaborate system of fluids, organs, chemicals, and electrical currents that define the human existence. The wisdom of the body, the blueprint of life, is truly represented in its ability to defend and heal itself. Over millions of years evolution of the human body has created a remarkable self-adjusting balance. This internal equilibrium can adapt itself to a temperature change of even a fraction of a degree, bathing the body in cooling perspiration when it becomes too warm. When too cold it begins to shiver, converting energy into heat.

The body consists of several primary systems such as the skeletal and the circulatory systems. Our immune system maintains our health, enabling us to fight a cold, ward off infection, or close a cut in our skin. The brain and nervous system is a perfectly coordinated mechanism that efficiently

regulates the body's life support systems. The human brain with infinite complexity is the most intricate structure known to man. Its potential power and many mysteries are still largely unknown and misunderstood. What uniquely separates humans from all other life is our knowledge of the self, the mind's own ability to be aware of itself. As awareness of the self has evolved, we've begun to understand the power of the mind and its influence over the body's health and well-being. Our natural environment contains many potentially harmful micro organisms that can enter the body and attack healthy cells. When this happens, we get sick and the immune system reacts to fight these harmful microbes and restore good health.

In a process not completely understood, the brain, through the immune system, helps the body recognize healthy cells while destroying and removing diseased cells. This internal intelligence, recognition of the self and non-self at the microscopic level, is one of life's greatest wonders. We've experienced many examples of our mind altering a physical change in our body in some way. For example, when watching a movie we often react as though the on-screen action is real. Dreams are another good example of the mind creating an image we often perceive as reality. The action doesn't happen to us, but the physical response does. A placebo can cause some people to respond to an illness in a positive physical way, even though there is no actual medicine involved. It is this type of stimulus-response that is the key to stimulating our immune system through the power of our own mind. This communications network between the mind and the body can literally be guided by a process called imagery. By mentally rehearsing or imagining our natural self healing processes at work, the immune system is stimulated. Researchers documented that the cells, tissues, organs, and muscles involved in the healing process become stronger or work more efficiently using positive imagery. The opposite is also true. Negative attitudes and stressful situations can weaken our immune system.

Imagery has been used successfully in medicine with impressive results. Imagery is regularly used by physicians treating cancer patients in conjunction with standard forms of medical therapy. To fully utilize immunoimagery it's important to have a basic understanding of the immune system. Let us take a guided tour through this process and actually see the body's immune system fighting disease.

The brain controls and integrates all body mechanisms through forty-three pairs of nerves leading to separated parts of the body. Different areas of the brain automatically control life support systems such as breathing and heartbeat as well as the intricate workings of the immune system. Neurons are the fundamental working units of the brain, spinal cord, and the nervous system. The brain alone has ten thousand million of them. The task of neurons is to generate, send, and receive signals through electrical and chemical impulses. Our thoughts are the results of these impulses. After the

brain translates the impulses received from different sensory neurons, it sends the proper response impulse back to the stimulated area. When the body needs food, for example, neurons send a message to the brain and stomach that translate into hunger. Through this intricate network, the brain communicates with the immune system to regulate our health and defend the body from harmful invaders.

Organs in our bodies such as our lungs, are made up of layers of tissue which in turn are made up of cells, the body's smallest living unit. During life's normal activity, healthy cells divide and grow as this time-lapsed photography shows. However, when harmful microbes enter and attack healthy cells, an immune response is triggered. The immune system is a miraculous mechanism of defense, attack, and repair consisting of a network of cells and organs that instantly respond to the presence of any disease-causing intruder. At all times the immune system surveys the identifying chemical markers of every molecule and cell in the body. Using these markers, the immune system can identify harmful cells and launch a full-scale attack to destroy them. Viruses, parasites, fungi and bacteria are common substances that trigger such an attack. These natural enemies often enter the body when we are undernourished, exhausted, or injured. Our skin, the body's first line of defense, keeps most of these harmful microbes out; however, they can enter through our eyes, nose, lungs, and throat.

The immune system is not contained within a single set of organs or vessels. The intricate networks of the lymphatic and the circulatory systems carry the cellular components and chemical messages of the immune system throughout every part of the body. Its army of defenders, white blood cells, can even pass single file through the body's smallest capillaries, to reach the battle area of infection. Over a trillion or more of white blood cells are present in nearly every tissue and organ. White blood cells originate in the bone marrow inside our long bones such as the legs and arms. Bone marrow produces millions of white blood cells daily, which are further programmed to patrol, attack, and destroy enemy invaders. They lead the body through the tiny vessels that feed them and sometimes travel to other glands to continue development such as the thymus or the spleen. The two main groups of white blood cells are called macrophages and lymphocytes. Other types of white blood cells amplify their effects. Macrophages destroy invader microbes and diseased or infected cells by eating them. Macrophages hunt their prey incessantly and can change their shape to pursue and devour a diseased cell. Here a macrophage uses its arm-like pseudopod to engulf and destroy a harmful invader. Macrophages are also called your body's trash collectors as they routinely consume pieces of dead tissue left over from the natural destruction of invading micro organisms. These materials are removed from the body to the lymphatic organs and vessels, an integral part of the immune system.

Lymphocytes are the white blood cells that distinguish between healthy cells and harmful invader cells. T-cells are lymphocytes that coordinate and communicate with the other types of cells in the immune system. Once T-cells become sensitized to the invader, they begin to multiply. Another subgroup, the killer T-cells, attack and destroy cancer cells and infected body cells before they have a chance to multiply. Another important lymphocyte, B-cells, produce a kind of chemical ammunition called antibodies. Antibodies are individually programmed by the brain's internal intelligence to seek out and destroy specific target microbes. Here a B-cell surrounded by harmful microbes uses its antibodies to destroy the enemy invaders. Together the macrophage and lymphocytes of the immune system win the battle against disease by destroying the enemy microbes. New cells divide and grow to replace damaged cells and good health is restored.

Now that we've seen our immune defenders under the microscope, let's recreate this process using animated characters. These lymphocytes have been color-coded for easy identification. The commander T-cell is orange, the killer T-cell is green and the B-cell is blue. Macrophages, the body's scavengers, are colored yellow. Harmful microbes enter the body and move into the bloodstream. The invader attacks and infects a normal cell telling it to produce more harmful agents. The immune defenses are triggered into action as macrophages first recognize that the intruders are not part of the body. Macrophages help T-cells identify the type of foreign invader using an identifying chemical handle on its surface. Once they have identified the enemy, T-cells become the commander, giving orders to the rest of the defense troops. The encoded T-cell then multiplies and creates specialized defense troops to fight the invader. Killer T-cells are signaled and search for infected cells to attack and destroy. Chemical messages are sent to alert other macrophages of the invasion. Other messages direct the macrophage to the battle area and help them attach to the infected cell. Finally, they eat and digest the invaders, making them harmless. If the immune defense troops become weak or are outnumbered, the commander T-cell sends for more powerful troops. Among these new recruits are the B-cells which produce and release antibodies, chemical bullets that destroy harmful microbes. Antibodies also stick to infected cells which help killer T-cells and macrophages quickly identify and destroy them. Helper cells spring into action by helping B-cells make more antibodies. When enough antibody has been made, suppressor cells direct B-cells to halt the production. Platoons of natural killers, NK cells, also search the area, killing infected cells and cancer cells. The immune defense troops--T-cells, B-cells, macrophages and others--finally destroy and remove the invader microbes. The long battle is ended as the immune system is again victorious. Gradually damaged cells are replaced by new cells and good health is restored.

# APPENDIX D

## Immunoimagery Audiotape Script

# APPENDIX D

## Immunoimagery Audiotape Script
## Music - Sounds of the Heart by Karunesh

My voice will guide you into a relaxed state. You will be invited to imagine with music your body's resourcefulness in fighting cancer. Each person does this a little differently, so trust your instincts and ignore any suggestions from me that don't seem to fit with you. We're ready to begin.

The first thing you'll want to do is just make yourself comfortable in your space. You might want to wiggle around a little or loosen anything that's tight. That's it...just whatever you need to do to feel comfortable. You can either make soft eyes or close your eyes...whatever you prefer. Take in a deep, deep breath through your mouth, hold onto it just a little, and let it go out through your mouth. You'll probably notice that there are some sounds in the room and just take note of them, and recognize what they are and let them fade gently into the background. You might want to take another deep breath, in up through the bottoms of your feet, up your legs, your torso, and out your mouth. That's it...just take another deep, deep breath, in and up, and out your mouth. You might even note a heaviness begin to set in your arms and legs as you breathe. And with each breath, you spread a calm, peaceful feeling. Your breath carries the tension out of your body as you exhale. So you can breathe in a peaceful, relaxed feeling. Let it seep the tension out of your body. Breathe in relaxed peacefulness...breathe out the tension. Just focus on breathing in the peacefulness...breathing out the tension. By now your feet may be feeling far away, as though your legs are ten feet long. Perhaps your hands are feeling far away at the end of your long, long arms. Breathe in a sense of calmness...breathe out tension. Breathe in...breathe out.

As the music begins I invite you to journey to a place deep inside your/your wife's body...to a place where all things are possible. You might have to become very small and find an opening in the body to squeeze through, but you'll be able to find a way in, and once you're in, you'll be able to move easily around the body and experience first hand those places where little miracles occur. The places where everything is possible. Take a moment to enjoy the panorama of color. What does it sound like in there? Does this inside space have a taste? What does it feel like to reach out and

touch these spaces as you move along? Do you have sense of rhythm or movement in this space?

As you journey inside your/your wife's body, you become aware of the production of millions of new white blood cells in the bone marrow. All up and down the bones, new white blood cells are made daily. It might not look anything like you imaged it would. What colors are the white blood cells? Do they make any sounds? If you reach out and touch them, what do they feel like? What if you tasted one? Do you have a sense of how the white blood cells move as they multiply?

There are different kinds of white blood cells and each kind is specialized to perform a specific job in fighting cancer. Take a moment to witness the white blood cells multiply purposefully, yet freely and easily as they dance in huge companies throughout your/your wife's blood stream...out of the blood stream and into every organ, tissue, and bone.

(pause)

It's unbelievable how fast they multiply and how far reaching their travels are. They are so clever...white blood cells can slip out of the blood vessels and into the bones, tissues, and organs. White blood cells are truly amazing. Just be with that process for a little while. Watch them multiply and multiply.

(pause)

Some of those specialized white blood cells are T-cells. Take a moment to notice your/your wife's T-cells. They're the ones that are trying to get your attention. Notice what color the T-cells are. If you tasted them, what would that be like? Do the T-cells have an odor? If you touch the T-cells what would they feel like? What would it be like to be a T-cell and move all around?

(pause)

Your body/your wife's body can produce many, many new T-cells. T-cells are smart. They have the ability to travel around the body and find cancer cells. T-cells are so smart, they do not attack self. They only attack foreign invaders like cancer. T-cells are playful while they multiply and they're playful while they find and destroy cancer. T-cells flourish when you are relaxed. T-cells are very good communicators. They organize the

immune system and they notify each other as well as other white blood cells when they find malignant cells in the body. T-cells also have incredibly long memories. They always remember what the foreign invaders are like. They immediately go to them and surround them. They can find very tiny, itty-bitty cancer cells. They call for help from other white blood cells and T-cells and together surround the foreign invaders and eat the cancer cells up, rendering them harmless. When T-cells are active and do their job, the body feels relief from pain. Take some time and watch the T-cells remember, go to, surround, eat, and digest cancer.

(pause)

They're capable of quite a process. Now let's take a moment to get a sense of what cancer cells are like. Some people believe that all of us have malignant cells in our body and that daily our white blood cells remove them before they can multiply. Cancer cells are confused and weak. They multiply like rabbits because they don't know any better. Take a moment and see if you can get a sense of what color cancer cells are? Where in your body/your wife's body would you look for cancer cells? Do the cancer cells emit a noise? Can you smell the cancer cells? Take a moment to scan your body/your wife's body looking for cancer cells. They're the ones that are stupid. They're foreign matter. Cancer cells have no purpose and cancer cells have no conscience. Just look around and see if you can spot them.

(pause)

Now take a moment to remember some of the resources that help you/your wife to fight off cancer cells...resources that are outside the body. There may have been medical treatment, kind thoughts from friends and family, prayers, love, people cheering you on...healing, hopeful images from others. Where are these supportive resources held within your body/your wife's body? Do they have a color? Do they move around? What might they sound like as they embrace your healing? Are there any smells associated with these resources? Just take some time to get a sense of the external resources to help you fight cancer, and what they feel like in your/your wife's body.

(pause)

We've spent some time getting a sense of your/your wife's internal cancer-fighting process, and the sense of either your or your wife's external resources. Now feel the strength and power of your wife's or your internal

cancer-fighting process working in harmony with your/her external resources. It can be a very, very powerful combination.

(pause)

Witness the T-cells multiply and enthusiastically move from where they are manufactured into your/your wife's bloodstream, tissues, and organs. The T-cells take command of the body's defenses and are cheered on by family, friends, and professionals. The T-cells skillfully identify and mark cancer cells for destruction. T-cells playfully, yet efficiently move to cancer cells and mark them with a chemical. After the diseased cells have been marked, armies of other T-cells are called upon to swarm to the marked cells, and when they get there, the T-cells have a lot of fun cooperating together throughout your/your wife's body. They engulf cancer cells, eat them, and digest them, making them harmless. Take some time to be with them as they accomplish important, healthful, playful work. Remember all the outside resources and people cheering those T-cells on, cheering the immune system, supporting all the work you're doing.

(pause)

They multiply. They move from where they're manufactured into the bloodstream, tissues, and organs and they're cheered on by a host of family, friends and professionals. They're skillful...playful...smart.

(pause)

You can manufacture however many you need to get the job done. Their memories guide them to the diseased cells. All the new ones sort of carry a collective memory from the others that preceded them, so they know exactly where to go in the body to find diseased cells.

(pause)

T-cells also have the knowledge of when there are enough of them. Then they stop producing and multiplying so many times when they know that they have enough to be effective and they slow down the multiplying process. They'll know that.

(pause)

You may wish to encourage your/your wife's T-cells to keep on multiplying as needed...to keep on searching...to continue marking cancer cells...and to help each other swarm, engulf and destroy the diseased cells. Perhaps you'll discover a way for the T-cells to continue their work in your/your wife's body after our journey has ended.

(pause)

Time is approaching for us to end this journey inside your/your wife's body. You might want to retrace some of your steps...pause along the way to re-experience some of your images and to remember what they felt like. And if you wish you can store these sensations in a special place in the body where you can easily find them again.

(pause)

It's time to end our journey and to gradually return to this room. As the music ends you may want to take a deep, deep breath in through the bottoms of your feet and out your mouth. And with another deep breath notice the sounds of the room creep back into your awareness. With each succeeding breath the sounds associated with this room might be coming closer and closer. And you might feel like you can feel your hands and feet again...become aware of what they feel like. You might even have the urge to wiggle your toes or shake out your hands. You can stretch a little. When you feel ready, you can open your eyes and have a look around.

# APPENDIX E

# IMAGE-CA

# APPENDIX E

NAME _____ DATE _____

## IMAGE-CA
## Interview Record and Scoring Sheet

*Jeanne Achterberg and G. Frank Lawlis*

**Biographical/Treatment Data**

Age _____ Sex _____ Marital Status _____

| Type of Treatment: | Date(s): |
|---|---|
| Surgery | On _____ |
| Radiation | from _____ to _____ |
| Chemotherapy/Immunotherapy | from _____ to _____ |
| Other | from _____ to _____ |
| Diagnosis: | Primary Site _____ |
| | Secondary Site(s) _____ |
| Current Disease Status: | _____ 1) no evidence of disease |
| | _____ 2) disease stabilized |
| | _____ 3) continued active disease |

IMAGE-CA Total Score (sten) _____

**Instructions**

This booklet is designed for recording and scoring information obtained from patient imagery drawings. After the patient has listened to the guided relaxation exercise, instruct him/her to draw, on a separate 8½ x 11-inch sheet of white paper, (1) the white blood cells, (2) any treatment being received, and (3) the cancer cells, all acting inside the body. When the drawings are completed, begin the interview using pages 3 and 4.

Following the interview, score the imagery/interview content according to the 14 Dimensions appearing on page 2. After scoring each of these scales, fold in page 4 so that **IMAGE CA - Summary Data** (page 5) is directly opposite page 2. Transcribe the 14 scores in column (2) of the table provided on page 5. Next, multiply each of the individual scores by the weights appearing in column (3) and enter the product in column (4). Add these components and enter the sum in the appropriate box marked "Weighted Sum." Then, in the appropriate sten conversion table, find the interval containing the obtained weighted sum and the corresponding sten score.

