CHAPTER 2

LITERATURE REVIEW

This chapter reviews the concept of fatigue, including definitions of fatigue, prevalence of cancer related fatigue, assessing and measuring fatigue, and impact of cancer-related fatigue. Next, theory of fatigue in cancer patients is presented. Then, come the reviews of factors that influence fatigue, including the empirical findings that support the relationships between the proposed factors and fatigue. Finally, the conceptual framework of the study is proposed.

Fatigue

Fatigue is a universal symptom associated with acute and chronic illness. However, it is also found in healthy individuals. Fatigue is the mechanism whereby the slowdown or cessation of function is initiated, allowing for regeneration and prevention of overuse of individual tissues or organs within the overall physiologic framework of the body (Eidelman, 1980 cited in Hart, Freel, & Milde, 1990). It is a normal protective mechanism that helps the body maintain physiologic equilibrium, and it is essential in warning the body of the need for rest and restoration (Hart, Freel, & Milde, 1990). Fatigue is an abnormal symptom when it occurs with less effort than usual, at unusual times, when rest is no longer restorative, or when diversion is not distracting (Hart, Freel, & Milde, 1990), such as in cancer patients.

Definitions of Fatigue

Fatigue is often defined by its proposed origin or cause such as, central versus peripheral fatigue, pathologic versus psychologic fatigue; by the exclusion of other diseases such as Chronic Fatigue Syndrome; or by its duration such as, acute versus chronic fatigue (Piper, 1993). In nursing, fatigue is described as a subjective phenomenon associated with many other terms, such as tiredness, weakness, lack of energy, exhaustion, lethargy, inability to concentrate, malaise, boredom, sleepiness, lack of motivation, and decreased mental status (Aistairs, 1987; Winningham, Nail, Burke, et al., 1994). In addition, differences in culture, meaning of words, and translation problems have influenced the meaning of fatigue (Glaus, 1998).

Aistars (1987) defined fatigue as "a condition characterized by subjective feelings of generalized weariness, exhaustion, and lack of energy resulting from prolonged stress that is directly or indirectly attributable to the disease process" (p. 25). Piper (1986) conceptualized fatigue as " a subjective feeling of tiredness that is influenced by circadian rhythm; it can vary in unpleasantness, intensity, and duration" (p. 220). Carpenito (2000) defined fatigue as "the self-recognized state in which an individual experiences an overwhelming, sustained sense of exhaustion and decreased capacity for physical and mental work that is not relieved by rest" (p. 371). Moreover, Carpenito (2000) categorized factors that caused fatigue as pathophysiologic, treatment-related, situational, and maturational.

Using the concept analysis, Ream and Richardson (1996) defined fatigue as "a subjective, unpleasant symptom which incorporates total body feeling ranging from tiredness to exhaustion creating an unrelenting overall condition which interferes with individuals' ability to function in their normal capacity" (p. 527). Lee and

colleagues (1994) defined fatigue as a perception of severity along a continuum ranging from full of energy and vitality to severe fatigue and exhaustion that results from the imbalance between resources and demands placed on women by their internal (physiologic) and external (social) environments. Aaronson and colleagues (1999) viewed fatigue as "an awareness of a decreased capacity for physical and/or mental activity due to an imbalance in the availability, utilization, and/or restoration of resources needed to perform activity" (p. 46).

Further, a panel of fatigue experts from the National Comprehensive Cancer Network (NCCN) defined cancer-related fatigue as, "An unusual, persistent, subjective sense of tiredness related to cancer or cancer treatment that interferes with usual functioning" (Arkinson, Barsevick, Cella, et al., 2000,p. 152). This definition reflects the unusual characteristics of cancer fatigue that healthy individuals experience, that is, fatigue in cancer patients is usually more severe, more distressful, and less likely to be relieved by rest. These specific characteristics are consistent with the definition proposed by Holley (2000) who conducted a qualitative study with 17 patients with various kinds of cancer. In this study, participants defined cancer-related fatigue by comparing it with typical fatigue as more rapid in onset, more intense, more energy-draining, longer lasting, and often unexpected.

In summary, it can be concluded that fatigue is defined as a subjective, unusual feeling or a lack of physical energy attributed to cancer and its treatment. Moreover, it causes discomfort and decreases both physical and mental activities, and is generally not relieved by rest.

Prevalence of Cancer-Related Fatigue

According to many studies, the prevalence of fatigue in women with breast cancer during treatment with adjuvant chemotherapy is approximately 70-94% (AHRQ, 2002; Greene et al., 1994; Jacobsen et al., 1999; Longman, Braden, & Mishel, 1996, 1997; Molassiotis & Chan, 2001; Sitzia & Huggins, 1998; Wyatt & Friedman, 1998). Moreover, fatigue remains severe and does not improve over time throughout chemotherapy treatment (Longman, Braden, & Mishel, 1997; Sitzia & Huggins, 1998; Wyatt & Friedman, 1998).

Longman, Braden, and Mishel (1996) studied the side effects of cancer treatment in 307 women with breast cancer by using the Side Effects Checklist. They found fatigue to be the most common, as well as the most problematic side effect. Subsequently, Longman, Braden, and Mishel (1997) extended their study with a longitudinal design among 53 of the 307 participants. Data were collected at 3 points: after treatment began, 6 to 8 weeks later, and then 12 weeks later. They found the prevalence rates of fatigue at 70%, 77%, and 79%, respectively. This suggests that fatigue is experienced by more patients as treatment continues over time.

Later, Sitzia and Huggins (1998) studied side effects in 52 patients with breast cancer receiving 6 cycles of Cyclophosphamide, Methotrexate and 5-Florouracil (CMF) by using the Worthing Chemotherapy Questionnaire 75 (WCQ-75) that is assured unless there is a “known” concern of its validity. The results consistently showed that the incidence of fatigue was approximately 90%, and that fatigue remained severe throughout chemotherapy.

Wyatt and Friedman (1998) investigated patterns of functional and psychosocial adjustment of midlife and older women after surgery for breast cancer.

They compared 30 subjects receiving follow-up adjuvant chemotherapy with 16 who did not. The presence and severity of the symptoms were measured at 3 time points post surgery: 6 weeks, 3 months, and 6 months. Fatigue and pain were found to be the most frequently reported symptoms in both groups. In women receiving adjuvant chemotherapy, 70% experienced fatigue after 6 weeks, 53% after 3 months, and 56% after 6 months, and fatigue did not improve over time. Jacobsen and colleagues (1999) also reported similar results. Even though the prevalence and severity of fatigue significantly increased after the start of chemotherapy, further the prevalence of fatigue showed a stable pattern. The U.S. Agency of Healthcare Research and Quality (AHRQ) reported that the prevalence of fatigue in breast cancer prior to starting chemotherapy was 4%, but increased to 91% after surgery and chemotherapy (AHRQ, 2002).

Fatigue is the most distressing side effect experienced during chemotherapy. It is also a long-term side effect of cancer treatment (Ashbury, Findlay, Reynolds & McKerracher, 1998; Knobf, 1986; Vogelzang et al., 1997).

Vogelzang and colleagues (1997) surveyed 419 cancer patients within 6 weeks to 1 year of last chemotherapy or radiotherapy. During treatment of cancer, 78% of patients experienced fatigue, of these 32% experienced daily fatigue. This finding is consistent with other studies (Ashbury, Findlay, Reynolds & McKerracher, 1998; Berger & Higginbotham, 2000).

In a survey of 913 Canadian cancer patients who had been treated within the previous 2 years, 78% reported fatigue as their most common symptom. In addition, they rated fatigue as either moderate (50%) or severe (37%) (Ashbury, Findlay, Reynolds & McKerracher, 1998).

Berger and Higginbotham (2000) studied 14 breast cancer patients both during and after adjuvant chemotherapy with doxorubicin and cyclophosphamide. In this pilot study, fatigue was found to be a significant problem throughout cycle three of cancer chemotherapy and continued at lower levels 2 months after the last treatment.

To compare fatigue between cancer and non-cancer groups, Irvine and colleagues (1994) conducted a prospective descriptive research study to investigate the prevalence of fatigue in 104 patients with different types of cancer—54 who received radiotherapy and 47 who received chemotherapy in comparison with a group of 53 healthy people. All participants were assessed using the Pearson Byars Fatigue Feeling Checklist. Radiotherapy patients were surveyed in the first week of a 5- or 6-week course of radiotherapy and during the last week of treatment. Chemotherapy patients were surveyed before receiving chemotherapy and 10-14 days after treatment. The healthy subjects were surveyed at only one point in time. The results indicated that there was no difference in the mean level of fatigue experienced in healthy subjects and those before the start of cancer treatment. However, cancer patients experienced a significant increase in fatigue over the course of radiotherapy and 14 days after treatment than was reported by healthy control subjects. This study suggests that before receiving cancer treatment, fatigue experienced by cancer patients is not different from fatigue experienced by healthy individuals because of the difference in timing of measurement.

In contrast, Jacobsen and colleagues (1999) investigated the characteristics, course of treatment, and correlations of fatigue in 54 women receiving adjuvant chemotherapy for breast cancer and in 54 women age-matched controls. Before the

start of chemotherapy and during the first three treatment cycles, subjects completed two fatigue questionnaires: the Fatigue Scale from the Profile of Mood States (POMS-F) measuring fatigue severity, and the Fatigue Symptom Inventory (FSI) assessing the frequency and severity of fatigue as well as its perceived interference with quality of life. The Memorial Symptom Assessment Scale (MSAS), assessing symptoms commonly associated with cancer and its treatment in terms of their prevalence, severity and distress, was administered in the clinic immediately before the start of each of the first 4 cycles of chemotherapy. An age-matched sample of women without cancer history was assessed at similar time intervals. Results showed that breast cancer patients experienced more fatigue than those without a previous history of cancer. These differences were evident before and after patients started chemotherapy. Fatigue increased among patients after treatment was started, but did not increase any further during the first 3 treatment cycles.

Broeckel and colleagues (1998) examined the characteristics and correlations of fatigue in 61 women with breast cancer who had completed chemotherapy within 3-36 months, and in 59 women with no history of cancer. All participants completed standardized self-report measures of fatigue—the Fatigue Scale from the Profile of Mood States (POMS-F) measuring fatigue severity, the Fatigue Symptom Inventory (FSI) assessing the frequency and severity as well as its perceived interference of quality of life, and the Multidimensional Fatigue Symptom Inventory (MFSI) assessing the complex nature of fatigue. Results revealed that former adjuvant chemotherapy patients reported approximately 1.5 times more severe fatigue ($p < .01$) and greater overall interference with quality of life because of fatigue ($p < .05$) as well as greater interference with ability to work ($p < .05$) and concentrate

($p < .05$) than women with no history of cancer. These results are supported by Andrykowski, Curran, and Lightner's (1998) study, comparing fatigue among 88 breast cancer patients who had completed surgery, radiotherapy, or chemotherapy treatment with 88 age-matched women with no history of cancer. The breast cancer group reported more fatigue, more weakness, and less vitality than those without cancer.