**INSTITUTE FOR PERSONALITY AND ABILITY TESTING, INC.**
**P. O. Box 188, Champaign, Illinois 61820**

## IMAGE-CA - Imagery Scoring Sheet



***Circle the number you feel best describes the imagery, based on the information you have available.***

### CANCER CELLS

| | 1 | 2 | 3 | 4 | 5 |
|---|---|---|---|---|---|
| 1. Vividness | very unclear | somewhat unclear | moderately vivid | quite vivid | maximumly vivid |
| 2. Activity | very active | quite active | moderately active | somewhat active | not at all active |
| 3. Strength | very strong | quite strong | moderately strong | moderately weak | quite weak |

### WHITE BLOOD CELLS (Immune System)

| | 1 | 2 | 3 | 4 | 5 |
|---|---|---|---|---|---|
| 4. Vividness | very unclear | somewhat unclear | moderately clear | quite vivid | maximumly vivid |
| 5. Activity | not active | some activity | moderately active | quite active | very active |
| 6. Numerosity (relative to Cancer Cells) | many more Ca than WBC | few more Ca than WBC | about the same WBC & Ca | few more WBC | many more WBC than Ca |
| 7. Size (relative to Cancer Cells) | Ca much larger than WBC | Ca somewhat larger | Ca and WBC about same | WBC little larger | WBC much larger than Ca |
| 8. Strength | quite weak | moderately weak | somewhat strong | quite strong | very strong |

### TREATMENT (Circle "3" if patient is not receiving treatment)

| | 1 | 2 | 3 | 4 | 5 |
|---|---|---|---|---|---|
| 9. Vividness | very unclear, confused | somewhat unclear | moderately clear | quite vivid | very vivid, clear |
| 10. Effectiveness | not at all effective | moderately ineffective | moderately effective | quite effective | highly effective |

### GENERAL

| | 1 | 2 | 3 | 4 | 5 |
|---|---|---|---|---|---|
| 11. How Symbolistic is visualization vs. How Concrete | very factual, concrete | moderately factual, concrete | mixed symbolistic/ factual | moderately symbolistic | highly symbolistic |
| 12. Overall Strength of Imagery vs. Weakness | very weak | quite weak | moderate | quite strong | very sound, strong |
| 13. Estimated regularity | not imaging | infrequent | moderately regular | high level of consistency | extremely frequent |
| 14. In your opinion, how is this type of imagery related to short-term disease management | continued active disease | some stabilization | considerable stabilization | eventual remission | rapid remission |

## IMAGE-CA - Interview Record



***Cancer***

1. Describe how your cancer cells look in your mind's eye.

2. Do you see the cancer cells moving around? If so, how? When?

3. How strong (tough) do you think your cells are? (Score on strength described or imputed to symbol chosen).

***White Blood Cells [WBC]***

4. Describe your WBC. (Score on vividness, clarity, continuity of description).

5. Do you see your WBC moving? If so, how? Where? (Score on activity or potential activity of symbol).

6. Do you see more cancer or more WBC? (Scoring on obvious response).

7. How big are your cancer cells? Your white blood cells?* (Score on relative difference with "5" indicating WBC significantly larger).

8. *How* do the WBC fight disease in your body? How well do you see the WBC as doing their job? (Score on strength or effectiveness).

***Treatment***

9. How does your treatment work to rid your body of disease? (Score on clarity and vividness).

10. How *well* does your treatment work to kill off disease? (Score on effectiveness described).

***Miscellaneous Response***

11. (Score on symbolism vs. concretion).

12. (Score on weak vs. strong).

13. How many times a day do you think about (or image) your cancer? (Record response).

14. (Score imagery on basis of how you would predict it related to disease from a clinical standpoint, i.e., "5" would indicate it predicted complete recovery, a "1" would predict a poor prognosis or death).

*Patient may be confused on difference between cancer *cell* and *tumor*. If so, some explanation or rewording may be required.

## IMAGE-CA - Summary Data *

| (1) Dimension | (2) Score | x | Weight | = | (4) Weighted Score |
|---|---|---|---|---|---|
| 1 | _____ | x | 1 | | _____ |
| 2 | _____ | x | 1 | | _____ |
| 3 | _____ | x | 3 | | _____ |
| 4 | _____ | x | 3 | | _____ |
| 5 | _____ | x | 4 | | _____ |
| 6 | _____ | x | 1 | | _____ |
| 7 | _____ | x | 3 | | _____ |
| 8 | _____ | x | 4 | | _____ |
| 9 | _____ | x | 2 | | _____ |
| 10 | _____ | x | 3 | | _____ |
| 11 | _____ | x | 1 | | _____ |
| 12 | _____ | x | 6 | | _____ |
| 13 | _____ | x | 1 | | _____ → ☐ Weighted Sum Without Dimension 14 (see Columns 5a and 6a below) |
| 14 | _____ | x | 16 | | _____ → ☐ Weighted Sum With Dimension 14 (see Columns 5b and 6b below) |

**Sten Conversion Table**
**For Use With Only 13 Dimensions**
(omitting clinical judgment, Dimension 14)

| (5a) Weighted Sum | (6a) Sten | |
|---|---|---|
| 165 or greater .... | 10 | Excellent imagery |
| 153-162 ..... | 9 | |
| 144-152 ..... | 8 | Good imagery |
| 134-143 ..... | 7 | |
| 125-133 ..... | 6 | Average imagery |
| 115-124 ..... | 5 | |
| 106-114 ..... | 4 | Less than average |
| 96-105 ..... | 3 | imagery |
| 87- 95 ..... | 2 | Poor imagery |
| less than 86 ..... | 1 | |

**Sten Conversion Table**
**For Use With All 14 Dimensions**

| (5b) Weighted Sum | (6b) Sten | |
|---|---|---|
| 247 or greater .... | 10 | Excellent imagery |
| 229-246 ..... | 9 | |
| 213-228 ..... | 8 | Good imagery |
| 195-212 ..... | 7 | |
| 178-194 ..... | 6 | Average imagery |
| 161-177 ..... | 5 | |
| 144-160 ..... | 4 | Less than average |
| 127-143 ..... | 3 | imagery |
| 110-126 ..... | 2 | Poor imagery |
| less than 109 .... | 1 | |

* *Note:* For individuals with relatively little experience using the IMAGE-CA drawing technique (less than 50 administrations), omission of Dimension 14 is advised. Therefore, the sten conversion table on the left of this page should be used. For a more detailed explanation of scoring procedures, see pp. 85-89, *Imagery of Cancer: An evaluation tool for the process of disease*, Achterberg & Lawlis, 1978.

# APPENDIX F

## Participants' Informed Consent Agreements

# APPENDIX F

## Participants' Informed Consent Agreements

### Husband's Informed Consent to Participate in Research Study

I, _____, the undersigned person, hereby knowingly and voluntarily consent to participate in learning guided imagery with my wife over a fifteen day period of time. I understand that the guided imagery included in this investigation is under careful study and that no benefits for its use can be promised, and the researcher in no way condones its use in place of standard medical treatment.

My participation in this study will occur in three two-hour educational or imagery sessions spaced one week apart. I understand that interviews about my specific images and their pictorial representations will be conducted and videotaped. In all resulting discussions or publications my identity will remain confidential; on all forms and in any specific descriptions I understand that I will be referred to by coded number. I consent to completing a standardized 32-item scale about my marriage. It has been explained that I will bear no cost for any of the sessions. I also understand that I may withdraw from this study at any time without penalty.

The above paragraphs have been explained to me and I have had an opportunity to ask any questions. I certify that I understand the contents of this form.

_____

Signature of Participant

_____

Signature of Witness

_____

Date

Wife's Informed Consent to Participate in the Research Study

I, _____, the undersigned person, hereby knowingly and voluntarily consent to learning guided imagery with my husband as well as to five blood draws over a fifteen day period of time (Day 1 -- one 12.5 cc draw; Days 8 & 15 -- two 12.5 cc draws). I understand that the blood will be drawn by a registered nurse, medical technologist, or licensed phlebotomist, and analyzed at the Immunology Laboratory at Sparrow Hospital. I understand that my physician has given medical approval for me to participate in these procedures. I realize that occasionally there is some discomfort associated with insertion of a needle, and that infrequently a bruise may appear at the site of the draw. I further understand that the guided imagery included in this investigation is under careful study and no benefits from its use can be promised, and the researcher in no way condones its use in place of standard medical treatment.

My participation in this study will occur in three two-hour educational or imagery sessions spaced one week apart. I understand that interviews about my specific images and their pictorial representations will be conducted and videotaped. In all resulting discussions or publications my identity will remain confidential; on all forms and in any specific descriptions I understand that I will be referred to by coded number. I consent to completing a standardized 32-item scale about my marriage. It has been explained that I will bear no cost for any of the sessions, blood draws, or blood test analyses. I also understand that I may withdraw from this study at any time without penalty.

The above paragraphs have been explained to me and I have had an opportunity to ask any questions. I certify that I understand the contents of this form.

_____

Signature of Participant

_____

Signature of Witness

_____

Date

# APPENDIX G

## Solicitation Letter to Potential Subjects

# APPENDIX G

## Solicitation Letter to Potential Subjects

September, 1994

Thank you for considering participation in this research study about guided imagery and breast cancer. During the past year you have probably undergone a series of exhausting treatments. I am interested in the role that guided imagery may have as an adjunctive therapy for cancer patients. As you read further you will see that I am asking for a lot from you and that you may not personally benefit from your participation in this study. However, it is my belief that the information obtained with your help will be useful to other women who will be diagnosed with breast cancer in the future.

In order to participate in this investigation you must be married and living with your husband, have had premenopausal breast cancer on one side only, and completed the course of medical treatment prescribed by your physician(s). Both husband and wife are asked to attend three one- to two-hour sessions, spaced one week apart and at the same time each week. You also must be willing to have five blood tests (one blood draw at the first session; and two blood draws one hour apart at both the second and third sessions). Your physician will need to verify that five blood draws within fifteen days are not contraindicated. (Husbands will not have blood tests.)

During the three sessions you and your husband will receive information about the body's defenses and will learn a guided imagery procedure. Following the imagery sessions you will be asked to make a drawing of your imagery. You will also participate in a tape-recorded interview about each of your specific images.

For the purpose of gathering background information, you would also have to agree to the release of specific medical information about your diagnosis and course of medical treatment. At each of the three sessions the wife will be asked to complete a brief questionnaire about recent illnesses, use of drugs, and life changes. Both husband and wife will also be asked to complete a 32-item scale about your marriage. Your confidentiality will be protected and all oral or written discussion of the study results will refer to participants only by an identification number.

There will be no cost to you for any of the blood tests or the informational and imagery sessions. Since this research is rather expensive, I do ask that you and your husband agree to participate only after careful thought and consideration. I will meet with you to show you the exact medical information requested, to outline the procedure of the three sessions, and to answer any questions that either of you may wish to ask.

I encourage you to contact me for more information if you believe you might be interested. There will be *no* pressure for you to participate for several reasons. First, you have been through a lot already and second, I only wish to solicit committed participants who will follow through with the three sessions which include five blood draws. Due to the expensive nature of this type of study, it will be important for participants to feel capable and willing to attend all three sessions at the agreed upon times. Following the completion of the study, you will have the opportunity to learn about the findings. I'm looking forward to hearing from you if you would like more information.

Cordially,

Ellen Leroi, M.A.
Department of Family and Child Ecology
Michigan State University
(517) 349-1027

# APPENDIX H

# UCRIHS

# APPENDIX H

**UNIVERSITY COMMITTEE ON RESEARCH INVOLVING HUMAN OR ANIMAL SUBJECTS**

The Graduate School
Michigan State University
118 Linton Hall

University and federal policies and procedures require that **all** research involving human or animal subjects receive prior approval from the appropriate review board. (See Faculty Handbook, p. 116-117 and the Academic Programs book, p. 60.)

**HUMAN SUBJECTS**

Does the thesis or dissertation you are submitting include research involving human subjects or materials of human origin? (Research involving human subjects includes surveys and telephone interviews used for research; materials of human origin include human blood and /or tissue.)

Yes ☒ No ☐

**If yes**, indicate UCRIHS log number for the approved protocol and attach the UCRIHS approval letter for that protocol to this form.

**UCRIHS Log Number:** 94-097

**ANIMAL SUBJECTS**

Does the thesis or dissertation you are proposing to submit include research involving vertebrate animals in any way?

Yes ☐ No ☒

**If yes**, and an animal use form was submitted to the All-University Committee on Animal Use and Care (AUCAUC), please list the approval number below and attach a copy of the AUCAUC approval letter to this form.

**AUF Number:**

**If yes**, but your project did not need an animal use form, provide a copy of the letter from the AUCAUC which cites the relevant exclusionary policy.

Ellen Leroi
Student's Name (print)

Donald Melcer, PhD
Major Professor's Name (print)

Ellen Leroi
Student's Signature

Donald Melcer
Major Professor's Signature

MICHIGAN STATE
UNIVERSITY

June 6, 1995

TO: Ellen Leroi
4431 Elmwood Drive
Okemos, Mi 48864

RE: IRB#: 94-097
TITLE: EFFICACY OF INDIVIDUAL AND CONJOINT GUIDED IMAGERY WITH BREAST CANCER PATIENTS
REVISION REQUESTED: N/A
CATEGORY: FULL REVIEW
APPROVAL DATE: 06/05/95

The University Committee on Research Involving Human Subjects'(UCRIHS) review of this project is complete. I am pleased to advise that the rights and welfare of the human subjects appear to be adequately protected and methods to obtain informed consent are appropriate. Therefore, the UCRIHS approved this project and any revisions listed above.

**RENEWAL:** UCRIHS approval is valid for one calendar year, beginning with the approval date shown above. Investigators planning to continue a project beyond one year must use the green renewal form (enclosed with the original approval letter or when a project is renewed) to seek updated certification. There is a maximum of four such expedited renewals possible. Investigators wishing to continue a project beyond that time need to submit it again for complete review.

**REVISIONS:** UCRIHS must review any changes in procedures involving human subjects, prior to initiation of the change. If this is done at the time of renewal, please use the green renewal form. To revise an approved protocol at any other time during the year, send your written request to the UCRIHS Chair, requesting revised approval and referencing the project's IRB # and title. Include in your request a description of the change and any revised instruments, consent forms or advertisements that are applicable.

**PROBLEMS/ CHANGES:** Should either of the following arise during the course of the work, investigators must notify UCRIHS promptly: (1) problems (unexpected side effects, complaints, etc.) involving human subjects or (2) changes in the research environment or new information indicating greater risk to the human subjects than existed when the protocol was previously reviewed and approved.

If we can be of any future help, please do not hesitate to contact us at (517)355-2180 or FAX (517)432-1171.

Sincerely,

David E. Wright, Ph.D.
UCRIHS Chair

DEW:kaa/lcp

cc: Donald Melcer

OFFICE OF
**RESEARCH AND GRADUATE STUDIES**

**University Committee on Research Involving Human Subjects (UCRIHS)**

Michigan State University
232 Administration Building
East Lansing, Michigan
48824-1046

517/355-2180
FAX: 517/432-1171

# APPENDIX I

## Medical Release and Information Forms

# APPENDIX I

## Medical Release and Information Forms

### Participant's Authorization for Disclosure of Medical Records

Patient Name _____

Birthdate _____

Information to be requested from:

Name _____

Address _____

_____

_____

Information to be released to:

Ellen Leroi, M.A.
Department of Family and Child Ecology
Unit 4 Paolucci Building
Michigan State University
East Lansing, MI 48824

I hereby consent to the disclosure of information contained in my medical record, including:

Date of breast cancer diagnosis: _____

Type of surgical treatment (please check)

_____ Lumpectomy date: _____

_____ Mastectomy date: _____

Number of lymph nodes removed: _____

_____ Breast reconstruction date: _____

Type of systemic treatment (please check)

_____ Chemotherapy
number of treatments: _____
treatment dates: _____
oncologist's name: _____
combination and amounts of chemical treatment: _____
_____
_____
_____
total length of time: _____

_____ Radiation
number of treatments: _____
treatment dates: _____
_____
radiology oncologist's name: _____
type and amount of radiation: _____
_____
_____
total length of time: _____

_____ Autologous Bone Marrow Transplant (ABMT)
date of procedure: _____
physician's name: _____

_____ Hormonal therapy
name of drug: _____
dose: _____
length of time used: _____
prescribing physician: _____

Pathology (please check)

_____ invasive

_____ non-invasive

type of cancer cells: _____

stage number: _____

size of tumor: _____

spread to lymph nodes? _____ how many? _____

presence of metastasis? _____ Please describe the extent: _____

_____

_____

_____ estrogen-receptor negative

_____ estrogen-receptor positive

Immune system function

_____ Please check if the patient shows evidence of the human immuno–deficiency virus (HIV), acquired immunodeficiency syndrome (AIDS) or AIDS related complex (ARC), information made confidential by Public Act 488 of 1988 as amended by Public Act 174 of the State of Michigan Health Code.

Purpose and Need for such Disclosure:

Participation in a Michigan State University doctoral dissertation research study.

I understand that I may revoke this authorization at any time and that this authorization pertains to fulfillment of the stated purpose of a research study. This authorization will automatically expire after six months from the date of signature.

I have read the above, and acknowledge that I am familiar with and fully understand the terms of this authorization.

Date: _____ Participant signature: _____

Date: _____ Witnessed by: _____

Participant Background and History

Name: _____

Address:_____

_____

Date of Birth:_____

Home Phone: _____ Work Phone: _____

Husband's Name:_____

His Work Phone:_____

His Date of Birth: _____

Month and Year of Breast Cancer Diagnosis: _____

Affected Side (left or right):_____

Please summarize in your own words what has happened (surgery, chemo-therapy, radiation, support groups, individual, couple or group therapy) from the time of breast cancer diagnosis until now.

Please briefly describe your knowledge and beliefs about guided imagery and any previous experiences that you may have had using this technique.

Wife's Reply:

Husband's reply:

Physician Approval Form

_____ has consulted with me about participating in a research study that requires five venipunctures within a two week period.

As the physician of Ms._____ , I see no contraindications in drawing 12.5 $cm^3$ of blood at each instance, according to the following schedule: Day 1, one venipuncture
Day 8, two venipunctures, about one hour apart
Day 15, two venipunctures, about one hour apart

_____
Physician Signature

_____
Physician Name (printed)

_____
Date

Participant Information Update

Session One

Name: _____ Today's Date: _____

1. Please list all medications (prescribed or over-the-counter) that you have taken during the past 30 days. [Name of medication, how much, how often, number of days taken]

2. Have you smoked marijuana or taken any street drugs during the past 30 days? _____ If yes, list all drugs, and how much and how often used.

3. Have you been ill during the past 30 days? _____ If yes, describe the conditions.

4. Have you visited a physician during the past 30 days? _____ If yes, for what purpose?

5. Have you received any medical treatment during the past 30 days? _____ If yes, describe the treatment.

6. Have there been any interpersonal or other changes during the past month? (e.g., ending or beginning a job; death of a family member, friend or pet; conflict with co-workers, family or friends; birth of a child; etc.) Please explain.

7. Please indicate below anything else that has happened during the past 30 days that you think might be important to share.

Participant Information Update

Session Two

Name: _____ Today's Date: _____

1. Please list all medications (prescribed or over-the-counter) that you have taken since our meeting last week. [Name of medication, how much, how often, number of days taken]

2. Have you smoked marijuana or taken any street drugs during the past week? _____ If yes, list all drugs, and how much and how often used.

3. Have you been ill during the past week? _____ If yes, describe the conditions.

4. Have you visited a physician during the past 7 days? _____ If yes, for what purpose?

5. Have you received any medical treatment since our last session? _____ If yes, describe the treatment.

6. Have there been any interpersonal or other changes during the past week? (e.g., ending or beginning a job; death of a family member, friend or pet; conflict with co-workers, family or friends; birth of a child; etc.) Please explain.

7. Please indicate below anything else that has happened during the past week that you think might be important to share.

Participant Information Update

Session Three

Name: _____ Today's Date: _____

1. Please list all medications (prescribed or over-the-counter) that you have taken since our meeting last week. [Name of medication, how much, how often, number of days taken]

2. Have you smoked marijuana or taken any street drugs during the past week? _____ If yes, list all drugs, and how much and how often used.

3. Have you been ill during the past week? _____ If yes, describe the conditions.

4. Have you visited a physician during the past 7 days? _____ If yes, for what purpose?

5. Have you received any medical treatment since our last session? _____ If yes, describe the treatment.

6. Have there been any interpersonal or other changes during the past week? (e.g., ending or beginning a job; death of a family member, friend or pet; conflict with co-workers, family or friends; birth of a child; etc.) Please explain.

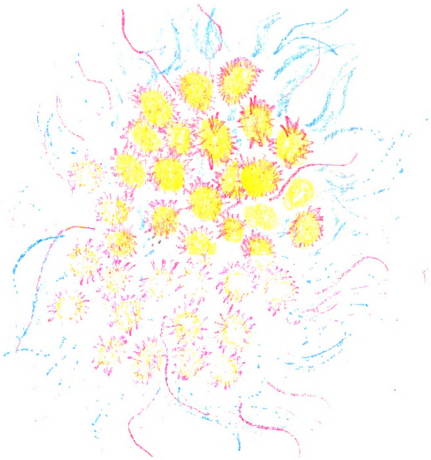
7. Please indicate below anything else that has happened during the past week that you think might be important to share.

# APPENDIX J

## Wives' IMAGE-CA Drawings

APPENDIX J
Wives' IMAGE-CA Drawings

1. Subject 1, image alone, 12-10-94

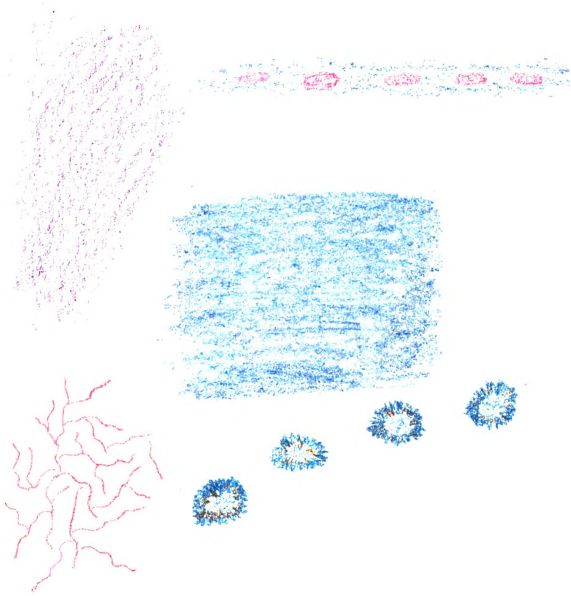


Subject 1, image together, 12-17-94


Subject 2, image alone, 12-18-94


Subject 2, image together, 12-11-94

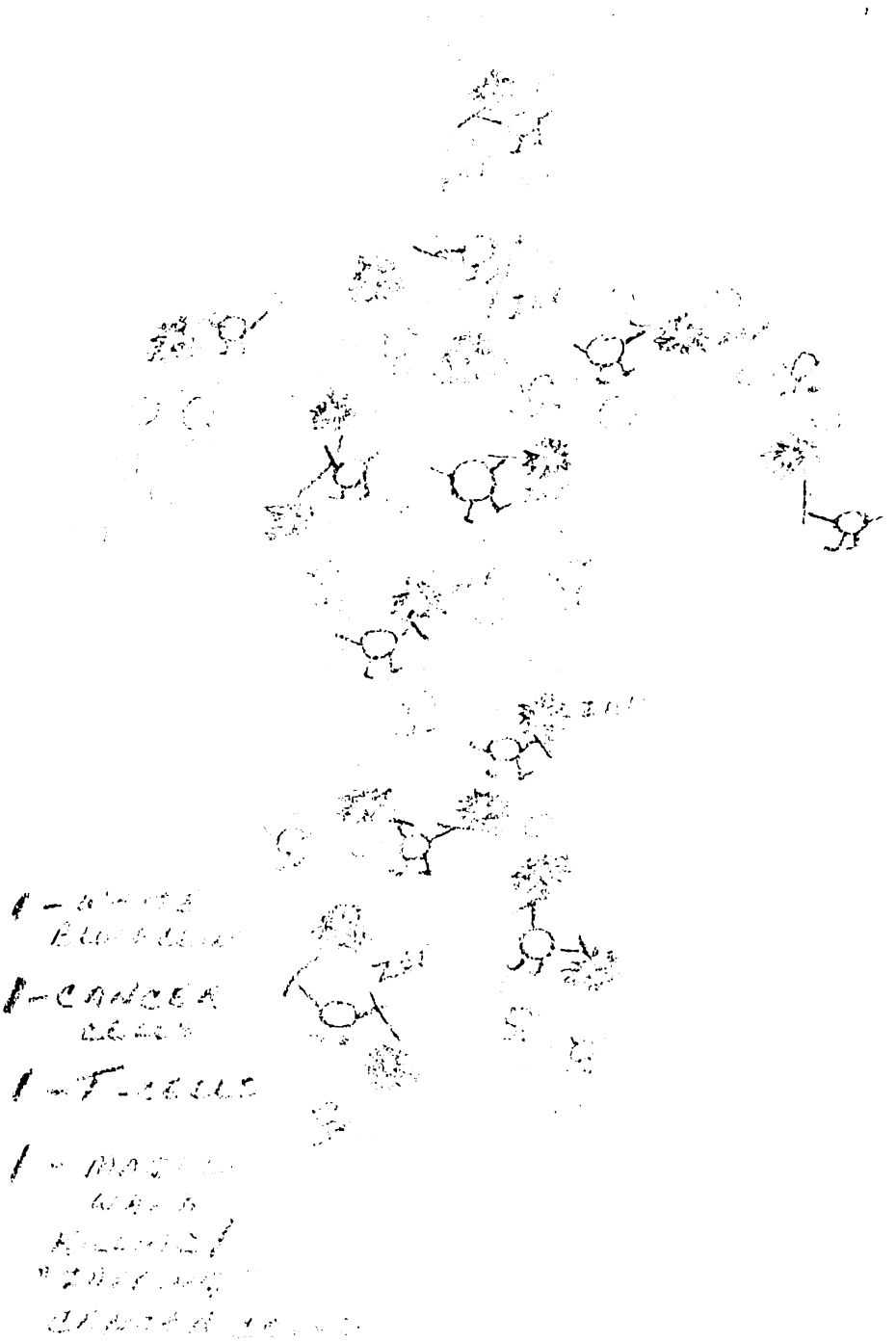
Subject 3, image alone, 2-5-95



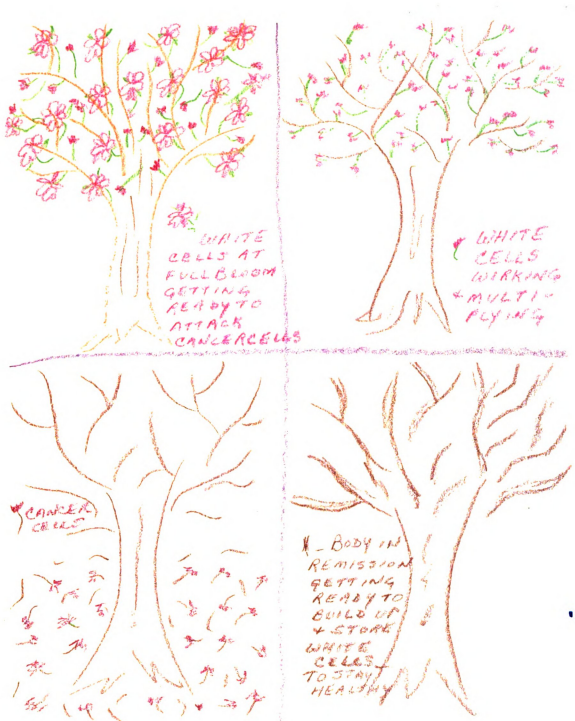
Subject 3, image together, 2-12-95


Subject 4, image alone, 5-21-95

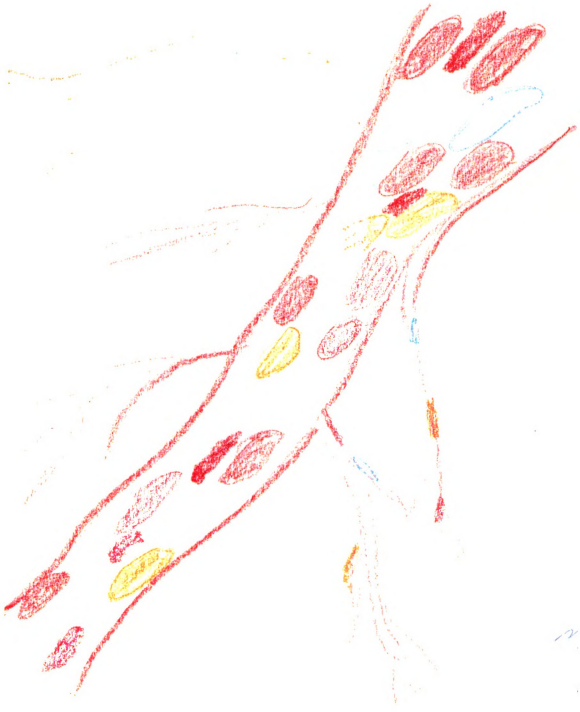

Subject 4, image together, 4-30-95



Subject 5, image alone, 8-20-95



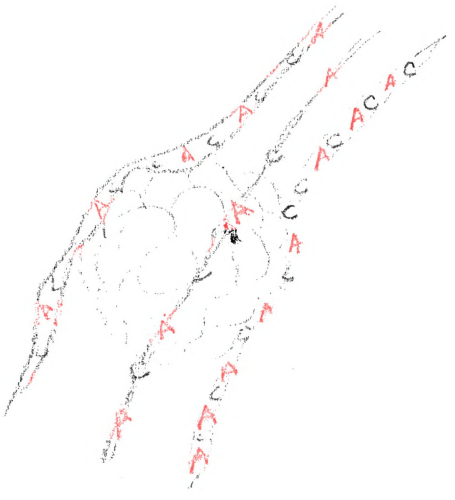

Subject 5, image together, 8-27-95



Subject 6, image alone, 1-21-96, drawing 1

Subject 6, image alone, 1-21-96, drawing 2

Subject 6, image alone, 1-21-96, drawing 3



Subject 6, image alone, 1-21-96, drawing 4

Subject 6, image alone, 1-21-96, drawing 5

Subject 6, image alone, 1-21-96, drawing 6


Subject 6, image together, 1-14-96, drawing 1

Subject 6, image together, 1-14-96, drawing 2

# APPENDIX K

## LogXact Output

APPENDIX K

LogXact Output

File: WBCALONE.DAT

Model: RESPONSE=ALONETOG+IMAGECA
Strat Var: <Unstratified>
Weight: <Unweighted>
#Obs: 12
#Groups: 12
Deviance : 9.8659 on 9 df

---

Tests ( 1 df) : <ALONETOG>

| Type of Test | Statistic | P-value | P-mid |
|---|---|---|---|
| Likelihood Ratio | 0.5110 | 0.4747 | NA |
| Wald | 0.4279 | 0.5130 | NA |
| Scores | 0.4520 | 0.5014 | NA |
| Exact (Conditional Scores) | 1.0000 | 1.0000 | 0.7500 |

---

Tests ( 1 df) : <IMAGECA>

| Type of Test | Statistic | P-value | P-mid |
|---|---|---|---|
| Likelihood Ratio | 6.0901 | 0.0136 | NA |
| Wald | 2.8053 | 0.0940 | NA |
| Scores | 4.8193 | 0.0281 | NA |
| Exact (Conditional Scores) | 4.0161 | 0.0400 | 0.0383 |

---

Tests ( 2 df) : <ALONETOG,IMAGECA>

| Type of Test | Statistic | P-value | P-mid |
|---|---|---|---|
| Likelihood Ratio | 6.4348 | 0.0401 | NA |
| Wald | 3.2662 | 0.1953 | NA |
| Scores | 5.1779 | 0.0751 | NA |
| Exact (Conditional Scores) | 4.7464 | 0.0682 | 0.0676 |

| VARIABLE | INFERENCE TYPE | <------- PARAMETER ESTIMATION --------> BETA | SE(BETA) | 95.0% (1-sided)BOUND | | P-VALUE ONE SIDED |
|---|---|---|---|---|---|---|
| ALONETOG | Asymptotic | -1.4360 | 2.1953 | -INF | 2.1749 | 0.2565 |
| | Exact | 0.0002 | <<MUE | -INF | 2.9452 | 0.5000 |
| IMAGECA | Asymptotic | -0.0682 | 0.0407 | -INF | -0.0012 | 0.0470 |
| | Exact | -0.0543 | NA | -INF | -0.0076 | 0.0200 |
| CONST | Asymptotic | 12.0648 | 7.6672 | -0.5467 | +INF | 0.0578 |
| | Exact | | | | | |

File: WBCALONE.DAT

Model: RESPONSE=ALONETOG+DAS
Strat Var: <Unstratified>
Weight: <Unweighted>
#Obs: 12
#Groups: 4
Deviance : 4.7271 on 1 df

---

Tests ( 1 df) : <ALONETOG>

| Type of Test | Statistic | P-value | P-mid |
|---|---|---|---|
| Likelihood Ratio | 0.4511 | 0.5018 | NA |
| Wald | 0.4306 | 0.5117 | NA |
| Scores | 0.4444 | 0.5050 | NA |
| Exact (Conditional Scores) | 0.3684 | 1.0000 | 0.8036 |

---

Tests ( 1 df) : <DAS>

| Type of Test | Statistic | P-value | P-mid |
|---|---|---|---|
| Likelihood Ratio | 2.9110 | 0.0880 | NA |
| Wald | 2.4312 | 0.1189 | NA |
| Scores | 2.8235 | 0.0929 | NA |
| Exact (Conditional Scores) | 2.3529 | 0.2400 | 0.1667 |