In brief, prevalence rates for fatigue differ in many studies because of differences in regimen and type of anticancer drugs, timing of measurement, measuring instruments, populations, and sample size. High prevalence rates were found during as well as after the administration of adjuvant chemotherapy. Moreover, most studies indicated that cancer patients experience more fatigue than those without cancer.

Assessing and Measuring Cancer-Related Fatigue

Fatigue assessment is recognized as an important aspect of oncology nursing. However, there is no widely accepted definition of fatigue as it is a complex, multicausal and multidimensional sensation (Piper, et al., 1987). Fatigue, like any other human experience, is capable of expression in three major ways, that is by physiological, behavioral response and verbal description (Richardson, 1998). Physiological, biochemical and behavioral approaches to assessment are often acknowledged as objective indicators of fatigue. However, in order to create a comprehensive picture of the nature and meaning of fatigue, subjective indicators must be acknowledged as the key to understanding fatigue experience (Piper et al.,

1989; Piper, 1991). Therefore, the best way to assess and measure fatigue is to determine the person's own perception of fatigue experience.

Due to overall lack of consensus in the literature on the definition of fatigue, it is not surprising that measuring fatigue has challenged investigators. Validity and reliability measures for perception of fatigue and its severity are important to both researchers and clinicians in measuring fatigue. Presently, measures are tailored to the situation in which studied, therefore limiting generalization of findings (Barnett, 2001). To quantify fatigue for research regardless of population of interest, Aaronson and colleagues (1999) discussed five important components of fatigue: (1) quantity of fatigue; (2) distress because of fatigue; (3) impact of fatigue on activity of daily living; (4) other correlations of fatigue; and (5) key biological parameters associated with fatigue. Further, due to the daily fluctuation of the severity of fatigue over time, the timing of the measurement is essential when assessing cancer- related fatigue (Wu & McSweeney, 2001). Measurements are then identified for each of these components to enable measures of fatigue across multiple studies that may result in more generalizable findings. For both clinical and research use, Wu and McSweeney (2001) concluded that cancer-related fatigue measures need to be brief, simple, sensitive enough to detect change over time, and stable enough to use repeatedly.

A number of self-report fatigue scales have been developed and broadly fall into two categories including unidimensional and multidimensional instruments. Instruments used to measure fatigue in cancer populations are as follows:

Unidimensional Instruments

Unidimensional fatigue measurements used in cancer patients include the Rhoten Fatigue Scale and the Profile of Mood State.

The Rhoten Fatigue Scale. The Rhoten Fatigue Scale (Rhoten, 1982) is a single-item, 11-point, graphic self-rating scale that asks patients to assess the severity of their current level of fatigue. The Rhoten Fatigue Scale, a unidimensional scale, is simple to administer, producing little burden upon the patients. However, its reliability cannot be assessed, as it is a single-item scale. In patients with ovarian cancer receiving chemotherapy, Pickard-Holley (1991) found a moderately strong correlation (r = .68) between the Rhoten Fatigue Scale and fatigue items on the Beck Depression Inventory and assessed reliability of the Rhoten Fatigue Scale using test-retest reliability, but did not report the result.

The Profile of Mood States (POMS). The Profile of Mood States (POMS) developed by McNair, Lorr, and Droppleman (1992), consists of 65-item, 5-point, adjective-rating scale and measures six mood states including depression, tension, anger, confusion, fatigue and vigor. Two POMS subscales, fatigue and vigor, are frequently used to measure fatigue in cancer patients. In a study of patients receiving cancer treatment, Meek and colleagues (2000) found good reliability and validity in the POMS fatigue subscale. The POMS fatigue and vigor subscales are short and easy to use. However, it was specifically developed for use as a mood scale for psychiatric patients, not to measure fatigue. Moreover, like other single-dimension measures, the POMS fatigue and vigor subscales measure only one aspect of fatigue.

Multidimensional Instruments

Multidimensional fatigue measurements used in cancer patients include the Multidimensional Fatigue Inventory, the Fatigue Symptom Inventory, and the Piper Fatigue Scale.

The Multidimensional Fatigue Inventory (MFI). The Multidimensional Fatigue Inventory (MFI) developed in Netherlands by Smets, Garssen, Bonke, and de Haes (1995) is a 20-item, 7-point self-report instrument. It is designed to measure five dimensions of fatigue including general fatigue, physical sensations, cognitive symptoms, reduced motivation, and reduced activity. These five dimensions were confirmed by factor analysis, and showed good internal consistency (Smets, Grarssen, Cull, & de Haes, 1996). Meek et al. (2000) tested the MFI in the American cancer population and found the results did not support five dimensions like those originally proposed. The different perceptions of fatigue may relate to cultural differences in the U.S. and Europe.

The Fatigue Symptom Inventory (FSI). The Fatigue Symptom Inventory (FSI) is a 14-item measure developed by Hann and colleagues (1998). It is designed to assess the frequency and severity of fatigue as well as its perceived disruptiveness. Frequency is measured as the number of days in the past week as well as the portion of each day respondents felt fatigued. Severity is measured in term of less, average, and most fatigue that respondents felt during the past week, as well as current fatigue. Perceived disruptiveness is assessed as the degree to which fatigue in the past week interferes with activities, work, enjoyment, and mood. Previous research

demonstrated the validity and reliability of the FSI in cancer patients (Broeckel et al., 1998; Hann, Denniston, & Baker, 2000).

The Piper Fatigue Scale (PFS). The Piper Fatigue Scale (PFS) is the first validated and best-developed multidimensional measure of cancer-related fatigue based on the Piper Integrated Fatigue Model. An early version consists of 76 visual analogue scales that assess subjective fatigue in temporal, intensity/severity, affective, and sensory dimensions (Piper, Lindsey, Dodd, et al., 1989). Due to its length and complicated format, Piper and colleagues revised the PFS in 1998 (Piper et al., 1998).

The revised PFS consists of 22 adjective-wording scales and 5 open-ended questions that measure four dimensions of subjective fatigue, including a) perception about timing of fatigue (temporal), b) mental, physical, and emotional symptoms of fatigue (sensory), c) emotional meaning attributed to fatigue (affective dimension), and d) impact and distress fatigue might have on the activities of daily living (intensity). These dimensions were confirmed using factor analysis (Piper et al., 1998). Empirical evidence that supported the high reliability of the PFS in cancer patients ranged from standardized alpha of 0.91 – 0.96 (Berger, 1998; Berger & Higginbotham, 2000; Berger & Walker, 2001; Woo et al., 1998). Moreover, Pritsanapanurangsei (2000) translated the revised PFS into Thai and used it in a fatigue study among Thai breast cancer patients. It also showed high internal consistency reliability (0.96 – 0.99). In addition, the Thai version of the PFS was used in other studies among Thai cancer patients, and was also found reliable (Saejew, 2001; Tohthong, 2002). The Thai version PFS is appropriate to use in this study due to its strong theoretical foundation, multidimensional measure of fatigue, and was found to be valid and high reliability.

In summary, fatigue is difficult to assess or measure because of its lack of a comprehensive definition. Its measurements used to assess cancer-related fatigue are either unidimensional or multidimensional. Although some instruments are available to measure fatigue in cancer patients, many lack validity or reliability. Therefore, the revised PFS is both validated and the best developed multidimensional instrument with a strong theoretical foundation. Moreover, it shows good internal consistency reliability in the original version and in the Thai version PFS.

Impact of Cancer-Related Fatigue

Fatigue poses many problems in many dimensions of quality of life or general well-being in cancer patients. Qualitative studies, which explored the experience of fatigue in cancer patients, showed consistent results of the impact of fatigue. These results can be summarized in four categories comprising physical, psychological, social, and economic/occupational (Chan & Molassiotis, 2000; Curt et al., 2000; Ferrell et al., 1996; Magnusson, Moler, Ekmant & Wallgren, 1999; Messias, Yeager, Dibble & Dodd, 1997), as follows:

Physical Impact. Physical manifestations of fatigue were most commonly described as a diminished energy level. Daily activities including walking distances, general household chores, and straightening up the house became more difficult (Chan & Molassiotis, 2000; Curt et al., 2000; Messias et al., 1997).

Psychological Impact. Most patients reported decreased motivation, and feelings including sadness, worry, concern, frustration, depression, or hopelessness regarding their fatigue (Chan & Molassiotis, 2000; Curt et al., 2000; Messias et al.,

1997). Several patients described how their self-esteem had been affected in term of feeling worthless and insecure (Magnusson et al., 1999).

Social Impact. Participating in social activities, such as going to a restaurant, keeping up with interpersonal relationships, and spending time with friends, also became more difficult. Exercise and shopping were also more difficult during episodes of fatigue (Curt et al., 2000; Magnusson et al., 1999). Motivation to engage in social activity was weakened, leaving chemotherapy patients with a sense of isolation and detachment (Chan & Molassiotis, 2000).

Economic/Occupational Impact. Fatigue has a tremendous impact on the patients' and their caregivers' occupations. A study found that three-forth of the patients changed their employment status as a result of fatigue, while others stopped working or took a medical leave. Further, patients' primary caregivers also took more time off from work, accepted fewer responsibilities or reduced their work hours which affected their families' income. Finally, due to fatigue, patients often hired people to help them with their daily household chores such as cooking and cleaning (Chan & Molassiotis, 2000; Curt et al., 2000).

Theory of Fatigue in Cancer Patients

Although the literature reports a high prevalence and high impact of fatigue in cancer patients, the exact mechanisms that produce fatigue are not yet known. However, it is believed that fatigue is the result of multiple factors (Dimeo et al., 1999; Smet et al., 1993). A review of literature found that most existing theories focus on the utilization of conservation of energy. However, other theories focus on

factors that directly or indirectly affect fatigue. These theories, published in the literature, are Ryden's Conceptual Framework of Energy Expenditure, Aistars' Organizing Framework, the Energy Analysis Model, Winningham's Psychobiological-Entropy Model, and the Piper Integrated Fatigue Model.

Ryden's Conceptual Framework of Energy Expenditure

Ryden's Conceptual Framework of Energy Expenditure (Ryden, 1977 as cited in Winningham et al., 1994). In this theory, fatigue is defined as a deficit of energy, with energy being defined as the ability to do work on biological, psychological, social, and cognitive levels. Individuals are depicted as open systems, and obtain energy from both internal (sleep, motivation, and spirituality) and environmental (food, water, and air) sources. Human physiological and psychological processes use these sources of energy to sustain life. When available energy exceeds the life-supporting needs, it can be used for nonessential activities including socializing. However, when energy demands increase to allow for healing during periods of sickness, little energy is left for nonessential activities. According to this model, women with breast cancer use energy to deal with the effects of breast cancer and chemotherapy, thus depleting energy reserves and causing fatigue.

Aistars' Organizing Framework

Aistars' Organizing Framework (Aistars, 1987) also depicts fatigue as an energy deficit. This theory explains those periods of under stimulation, such as inactivity and boredom, which can produce stress through feedback systems. Aistars conceptualized fatigue in cancer patients is a response to continual stress caused by

multiple physiological (pain, infection, and anemia), psychological, and situational factors related to cancer or its treatment. Stored energy is depleted when the individual copes with prolong stressors on a constant basis with no opportunity to restore energy. This model provides an understandable and concise explanation of fatigue and the processes that lead to it. Moreover, it can be applied to individuals with any form of chronic illness, not just cancer.

The Energy Analysis Model

The Energy Analysis Model (Irvine et al., 1994) also draws on Ryden's Conceptual Framework. Like Ryden's framework, this theory proposes that the human body is an open system dependent on energy sources from internal and external sources. It conceptualizes fatigue as arising when external supplies are decreased (by dehydration or anorexia), internal supplies are interrupted (by anxiety, anemia, or lack of sleep), and energy demands are high (following physical or cognitive/emotional over-exertion). The Energy Analysis Model expands on previous theories by adding the variable, energy-response modifier. This variable is the mechanism by which Irvine accounts for factors that are unique to the energy metabolism and expenditure of cancer patients. Unfortunately, this theory does not clarify how the energy-response modifiers affect fatigue.

Winningham's Psychobiological-Entropy Model

Winningham's Psychobiological-Entropy Model (Winningham, 1996) defines fatigue as an energy deficit that occurs as a result of pre-existing conditions, disease, related symptoms, treatment, environmental influences, and inactivity. The

model proposes that primary fatigue in cancer patients is unique compared to other primary symptoms of cancer such as diarrhea, nausea/vomiting, and pain, all of which lead to a decrease in physical activity. Decreased activity produced by these primary cancer symptoms results in secondary fatigue which in turn leads to a cycle of decreased activity, and reduced functional status. Moreover, this model suggests interventions for prevention of fatigue. First, the symptoms and factors that contribute to primary fatigue should be managed, followed by achieving an optimal balance between restorative rest and activity.

Piper Integrated Fatigue Model

The Piper Integrated Fatigue Model: PIF (Piper et al., 1987) was developed from a deductive approach based on a review of fatigue literature from five disciplines, including physiology, psychology, ergonomics, medicine, and nursing. It describes 14 biological, physiological, psychological, and social factors that influence the subjective and objective (physiological, biochemical, and behavioral) signs and symptoms of fatigue. These factors or patterns include innate host factors, accumulation of metabolites, changes in energy and energy substrates, activity/ rest, sleep/ wake, disease, treatments, environment, symptoms, psychological, changes in regulation/ transmission, social, life events, and oxygenation patterns (see Figure 2-1). Additionally, it supports the idea that fatigue becomes more complicated to manage when it becomes a chronic symptom.

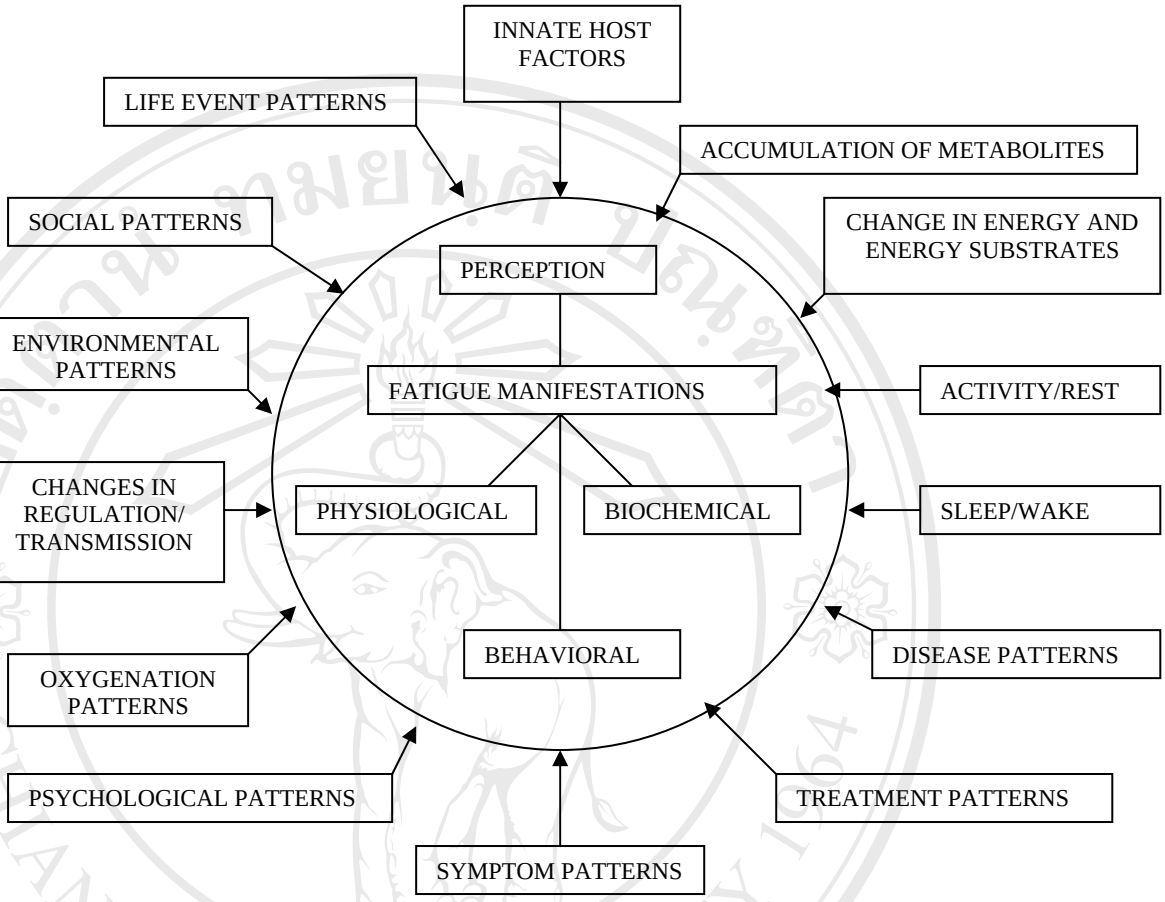


Figure 2-1 Integrated Fatigue Model (Redrawn from Piper, B. F., Lindsey, A. M., & Dodd, M. J. (1987). Fatigue mechanisms in cancer patients: Developing nursing theory. Oncology Nursing Forum, 14, p.19)

Innate host factors. Innate host factors such as age, gender, genetic makeup, race, and unique circadian rhythms may influence fatigue (Piper et al., 1987). Subjective fatigue is thought to be common in premature infants and the elderly because they are at risk for respiratory muscle fatigue due to age-related muscle fiber differences (Piper, 1993).

Accumulation of metabolites. Accumulation of various metabolites has been associated with fatigue. In cancer patients, the accumulation of lactate,

hydrogen ions, and cell destruction end products are likely mechanisms of fatigue (Piper et al, 1987; Piper, 1991).

Changes in energy and energy substrate patterns. Changes in energy production and substrate patterns can profoundly influence human performance and development of fatigue. In cancer patients, changes in energy patterns are common and may result from abnormalities in energy expenditure, cancer cachexia, anorexia, infection, fever, and nausea/vomiting (Piper et al., 1987; Piper, 1991). These conditions affect their nutritional status which influences energy expenditure, thus producing fatigue.

Activity/rest patterns. Activity is broadly defined and applied to work, exercise, mobility, and leisure activities. Activity can play an important role in the prevention, cause, and alleviation of fatigue (Piper et al., 1987; Piper, 1991). Further, unnecessary prolonged bed rest and immobility contribute to weakness and fatigue (Winningham et al., 1994). Skeletal muscles that are not exercised lose their oxidative capacity. When this occurs, more oxygen is required for performance of comparable work than in conditioned muscles. Less activity, therefore, can contribute significantly to the development of fatigue (Astrand & Rodahl, 1986 cited in Piper, 1993).

Sleep/wake patterns. Alterations in the sleep/wake cycle can also lead to fatigue (Piper et al., 1987). Restful sleep increases the blood supply and energy to the brain, giving a refreshed feeling after waking up (Gall, 1996). On the other hand, a lack of restful sleep at night leads to an increase in sleepiness and fatigue during the day (Piper, 1993).

Disease patterns. The most common symptom of cancer and other chronic diseases is fatigue (Piper et al., 1987). In cancer patients, fatigue has been demonstrated to increase as the progression of cancer increases (Glaus, 1998).

Treatment Patterns. Treatment is one of the many proposed causes in the development of cancer-related fatigue (Jacobs & Piper, 1996). Various medical treatments, such as chemotherapy, surgery, radiotherapy, and biological response modifiers are associated with fatigue (Piper et al., 1987). Moreover, a combination of treatment such as radiotherapy and chemotherapy produce higher fatigue than a single treatment (Woo et al., 1998). Antineoplastic drugs, that cross the blood-brain barrier or have neurotoxicities, may be more likely to produce fatigue than other agents (Piper et al., 1987).

Symptom patterns. Pain, nausea, and vomiting are common symptoms of symptom distress of cancer and cancer treatment. These symptoms may increase energy expenditure thus, causing fatigue. Further, assessment and control of these symptoms may reduce or prevent fatigue in cancer patients (Piper et al., 1987).

Psychological patterns. Psychological factors such as unusual response to stressors (coping strategies), depression, anxiety, degree of motivation, distraction, boredom, and beliefs and attitudes may influence fatigue (Piper et al., 1987; Piper, 1991; Piper, 1993). Psychological disturbances, including anxiety and depression, are common in cancer patients (Andrykowski et al., 1998; Mock et al., 1997) and persist over time (Longman et al., 1999).

Oxygenation patterns. Any factor that alters or interferes with the ability to obtain or maintain an adequate oxygen level can also influence fatigue (Piper et al., 1987; Piper, 1991), such as anemia, which is a common symptom in cancer and its treatment. Easiness of fatigue and reduced endurance are associated with anemia (Piper, 1993).

Changes in regulation/transmission patterns. Fluid or electrolyte imbalance can potentially affect neurotransmission and muscle force, resulting in fatigue. Neurotransmitters such as tryptophan, serotonin, and melatonin can also influence sleep, circadian rhythms, and in turn fatigue (Piper et al., 1987; Piper, 1991, 1993).

Environmental patterns. Noise, temperature, and allergens may contribute to fatigue as well (Piper et al., 1987, Piper, 1991).