---

Tests ( 2 df) : <ALONETOG,DAS>

| Type of Test | Statistic | P-value | P-mid |
|---|---|---|---|
| Likelihood Ratio | 3.2557 | 0.1963 | NA |
| Wald | 2.5360 | 0.2814 | NA |
| Scores | 3.0857 | 0.2138 | NA |
| Exact (Conditional Scores) | 2.8286 | 0.4242 | 0.3965 |

| VARIABLE | INFERENCE TYPE | <------- PARAMETER ESTIMATION --------> BETA | SE(BETA) | 95.0% (1-sided)BOUND | | P-VALUE ONE SIDED |
|---|---|---|---|---|---|---|
| ALONETOG | Asymptotic | 0.9163 | 1.3964 | -1.3806 | +INF | 0.2559 |
| | Exact | 0.7631 | NA | -1.9274 | +INF | 0.5000 |
| DAS | Asymptotic | -2.3026 | 1.4767 | -INF | 0.1264 | 0.0595 |
| | Exact | -1.8409 | NA | -INF | 0.7027 | 0.1600 |
| CONST | Asymptotic | 0.6931 | 1.2935 | -1.4344 | +INF | 0.2960 |
| | Exact | | | | | |

File: WBCALONE.DAT

Model: RESPONSE=ALONETOG+DAS#
Strat Var: <Unstratified>
Weight: <Unweighted>
#Obs: 12
#Groups: 12
Deviance : 14.4652 on 9 df

---

Tests ( 1 df) : <ALONETOG>

| Type of Test | Statistic | P-value | P-mid |
|---|---|---|---|
| Likelihood Ratio | 0.3915 | 0.5315 | NA |
| Wald | 0.3812 | 0.5369 | NA |
| Scores | 0.3881 | 0.5333 | NA |
| Exact (Conditional Scores) | 0.3333 | 1.0000 | 0.8125 |

---

Tests ( 1 df) : <DAS#>

| Type of Test | Statistic | P-value | P-mid |
|---|---|---|---|
| Likelihood Ratio | 1.4908 | 0.2221 | NA |
| Wald | 1.3110 | 0.2522 | NA |
| Scores | 1.4351 | 0.2309 | NA |
| Exact (Conditional Scores) | 1.1959 | 0.3000 | 0.2950 |

---

Tests ( 2 df) : <ALONETOG,DAS#>

| Type of Test | Statistic | P-value | P-mid |
|---|---|---|---|
| Likelihood Ratio | 1.8355 | 0.3994 | NA |
| Wald | 1.5364 | 0.4639 | NA |
| Scores | 1.7370 | 0.4196 | NA |
| Exact (Conditional Scores) | 1.5922 | 0.4697 | 0.4678 |

| VARIABLE | INFERENCE TYPE | <------- PARAMETER ESTIMATION BETA | SE(BETA) | 95.0% (1-sided)BOUND | -------> | P-VALUE ONE SIDED |
|---|---|---|---|---|---|---|
| ALONETOG | Asymptotic | 0.7900 | 1.2795 | -1.3146 | +INF | 0.2685 |
| | Exact | 0.6932 | NA | -1.8549 | +INF | 0.5000 |
| DAS# | Asymptotic | -0.0516 | 0.0451 | -INF | 0.0225 | 0.1261 |
| | Exact | -0.0426 | NA | -INF | 0.0230 | 0.1567 |
| CONST | Asymptotic | 4.7783 | 4.7982 | -3.1140 | +INF | 0.1597 |
| | Exact | | | | | |

**File: LYMPHSAL.DAT**

Model: RESPONSE=ALONETOG+IMAGECA
Strat Var: <Unstratified>
Weight: <Unweighted>
#Obs: 12
#Groups: 12
Deviance : 7.7189 on 9 df

---

Tests ( 1 df) : <ALONETOG>

| Type of Test | Statistic | P-value | P-mid |
|---|---|---|---|
| Likelihood Ratio | 0.0054 | 0.9416 | NA |
| Wald | 0.0054 | 0.9413 | NA |
| Scores | 0.0054 | 0.9413 | NA |
| Exact (Conditional Scores) | DEGENERATE | ? | ? |

---

Tests ( 1 df) : <IMAGECA>

| Type of Test | Statistic | P-value | P-mid |
|---|---|---|---|
| Likelihood Ratio | 7.5574 | 0.0060 | NA |
| Wald | 3.5698 | 0.0588 | NA |
| Scores | 6.1836 | 0.0129 | NA |
| Exact (Conditional Scores) | 5.1530 | 0.0133 | 0.0111 |

---

Tests ( 2 df) : <ALONETOG,IMAGECA>

| Type of Test | Statistic | P-value | P-mid |
|---|---|---|---|
| Likelihood Ratio | 8.9166 | 0.0116 | NA |
| Wald | 3.9385 | 0.1396 | NA |
| Scores | 6.8298 | 0.0329 | NA |
| Exact (Conditional Scores) | 6.2607 | 0.0173 | 0.0168 |

| VARIABLE | INFERENCE TYPE | <------- PARAMETER ESTIMATION --------> BETA | SE(BETA) | 95.0% (1-sided)BOUND | | P-VALUE ONE SIDED |
|---|---|---|---|---|---|---|
| ALONETOG | Asymptotic | 0.1510 | 2.0519 | -3.2241 | +INF | 0.4707 |
| | Exact | Degenerate | NA | ? | ? | ? |
| IMAGECA | Asymptotic | -0.0775 | 0.0410 | -INF | -0.0100 | 0.0294 |
| | Exact | -0.0556 | NA | -INF | -0.0106 | 0.0133 |
| CONST | Asymptotic | 13.7900 | 7.7344 | 1.0681 | +INF | 0.0373 |
| | Exact | | | | | |

File: LYMPHSAL.DAT

Model: RESPONSE=ALONETOG+DAS
Strat Var: <Unstratified>
Weight: <Unweighted>
#Obs: 12
#Groups: 4
Deviance : 0.7338 on 1 df

---

Tests ( 1 df) : <ALONETOG>

| Type of Test | Statistic | P-value | P-mid |
|---|---|---|---|
| Likelihood Ratio | 1.3592 | 0.2437 | NA |
| Wald | 1.2812 | 0.2577 | NA |
| Scores | 1.3333 | 0.2482 | NA |
| Exact (Conditional Scores) | 1.1053 | 0.5810 | 0.4607 |

---

Tests ( 1 df) : <DAS>

| Type of Test | Statistic | P-value | P-mid |
|---|---|---|---|
| Likelihood Ratio | 0.0000 | 1.0000 | NA |
| Wald | 0.0000 | 1.0000 | NA |
| Scores | 0.0000 | 1.0000 | NA |
| Exact (Conditional Scores) | 0.0000 | 1.0000 | 0.7756 |

---

Tests ( 2 df) : <ALONETOG,DAS>

| Type of Test | Statistic | P-value | P-mid |
|---|---|---|---|
| Likelihood Ratio | 1.3592 | 0.5068 | NA |
| Wald | 1.2812 | 0.5270 | NA |
| Scores | 1.3333 | 0.5134 | NA |
| Exact (Conditional Scores) | 1.2222 | 0.8095 | 0.7549 |

| VARIABLE | INFERENCE TYPE | <------- PARAMETER ESTIMATION --------> BETA | SE(BETA) | 95.0% (1-sided)BOUND | | P-VALUE ONE SIDED |
|---|---|---|---|---|---|---|
| ALONETOG | Asymptotic | 1.3863 | 1.2247 | -0.6282 | +INF | 0.1288 |
| | Exact | 1.1247 | NA | -1.0956 | +INF | 0.2905 |
| DAS | Asymptotic | 0.0000 | 1.2990 | -2.1367 | +INF | 0.5000 |
| | Exact | 0.0000 | NA | -2.6498 | +INF | 0.7244 |
| CONST | Asymptotic | -0.6931 | 1.2247 | -INF | 1.3214 | 0.2857 |
| | Exact | | | | | |

File: LYMPHSAL.DAT

Model: RESPONSE=ALONETOG+DAS#
Strat Var: <Unstratified>
Weight: <Unweighted>
#Obs: 12
#Groups: 12
Deviance : 14.2804 on 9 df

---

Tests ( 1 df) : <ALONETOG>

| Type of Test | Statistic | P-value | P-mid |
|---|---|---|---|
| Likelihood Ratio | 1.4759 | 0.2244 | NA |
| Wald | 1.3527 | 0.2448 | NA |
| Scores | 1.4360 | 0.2308 | NA |
| Exact (Conditional Scores) | 2.0000 | 0.5000 | 0.3750 |

---

Tests ( 1 df) : <DAS#>

| Type of Test | Statistic | P-value | P-mid |
|---|---|---|---|
| Likelihood Ratio | 0.9959 | 0.3183 | NA |
| Wald | 0.9051 | 0.3414 | NA |
| Scores | 0.9651 | 0.3259 | NA |
| Exact (Conditional Scores) | 0.8043 | 0.3911 | 0.3867 |

---

Tests ( 2 df) : <ALONETOG,DAS#>

| Type of Test | Statistic | P-value | P-mid |
|---|---|---|---|
| Likelihood Ratio | 2.3551 | 0.3080 | NA |
| Wald | 1.8803 | 0.3906 | NA |
| Scores | 2.1912 | 0.3343 | NA |
| Exact (Conditional Scores) | 2.0086 | 0.3485 | 0.3474 |

---

| VARIABLE | INFERENCE TYPE | <------- PARAMETER ESTIMATION --------> BETA | SE(BETA) | 95.0% (1-sided)BOUND | | P-VALUE ONE SIDED |
|---|---|---|---|---|---|---|
| ALONETOG | Asymptotic | 1.5190 | 1.3061 | -0.6293 | +INF | 0.1224 |
| | Exact | 0.8813 | <<MUE | -1.2456 | +INF | 0.2500 |
| DAS# | Asymptotic | -0.0429 | 0.0451 | -INF | 0.0312 | 0.1707 |
| | Exact | -0.0355 | NA | -INF | 0.0293 | 0.1956 |
| CONST | Asymptotic | 3.8650 | 4.8156 | -4.0560 | +INF | 0.2111 |
| | Exact | | | | | |

**File: CD3ALONE.DAT**

Model: RESPONSE=ALONETOG+IMAGECA
Strat Var: <Unstratified>
Weight: <Unweighted>
#Obs: 12
#Groups: 12
Deviance : 9.7278 on 9 df

---

Tests ( 1 df) : <ALONETOG>

| Type of Test | Statistic | P-value | P-mid |
|---|---|---|---|
| Likelihood Ratio | 0.5422 | 0.4615 | NA |
| Wald | 0.4498 | 0.5024 | NA |
| Scores | 0.4768 | 0.4899 | NA |
| Exact (Conditional Scores) | DEGENERATE | ? | ? |

---

Tests ( 1 df) : <IMAGECA>

| Type of Test | Statistic | P-value | P-mid |
|---|---|---|---|
| Likelihood Ratio | 6.2282 | 0.0126 | NA |
| Wald | 2.8078 | 0.0938 | NA |
| Scores | 4.8987 | 0.0269 | NA |
| Exact (Conditional Scores) | 4.0822 | 0.0367 | 0.0350 |

---

Tests ( 2 df) : <ALONETOG,IMAGECA>

| Type of Test | Statistic | P-value | P-mid |
|---|---|---|---|
| Likelihood Ratio | 6.5729 | 0.0374 | NA |
| Wald | 3.2729 | 0.1947 | NA |
| Scores | 5.2575 | 0.0722 | NA |
| Exact (Conditional Scores) | 4.8194 | 0.0657 | 0.0650 |

| VARIABLE | INFERENCE TYPE | <------- PARAMETER ESTIMATION --------> BETA | SE(BETA) | 95.0% (1-sided)BOUND | | P-VALUE ONE SIDED |
|---|---|---|---|---|---|---|
| ALONETOG | Asymptotic | -1.4990 | 2.2351 | -INF | 2.1775 | 0.2512 |
| | Exact | Degenerate | NA | ? | ? | ? |
| IMAGECA | Asymptotic | -0.0699 | 0.0417 | -INF | -0.0013 | 0.0469 |
| | Exact | -0.0555 | NA | -INF | -0.0092 | 0.0167 |
| CONST | Asymptotic | 12.3815 | 7.8539 | -0.5370 | +INF | 0.0575 |
| | Exact | | | | | |

File: CD3ALONE.DAT

Model: RESPONSE=ALONETOG+DAS
Strat Var: <Unstratified>
Weight: <Unweighted>
#Obs: 12
#Groups: 4
Deviance : 0.1913 on 1 df

---

Tests ( 1 df) : <ALONETOG>

| Type of Test | Statistic | P-value | P-mid |
|---|---|---|---|
| Likelihood Ratio | 0.3498 | 0.5542 | NA |
| Wald | 0.3438 | 0.5576 | NA |
| Scores | 0.3478 | 0.5553 | NA |
| Exact (Conditional Scores) | 0.2877 | 1.0000 | 0.8155 |

---

Tests ( 1 df) : <DAS>

| Type of Test | Statistic | P-value | P-mid |
|---|---|---|---|
| Likelihood Ratio | 0.1756 | 0.6752 | NA |
| Wald | 0.1751 | 0.6757 | NA |
| Scores | 0.1765 | 0.6744 | NA |
| Exact (Conditional Scores) | 0.1471 | 1.0000 | 0.7933 |

---

Tests ( 2 df) : <ALONETOG,DAS>

| Type of Test | Statistic | P-value | P-mid |
|---|---|---|---|
| Likelihood Ratio | 0.5203 | 0.7709 | NA |
| Wald | 0.4988 | 0.7793 | NA |
| Scores | 0.5143 | 0.7733 | NA |
| Exact (Conditional Scores) | 0.4714 | 1.0000 | 0.9217 |

| VARIABLE | INFERENCE TYPE | <------- PARAMETER ESTIMATION --------> BETA | SE(BETA) | 95.0% (1-sided)BOUND | | P-VALUE ONE SIDED |
|---|---|---|---|---|---|---|
| ALONETOG | Asymptotic | 0.7037 | 1.2002 | -1.2704 | +INF | 0.2788 |
| | Exact | 0.5786 | NA | -1.6932 | +INF | 0.5000 |
| DAS | Asymptotic | -0.5264 | 1.2582 | -INF | 1.5431 | 0.3378 |
| | Exact | -0.4366 | NA | -INF | 2.1018 | 0.5733 |
| CONST | Asymptotic | -0.3519 | 1.1796 | -INF | 1.5884 | 0.3827 |
| | Exact | | | | | |

File: CD3ALONE.DAT

Model: RESPONSE=ALONETOG+DAS#
Strat Var: <Unstratified>
Weight: <Unweighted>
#Obs: 12
#Groups: 12
Deviance : 15.2374 on 9 df

---

Tests ( 1 df) : <ALONETOG>

| Type of Test | Statistic | P-value | P-mid |
|---|---|---|---|
| Likelihood Ratio | 0.3662 | 0.5451 | NA |
| Wald | 0.3586 | 0.5493 | NA |
| Scores | 0.3637 | 0.5465 | NA |
| Exact (Conditional Scores) | 0.3333 | 1.0000 | 0.8125 |

---

Tests ( 1 df) : <DAS#>

| Type of Test | Statistic | P-value | P-mid |
|---|---|---|---|
| Likelihood Ratio | 0.7185 | 0.3966 | NA |
| Wald | 0.6772 | 0.4106 | NA |
| Scores | 0.7065 | 0.4006 | NA |
| Exact (Conditional Scores) | 0.5888 | 0.4933 | 0.4883 |

---

Tests ( 2 df) : <ALONETOG,DAS#>

| Type of Test | Statistic | P-value | P-mid |
|---|---|---|---|
| Likelihood Ratio | 1.0632 | 0.5877 | NA |
| Wald | 0.9578 | 0.6195 | NA |
| Scores | 1.0292 | 0.5977 | NA |
| Exact (Conditional Scores) | 0.9434 | 0.6162 | 0.6143 |

| VARIABLE | INFERENCE TYPE | <------- PARAMETER ESTIMATION BETA | SE(BETA) | 95.0% (1-sided) BOUND | | P-VALUE ONE SIDED |
|---|---|---|---|---|---|---|
| ALONETOG | Asymptotic | 0.7375 | 1.2315 | -1.2882 | +INF | 0.2746 |
| | Exact | 0.6932 | NA | -1.8549 | +INF | 0.5000 |
| DAS# | Asymptotic | -0.0346 | 0.0421 | -INF | 0.0346 | 0.2053 |
| | Exact | -0.0287 | NA | -INF | 0.0343 | 0.2433 |
| CONST | Asymptotic | 2.9962 | 4.5238 | -4.4448 | +INF | 0.2539 |
| | Exact | | | | | |