Social patterns. Social support, cultural beliefs, and economic factors may have an effect on fatigue (Piper et al., 1987). The availability and quantity of social support have an important effect on subjective fatigue in women receiving chemotherapy (Jamar, 1989). For example, patients who have family or friends to help them with their daily responsibilities are likely to gain more rest and consequently experience less fatigue.

Life event patterns. Life event patterns such as transitional events associated with growth and development may be related to fatigue in cancer patients (Piper et al., 1987; Piper, 1991, 1993). Moreover, during diagnosis and treatment, women may experience fatigue from psychological distress (fear, anxiety, and

depression) that stimulates stress hormone producing energy expenditure leading to fatigue.

In summary, fatigue is often the result of multiple factors. The PIF has practical use in understanding fatigue and its influencing factors in women with breast cancer, and can be used as a framework to explain the underlining mechanism of chemotherapy-induced fatigue (Piper et al., 1987). The PIF model helps delineate objective and subjective indicators that guide nursing assessment. Moreover, it provides a framework for the clinical approach and research. Unfortunately, it does not clarify the relationships among the influencing factors in the PIF model. Therefore, using the PIF model with evidence from literature as the framework for this study strengthens the causal relationships for developing a causal model for predicting fatigue.

Factors Influencing Fatigue

The PIF (Piper et al., 1987) explains 14 patterns or factors that most likely influence fatigue. In the present study, 7 of the 14 patterns are proposed to affect fatigue: treatment, energy and energy substrate, oxygenation, symptom, sleep/wake, social, and psychological patterns. Seven additional patterns including innate host factors, life event, disease, activity/ exercise, environment, accumulation of metabolites, and regulatory/ transmission patterns from the PIF Model are excluded from the study's conceptual framework. These patterns were considered to be similar among breast cancer women receiving adjuvant chemotherapy, and relatively constant variables, as well as difficult to measure or modify.

Innate host pattern and *disease pattern* were excluded as constant variables, since all participants were women and had breast cancer. Further, these factors can not be managed or modified. *Life event patterns* were considered similar among women with breast cancer because all had been diagnosed with breast cancer and received surgery and chemotherapy. *Activity/ exercise patterns* were both minimal and similar among these women since they were not engaged in any extensive exercise program during chemotherapy treatment. *Accumulation of metabolites* considered as cell destruction end products such as lactate and hydrogen ions, as well as *regulatory/ transmission patterns* represented by neurotransmitters such as melatonin, were difficult to determine, as they required special laboratory investigation. Finally, e*nvironment patterns* were difficult to control as all participants were outpatients and resided in their homes.

In this study, the variable in the treatment pattern was the chemotherapy protocol. Body mass index (BMI) was included in the energy and energy substrate pattern. Anemia was represented by the hemoglobin level in the oxygenation pattern. The sleep/ wake pattern was represented by sleep disturbance. Pain, nausea and vomiting as symptom distress represented the symptom pattern. The social pattern and cultural belief was represented by social support (family and friend support) and Buddhist practices. Finally, anxiety and depression were the variables in the psychological pattern.

Treatment Patterns

Treatment (such as surgery, chemotherapy, radiotherapy, and biological response modifiers) is one of many causes of cancer-related fatigue, (Jacob & Piper,

1996). For breast cancer treatment, mastectomy followed by adjuvant chemotherapy is recommended as a standard treatment for women with early stage breast cancer, in the attempt to eradicate or prevent occult micro-metastasis disease and to increase the disease-free survival rates (Gaston-Jobansson, Fall-Dickson, Bakos & Kennedy, 1999; Goodman, 1991).

The standard regimens for stage I or II breast cancer is steadily evolving and currently involves one of the three regimens: 1) cyclophosphamide, methotrexate, and 5-FU: CMF every 21 day cycle (on days 1) or 28 day cycle (on days1 and 8); 2) cyclophosphamide, adriamycin, and 5-FU: CAF every 21 day cycle (on days 1); or 28 day cycle (on days1 and 8); and 3) adriamycin and cyclophosphamide: AC every 21 day cycle (on days 1), for 4 to 6 months. Then, followed by 5 years of oral tamoxifen (TAM) for women who have estrogen receptor positive tumors (Fisher, Wickerham, & Redmond, 1992). These standard regimens or protocols used are categorical with the anthracycline (adriamycin: CAF, AC), or non-anthracycline (non-adriamycin: CMF) protocol (Neskovic-Konstantinovic, 2000).

Relationship of Chemotherapy Protocol to Fatigue

The common notion among oncology nurses is that specific chemotherapy agents of the adriamycin-based protocol, are associated with more side effects, including fatigue, than non-adriamycin protocol (Berger & Walker, 2001), since, anthracycline agents, in particular adriamycin, are the high emetic potential agents influencing severity of nausea and vomiting (McKenry & Salerno, 1995). Other side effects include myelosuppression, in particular granulocytopenia, severity of mucositis, alopecia, and fatigue. Further, the development of cardiotoxicity has been

a major concern with adriamycin treatment (Lehne, 1998; Vermorken, 2003). While non-anthracycline agents, including methotrexate, cyclophosphamide, and 5FU (CMF) have low emetic potential (McKenry & Salerno, 1995) they may be less likely to produce fatigue than antharcycline agents. The study by A'Hern, Smith and Ebbs (1993) supported the conviction that breast cancer treatment, CAF: adriamycin-containing protocols, produce more effective treatment and more side effects than the CMF protocol (Ratanatharathorn, 2002).

Further, Pritsanapanurungsei (2000) studied fatigue in 30 breast cancer patients receiving the first three courses of the CMF protocol. Results indicated that mean scores of fatigue were at the low level (mean 2.89-3.01, possible range 0-10), while Berger and colleagues (2003) found in their study of 25 women with breast cancer receiving the first three cycle of the adriamycin-based chemotherapy, that mean fatigue intensity scores remained mild (< 4, possible range 0-10). However, half of the study participants' scores were in the moderate (4-6.9) to severe (7-10) range at each measurement point.

Literature review found few studies that compared fatigue among chemotherapy protocols. Piper (1992) examined the variables of cycle length (21-day versus 28-day) and inclusion of adriamycin in the regimen. No changes were found for any of the outcome fatigue indicators by length of chemotherapy cycle or by the inclusion of adriamycin in the treatment regimen. Similarly, Greene, Nail, Fieler, Dudgeon, and Jones (1994) compared the incidence and severity of patient-reported side effects for three combination chemotherapy regimens used in the treatment of stage I-IV breast cancer. These regimens included CMF, CAF, and cyclophosphamide, mitoxantrone, and 5-FU (CNF). Eighty-six women with breast

cancer rated the severity of side effects. Data were collected during the first and second cycles on the second and fifth days after chemotherapy. The findings revealed no differences in reported fatigue among these regimens at any time.

Dalopakarn (2002) also found, in 160 Thai women with breast cancer receiving non-adriamycin (56.9%) and adriamycin-based protocol (43.1%), no difference in mean scores of fatigue reported between protocols.

However, Berger and Walker (2001) studied 60 women during the first three cycles of adjuvant breast cancer chemotherapy and found that chemotherapy protocols that contain intravenous adriamycin were directly associated with high fatigue at the first treatment cycle ($\beta = .26$, $p = .02$). Thus, this factor should be further investigated.

Energy and Energy Substrate Patterns

Piper and colleagues (1987) suggested that changes in energy and energy substrate and production could profoundly influence human performance and development of fatigue. In cancer patients, change in energy may result from the side effects of cancer chemotherapy including nausea, vomiting, diarrhea, and a decrease of appetite contributing to weight loss, malnutrition, dehydration, and decreased energy (Kalman & Villani, 1997). Lack of energy leads to a decrease in cardio-respiratory and musculoskeletal functions, muscle fiber atrophy, and necrotic fibers, thus influence fatigue (Irvine et al., 1994; Kalman & Villani, 1997; Winningham, 2001).

Nutritional status is the variable selected to measure energy storage patterns and is defined as a caloric reserve status. Although this variable broadly represents

the cellular processes, it provides quantitative data that can be used to classify subjects as having either inadequate, normal or excess nutritional reserves. Caloric reserve stored as body fat was determined using the body mass index (BMI).

BMI is commonly used in determining body fat and nutritional risk (Zeman & Ney, 1988). BMI is calculated as total body weight in kilograms divided by height in meters squared. In addition, weight and height data are easy to obtain and simple to use in evaluating cachexia and obesity, as well as the patients' nutritional risk (Sarhill, Mahmoud, Christie & Tahir, 2003). Calle and colleagues (1999) therefore recommended that serial measurements of BMI should be conducted to evaluate the nutritional status in cancer patients. According to WHO, a normal BMI is between 18.5 to 24.9 Kg/m^2; inadequate nutritional status is BMI < 18.5 Kg/m^2; and excess nutritional status is BMI > 24.9 Kg/m^2 (Calle, Thun, Petrelli, Rodriguez, et al., 1999).

Relationship of BMI to Fatigue

Literature review found few studies that directly examine BMI and fatigue. Previous studies found that weight loss (Blesch et al., 1991; Irvine et al., 1994) was related to fatigue in cancer patients during cancer treatment. Only one study (Berger & Walker, 2001) found BMI related to fatigue.

Blesch and colleagues (1991) studied the relationship between fatigue and physiological, biochemical, and behavioral factors using the conceptual framework of Piper (1987) in 77 cancer patients undergoing radiotherapy and/ or chemotherapy for lung cancer (n = 33) and breast cancer (n = 44). Fatigue was measured using the Rhoten Fatigue Scale. They found that no biochemical factors related to fatigue. Only weight change (weight loss) correlated significantly with fatigue.

Irvine and colleagues (1994) conducted a prospective study to investigate the correlation of fatigue in 101 patients (54 received radiotherapy and 47 received chemotherapy) with various types of cancer. The majority was female (96%) and had breast cancer (62%). The results revealed that cancer patients experienced a significant increase in fatigue over the course of radiotherapy and 14 days after chemotherapy. Further, fatigue had a significant relationship with weight loss ($p < .05$).

Berger and Walker (2001) conducted a prospective, correlational study with repeated measures in 60 women receiving the first three cycles of adjuvant breast cancer chemotherapy. Results showed that only a trend in a lower BMI directly influenced fatigue at the midpoint of the first treatment cycle ($\beta = -.19$, $p = .10$).

Conversely, Beach and colleagues (2001) conducted a prospective study of 75 lung cancer patients (53% female) receiving radiotherapy. Weight loss over the course of treatment was found not to be correlated with fatigue. However, only 45 participants completed all visits, and the sample may not have been large enough to demonstrate statistical significance. Thus, BMI needed to be investigated, and was anticipated to have a negative relationship to fatigue severity.

Oxygenation Patterns

Any factor that alters or interferes with the ability to obtain or maintain adequate oxygenation levels in the blood can influence fatigue (Piper et al., 1987). Further, easiness of fatigue and reduced endurance are associated with anemia (Piper, 1993).

Anemia is defined as a deficiency of red blood cells or a condition where hemoglobin concentration is below 12 gm/dL for women, which leads to a reduction in the oxygen-carrying capacity of blood (Cella, 1998; Yellen, Cella, Webster, Blendowski, & Kaplan, 1997). Anemia is a common result of chemotherapy induction from the myelosuppressive effects (Winningham & Barton-Burke, 2000; Yellen et al., 1997). Therefore the hemoglobin level is examined as a biological measure of anemia.

Relationship of Hemoglobin Level to Fatigue

Muscle cells and organs are impaired when oxygen supply is decreased, as found in a low hemoglobin level (Winningham, 1996). Further, a decrease in the oxygen supply leads to fatigue. Piper and colleagues (1989) found that women with breast cancer who had higher hematocrit or hemoglobin values on day 10 or 14 of the first cycle had more vigor than those with lower hematocrit and hemoglobin values.

Jamar (1989) explored the relationship between fatigue and anemia in a cross-sectional study of 16 women with ovarian cancer treated with chemotherapy. Jamar found an inverse correlation between fatigue and hematocrit level such that the higher the fatigue, the lower the hematocrit level.

Further, Mendoza and colleagues (1999) found that fatigue measured by the Brief Fatigue Inventory was statistically significantly correlated with hemoglobin levels ($r = -.36$, $p < .001$) in 305 cancer patients. Hemoglobin also was significantly related to the fatigue subscale of the POMS-Fatigue ($r = -.34$, $p < .001$).

Cella and colleagues (2002) explored and compared fatigue among anemic and non-anemic cancer patients, and control subjects, and found that fatigue in anemic

patients was higher than in non-anemic patients and control subjects ($p < .001$). Moreover, in the anemic group, level of anemia was a significant predictor of fatigue ($p < .001$). Hwang and colleagues (2003) also found, in a study of 180 cancer patients, that hemoglobin was an independent predictor of fatigue.

Conversely, Blesch and colleagues (1991) studied the relationship between fatigue and physiological, biochemical, and behavioral factors using the conceptual framework of Piper (1987) in 77 cancer patients undergoing radiotherapy and/ or chemotherapy for lung cancer ($n = 33$) or breast cancer ($n = 44$). Blesch and colleagues found that no biochemical factors, including hematocrit, hemoglobin, serum albumin, or white blood count related to fatigue. This suggests that the blood levels in this study might have been taken from medical records, and may not currently reflect the participants' self-assessment of fatigue, thus suggesting the nonsignificant findings and lack of correlation with fatigue in their study. This explanation is supported by findings demonstrating significant relationships between current measurements of hemoglobin level and fatigue in recent studies (Jacobsen, Garland, Booth-Jones, et al., 2004; Lind, Vernon, Cruickshank, et al., 2002).

Lind and colleagues (2002) studied the level of hemoglobin and quality of life in 179 anemic cancer patients (hemoglobin level < 12 gm/dl for female and < 13 gm/dl for male). Quality of life assessment forms (including fatigue subscale) were completed at the same time as hemoglobin levels were assessed. Results from both partial correlation and regression showed that hemoglobin level and fatigue subscale in quality of life have a significant positive association ($r = .28$, $p < .001$), and with regression coefficient ($\beta = 3.14$, $p < .001$), indicating that the higher the hemoglobin level the lower the fatigue level (the better the quality of life).

Jacobsen and colleagues (2004) examined in a prospective study the relationship between hemoglobin level and fatigue, as well as hemoglobin level and cognitive functioning. All 77 cancer patients completed the Fatigue Symptom Inventory (FSI) which measures fatigue on the day prior to start of the first chemotherapy cycle and on the day prior to start the fourth treatment cycle (as a follow-up assessment). Hemoglobin levels were also measured at corresponding timepoints. Results showed that hemoglobin levels declined significantly over time, but no significant changes were evident between the two assessment points in the average of total fatigue scores. However, regression analyses demonstrated that change in fatigue disruptiveness was the only variable significantly related to change in hemoglobin ($\beta = -.22$, $p < .05$), such that the greater decline in hemoglobin, the greater increase in fatigue disruptiveness.

Symptom Patterns

According to the Piper Integrated Fatigue Model, Piper and colleagues (1987) explained symptom patterns as the experience of physical symptoms such as pain, nausea and vomiting, constipation, or diarrhea that are hypothesized to have an influence on fatigue. These symptoms were previously identified as symptom distress during cancer treatments (McCorkle &Young, 1978; Rhodes & Watson, 1987).

McCorkle and Young (1978) found that fatigue, pain, appetite and coughing were the four most frequent contributors to symptom distress in a sample of 53 lung and breast cancer patients. Ehlke (1988) also reported fatigue, insomnia, nausea and pain as the four most commonly encountered symptoms that produced distress in 107 outpatients with breast cancer. Consistently higher scores for fatigue, insomnia, and

nausea occurrence across the three data collection points, at the start of chemotherapy, at the nadir, and at the end of the first chemotherapy cycle, support the work of Boehmke (2004) who measured symptom distress in 120 women with early-stage breast cancer.

In addition, pain has been reported in 47% of breast cancer patients receiving treatment in the outpatient setting (Miaskowski & Dibble, 1995). Finally, pain sensation was often reported as severe and distressing (Baron, 1998). These results are consistent with the view that the most frequently occurring symptoms reflecting distress from the chemotherapy regimens used for adjuvant breast cancer chemotherapy include fatigue, nausea and vomiting, pain, and sleep difficulty. Therefore, pain, and nausea and vomiting were examined as symptom patterns to identify the predictors of fatigue in this study.

Relationship of Pain, Nausea and Vomiting to Fatigue

Symptom distress, including pain, and nausea and vomiting, predisposing as stressor for women with breast cancer, may increase the expenditure of energy thus causing fatigue (Aistars, 1987; Hart & Freel, 1982) by stimulating the sympathetic nervous system to release stress hormones. When body organs have been stimulated for a long time, they will deplete energy reservation, leading to fatigue (Selye, 1976).

Many studies support that fatigue is positively related to physical symptom distress during cancer treatment (Berger & Walker, 2001; Dalopakarn, 2002; Irvine et al., 1994; Lam, 1997), severity of specific physical symptoms, such as pain (Blesch et al., 1991; Bower et al., 2000; Jacobsen et al., 1999), and nausea and vomiting (Jacobsen et al., 1999; Pritsanapanurungsei, 2000; Stone et al., 2001).

Irvine and colleagues (1994) conducted a prospective descriptive study to investigate the correlation of fatigue in 101 patients with different types of cancer. Most patients were female (96%) and had breast cancer (62%); 54 received radiotherapy and 47 received chemotherapy. Chemotherapy patients were surveyed before receiving chemotherapy (time 1) and 10-14 days after treatment (time 2). Fatigue at time 2 was significantly related to symptom distress, mood disturbance and functional ability ($p < .0001$). Moreover, symptom distress explained 29% of the variance in fatigue scores, while mood disturbance explained an additional 4% ($p < .0001$). The results indicate a strong relationship between symptom distress and fatigue.

Glover, Miaskowski, Dibble and Dodd (1995) evaluated the problems of pain and fatigue in oncology outpatients. The results showed that oncology outpatients who experienced cancer-related pain reported significantly higher levels of fatigue compared to pain-free patients. This finding suggests a positive relationship between cancer pain and fatigue.

In an unpublished master's thesis, Lam (1997) conducted a secondary analysis using path analysis in 101 women with breast cancer. Results showed that physical symptom distress (including pain, and nausea and vomiting) had a direct effect on fatigue, as well as having an indirect effect through its effect on psychological distress.

Berger and Walker (2001) tested the explanatory model of fatigue in 60 women receiving three adjuvant breast cancer chemotherapy cycles using the Piper Integrated Fatigue Model. Results showed that symptom distress (nausea, sleep, and

mood) made the largest independent contribution to explanation of fatigue at all three treatment times with β's ranging from .45 to .76 ($p < .001$).

In Thailand, Pritsanapanurungsie (2000) conducted a descriptive study aimed to examine patterns of fatigue and related factors among 30 breast cancer patients receiving the first three courses of chemotherapy. Instruments consisted of the Piper Fatigue Scale and a modified form of the Rhodes Index of Nausea and Vomiting Form II. There were significantly positive relationships ($p < .01$) between fatigue and nausea and vomiting at the first, second, and third course of chemotherapy ($r = .356$, .455, and .358, respectively).

Dalopakarn (2002) also investigated factors related to fatigue in 160 Thai breast cancer women receiving chemotherapy. Results showed that symptom distress was significant positively related to fatigue ($r = .80$, $p < .01$), and accounted for 64% of the variance in fatigue scores ($p = .00$).

Relationship of Pain, and Nausea and Vomiting to Anxiety and Depression

In a neuropsychiatry study, results suggest that depression and pain might also share similar neurotransmitter deficits. Ward and colleagues (1982) found that depression and anxiety were significantly correlated with the severity of pain in patients with both pain and depression. Serotonin, norepinephrine, and other biogenic amines may modulate paleospinothalamic tract transmissions and the endogenous pain control system, as well as the patients' moods. Thus, alterations in the level of these biogenic amines may lead to both pain and depression (Schuster & Goctz, 1994).

Spiegel, Sands, and Koopman (1994) explored the relationship between pain and depression among 96 subjects (48 in the high-pain group and 48 in the low-pain group). Prevalence of depression was found to be significantly higher in the high-pain group rather than in the low-pain group. Pain intensity was also found to correlate significantly with total mood disturbance including anxiety and depression.

Lam (1997) conducted a secondary analysis to examine interrelationships among physical symptom distress, psychological distress and fatigue in 101 women with breast cancer. Results from path analysis indicated that physical symptom distress including pain, and nausea and vomiting, had a direct effect on fatigue, and on psychological distress including anxiety and depression. Moreover, physical symptom distress had an indirect effect on fatigue through psychological distress. Therefore, psychological distress may be a mediator between physical symptom distress and fatigue.

In another study of 127 women with stage II-IV breast cancer who had completed adjuvant chemotherapy and were waiting for transplantation, Gaston-Johansson and colleagues (1999) found that 91% reported fatigue, and 47% reported pain, while 54% reported depression. Moreover, fatigue, pain, and depression were significantly correlated with each other.

Ciaramella and Poli (2001) evaluated whether depressed patients were more likely to experience pain, or whether pain and depression was a cluster that occurred concurrently. They found that patients who reported depression many years were not more likely to be in pain at the time of evaluation. However, they found that patients who were currently depressed reported more pain than those who were not depressed ($\chi^2 = 12.42$, $p < .001$). They therefore hypothesized that pain preceded depression.

Similarly, in Thailand, Dalopakarn (2002) studied factors related to fatigue in 160 breast cancer patients receiving chemotherapy. Results showed that symptom distress was positively related to depression ($r = .58$; $p < .01$).