**File: CD4ALONE.DAT**

Model: RESPONSE=ALONETOG+IMAGECA
Strat Var: <Unstratified>
Weight: <Unweighted>
#Obs: 12
#Groups: 12
Deviance : 7.7189 on 9 df

---

Tests ( 1 df) : <ALONETOG>

| Type of Test | Statistic | P-value | P-mid |
|---|---|---|---|
| Likelihood Ratio | 0.0054 | 0.9416 | NA |
| Wald | 0.0054 | 0.9413 | NA |
| Scores | 0.0054 | 0.9413 | NA |
| Exact (Conditional Scores) | DEGENERATE | ? | ? |

---

Tests ( 1 df) : <IMAGECA>

| Type of Test | Statistic | P-value | P-mid |
|---|---|---|---|
| Likelihood Ratio | 7.5574 | 0.0060 | NA |
| Wald | 3.5698 | 0.0588 | NA |
| Scores | 6.1836 | 0.0129 | NA |
| Exact (Conditional Scores) | 5.1530 | 0.0133 | 0.0111 |

---

Tests ( 2 df) : <ALONETOG,IMAGECA>

| Type of Test | Statistic | P-value | P-mid |
|---|---|---|---|
| Likelihood Ratio | 8.9166 | 0.0116 | NA |
| Wald | 3.9385 | 0.1396 | NA |
| Scores | 6.8298 | 0.0329 | NA |
| Exact (Conditional Scores) | 6.2607 | 0.0173 | 0.0168 |

---

| VARIABLE | INFERENCE TYPE | <------- PARAMETER ESTIMATION --------> BETA | SE(BETA) | 95.0% (1-sided)BOUND | | P-VALUE ONE SIDED |
|---|---|---|---|---|---|---|
| ALONETOG | Asymptotic | 0.1510 | 2.0519 | -3.2241 | +INF | 0.4707 |
| | Exact Degenerate | | NA | ? | ? | ? |
| IMAGECA | Asymptotic | -0.0775 | 0.0410 | -INF | -0.0100 | 0.0294 |
| | Exact | -0.0556 | NA | -INF | -0.0106 | 0.0133 |
| CONST | Asymptotic | 13.7900 | 7.7344 | 1.0681 | +INF | 0.0373 |
| | Exact | | | | | |

---

File: CD4ALONE.DAT

Model: RESPONSE=ALONETOG+DAS
Strat Var: <Unstratified>
Weight: <Unweighted>
#Obs: 12
#Groups: 4
Deviance : 0.7338 on 1 df

Tests ( 1 df) : <ALONETOG>

| Type of Test | Statistic | P-value | P-mid |
|---|---|---|---|
| Likelihood Ratio | 1.3592 | 0.2437 | NA |
| Wald | 1.2812 | 0.2577 | NA |
| Scores | 1.3333 | 0.2482 | NA |
| Exact (Conditional Scores) | 1.1053 | 0.5810 | 0.4607 |

Tests ( 1 df) : <DAS>

| Type of Test | Statistic | P-value | P-mid |
|---|---|---|---|
| Likelihood Ratio | 0.0000 | 1.0000 | NA |
| Wald | 0.0000 | 1.0000 | NA |
| Scores | 0.0000 | 1.0000 | NA |
| Exact (Conditional Scores) | 0.0000 | 1.0000 | 0.7756 |

Tests ( 2 df) : <ALONETOG,DAS>

| Type of Test | Statistic | P-value | P-mid |
|---|---|---|---|
| Likelihood Ratio | 1.3592 | 0.5068 | NA |
| Wald | 1.2812 | 0.5270 | NA |
| Scores | 1.3333 | 0.5134 | NA |
| Exact (Conditional Scores) | 1.2222 | 0.8095 | 0.7549 |

| VARIABLE | INFERENCE TYPE | <------- PARAMETER ESTIMATION -------> BETA | SE(BETA) | 95.0% (1-sided)BOUND | | P-VALUE ONE SIDED |
|---|---|---|---|---|---|---|
| ALONETOG | Asymptotic | 1.3863 | 1.2247 | -0.6282 | +INF | 0.1288 |
| | Exact | 1.1247 | NA | -1.0956 | +INF | 0.2905 |
| DAS | Asymptotic | 0.0000 | 1.2990 | -2.1367 | +INF | 0.5000 |
| | Exact | 0.0000 | NA | -2.6498 | +INF | 0.7244 |
| CONST | Asymptotic | -0.6931 | 1.2247 | -INF | 1.3214 | 0.2857 |
| | Exact | | | | | |

File: CD4ALONE.DAT

Model: RESPONSE=ALONETOG+DAS#
Strat Var: <Unstratified>
Weight: <Unweighted>
#Obs: 12
#Groups: 12
Deviance : 14.2804 on 9 df

---

Tests ( 1 df) : <ALONETOG>

| Type of Test | Statistic | P-value | P-mid |
|---|---|---|---|
| Likelihood Ratio | 1.4759 | 0.2244 | NA |
| Wald | 1.3527 | 0.2448 | NA |
| Scores | 1.4360 | 0.2308 | NA |
| Exact (Conditional Scores) | 2.0000 | 0.5000 | 0.3750 |

---

Tests ( 1 df) : <DAS#>

| Type of Test | Statistic | P-value | P-mid |
|---|---|---|---|
| Likelihood Ratio | 0.9959 | 0.3183 | NA |
| Wald | 0.9051 | 0.3414 | NA |
| Scores | 0.9651 | 0.3259 | NA |
| Exact (Conditional Scores) | 0.8043 | 0.3911 | 0.3867 |

---

Tests ( 2 df) : <ALONETOG,DAS#>

| Type of Test | Statistic | P-value | P-mid |
|---|---|---|---|
| Likelihood Ratio | 2.3551 | 0.3080 | NA |
| Wald | 1.8803 | 0.3906 | NA |
| Scores | 2.1912 | 0.3343 | NA |
| Exact (Conditional Scores) | 2.0086 | 0.3485 | 0.3474 |

---

| VARIABLE | INFERENCE TYPE | <------- PARAMETER ESTIMATION --------> BETA | SE(BETA) | 95.0% (1-sided)BOUND | | P-VALUE ONE SIDED |
|---|---|---|---|---|---|---|
| ALONETOG | Asymptotic | 1.5190 | 1.3061 | -0.6293 | +INF | 0.1224 |
| | Exact | 0.8813 | <<MUE | -1.2456 | +INF | 0.2500 |
| DAS# | Asymptotic | -0.0429 | 0.0451 | -INF | 0.0312 | 0.1707 |
| | Exact | -0.0355 | NA | -INF | 0.0293 | 0.1956 |
| CONST | Asymptotic | 3.8650 | 4.8156 | -4.0560 | +INF | 0.2111 |
| | Exact | | | | | |

---

**File: CD8ALONE.DAT**

Model: RESPONSE=ALONETOG+IMAGECA
Strat Var: <Unstratified>
Weight: <Unweighted>
#Obs: 12
#Groups: 12
Deviance : 4.6449 on 9 df

---

Tests ( 1 df) : <ALONETOG>

| Type of Test | Statistic | P-value | P-mid |
|---|---|---|---|
| Likelihood Ratio | 5.6034 | 0.0179 | NA |
| Wald | 1.1947 | 0.2744 | NA |
| Scores | 2.1342 | 0.1440 | NA |
| Exact (Conditional Scores) | DEGENERATE | ? | ? |

---

Tests ( 1 df) : <IMAGECA>

| Type of Test | Statistic | P-value | P-mid |
|---|---|---|---|
| Likelihood Ratio | 11.9907 | 0.0005 | NA |
| Wald | 1.2270 | 0.2680 | NA |
| Scores | 6.2652 | 0.0123 | NA |
| Exact (Conditional Scores) | 5.2210 | 0.0100 | 0.0088 |

---

Tests ( 2 df) : <ALONETOG,IMAGECA>

| Type of Test | Statistic | P-value | P-mid |
|---|---|---|---|
| Likelihood Ratio | 11.9907 | 0.0025 | NA |
| Wald | 1.2710 | 0.5297 | NA |
| Scores | 6.2652 | 0.0436 | NA |
| Exact (Conditional Scores) | 5.7431 | 0.0368 | 0.0363 |

| VARIABLE | INFERENCE TYPE | <------- PARAMETER ESTIMATION --------> BETA | SE(BETA) | 95.0% (1-sided)BOUND | | P-VALUE ONE SIDED |
|---|---|---|---|---|---|---|
| ALONETOG | Asymptotic | -50.3429 | 46.0584 | -INF | 25.4164 | 0.1372 |
| | Exact Degenerate | NA | ? | ? | | ? |
| IMAGECA | Asymptotic | -1.0179 | 0.9189 | -INF | 0.4936 | 0.1340 |
| | Exact | -0.5523 | NA | -INF | -0.0227 | 0.0050 |
| CONST | Asymptotic | 203.7922 | 184.5096 | -99.6990 | +INF | 0.1347 |
| | Exact | | | | | |

File: CD8ALONE.DAT

Model: RESPONSE=ALONETOG+DAS
Strat Var: <Unstratified>
Weight: <Unweighted>
#Obs: 12
#Groups: 4
Deviance : 0.0000 on 1 df

---

Tests ( 1 df) : <ALONETOG>

| Type of Test | Statistic | P-value | P-mid |
|---|---|---|---|
| Likelihood Ratio | 0.0000 | 1.0000 | NA |
| Wald | 0.0000 | 1.0000 | NA |
| Scores | 0.0000 | 1.0000 | NA |
| Exact (Conditional Scores) | 0.0000 | 1.0000 | 0.7905 |

---

Tests ( 1 df) : <DAS>

| Type of Test | Statistic | P-value | P-mid |
|---|---|---|---|
| Likelihood Ratio | 0.0000 | 1.0000 | NA |
| Wald | 0.0000 | 1.0000 | NA |
| Scores | 0.0000 | 1.0000 | NA |
| Exact (Conditional Scores) | 0.0000 | 1.0000 | 0.7800 |

---

Tests ( 2 df) : <ALONETOG,DAS>

| Type of Test | Statistic | P-value | P-mid |
|---|---|---|---|
| Likelihood Ratio | 0.0000 | 1.0000 | NA |
| Wald | 0.0000 | 1.0000 | NA |
| Scores | 0.0000 | 1.0000 | NA |
| Exact (Conditional Scores) | 0.0000 | 1.0000 | 0.9048 |

| VARIABLE | INFERENCE TYPE | <------- PARAMETER ESTIMATION --------> BETA | SE(BETA) | 95.0% (1-sided)BOUND | | P-VALUE ONE SIDED |
|---|---|---|---|---|---|---|
| ALONETOG | Asymptotic | 0.0000 | 1.1547 | -INF | 1.8993 | 0.5000 |
| | Exact | 0.0000 | NA | -INF | 2.2410 | 0.7095 |
| DAS | Asymptotic | 0.0000 | 1.2247 | -INF | 2.0145 | 0.5000 |
| | Exact | 0.0000 | NA | -INF | 2.4932 | 0.7200 |
| CONST | Asymptotic | 0.0000 | 1.1547 | -INF | 1.8993 | 0.5000 |
| | Exact | | | | | |

File: CD8ALONE.DAT

Model: RESPONSE=ALONETOG+DAS#
Strat Var: <Unstratified>
Weight: <Unweighted>
#Obs: 12
#Groups: 12
Deviance : 16.3412 on 9 df

---

Tests ( 1 df) : <ALONETOG>

| Type of Test | Statistic | P-value | P-mid |
|---|---|---|---|
| Likelihood Ratio | 0.0000 | 1.0000 | NA |
| Wald | 0.0000 | 1.0000 | NA |
| Scores | 0.0000 | 1.0000 | NA |
| Exact (Conditional Scores) | 0.0000 | 1.0000 | 0.7500 |

---

Tests ( 1 df) : <DAS#>

| Type of Test | Statistic | P-value | P-mid |
|---|---|---|---|
| Likelihood Ratio | 0.2943 | 0.5875 | NA |
| Wald | 0.2872 | 0.5920 | NA |
| Scores | 0.2919 | 0.5890 | NA |
| Exact (Conditional Scores) | 0.2433 | 0.6200 | 0.6175 |

---

Tests ( 2 df) : <ALONETOG,DAS#>

| Type of Test | Statistic | P-value | P-mid |
|---|---|---|---|
| Likelihood Ratio | 0.2943 | 0.8632 | NA |
| Wald | 0.2872 | 0.8662 | NA |
| Scores | 0.2919 | 0.8642 | NA |
| Exact (Conditional Scores) | 0.2676 | 0.8355 | 0.8344 |

| VARIABLE | INFERENCE TYPE | <------- PARAMETER ESTIMATION --------> BETA | SE(BETA) | 95.0% (1-sided)BOUND | | P-VALUE ONE SIDED |
|---|---|---|---|---|---|---|
| ALONETOG | Asymptotic | 0.0000 | 1.1690 | -1.9228 | +INF | 0.5000 |
| | Exact | 0.0000 | NA | -INF | 3.6508 | 0.7500 |
| DAS# | Asymptotic | -0.0212 | 0.0395 | -INF | 0.0439 | 0.2960 |
| | Exact | -0.0177 | NA | -INF | 0.0404 | 0.3100 |
| CONST | Asymptotic | 2.2859 | 4.3464 | -4.8633 | +INF | 0.2995 |
| | Exact | | | | | |

**File: SEGSALON.DAT**

Model: RESPONSE=ALONETOG+IMAGECA
Strat Var: <Unstratified>
Weight: <Unweighted>
#Obs: 12
#Groups: 12
Deviance : 12.3473 on 9 df

---

Tests ( 1 df) : <ALONETOG>

| Type of Test | Statistic | P-value | P-mid |
|---|---|---|---|
| Likelihood Ratio | 1.9076 | 0.1672 | NA |
| Wald | 1.7597 | 0.1847 | NA |
| Scores | 1.9885 | 0.1585 | NA |
| Exact (Conditional Scores) | 1.5000 | 0.6667 | 0.5000 |

---

Tests ( 1 df) : <IMAGECA>

| Type of Test | Statistic | P-value | P-mid |
|---|---|---|---|
| Likelihood Ratio | 0.6976 | 0.4036 | NA |
| Wald | 0.6592 | 0.4168 | NA |
| Scores | 0.7008 | 0.4025 | NA |
| Exact (Conditional Scores) | 0.5840 | 0.5333 | 0.5278 |

---

Tests ( 2 df) : <ALONETOG,IMAGECA>

| Type of Test | Statistic | P-value | P-mid |
|---|---|---|---|
| Likelihood Ratio | 3.9533 | 0.1385 | NA |
| Wald | 3.0221 | 0.2207 | NA |
| Scores | 3.6733 | 0.1594 | NA |
| Exact (Conditional Scores) | 3.3672 | 0.2020 | 0.2014 |

| VARIABLE | INFERENCE TYPE | <------- PARAMETER ESTIMATION --------> BETA | SE(BETA) | 95.0% (1-sided)BOUND | | P-VALUE ONE SIDED |
|---|---|---|---|---|---|---|
| ALONETOG | Asymptotic | 1.9477 | 1.4683 | -0.4674 | +INF | 0.0923 |
| | Exact | 0.4810 | <<MUE | -1.3585 | +INF | 0.3333 |
| IMAGECA | Asymptotic | -0.0166 | 0.0205 | -INF | 0.0171 | 0.2084 |
| | Exact | -0.0136 | NA | -INF | 0.0179 | 0.2556 |
| CONST | Asymptotic | 1.5051 | 3.9408 | -4.9770 | +INF | 0.3513 |
| | Exact | | | | | |

File: SEGSALON.DAT

Model: RESPONSE=ALONETOG+DAS
Strat Var: <Unstratified>
Weight: <Unweighted>
#Obs: 12
#Groups: 4
Deviance : 2.7692 on 1 df

---

Tests ( 1 df) : <ALONETOG>

| Type of Test | Statistic | P-value | P-mid |
|---|---|---|---|
| Likelihood Ratio | 3.3171 | 0.0686 | NA |
| Wald | 2.7212 | 0.0990 | NA |
| Scores | 3.1304 | 0.0768 | NA |
| Exact (Conditional Scores) | 2.5890 | 0.2619 | 0.2024 |

---

Tests ( 1 df) : <DAS>

| Type of Test | Statistic | P-value | P-mid |
|---|---|---|---|
| Likelihood Ratio | 0.2318 | 0.6302 | NA |
| Wald | 0.2267 | 0.6340 | NA |
| Scores | 0.2308 | 0.6310 | NA |
| Exact (Conditional Scores) | 0.1923 | 1.0000 | 0.7778 |

---

Tests ( 2 df) : <ALONETOG,DAS>

| Type of Test | Statistic | P-value | P-mid |
|---|---|---|---|
| Likelihood Ratio | 3.4876 | 0.1749 | NA |
| Wald | 2.7619 | 0.2513 | NA |
| Scores | 3.2571 | 0.1962 | NA |
| Exact (Conditional Scores) | 2.9857 | 0.3131 | 0.2879 |