Interrelationship Among Pain, Nausea and Vomiting, and Sleep Disturbance

Symptom distress, such as pain, has been hypothesized to disrupt sleep that is vital to recovery and repair of tissue and may offer a temporary cessation of the psychological awareness of pain. Poor sleep can lead to difficulty managing pain. In this way, a cycle of pain and poor sleep may become self-perpetuating (Lewin & Dahl, 1999). Moreover, Hu and Silberfarb (1991) suggested that sleep disturbance is secondary to pain experienced by breast cancer patients.

Previous studies have determined correlations within symptom distress, including pain, and nausea and vomiting. Results showed that symptom distress had a positive relationship to sleep disturbance. Cimprich (1999) investigated sleep quality, fatigue, and symptom distress in breast cancer patients who had not yet undergone treatment of any kind. Results showed that insomnia or sleep disturbance was related to high levels of symptom distress. Further, insomnia was the most frequent symptom reported with 88% of the sample.

Beck and Schwartz (2000 cited in Dodd et al., 2001) conducted a cross-sectional study of 84 inpatients and outpatients to examine the intensity of pain on fatigue and sleep quality. A significant difference existed in global sleep quality and fatigue based on the degree of pain intensity. The poor quality of sleep was associated with severe pain. The investigators concluded that pain is a significant contributing factor to insomnia. This hypothesis is consistent with the cross-sectional,

correlational studies (Morin, Gibson, & Wade, 1998; Wilson, Eriksson, D'Eon, Mikail, & Emery, 2002) that found sleep disturbance was positively associated with pain severity.

In Thailand, Pritsanapanurungsei (2000) conducted a prospective study to investigate the pattern of fatigue and related factors among 30 women with early stage breast cancer receiving three courses of CMF protocol. The findings revealed that both nausea and vomiting and sleep disturbance were positively correlated to fatigue at all three courses of chemotherapy ($p < .01$). In addition, there was a positive relationship between nausea and vomiting and sleep disturbance during all courses ($p < .01$).

Dalopakarn (2002) investigated factors related to fatigue in 160 women with breast cancer receiving chemotherapy. Results showed that symptom distress was negatively correlated with sleep quality ($r = -.645$, $p < .01$).

In addition, extreme vomiting can lead to physical damage including esophageal tears, gastric herniation, rib fracture, and dislocation of intervertebral discs contributing to perceived pain (Morrow, Roscoe, Hickok, Andrews & Matteson, 2002). Thus, vomiting was positively associated with pain.

Sleep/ Wake Patterns

Piper and colleagues (1987) identified alteration in sleep/ wake cycle or sleep disorders as a factor related to fatigue. Adequate sleep is essential for maintaining energy (Hart et al., 1990). During sleep, the body organs' need for energy is decreased; parasympathetic nervous system is stimulated to increase the blood supply and energy to the brain, making the individual feel refreshed after

waking (Gall, 1996). A lack of restful sleep can lead to increased sleepiness and fatigue during the day (Piper, 1993). Therefore, sleep disturbance that causes exhaustion may lead to physical changes and inevitably to fatigue (Dixon & Hickey, 1993; Nail & Winningham, 1995).

Sleep disturbance is a common complaint in women with breast cancer (Ancoli-Israel, Moore, & Jones, 2001; Knobf, 1986; Silberfarb, Hauri, Oxman, et al., 1993). Previous studies on sleep in cancer patients indicate that patients' complaints range from difficultly falling asleep to difficult staying asleep with frequent and prolonged night time awakenings both prior to (Cimprich, 1999) and during treatment (Engstrom, Stroh, Rose, et al., 1999; Owen, Parker, & McGuire, 1999). Reports of sleep problems in cancer patients suggest that disrupted sleep may play an important role in the discomfort experienced by these patients; however, sleep disturbances have received inadequate attention (Yellen & Dyonzak, 1996).

Owen et al. (1999) compared sleep quality in cancer patients with different types of cancer and healthy subjects. They found that cancer patients reported significantly poorer overall sleep quality and more daytime dysfunction than did healthy subjects.

Tucker (1998) examined the incidence and characteristics of sleep disturbance in 67 women with breast cancer receiving chemotherapy during seven days following initial chemotherapy treatment. The incidence of insomnia over the week ranged from 54-64%; a dramatically higher incidence than previously documented in community-based surveys. Participants most commonly reported early morning awakenings, followed by difficulty in maintaining sleep and difficulty initiating sleep, respectively.

In another survey, Engstrom and colleagues (1999) investigated sleep alterations in 150 patients with lung cancer (n= 57) and with breast cancer (n= 93) in various stages with different treatments. Although 44% reported a sleep problem, only 17% communicated the problem to their health care provider. Engstrom and colleagues later interviewed an additional 42 patients and found 45% (n= 20) reported a sleep problem in the previous month, of which half rated it as moderate, severe, or intolerable. Of those who reported a sleep problem, 90% (n= 18) complained of waking during the night, 85% (n= 17) complained of sleeping fewer hours than normal, 75% (n= 15) complained of difficulty falling back to sleep, and 39% (n= 8) reported napping at unusual times. The findings help identify the type of sleep complaints that cancer patient experience.

Relationship of Sleep Disturbance to Fatigue

Research findings support a positive relationship between sleep disturbance and fatigue in breast cancer patients receiving chemotherapy (Berger & Farr, 1999; Berger & Higginbotham, 2000; Broeckel et al, 1998; Dalopakarn, 2002; Davidson et al., 2002; Pritsanapanurungsei, 2000). Berger and Farr (1999) reported that women receiving chemotherapy for breast cancer who had sleep disturbance, more daytime sleep and night time awakening, reported more fatigue.

Later, Berger and Higginbotham (2000) conducted a prospective, descriptive study to examine relationships between activity, sleep, symptom distress, health status and fatigue during and following adjuvant chemotherapy—doxorubicin and cyclophosphamide—in 14 women with stage I or II breast cancer receiving four cycles of chemotherapy. The study showed that women had difficulty obtaining

quality sleep during and following chemotherapy, and approximately half of the sample experienced prolonged total rest time and trouble falling back to sleep. Further, women with higher fatigue had less efficient sleep, spent more time in bed and awake during the night than those with lower fatigue. Fatigue was also found to be correlated with symptom distress, lower activity, and poorer physical and social health status. Despite the limitation of a small sample size, these findings suggest that individualized intervention to manage symptoms, promote sleep, and encourage pacing of activity/rest cycles may assist in modifying fatigue and maintaining quality of life during and following chemotherapy.

In a cross-sectional study of 982 cancer patients, Davidson and colleagues (2002) examined the nature and prevalence of sleep problems. The most prevalent problems for the women with breast cancer were fatigue (48%), insomnia (38%), and excessive sleepiness (28%). Recent cancer treatment was associated with excessive fatigue and sleepiness regardless of type of cancer. Patients with insomnia identified waking several times as the most common type of insomnia (76%) followed by trouble falling asleep (44%), waking for a long time (35%), and waking up too early (33%). The most frequently identified contributors to insomnia were thoughts, concerns, and pain/discomfort. In a logistic regression analysis, one of variables associated with increased risk of insomnia was fatigue (β= .25, OR= 2.49, 95% CI = 1.75-3.55). That is, patients who reported being overly fatigued were 2.5 times more likely to have insomnia than others (Davidson et al., 2002).

In Thailand, Pritsanapanurungsie (2000) conducted a study which aimed to examine the relationship between fatigue and sleep disturbance among 30 breast cancer patients receiving the first-three courses of chemotherapy. Instruments

included the Piper Fatigue Scale and the Sleep Disturbance Scale. Results found that after receiving chemotherapy, a positive relationship ($p < .01$) between fatigue and sleep disturbances during all three courses of chemotherapy ($r = .468$, .567, and .540, respectively) were noted. This was consistent with Dalopakarn's cross-sectional study, which found a negative correlation between sleep quality and fatigue ($r = -.654$, $p < .05$) in 160 breast cancer patients receiving chemotherapy (Dalopakarn, 2002).

Relationship of Sleep Disturbance to Anxiety and Depression

Inadequate or unrefreshed sleep may be important not only to the expression of fatigue, but also to the patient's quality of life and treatment tolerance. In addition, it may influence the development of mood disorders and clinical depression (Ancoli-Israel, Moore, & Jones, 2001). Sheely (1996) suggest that sleep disturbance is associated with pain, which is one element of symptom distress, as well as with psychological distress, including anxiety and depression symptoms. Broeckel and colleagues (1998) also found a positive relationship among fatigue, depression, poor sleep quality, and sleeping during the day in breast cancer patients.

Moreover, Redeker, Lev and Ruggiero (2000) examined the relationship among insomnia, fatigue, and psychological factors of anxiety and depression in 263 cancer patients (18% breast cancer) undergoing chemotherapy. They found that insomnia, fatigue, depression and anxiety had a positive correlation with one another ($r = .26$ to $r = .69$, $p< .001$). Similar to these findings, Dalopakarn (2002) found in Thailand that quality of sleep was negatively related to depression in women with breast cancer receiving chemotherapy ($r = -.480$, $p < .01$).

Social Patterns

Social patterns influence fatigue and are comprised of support from individuals who are close to the patients and to the patient's perceived social support, cultural beliefs and economic factors (Piper et al., 1987). Social support and Buddhist practices were represented as socio-cultural in social patterns in this study.

Social Support

Social support is an important and interesting concept studied in socio-psychological and health behavior as well as in nursing science for a long time. It has been proven to be a predictor of physical and psychological well-being, an effective coping resources, and a buffer against stressful experiences as well as symptoms (Uphold, Lenz, & Soeken, 2000).

Definition of Social Support

The concept of social support has been used extensively in both the theoretical and research literature. However, there is a lack of agreement about the definition of social support, nor is there consensus on the measurement of social support (Hupcey, 1998; Stewart, 1993; Thoits, 1995). Its definition depends on the perspective of the theorist. According to the literature, social support can be described in two dimensions as structural and functional (House, 1981; Stewart, 1993; Thoits, 1995).

Structural dimension of support refers to the providers of supportive actions or social networks such as family, friends, neighbors, or co-workers (House, 1981; Stewart, 1993; Thoits, 1995).

Functional dimension of support refers to various types of assistance available or actually received. Functional social support includes emotional, instrumental (tangible), informational, and appraisal support (House, 1981; Stewart, 1993; Thoits, 1995).

Emotional support involves the provision of care, empathy, trust, and love (House, 1981; Krause, 1986). Moreover, Cobb (1976) defined emotional support as being cared for, loved, esteemed, valued, and belonging to a network of mutual obligation. Further, Kahn and Antonucci (1980) and Norbeck and colleagues (1981) found emotional support to be an affective form of assistance composed of admiration, respect, and love. According to House (1981), emotional support is the most important type of support, which improves psychological adjustment (Funch & Mettlin, 1982; Kaveevivitchai, 1993).

Instrumental support involves the provision of tangible goods and services, or tangible aid, such as financial assistance or performing tasks for others (House, 1981; Krause, 1986). This support appeared to improve disposition and physical recovery (Funch & Mettlin, 1982).

Informational support refers to the provision of knowledge or information relevant to the particular situation that an individual is experiencing, such as during the time of stress (House, 1981) and during the problem-solving process (Tilden & Weinert, 1987). Informational support may be beneficial when provided by health care professionals (Dunkel-Schetter, 1984; Fridfinnsdottir, 1997).

Appraisal support refers to affirmation, feedback, or social comparison (House, 1981). Kahn and Antonucci (1980) also defined appraisal support as affirmation support, including expressions that assure the appropriateness

of acts or statements made by another. This type of support tends to relieve uncertainty and emotional distress (Mishel & Braden, 1987). Therefore, different types of social support have different effects.

Family Support and Friend Support as a Social Support in Breast Cancer

Three main sources of support for breast cancer patients have been identified: family, health care professionals, and other patients or friends (Meyerowitz, et al., 1979). However, the findings from a meta-synthesis study that clarified social support among 47 qualitative studies indicates that social support networks consist primarily of family and friends, and not health care professionals (Finfgeld-Connett, 2005). Therefore, in this study social support refers to the perception of support provided by family members and friends that was measured by Family APGAR and Friend APGAR Questionnaire (Smilkstein, 1978, 1982).

Smilkstein and colleagues (1982) noted, " Family is the first and frequently the foremost of social support systems…" (p. 311). Further, they suggest that friends are also relevant to an individual. In addition, Smilkstein (1978, 1982) defined family support and friend support as the provision of assistance given by family members or friends including adaptation, partnership, growth, affection, and resolve/ commitment.

Functional dimensions of family support and friend support. Family support and friend support used in this study are comprised of adaptation, partnership, growth, affection, and resolve (Smilkstein, 1978).

Smilkstein (1978, p. 1232) stated that a*daptation* is the utilization of intra and extra familial resources for problem solving when family equilibrium is stressed

during a crisis. *Partnership* is the sharing of decision making and nurturing responsibilities by family members. *Growth* is the physical and emotional maturation and self-fulfillment that is achieved by family members through mutual support and guidance. *Affection* is the caring or loving relationship that exists among family members. *Resolve* is the commitment to devote time to other members of the family for physical and emotional nurturing. It also usually involves a decision to share wealth and space.

Considering the functional dimensions of support of Smilkstein (1978), Norwood (1996) noted that adaptation and resolve were equal to aid; partnership and growth were equal to affirmation; and affection was equal to affect.

According to three key elements of social support, Kahn and Antonucci (1980) referred affect to emotional support, and affirmation to appraisal support, as well as aid to instrumental support. Therefore, in this study, family support and friend support is composed of three types of support: emotional support, instrumental support, and appraisal support.

Effects of Family Support and Friend Support on Fatigue

Previous studies have indicated that social support in terms of family support and friend support is a predictor of psychological well-being and physical health that decrease fatigue, anxiety, and depression.

Relationship of Family Support and Friend Support to Fatigue

Women with cancer who have family or friends that are available to assist them with their daily responsibilities are able to rest more when needed. The

availability and quantity of social support have an important effect on the subjective perception of fatigue in women receiving chemotherapy (Jamar, 1989). Social support, including family support and friend support, is influential in the patient's adjustment to breast cancer (Feather & Wainstock, 1989; Kaveevivitchai, 1993), and is believed to influence fatigue perception.

Few studies have examined the effects of social support on fatigue in cancer patients. However, those results are consistent in that social support has a negative or inverse relationship with fatigue (Dalopakarn, 2002; Jamar, 1989).

Jamar (1989) conducted a one-time, semi-structural interview among 16 women with ovarian cancer in various stages at various points during their chemotherapy regimens. The degree of social support was determined by selected demographic variables, single versus married; living alone versus living with someone else. No formal measure of social support was used. Single parents and women without assistance in the home were found to have higher fatigue levels than married women ($p < .01$).

Dalopakarn (2002) conducted a cross-sectional study to examine factors related to fatigue in 160 Thai women with breast cancer receiving chemotherapy. The results showed that social support composed of emotional, instrumental, information, and appraisal support, had a significantly negative relationship to fatigue ($r = -.411$, $p < .001$).

Relationship of Family Support and Friend Support to Anxiety and Depression

Theoretically, the perception of social support, including family support and friend support, as the perception that an individual is accepted and valued in the individual's interpersonal environment bolsters esteem, confidence, and efficacy, which guard against psychological distress including anxiety and depression (Stice, Rogan & Randall, 2004). The stress-buffering model asserts that social support mitigates the relationship between stressful life events and depression (Windle, 1992).

Roberts, Cox, Shannon and Wells (1994) explored the effects of perceived social support from friends, family, and spouses on psychological adjustment among 135 newly-diagnosed breast cancer patients. The results showed that social support improved psychological adjustment. This finding is congruent with Kaveevivitchai's (1993) study that found social support decreased stress and psychological distress among Thai women with breast cancer. Moreover, deficits in perceived support predicted future increases in depressive symptoms, especially in females (Stice & Bearman, 2001; Windle, 1992).

In terms of peer support or support from other cancer patients, the patients' mood significantly improved when participating in a cancer support group with those who did not (Spiegel, Bloom & Yalom, 1981). In addition, a lower level of anxiety and depression in breast cancer patients who attended a support group was noted in a previous study (Irvine, Brown, Crooks, Roberts & Browne, 1991). Finally, coping and survival time improved among metastatic breast cancer patients who attended a support group (Spiegel, Bloom, Kraemer, & Gottheil, 1989; Goodwin et al., 2001).

Dalopakarn (2002) conducted a cross-sectional study to examine factors related to fatigue in 160 Thai women with breast cancer. The results showed that social support had a significantly negative relationship to depression ($r = -.424$, $p < .001$).

Interrelations Among Family Support, Friend Support, Pain, Nausea and Vomiting, and Sleep Disturbance

Bloom (1982) reported that the perception of social support, measured by family cohesiveness and frequency of social contact, is the strongest predictor of healthy coping responses to mastectomy. Successful adjustment has been found in women with breast cancer who experience communication and support from others, believe they have control over their disease process and side effects of treatment, and take responsibility for changing their lifestyle by complying with medical regimens (Kaveevivitchai, 1993). As such, social support is negatively associated with side effect symptoms from disease and treatment including pain, nausea and vomiting.

Dalopakarn (2002) conducted a cross-sectional study to examine the factors related to fatigue in 160 Thai women with breast cancer. The results showed that social support had a significantly negative associated with symptom distress ($r = -.33$, $p < .001$) that included pain, nausea and vomiting, and sleep disturbance.

Recently, Rustoen, Wahl, Hanestad, Lerdal, Paul, and Miaskowski (2004) studied gender differences in pain among Norwegian adults. They found that in women, marital status explained a significant amount of the variance in pain. Widows reported higher pain intensity scores than did married women. Thus, perceived

support from family, including spouse support, is negatively associated with pain intensity.

Family Support and Friend Support in Thai Culture

In Thai culture, a family holds strong intimate relationships with other family members. Closely connected, family members therefore are responsible for providing support to a family member who is suffering from an illness (Caffrey, 1992; Charoenkitkarn, 2000; Phengjard, 2001). Studies in Thailand reveal that social support, including support from family and friends, is essential for survival and adaptation to a serious illness (Chanpuang, 1991; Janda, 2002; Yanwaree, 2002). However, limited studies have explored the effect of social support on fatigue in cancer patients (Dalopakarn). Therefore, family and friend support should be explored in this study.

Buddhist Practices

Buddhism is the major religion (95%) in Thailand and therefore plays an important role among Thais, especially when they become ill (Komin, 1990; Pongpruk, 1998). As such, Buddhist teachings greatly influence how people deal with a serious illness and accept suffering (Pongpruk, 1998). Buddhists believe in Karma as a source of dealing with negative feelings and problematic situations that arise during treatments, including cancer (Pongpruk, 1998; Junda, 2004). Further, Thais perform Buddhist practices to acquire “Boon” or merit by giving food to the monks; as an offering, building and renovating temples; and by showing kindness and compassion to all living creatures (Khantipalo, 1995). Consequently, Buddhism

profoundly influences a Thai's daily life (Pongpruk, 1998; Sethabouppha, 2001). In this study, Buddhist practices act as socio-cultural events in the social patterns of the PIF model that influence fatigue.

Effects of Buddhist Practices on Fatigue

Research documents show that Buddhist practices operate as a mediator variable between physical symptom distress and psychological distress, as well as between physical symptom distress and fatigue.

Buddhist Practices as a Mediator Variable Between Symptom Distress and Psychological Distress

Several qualitative female cancer studies (Chaithaneeyachati, 2002; Chunlestskul, 1998; Junda, 2004; Kaveevivitchai, 1993; Pongpruk, 1998; Tiansawad & Jaruwacharapanichkul, 1997) found that when facing suffering from cancer treatment including pain, nausea and vomiting, and sleep problems, Thai women often perform Buddhist practices such as praying, making merit (giving money or food to monks), listening to dharma tapes, and practicing meditation, in order to cope with their suffering from disease and treatment. Thus, Buddhist practices as coping strategies are significant predictors of patients' stress level. In addition, Buddhist practices promote positive attitudes that contribute to positive hope. Hope is another way of reinterpreting negative thought process contributing to decrease in psychological distress that includes anxiety and depression.

Meditation, a popular Buddhist practice, is a way of mindfulness through the contemplation of body, feeling, and mind; or development and cultivation of the mind

(Bhavana, n.d.). People who practice right concentration will achieve mindfulness or inner freedom from suffering (Chaithaneeyachati, 2002; Pongpruk, 1998). In addition, the ways of practice in keeping the Buddha's precepts (Sila), donating or giving material things or making merit to support bhikkhus, and giving to the poor (Dana), are widely performed by Thais to help them feel good and peaceful, as well as to found wholesome mental states (Khantipalo, 1995). Previous studies show that Buddhist practices are helpful in relieving psychological distress in the form of anxiety and depression, in particular in people who suffering from AIDS (Dane, 1992), burns (Setakasikorn, 1997), and rheumatoid arthritis (Petmaneechote, 2000).

Women with AIDS in northern Thailand reported that meditation helped them to gain strength, relax, and think positively (Dane, 1992) which contributed to peace of mind, and relieving emotional distress.

Setakasikorn (1997) conducted a quasi-experimental study to examine the effects of Buddhist meditation in 20 burn patients. The results indicated that the experimental group significantly reduced anxiety while the control group experienced increased pain and anxiety after intervention. A comparison between the two groups revealed that the experimental group felt relaxed and less anxiety than the control group. These findings are consistent with Petmaneechote's (2000) study in Thai rheumatoid arthritis patients, who found that the mean scores of anxiety in the practicing group were statistically lower than those of the control ($p < .05$).