---

| VARIABLE | INFERENCE TYPE | <------- PARAMETER ESTIMATION --------> BETA | SE(BETA) | 95.0% (1-sided)BOUND | | P-VALUE ONE SIDED |
|---|---|---|---|---|---|---|
| ALONETOG | Asymptotic | 2.3589 | 1.4300 | 0.0068 | +INF | 0.0495 |
| | Exact | 1.8615 | NA | -0.5332 | +INF | 0.1310 |
| DAS | Asymptotic | -0.7002 | 1.4708 | -INF | 1.7190 | 0.3170 |
| | Exact | -0.5824 | NA | -INF | 2.3390 | 0.5778 |
| CONST | Asymptotic | -1.1795 | 1.3789 | -INF | 1.0886 | 0.1962 |
| | Exact | | | | | |

File: SEGSALON.DAT

Model: RESPONSE=ALONETOG+DAS#
Strat Var: <Unstratified>
Weight: <Unweighted>
#Obs: 12
#Groups: 12
Deviance : 13.0283 on 9 df

---

Tests ( 1 df) : <ALONETOG>

| Type of Test | Statistic | P-value | P-mid |
|---|---|---|---|
| Likelihood Ratio | 3.2600 | 0.0710 | NA |
| Wald | 2.7195 | 0.0991 | NA |
| Scores | 3.0889 | 0.0788 | NA |
| Exact (Conditional Scores) | 1.9565 | 0.3500 | 0.2750 |

---

Tests ( 1 df) : <DAS#>

| Type of Test | Statistic | P-value | P-mid |
|---|---|---|---|
| Likelihood Ratio | 0.0166 | 0.8976 | NA |
| Wald | 0.0165 | 0.8977 | NA |
| Scores | 0.0166 | 0.8976 | NA |
| Exact (Conditional Scores) | 0.0138 | 0.9444 | 0.9111 |

---

Tests ( 2 df) : <ALONETOG,DAS#>

| Type of Test | Statistic | P-value | P-mid |
|---|---|---|---|
| Likelihood Ratio | 3.2723 | 0.1947 | NA |
| Wald | 2.7229 | 0.2563 | NA |
| Scores | 3.0980 | 0.2125 | NA |
| Exact (Conditional Scores) | 2.8398 | 0.3359 | 0.3321 |

| VARIABLE | INFERENCE TYPE | <------- PARAMETER ESTIMATION --------> BETA | SE(BETA) | 95.0% (1-sided)BOUND | | P-VALUE ONE SIDED |
|---|---|---|---|---|---|---|
| ALONETOG | Asymptotic | 2.3064 | 1.3986 | 0.0059 | +INF | 0.0496 |
| | Exact | 1.4929 | NA | -0.6350 | +INF | 0.1750 |
| DAS# | Asymptotic | 0.0059 | 0.0455 | -0.0690 | +INF | 0.4488 |
| | Exact | 0.0049 | NA | -0.0687 | +INF | 0.4889 |
| CONST | Asymptotic | -2.2431 | 5.0676 | -INF | 6.0923 | 0.3290 |
| | Exact | | | | | |

**File: WBCFIRST.DAT**

Model: RESPONSE=SEQUENCE+IMAGECA
Strat Var: <Unstratified>
Weight: <Unweighted>
#Obs: 12
#Groups: 12
Deviance : 9.3302 on 9 df

---

Tests ( 1 df) : <SEQUENCE>

| Type of Test | Statistic | P-value | P-mid |
|---|---|---|---|
| Likelihood Ratio | 1.0467 | 0.3063 | NA |
| Wald | 1.0056 | 0.3160 | NA |
| Scores | 1.1129 | 0.2915 | NA |
| Exact (Conditional Scores) | DEGENERATE | ? | ? |

---

Tests ( 1 df) : <IMAGECA>

| Type of Test | Statistic | P-value | P-mid |
|---|---|---|---|
| Likelihood Ratio | 3.7148 | 0.0539 | NA |
| Wald | 2.6134 | 0.1060 | NA |
| Scores | 3.3658 | 0.0666 | NA |
| Exact (Conditional Scores) | 2.8049 | 0.0778 | 0.0667 |

---

Tests ( 2 df) : <SEQUENCE,IMAGECA>

| Type of Test | Statistic | P-value | P-mid |
|---|---|---|---|
| Likelihood Ratio | 6.9705 | 0.0306 | NA |
| Wald | 3.5975 | 0.1655 | NA |
| Scores | 5.7888 | 0.0553 | NA |
| Exact (Conditional Scores) | 5.3064 | 0.0505 | 0.0492 |

---

| VARIABLE | INFERENCE TYPE | <------- PARAMETER ESTIMATION --------> BETA | SE(BETA) | 95.0% (1-sided)BOUND | | P-VALUE ONE SIDED |
|---|---|---|---|---|---|---|
| SEQUENCE | Asymptotic | 1.6705 | 1.6658 | -1.0695 | +INF | 0.1580 |
| | Exact Degenerate | NA | | ? | ? | ? |
| IMAGECA | Asymptotic | -0.0474 | 0.0293 | -INF | 0.0008 | 0.0530 |
| | Exact | -0.0358 | NA | -INF | -0.0011 | 0.0444 |
| CONST | Asymptotic | 7.0111 | 5.2408 | -1.6092 | +INF | 0.0905 |
| | Exact | | | | | |

---

File: WBCFIRST.DAT

Model: RESPONSE=SEQUENCE+DAS
Strat Var: <Unstratified>
Weight: <Unweighted>
#Obs: 12
#Groups: 4
Deviance : NA on NA df

---

Tests ( 1 df) : <SEQUENCE>

| Type of Test | Statistic | P-value | P-mid |
|---|---|---|---|
| Likelihood Ratio | ? | ? | NA |
| Wald | ? | ? | NA |
| Scores | 4.0000 | 0.0455 | NA |
| Exact (Conditional Scores) | 3.3158 | 0.2143 | 0.1607 |

---

Tests ( 1 df) : <DAS>

| Type of Test | Statistic | P-value | P-mid |
|---|---|---|---|
| Likelihood Ratio | ? | ? | NA |
| Wald | ? | ? | NA |
| Scores | 3.6923 | 0.0547 | NA |
| Exact (Conditional Scores) | 3.0769 | 0.1778 | 0.1111 |

---

Tests ( 2 df) : <SEQUENCE,DAS>

| Type of Test | Statistic | P-value | P-mid |
|---|---|---|---|
| Likelihood Ratio | ? | ? | NA |
| Wald | ? | ? | NA |
| Scores | 5.8286 | 0.0542 | NA |
| Exact (Conditional Scores) | 5.3429 | 0.0657 | 0.0581 |

| VARIABLE | INFERENCE TYPE | <------- PARAMETER ESTIMATION --------> BETA | SE(BETA) | 95.0% (1-sided)BOUND | | P-VALUE ONE SIDED |
|---|---|---|---|---|---|---|
| SEQUENCE | Asymptotic | ? | ? | ? | ? | ? |
| | Exact | 1.5099 | <<MUE | -0.4598 | +INF | 0.1071 |
| DAS | Asymptotic | ? | ? | ? | ? | ? |
| | Exact | -1.3992 | <<MUE | -INF | 0.6457 | 0.1333 |
| CONST | Asymptotic | ? | ? | ? | ? | ? |
| | Exact | | | | | |

File: WBCFIRST.DAT

Model: RESPONSE=SEQUENCE+DAS#
Strat Var: <Unstratified>
Weight: <Unweighted>
#Obs: 12
#Groups: 12
Deviance : 11.0138 on 9 df

---

Tests ( 1 df) : <SEQUENCE>

| Type of Test | Statistic | P-value | P-mid |
|---|---|---|---|
| Likelihood Ratio | 3.8428 | 0.0500 | NA |
| Wald | 2.7089 | 0.0998 | NA |
| Scores | 3.4932 | 0.0616 | NA |
| Exact (Conditional Scores) | 3.0000 | 0.2500 | 0.1875 |

---

Tests ( 1 df) : <DAS#>

| Type of Test | Statistic | P-value | P-mid |
|---|---|---|---|
| Likelihood Ratio | 2.0311 | 0.1541 | NA |
| Wald | 1.5780 | 0.2090 | NA |
| Scores | 1.8767 | 0.1707 | NA |
| Exact (Conditional Scores) | 1.5639 | 0.2333 | 0.2278 |

---

Tests ( 2 df) : <SEQUENCE,DAS#>

| Type of Test | Statistic | P-value | P-mid |
|---|---|---|---|
| Likelihood Ratio | 5.2868 | 0.0711 | NA |
| Wald | 2.9818 | 0.2252 | NA |
| Scores | 4.4798 | 0.1065 | NA |
| Exact (Conditional Scores) | 4.1065 | 0.1162 | 0.1155 |

| VARIABLE | INFERENCE TYPE | <------- PARAMETER ESTIMATION BETA | SE(BETA) | 95.0% (1-sided)BOUND | -------> | P-VALUE ONE SIDED |
|---|---|---|---|---|---|---|
| SEQUENCE | Asymptotic | 2.8724 | 1.7452 | 0.0018 | +INF | 0.0499 |
| | Exact | 1.3476 | <<MUE | -0.5396 | +INF | 0.1250 |
| DAS# | Asymptotic | -0.0735 | 0.0585 | -INF | 0.0227 | 0.1045 |
| | Exact | -0.0595 | NA | -INF | 0.0199 | 0.1222 |
| CONST | Asymptotic | 5.9421 | 5.8725 | -3.7173 | +INF | 0.1558 |
| | Exact | | | | | |

**File: LYMPHSFI.DAT**

Model: RESPONSE=SEQUENCE+IMAGECA
Strat Var: <Unstratified>
Weight: <Unweighted>
#Obs: 12
#Groups: 12
Deviance : 7.7133 on 9 df

---

Tests ( 1 df) : <SEQUENCE>

| Type of Test | Statistic | P-value | P-mid |
|---|---|---|---|
| Likelihood Ratio | 0.0110 | 0.9163 | NA |
| Wald | 0.0112 | 0.9158 | NA |
| Scores | 0.0112 | 0.9157 | NA |
| Exact (Conditional Scores) | DEGENERATE | ? | ? |

---

Tests ( 1 df) : <IMAGECA>

| Type of Test | Statistic | P-value | P-mid |
|---|---|---|---|
| Likelihood Ratio | 7.5631 | 0.0060 | NA |
| Wald | 3.7265 | 0.0536 | NA |
| Scores | 6.1631 | 0.0130 | NA |
| Exact (Conditional Scores) | 5.1359 | 0.0178 | 0.0156 |

---

Tests ( 2 df) : <SEQUENCE,IMAGECA>

| Type of Test | Statistic | P-value | P-mid |
|---|---|---|---|
| Likelihood Ratio | 8.9223 | 0.0115 | NA |
| Wald | 3.9291 | 0.1402 | NA |
| Scores | 6.8117 | 0.0332 | NA |
| Exact (Conditional Scores) | 6.2440 | 0.0216 | 0.0211 |

| VARIABLE | INFERENCE TYPE | <------- PARAMETER ESTIMATION --------> BETA | SE(BETA) | 95.0% (1-sided)BOUND | | P-VALUE ONE SIDED |
|---|---|---|---|---|---|---|
| SEQUENCE | Asymptotic | 0.2095 | 1.9824 | -3.0512 | +INF | 0.4579 |
| | Exact Degenerate | NA | | ? | ? | ? |
| IMAGECA | Asymptotic | -0.0775 | 0.0401 | -INF | -0.0115 | 0.0268 |
| | Exact | -0.0555 | NA | -INF | -0.0083 | 0.0178 |
| CONST | Asymptotic | 13.7646 | 7.5268 | 1.3841 | +INF | 0.0337 |
| | Exact | | | | | |

File: LYMPHSFI.DAT

Model: RESPONSE=SEQUENCE+DAS
Strat Var: <Unstratified>
Weight: <Unweighted>
#Obs: 12
#Groups: 4
Deviance : 0.7338 on 1 df

---

Tests ( 1 df) : <SEQUENCE>

| Type of Test | Statistic | P-value | P-mid |
|---|---|---|---|
| Likelihood Ratio | 1.3592 | 0.2437 | NA |
| Wald | 1.2812 | 0.2577 | NA |
| Scores | 1.3333 | 0.2482 | NA |
| Exact (Conditional Scores) | 1.1053 | 0.5810 | 0.4607 |

---

Tests ( 1 df) : <DAS>

| Type of Test | Statistic | P-value | P-mid |
|---|---|---|---|
| Likelihood Ratio | 0.0000 | 1.0000 | NA |
| Wald | 0.0000 | 1.0000 | NA |
| Scores | 0.0000 | 1.0000 | NA |
| Exact (Conditional Scores) | 0.0000 | 1.0000 | 0.7756 |

---

Tests ( 2 df) : <SEQUENCE,DAS>

| Type of Test | Statistic | P-value | P-mid |
|---|---|---|---|
| Likelihood Ratio | 1.3592 | 0.5068 | NA |
| Wald | 1.2812 | 0.5270 | NA |
| Scores | 1.3333 | 0.5134 | NA |
| Exact (Conditional Scores) | 1.2222 | 0.8095 | 0.7549 |

| VARIABLE | INFERENCE TYPE | <------- PARAMETER ESTIMATION --------> BETA | SE(BETA) | 95.0% (1-sided)BOUND | | P-VALUE ONE SIDED |
|---|---|---|---|---|---|---|
| SEQUENCE | Asymptotic | 1.3863 | 1.2247 | -0.6282 | +INF | 0.1288 |
| | Exact | 1.1247 | NA | -1.0956 | +INF | 0.2905 |
| DAS | Asymptotic | 0.0000 | 1.2990 | -2.1367 | +INF | 0.5000 |
| | Exact | 0.0000 | NA | -2.6498 | +INF | 0.7244 |
| CONST | Asymptotic | -0.6931 | 1.2247 | -INF | 1.3214 | 0.2857 |
| | Exact | | | | | |

File: LYMPHSFI.DAT

Model: RESPONSE=SEQUENCE+DAS#
Strat Var: <Unstratified>
Weight: <Unweighted>
#Obs: 12
#Groups: 12
Deviance : 14.2804 on 9 df

---

Tests ( 1 df) : <SEQUENCE>

| Type of Test | Statistic | P-value | P-mid |
|---|---|---|---|
| Likelihood Ratio | 1.4759 | 0.2244 | NA |
| Wald | 1.3527 | 0.2448 | NA |
| Scores | 1.4360 | 0.2308 | NA |
| Exact (Conditional Scores) | 2.0000 | 0.5000 | 0.3750 |

---

Tests ( 1 df) : <DAS#>

| Type of Test | Statistic | P-value | P-mid |
|---|---|---|---|
| Likelihood Ratio | 0.9959 | 0.3183 | NA |
| Wald | 0.9051 | 0.3414 | NA |
| Scores | 0.9651 | 0.3259 | NA |
| Exact (Conditional Scores) | 0.8043 | 0.3911 | 0.3867 |

---

Tests ( 2 df) : <SEQUENCE,DAS#>

| Type of Test | Statistic | P-value | P-mid |
|---|---|---|---|
| Likelihood Ratio | 2.3551 | 0.3080 | NA |
| Wald | 1.8803 | 0.3906 | NA |
| Scores | 2.1912 | 0.3343 | NA |
| Exact (Conditional Scores) | 2.0086 | 0.3485 | 0.3474 |

| VARIABLE | INFERENCE TYPE | <------- PARAMETER ESTIMATION --------> BETA | SE(BETA) | 95.0% (1-sided)BOUND | | P-VALUE ONE SIDED |
|---|---|---|---|---|---|---|
| SEQUENCE | Asymptotic | 1.5190 | 1.3061 | -0.6293 | +INF | 0.1224 |
| | Exact | 0.8813 | <<MUE | -1.2456 | +INF | 0.2500 |
| DAS# | Asymptotic | -0.0429 | 0.0451 | -INF | 0.0312 | 0.1707 |
| | Exact | -0.0355 | NA | -INF | 0.0293 | 0.1956 |
| CONST | Asymptotic | 3.8650 | 4.8156 | -4.0560 | +INF | 0.2111 |
| | Exact | | | | | |

**File: CD3FIRST.DAT**

Model: RESPONSE=SEQUENCE+IMAGECA
Strat Var: <Unstratified>
Weight: <Unweighted>
#Obs: 12
#Groups: 12
Deviance : 9.7956 on 9 df

---

Tests ( 1 df) : <SEQUENCE>

| Type of Test | Statistic | P-value | P-mid |
|---|---|---|---|
| Likelihood Ratio | 0.4743 | 0.4910 | NA |
| Wald | 0.4032 | 0.5255 | NA |
| Scores | 0.4267 | 0.5136 | NA |
| Exact (Conditional Scores) | DEGENERATE | ? | ? |

---

Tests ( 1 df) : <IMAGECA>

| Type of Test | Statistic | P-value | P-mid |
|---|---|---|---|
| Likelihood Ratio | 6.1603 | 0.0131 | NA |
| Wald | 2.8793 | 0.0897 | NA |
| Scores | 5.0599 | 0.0245 | NA |
| Exact (Conditional Scores) | 4.2166 | 0.0433 | 0.0417 |

---

Tests ( 2 df) : <SEQUENCE,IMAGECA>

| Type of Test | Statistic | P-value | P-mid |
|---|---|---|---|
| Likelihood Ratio | 6.5050 | 0.0387 | NA |
| Wald | 3.2340 | 0.1985 | NA |
| Scores | 5.3598 | 0.0686 | NA |
| Exact (Conditional Scores) | 4.9132 | 0.0682 | 0.0676 |

| VARIABLE | INFERENCE TYPE | <------- PARAMETER ESTIMATION --------> BETA | SE(BETA) | 95.0% (1-sided)BOUND | | P-VALUE ONE SIDED |
|---|---|---|---|---|---|---|
| SEQUENCE | Asymptotic | -1.3268 | 2.0896 | -INF | 2.1103 | 0.2627 |
| | Exact Degenerate | | NA | ? | ? | ? |
| IMAGECA | Asymptotic | -0.0667 | 0.0393 | -INF | -0.0020 | 0.0449 |
| | Exact | -0.0536 | NA | -INF | -0.0063 | 0.0233 |
| CONST | Asymptotic | 11.7758 | 7.3620 | -0.3336 | +INF | 0.0549 |
| | Exact | | | | | |

File: CD3FIRST.DAT

Model: RESPONSE=SEQUENCE+DAS
Strat Var: <Unstratified>
Weight: <Unweighted>
#Obs: 12
#Groups: 4
Deviance : 0.1913 on 1 df

---

Tests ( 1 df) : <SEQUENCE>

| Type of Test | Statistic | P-value | P-mid |
|---|---|---|---|
| Likelihood Ratio | 0.3498 | 0.5542 | NA |
| Wald | 0.3438 | 0.5576 | NA |
| Scores | 0.3478 | 0.5553 | NA |
| Exact (Conditional Scores) | 0.2877 | 1.0000 | 0.8155 |

---

Tests ( 1 df) : <DAS>

| Type of Test | Statistic | P-value | P-mid |
|---|---|---|---|
| Likelihood Ratio | 0.1756 | 0.6752 | NA |
| Wald | 0.1751 | 0.6757 | NA |
| Scores | 0.1765 | 0.6744 | NA |
| Exact (Conditional Scores) | 0.1471 | 1.0000 | 0.7933 |

---

Tests ( 2 df) : <SEQUENCE,DAS>

| Type of Test | Statistic | P-value | P-mid |
|---|---|---|---|
| Likelihood Ratio | 0.5203 | 0.7709 | NA |
| Wald | 0.4988 | 0.7793 | NA |
| Scores | 0.5143 | 0.7733 | NA |
| Exact (Conditional Scores) | 0.4714 | 1.0000 | 0.9217 |

| VARIABLE | INFERENCE TYPE | <------- PARAMETER ESTIMATION --------> BETA | SE(BETA) | 95.0% (1-sided)BOUND | | P-VALUE ONE SIDED |
|---|---|---|---|---|---|---|
| SEQUENCE | Asymptotic | 0.7037 | 1.2002 | 1.2704 | +INF | 0.2788 |
| | Exact | 0.5786 | NA | -1.6932 | +INF | 0.5000 |
| DAS | Asymptotic | -0.5264 | 1.2582 | -INF | 1.5431 | 0.3378 |
| | Exact | -0.4366 | NA | -INF | 2.1018 | 0.5733 |
| CONST | Asymptotic | -0.3519 | 1.1796 | -INF | 1.5884 | 0.3827 |
| | Exact | | | | | |

File: CD3FIRST.DAT

Model: RESPONSE=SEQUENCE+DAS#
Strat Var: <Unstratified>
Weight: <Unweighted>
#Obs: 12
#Groups: 12
Deviance : 15.2374 on 9 df

---

Tests ( 1 df) : <SEQUENCE>

| Type of Test | Statistic | P-value | P-mid |
|---|---|---|---|
| Likelihood Ratio | 0.3662 | 0.5451 | NA |
| Wald | 0.3586 | 0.5493 | NA |
| Scores | 0.3637 | 0.5465 | NA |
| Exact (Conditional Scores) | 0.3333 | 1.0000 | 0.8125 |

---

Tests ( 1 df) : <DAS#>

| Type of Test | Statistic | P-value | P-mid |
|---|---|---|---|
| Likelihood Ratio | 0.7185 | 0.3966 | NA |
| Wald | 0.6772 | 0.4106 | NA |
| Scores | 0.7065 | 0.4006 | NA |
| Exact (Conditional Scores) | 0.5888 | 0.4933 | 0.4883 |

---

Tests ( 2 df) : <SEQUENCE,DAS#>

| Type of Test | Statistic | P-value | P-mid |
|---|---|---|---|
| Likelihood Ratio | 1.0632 | 0.5877 | NA |
| Wald | 0.9578 | 0.6195 | NA |
| Scores | 1.0292 | 0.5977 | NA |
| Exact (Conditional Scores) | 0.9434 | 0.6162 | 0.6143 |

---

| VARIABLE | INFERENCE TYPE | <------- PARAMETER ESTIMATION --------> BETA | SE(BETA) | 95.0% (1-sided)BOUND | | P-VALUE ONE SIDED |
|---|---|---|---|---|---|---|
| SEQUENCE | Asymptotic | 0.7375 | 1.2315 | -1.2882 | +INF | 0.2746 |
| | Exact | 0.6932 | NA | -1.8549 | +INF | 0.5000 |
| DAS# | Asymptotic | -0.0346 | 0.0421 | -INF | 0.0346 | 0.2053 |
| | Exact | -0.0287 | NA | -INF | 0.0343 | 0.2433 |
| CONST | Asymptotic | 2.9962 | 4.5238 | -4.4448 | +INF | 0.2539 |
| | Exact | | | | | |

---

**File: CD4FIRST.DAT**

Model: RESPONSE=SEQUENCE+IMAGECA
Strat Var: <Unstratified>
Weight: <Unweighted>
#Obs: 12
#Groups: 12
Deviance : 7.7133 on 9 df

---

Tests ( 1 df) : <SEQUENCE>

| Type of Test | Statistic | P-value | P-mid |
|---|---|---|---|
| Likelihood Ratio | 0.0110 | 0.9163 | NA |
| Wald | 0.0112 | 0.9158 | NA |
| Scores | 0.0112 | 0.9157 | NA |
| Exact (Conditional Scores) | DEGENERATE | ? | ? |

---

Tests ( 1 df) : <IMAGECA>

| Type of Test | Statistic | P-value | P-mid |
|---|---|---|---|
| Likelihood Ratio | 7.5631 | 0.0060 | NA |
| Wald | 3.7265 | 0.0536 | NA |
| Scores | 6.1631 | 0.0130 | NA |
| Exact (Conditional Scores) | 5.1359 | 0.0178 | 0.0156 |

---

Tests ( 2 df) : <SEQUENCE,IMAGECA>

| Type of Test | Statistic | P-value | P-mid |
|---|---|---|---|
| Likelihood Ratio | 8.9223 | 0.0115 | NA |
| Wald | 3.9291 | 0.1402 | NA |
| Scores | 6.8117 | 0.0332 | NA |
| Exact (Conditional Scores) | 6.2440 | 0.0216 | 0.0211 |

| VARIABLE | INFERENCE TYPE | <------- PARAMETER ESTIMATION --------> BETA | SE(BETA) | 95.0% (1-sided)BOUND | | P-VALUE ONE SIDED |
|---|---|---|---|---|---|---|
| SEQUENCE | Asymptotic | 0.2095 | 1.9824 | -3.0512 | +INF | 0.4579 |
| | Exact Degenerate | NA | | ? | ? | ? |
| IMAGECA | Asymptotic | -0.0775 | 0.0401 | -INF | -0.0115 | 0.0268 |
| | Exact | -0.0555 | NA | -INF | -0.0083 | 0.0178 |
| CONST | Asymptotic | 13.7646 | 7.5268 | 1.3841 | +INF | 0.0337 |
| | Exact | | | | | |

File: CD4FIRST.DAT

Model: RESPONSE=SEQUENCE+DAS
Strat Var: <Unstratified>
Weight: <Unweighted>
#Obs: 12
#Groups: 4
Deviance : 0.7338 on 1 df

---

Tests ( 1 df) : <SEQUENCE>

| Type of Test | Statistic | P-value | P-mid |
|---|---|---|---|
| Likelihood Ratio | 1.3592 | 0.2437 | NA |
| Wald | 1.2812 | 0.2577 | NA |
| Scores | 1.3333 | 0.2482 | NA |
| Exact (Conditional Scores) | 1.1053 | 0.5810 | 0.4607 |

---

Tests ( 1 df) : <DAS>

| Type of Test | Statistic | P-value | P-mid |
|---|---|---|---|
| Likelihood Ratio | 0.0000 | 1.0000 | NA |
| Wald | 0.0000 | 1.0000 | NA |
| Scores | 0.0000 | 1.0000 | NA |
| Exact (Conditional Scores) | 0.0000 | 1.0000 | 0.7756 |

---

Tests ( 2 df) : <SEQUENCE,DAS>

| Type of Test | Statistic | P-value | P-mid |
|---|---|---|---|
| Likelihood Ratio | 1.3592 | 0.5068 | NA |
| Wald | 1.2812 | 0.5270 | NA |
| Scores | 1.3333 | 0.5134 | NA |
| Exact (Conditional Scores) | 1.2222 | 0.8095 | 0.7549 |

| VARIABLE | INFERENCE TYPE | <------- PARAMETER ESTIMATION --------> BETA | SE(BETA) | 95.0% (1-sided)BOUND | | P-VALUE ONE SIDED |
|---|---|---|---|---|---|---|
| SEQUENCE | Asymptotic | 1.3863 | 1.2247 | -0.6282 | +INF | 0.1288 |
| | Exact | 1.1247 | NA | -1.0956 | +INF | 0.2905 |
| DAS | Asymptotic | 0.0000 | 1.2990 | -2.1367 | +INF | 0.5000 |
| | Exact | 0.0000 | NA | -2.6498 | +INF | 0.7244 |
| CONST | Asymptotic | -0.6931 | 1.2247 | -INF | 1.3214 | 0.2857 |
| | Exact | | | | | |

File: CD4FIRST.DAT

Model: RESPONSE=SEQUENCE+DAS#
Strat Var: <Unstratified>
Weight: <Unweighted>
#Obs: 12
#Groups: 12
Deviance : 14.2804 on 9 df

---

Tests ( 1 df) : <SEQUENCE>

| Type of Test | Statistic | P-value | P-mid |
|---|---|---|---|
| Likelihood Ratio | 1.4759 | 0.2244 | NA |
| Wald | 1.3527 | 0.2448 | NA |
| Scores | 1.4360 | 0.2308 | NA |
| Exact (Conditional Scores) | 2.0000 | 0.5000 | 0.3750 |

---

Tests ( 1 df) : <DAS#>

| Type of Test | Statistic | P-value | P-mid |
|---|---|---|---|
| Likelihood Ratio | 0.9959 | 0.3183 | NA |
| Wald | 0.9051 | 0.3414 | NA |
| Scores | 0.9651 | 0.3259 | NA |
| Exact (Conditional Scores) | 0.8043 | 0.3911 | 0.3867 |

---

Tests ( 2 df) : <SEQUENCE,DAS#>

| Type of Test | Statistic | P-value | P-mid |
|---|---|---|---|
| Likelihood Ratio | 2.3551 | 0.3080 | NA |
| Wald | 1.8803 | 0.3906 | NA |
| Scores | 2.1912 | 0.3343 | NA |
| Exact (Conditional Scores) | 2.0086 | 0.3485 | 0.3474 |

---

| VARIABLE | INFERENCE TYPE | <------- PARAMETER ESTIMATION --------> BETA | SE(BETA) | 95.0% (1-sided)BOUND | | P-VALUE ONE SIDED |
|---|---|---|---|---|---|---|
| SEQUENCE | Asymptotic | 1.5190 | 1.3061 | -0.6293 | +INF | 0.1224 |
| | Exact | 0.8813 | <<MUE | -1.2456 | +INF | 0.2500 |
| DAS# | Asymptotic | -0.0429 | 0.0451 | -INF | 0.0312 | 0.1707 |
| | Exact | -0.0355 | NA | -INF | 0.0293 | 0.1956 |
| CONST | Asymptotic | 3.8650 | 4.8156 | -4.0560 | +INF | 0.2111 |
| | Exact | | | | | |

---

**File: CD8FIRST.DAT**

Model: RESPONSE=SEQUENCE+IMAGECA
Strat Var: <Unstratified>
Weight: <Unweighted>
#Obs: 12
#Groups: 12
Deviance : 6.8665 on 9 df

---

Tests ( 1 df) : <SEQUENCE>

| Type of Test | Statistic | P-value | P-mid |
|---|---|---|---|
| Likelihood Ratio | 3.3818 | 0.0659 | NA |
| Wald | 0.5568 | 0.4556 | NA |
| Scores | 2.0183 | 0.1554 | NA |
| Exact (Conditional Scores) | DEGENERATE | ? | ? |

---

Tests ( 1 df) : <IMAGECA>

| Type of Test | Statistic | P-value | P-mid |
|---|---|---|---|
| Likelihood Ratio | 9.7691 | 0.0018 | NA |
| Wald | 0.6837 | 0.4083 | NA |
| Scores | 6.5726 | 0.0104 | NA |
| Exact (Conditional Scores) | 5.4772 | 0.0200 | 0.0188 |

---

Tests ( 2 df) : <SEQUENCE,IMAGECA>

| Type of Test | Statistic | P-value | P-mid |
|---|---|---|---|
| Likelihood Ratio | 9.7691 | 0.0076 | NA |
| Wald | 0.9017 | 0.6371 | NA |
| Scores | 6.5726 | 0.0374 | NA |
| Exact (Conditional Scores) | 6.0249 | 0.0390 | 0.0384 |

---

| VARIABLE | INFERENCE TYPE | <------- PARAMETER ESTIMATION --------> BETA | SE(BETA) | 95.0% (1-sided)BOUND | | P-VALUE ONE SIDED |
|---|---|---|---|---|---|---|
| SEQUENCE | Asymptotic | -9.0868 | 12.1780 | -INF | 10.9442 | 0.2278 |
| | Exact Degenerate | NA | | ? | ? | ? |
| IMAGECA | Asymptotic | -0.2062 | 0.2493 | -INF | 0.2040 | 0.2042 |
| | Exact | -0.1661 | NA | -INF | -0.0136 | 0.0100 |
| CONST | Asymptotic | 40.4315 | 49.6634 | -41.2576 | +INF | 0.2078 |
| | Exact | | | | | |

---

File: CD8FIRST.DAT

Model: RESPONSE=SEQUENCE+DAS
Strat Var: <Unstratified>
Weight: <Unweighted>
#Obs: 12
#Groups: 4
Deviance : 0.0000 on 1 df

---

Tests ( 1 df) : <SEQUENCE>

| Type of Test | Statistic | P-value | P-mid |
|---|---|---|---|
| Likelihood Ratio | 0.0000 | 1.0000 | NA |
| Wald | 0.0000 | 1.0000 | NA |
| Scores | 0.0000 | 1.0000 | NA |
| Exact (Conditional Scores) | 0.0000 | 1.0000 | 0.7905 |

---

Tests ( 1 df) : <DAS>

| Type of Test | Statistic | P-value | P-mid |
|---|---|---|---|
| Likelihood Ratio | 0.0000 | 1.0000 | NA |
| Wald | 0.0000 | 1.0000 | NA |
| Scores | 0.0000 | 1.0000 | NA |
| Exact (Conditional Scores) | 0.0000 | 1.0000 | 0.7800 |

---

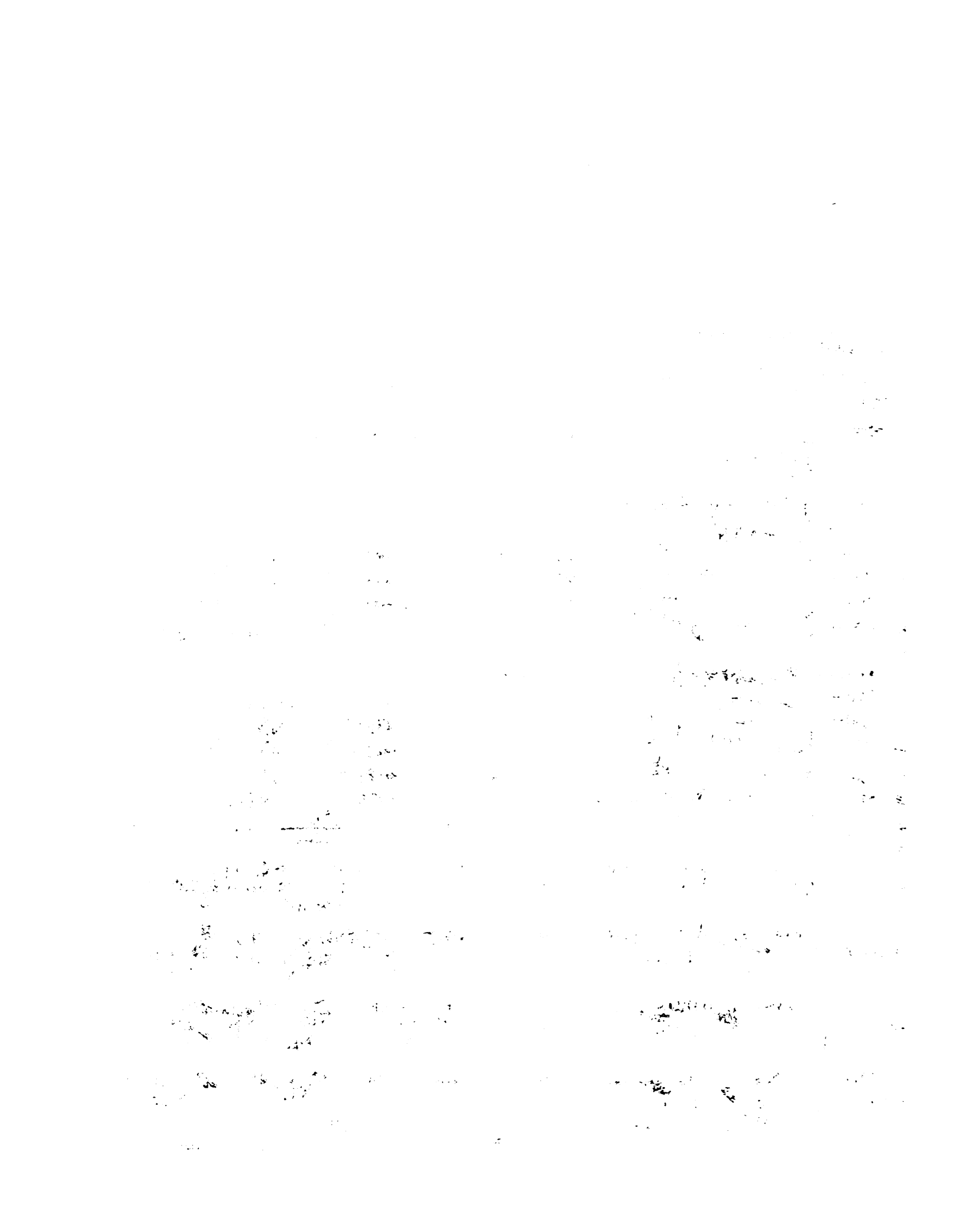
Tests ( 2 df) : <SEQUENCE,DAS>

| Type of Test | Statistic | P-value | P-mid |
|---|---|---|---|
| Likelihood Ratio | 0.0000 | 1.0000 | NA |
| Wald | 0.0000 | 1.0000 | NA |
| Scores | 0.0000 | 1.0000 | NA |
| Exact (Conditional Scores) | 0.0000 | 1.0000 | 0.9048 |

---

| VARIABLE | INFERENCE TYPE | <------- PARAMETER ESTIMATION --------> BETA | SE(BETA) | 95.0% (1-sided)BOUND | | P-VALUE ONE SIDED |
|---|---|---|---|---|---|---|
| SEQUENCE | Asymptotic | 0.0000 | 1.1547 | -INF | 1.8993 | 0.5000 |
| | Exact | 0.0000 | NA | -INF | 2.2410 | 0.7095 |
| DAS | Asymptotic | 0.0000 | 1.2247 | -INF | 2.0145 | 0.5000 |
| | Exact | 0.0000 | NA | -INF | 2.4932 | 0.7200 |
| CONST | Asymptotic | 0.0000 | 1.1547 | -INF | 1.8993 | 0.5000 |
| | Exact | | | | | |

---



File: CD8FIRST.DAT

Model: RESPONSE=SEQUENCE+DAS#
Strat Var: <Unstratified>
Weight: <Unweighted>
#Obs: 12
#Groups: 12
Deviance : 16.3412 on 9 df

---

Tests ( 1 df) : <SEQUENCE>

| Type of Test | Statistic | P-value | P-mid |
|---|---|---|---|
| Likelihood Ratio | 0.0000 | 1.0000 | NA |
| Wald | 0.0000 | 1.0000 | NA |
| Scores | 0.0000 | 1.0000 | NA |
| Exact (Conditional Scores) | 0.0000 | 1.0000 | 0.7500 |

---

Tests ( 1 df) : <DAS#>

| Type of Test | Statistic | P-value | P-mid |
|---|---|---|---|
| Likelihood Ratio | 0.2943 | 0.5875 | NA |
| Wald | 0.2872 | 0.5920 | NA |
| Scores | 0.2919 | 0.5890 | NA |
| Exact (Conditional Scores) | 0.2433 | 0.6200 | 0.6175 |

---

Tests ( 2 df) : <SEQUENCE,DAS#>

| Type of Test | Statistic | P-value | P-mid |
|---|---|---|---|
| Likelihood Ratio | 0.2943 | 0.8632 | NA |
| Wald | 0.2872 | 0.8662 | NA |
| Scores | 0.2919 | 0.8642 | NA |
| Exact (Conditional Scores) | 0.2676 | 0.8355 | 0.8344 |

| VARIABLE | INFERENCE TYPE | <------- PARAMETER ESTIMATION ------> BETA | SE(BETA) | 95.0% (1-sided)BOUND | | P-VALUE ONE SIDED |
|---|---|---|---|---|---|---|
| SEQUENCE | Asymptotic | 0.0000 | 1.1690 | -1.9228 | +INF | 0.5000 |
| | Exact | 0.0000 | NA | -INF | 3.6508 | 0.7500 |
| DAS# | Asymptotic | -0.0212 | 0.0395 | -INF | 0.0439 | 0.2960 |
| | Exact | -0.0177 | NA | -INF | 0.0404 | 0.3100 |
| CONST | Asymptotic | 2.2859 | 4.3464 | -4.8633 | +INF | 0.2995 |
| | Exact | | | | | |

**File: SEGSFIRS.DAT**

Model: RESPONSE=SEQUENCE+IMAGECA
Strat Var: <Unstratified>
Weight: <Unweighted>
#Obs: 12
#Groups: 12
Deviance : 12.4432 on 9 df

---

Tests ( 1 df) : <SEQUENCE>

| Type of Test | Statistic | P-value | P-mid |
|---|---|---|---|
| Likelihood Ratio | 1.8117 | 0.1783 | NA |
| Wald | 1.6652 | 0.1969 | NA |
| Scores | 1.8573 | 0.1729 | NA |
| Exact (Conditional Scores) | 0.5000 | 1.0000 | 0.6667 |

---

Tests ( 1 df) : <IMAGECA>

| Type of Test | Statistic | P-value | P-mid |
|---|---|---|---|
| Likelihood Ratio | 0.6017 | 0.4379 | NA |
| Wald | 0.5722 | 0.4494 | NA |
| Scores | 0.5975 | 0.4395 | NA |
| Exact (Conditional Scores) | 0.4980 | 0.5222 | 0.5111 |

---

Tests ( 2 df) : <SEQUENCE,IMAGECA>

| Type of Test | Statistic | P-value | P-mid |
|---|---|---|---|
| Likelihood Ratio | 3.8574 | 0.1453 | NA |
| Wald | 2.9294 | 0.2311 | NA |
| Scores | 3.5656 | 0.1682 | NA |
| Exact (Conditional Scores) | 3.2685 | 0.2083 | 0.2071 |

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| VARIABLE | INFERENCE TYPE | <------- PARAMETER ESTIMATION --------> BETA | SE(BETA) | 95.0% (1-sided)BOUND | | P-VALUE ONE SIDED |
|---|---|---|---|---|---|---|
| SEQUENCE | Asymptotic | 1.9077 | 1.4783 | -0.5240 | +INF | 0.0985 |
| | Exact | -0.6929 | <<MUE | -3.6378 | +INF | 0.6667 |
| IMAGECA | Asymptotic | -0.0163 | 0.0215 | -INF | 0.0191 | 0.2247 |
| | Exact | -0.0134 | NA | -INF | 0.0175 | 0.2333 |
| CONST | Asymptotic | 1.4513 | 4.1241 | -5.3323 | +INF | 0.3625 |
| | Exact | | | | | |

File: SEGSFIRS.DAT

Model: RESPONSE=SEQUENCE+DAS
Strat Var: <Unstratified>
Weight: <Unweighted>
#Obs: 12
#Groups: 4
Deviance : 2.7692 on 1 df

---

Tests ( 1 df) : <SEQUENCE>

| Type of Test | Statistic | P-value | P-mid |
|---|---|---|---|
| Likelihood Ratio | 3.3171 | 0.0686 | NA |
| Wald | 2.7212 | 0.0990 | NA |
| Scores | 3.1304 | 0.0768 | NA |
| Exact (Conditional Scores) | 2.5890 | 0.2619 | 0.2024 |

---

Tests ( 1 df) : <DAS>

| Type of Test | Statistic | P-value | P-mid |
|---|---|---|---|
| Likelihood Ratio | 0.2318 | 0.6302 | NA |
| Wald | 0.2267 | 0.6340 | NA |
| Scores | 0.2308 | 0.6310 | NA |
| Exact (Conditional Scores) | 0.1923 | 1.0000 | 0.7778 |

---

Tests ( 2 df) : <SEQUENCE,DAS>

| Type of Test | Statistic | P-value | P-mid |
|---|---|---|---|
| Likelihood Ratio | 3.4876 | 0.1749 | NA |
| Wald | 2.7619 | 0.2513 | NA |
| Scores | 3.2571 | 0.1962 | NA |
| Exact (Conditional Scores) | 2.9857 | 0.3131 | 0.2879 |

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| VARIABLE | INFERENCE TYPE | <------- PARAMETER ESTIMATION --------> BETA | SE(BETA) | 95.0% (1-sided)BOUND | | P-VALUE ONE SIDED |
|---|---|---|---|---|---|---|
| SEQUENCE | Asymptotic | 2.3589 | 1.4300 | 0.0068 | +INF | 0.0495 |
| | Exact | 1.8615 | NA | -0.5332 | +INF | 0.1310 |
| DAS | Asymptotic | -0.7002 | 1.4708 | -INF | 1.7190 | 0.3170 |
| | Exact | -0.5824 | NA | -INF | 2.3390 | 0.5778 |
| CONST | Asymptotic | -1.1795 | 1.3789 | -INF | 1.0886 | 0.1962 |
| | Exact | | | | | |

File: SEGSFIRS.DAT

Model: RESPONSE=SEQUENCE+DAS#
Strat Var: <Unstratified>
Weight: <Unweighted>
#Obs: 12
#Groups: 12
Deviance : 13.0283 on 9 df

---

Tests ( 1 df) : <SEQUENCE>

| Type of Test | Statistic | P-value | P-mid |
|---|---|---|---|
| Likelihood Ratio | 3.2600 | 0.0710 | NA |
| Wald | 2.7195 | 0.0991 | NA |
| Scores | 3.0889 | 0.0788 | NA |
| Exact (Conditional Scores) | 1.9565 | 0.3500 | 0.2750 |

---

Tests ( 1 df) : <DAS#>

| Type of Test | Statistic | P-value | P-mid |
|---|---|---|---|
| Likelihood Ratio | 0.0166 | 0.8976 | NA |
| Wald | 0.0165 | 0.8977 | NA |
| Scores | 0.0166 | 0.8976 | NA |
| Exact (Conditional Scores) | 0.0138 | 0.9444 | 0.9111 |

---

Tests ( 2 df) : <SEQUENCE,DAS#>

| Type of Test | Statistic | P-value | P-mid |
|---|---|---|---|
| Likelihood Ratio | 3.2723 | 0.1947 | NA |
| Wald | 2.7229 | 0.2563 | NA |
| Scores | 3.0980 | 0.2125 | NA |
| Exact (Conditional Scores) | 2.8398 | 0.3359 | 0.3321 |

| VARIABLE | INFERENCE TYPE | <------- PARAMETER ESTIMATION --------> BETA | SE(BETA) | 95.0% (1-sided)BOUND | | P-VALUE ONE SIDED |
|---|---|---|---|---|---|---|
| SEQUENCE | Asymptotic | 2.3064 | 1.3986 | 0.0059 | +INF | 0.0496 |
| | Exact | 1.4929 | NA | -0.6350 | +INF | 0.1750 |
| DAS# | Asymptotic | 0.0059 | 0.0455 | -0.0690 | +INF | 0.4488 |
| | Exact | 0.0049 | NA | -0.0687 | +INF | 0.4889 |
| CONST | Asymptotic | -2.2431 | 5.0676 | -INF | 6.0923 | 0.3290 |
| | Exact | | | | | |

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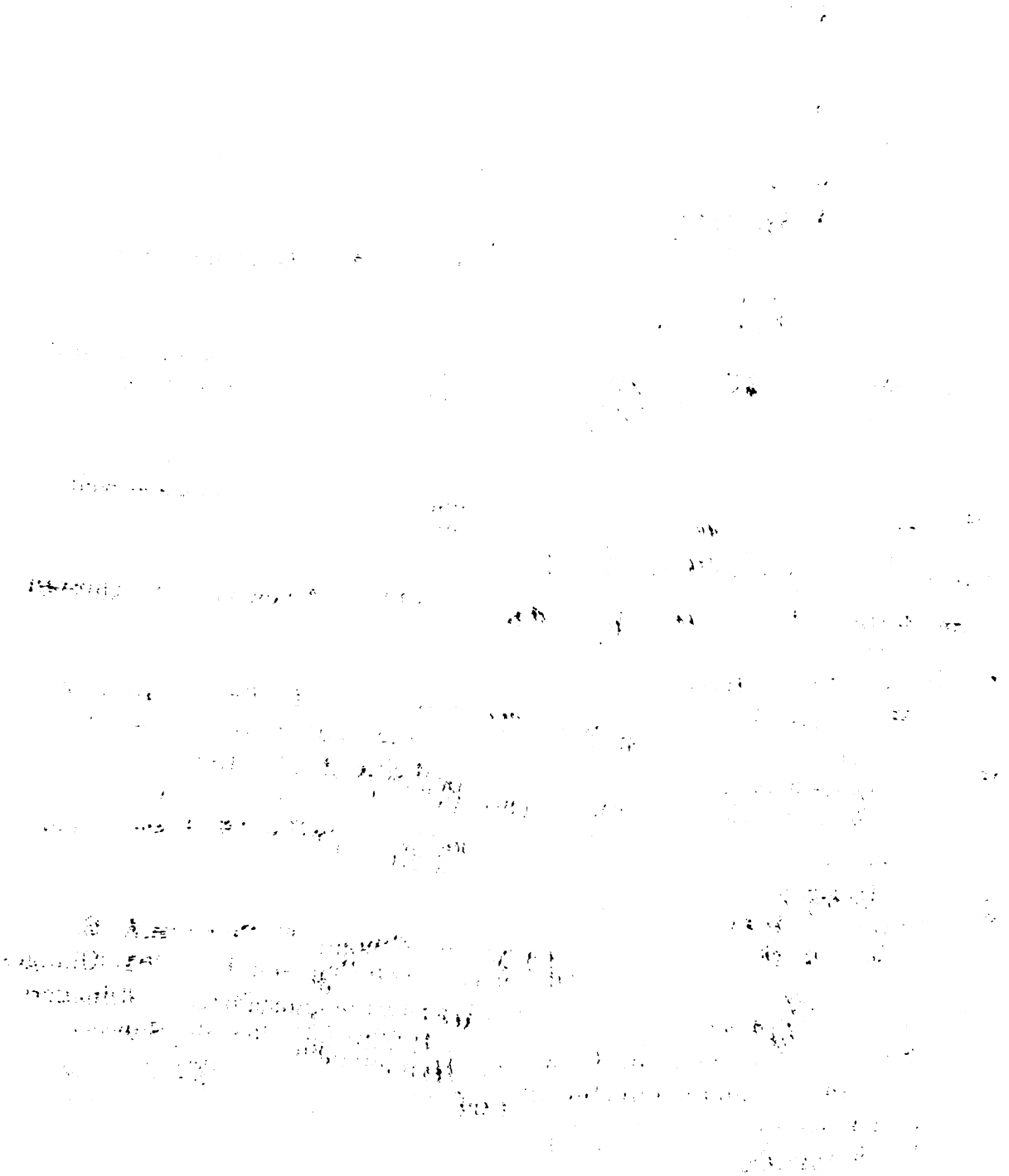

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