Therefore, Buddhist practices may be a mediating variable between physical symptoms and psychological symptoms. However, the direct or indirect relationship of Buddhist practices with fatigue through psychological symptoms has not been

examined. Thus, in order to explain the connection between Buddhist practices and fatigue during chemotherapy, the relationship needs to be studied.

Relationship of Buddhist Practices to Fatigue

Even though the relationship between Buddhist practices and fatigue in cancer patients has not been tested directly, there are several fatigue management studies showing that Thai women use Buddhist practices for relieving fatigue, both in cancer patients receiving chemotherapy (Kongsaktrakul, 2004; Pritsanapanurungsie, 2000), and postpartum women (Theerakulchai, 2004).

Pritsanapanurungsie (2000) studied factors related to fatigue and self-care in Thai breast cancer patients receiving chemotherapy, and found that 60% of participants used Buddhist practices such as listening to dharma tapes, praying, and practicing meditation, as self-care actions to deal with fatigue. These practices were highly effective in relieving fatigue. Kongsaktrakul's (2004) found that 80.8% of the participants, including breast and lung cancer patients, listened to dharma tapes, but only half used meditation as strategies to manage fatigue.

Further, Buddhist practices were found to help manage fatigue in postpartum women. Theerakulchai (2004) studied fatigue and fatigue management in Thai postpartum women, and found that participants performed merit making, praying, and meditation, which helped prevent psychological fatigue.

Psychological Patterns

According to Piper and colleagues (1987), psychological patterns are defined as psychological responses to an illness and/ or therapy, which can contribute

to loss of desire to live and overall weakness resulting in fatigue. In addition, Piper proposed anxiety and depression as psychological responses in reaction to stress, which influences fatigue. In this study, therefore, psychological distress including anxiety and depression are represented as psychological patterns.

Hoskins (1997), and Thompson and Shear (1998), reported that breast cancer patients receiving chemotherapy (Schreier & Williams, 2004) were anxious and depressed. These emotions were found to have high incidence and increased continuously during treatment.

Anxiety is known to intensify physical symptoms and thus influence overall quality of life. In addition, it causes significant distress and impairment in interpersonal, social, and/ or occupational functioning. Feelings of depression are also experienced by these patients due to the sense of hopelessness, which results from anxiety (Kelter, Schwecke, & Bostrom, 1999). "Secondary depression" often arises because of anxiety, and occurs in between 30-50% of anxiety patients (Dealy et al., 1981 as cited in Thongsawan, 2000).

Depression is a common psychological disturbance in cancer patients (Andrykowski et al., 1998; Mock et al., 1997), especially among breast cancer patients receiving chemotherapy (Pasacreta, 1997). The prevalence of depression in cancer patients ranges from 15% to 70% (Newport & Nemeroff, 1998). However, most cancer studies report an incidence of mild to moderate depression from 20% to 35% (Berard et al., 1998; Bottomley, 1998; Newport & Nemeroff, 1998; Pasacreta, 1997) with higher depression in those with advanced cancer (Grassi et al., 1996). Further, symptoms of depression affect treatment outcomes, physical health, and overall quality of life.

Depression and anxiety are linked. Depression is an emotion with a strong physical side. It can often come after a period of anxiety, be caused by anxiety, or go hand in hand with it (Kelter, Schwecke, & Bostrom, 1999; Newport & Nemeroff, 1998).

Relationship of Anxiety and Depression to Fatigue

Depression is thought to be a principle cause of fatigue in cancer patients (Jacob & Piper, 1996) by depleting energy storage (Aistars, 1987). Breast cancer is considered a threatening situation. The experience of physical symptom distress resulting from cancer and treatment may further increase the degree of already existing psychological distress including anxiety and depression. Therefore, women receiving chemotherapy for breast cancer who experience distress from physical symptoms may feel psychological distress, and have a higher level of fatigue than those who do not (Nail & King, 1987). Thus, physical symptom distress contributes to psychological distress including anxiety and depression, and together contribute to fatigue.

Studies investigating fatigue in various types of cancer, including breast cancer undergoing active treatment, found that fatigue correlated with overall psychological distress including anxiety and depression. In addition, psychological distress was also found to be a significant predictor of fatigue.

Blesch and colleagues (1991) studied 77 cancer patients undergoing radiotherapy and/or chemotherapy for lung cancer (n = 33) and breast cancer (n = 44). Significant correlation of fatigue and the level of pain (r = .48), anxiety (r = .40), depression (r = .46), vigor (r = -.30), and global mood state (r = .48) were found.

Consistent with this study, Irvine and colleagues (1994) found that mood disturbance correlated with fatigue ($r = .47$, $p < .0001$) in 101 cancer patients (96% female, 62% breast cancer) receiving either radiotherapy or chemotherapy. Further, they found that symptom distress and mood disturbance together explained 33% of variance in the level of fatigue.

Dimeo et al. (1997) studied the relationship among fatigue, psychological distress and physical performance in 78 cancer patients. Intensity of fatigue showed a strong positive correlation ($p < .001$) with several indicators of psychological distress such as depression and anxiety ($r = 0.68$, and $r = 0.63$, respectively).

To examine relationships among physical symptom distress, psychological distress, and fatigue in 101 women with breast cancer receiving radiotherapy, Lam (1997) conducted a secondary analysis using path analysis. Results revealed that psychological distress had a direct effect on fatigue. Physical symptom distress had both direct and indirect effects on fatigue through psychological distress. Therefore, psychological distress is a mediator between fatigue and physical symptoms.

Redeker, Lev and Ruggiero (2000) examined the relationship between fatigue and the psychological factors of anxiety and depression in 263 cancer patients (18% breast cancer) undergoing chemotherapy. Fatigue had a positive correlation with depression and anxiety ($r = .43$ and $r = .44$, $p < .001$, respectively).

In Thailand, Dalopakarn (2002) explored factors that related fatigue in breast cancer patients. Results showed that depression was positively related to fatigue at a moderate to high level ($r = .699$, $p < .01$). In addition, depression accounted for 8% of the variance in fatigue scores.

Summary Factors Influencing Fatigue in the Study

Adjuvant chemotherapy in breast cancer represented as treatment patterns in the PIF model. Adjuvant chemotherapy is categorized to protocol with or without adriamycin. Previous research results do not show a consistent relationship between the chemotherapy protocol and fatigue severity. Thus, the chemotherapy protocol needs investigation, and it is anticipated to have a positive relationship to fatigue severity.

BMI is used to determine the nutritional status that is derived from the energy and energy substrate patterns of the PIF Model. Previous research supported a negative relationship between BMI and fatigue.

A low hemoglobin level is defined as a deficiency of red blood cells which leads to a reduction in oxygen-carrying capacity to body organs. Previous studies have documented a relationship between fatigue and anemia in cancer patients. However, the results are inconsistent, which may be accounted for by the different timepoints of measuring hemoglobin and subjective fatigue. In this study, hemoglobin levels are anticipated to have a negative direct effect on fatigue.

Pain, and nausea and vomiting as symptom distress, and sleep disturbance, are represented in symptom patterns and sleep/ wake patterns in the PIF Model. Literature reviews found symptom distress and sleep disturbance to be positively related to fatigue and psychological distress, including anxiety and depression. In addition, previous studies in breast cancer patients showed consistent results in that pain, nausea and vomiting, and sleep disturbance have a positive relationship with each other. Therefore, it can be hypothesized that pain, nausea and vomiting, and sleep disturbance are positively interrelated with each other.

Family support and friend support are identified as the major supports for breast cancer patients. Patients' perceive support from family and friend as individuals is accepted and valued by the individuals as an element of interpersonal environment that bolsters esteem, confidence, and efficacy, which in turn protect against psychological distress, including anxiety and depression. Further, family and friends contribute to a decrease of fatigue by assisting women with their daily responsibilities, so that they have more time to rest. In Thailand, however, only limited studies have explored the effect of social support on fatigue. In this study, therefore, social support in terms of family support and friend support is hypothesized to have a negative direct effect on anxiety, depression, and fatigue.

Buddhist practices are represented as socio-cultural patterns in the PIF Model. Previous literature supports the view that Thai women with cancer perform Buddhist practices when facing symptoms related to their treatment such as pain, nausea and vomiting, and sleep problems. In addition, Buddhist practices help to decrease emotional distress, promote mental health, and relieve fatigue. In this study, Buddhist practices act as a mediator variable between symptom distress and psychological distress, as well as fatigue. Therefore, Buddhist practices are hypothesized to have a negative direct effect on anxiety and depression, as well as fatigue.

Anxiety and depression are thought to be psychological patterns in the PIF Model, with depression often following a period of anxiety. Further, most studies accept that anxiety and depression are positively related to and significant predictors of fatigue. In addition, anxiety and depression are anticipated to be mediators between physical symptoms and fatigue.

The Conceptual Framework of the Study

The model for this predicting fatigue is composed of selected factors from the PIF model (Piper et al., 1987). In current study, 7 of the 14 patterns are regarded as affecting fatigue, including treatment (chemotherapy protocol), energy and energy substrate (BMI), oxygenation (hemoglobin level), symptoms (pain, and nausea and vomiting), sleep/wake (sleep disturbance), social (family and friend support, and Buddhist practices), and psychological patterns (anxiety and depression).

In this conceptual framework, women with breast cancer receive adjuvant chemotherapy (treatment patterns), including protocol with or without anthracycline agents (adriamycin), a common modality treatment for breast cancer. Previous studies (Berger, 1998; Berger & Walker, 2001) indicate that protocol containing adriamycin increased the severity of fatigue more than protocols without adriamycin treatment. Moreover, anemia or a decreased hemoglobin level as oxygenation patterns, and nutritional status in terms of body mass index as energy and energy substrate patterns, are considered factors that contribute to fatigue (Berger & Walker, 2001; Jamar, 1989; Mendoza et al., 1999; Piper et al., 1989).

The presence and the severity of pain, nausea and vomiting, and sleep disturbance, which are common side effects of chemotherapy (Boehmke, 2004; Ehlke, 1988; McCorkle & Young, 1978), are recognized as contributing to anxiety and depression (Dalopakarn, 2002; Gaston-Johansson et al., 1999; Lam, 1997), as well as to fatigue (Dalopakarn, 2002, Irvine et al., 1994; Lam, 1997). Therefore, psychological distress symptoms are considered mediating variables between physical symptoms and fatigue. Furthermore, when facing suffering, including pain, nausea and vomiting, and sleep problems, Thai women often increase performance of

Buddhist practices such as praying, keeping the five precepts (Sila), giving things or money to bhikkhus, or to the poor (Dana), and practicing meditation or developing cultivation of the mind (Bhavana) as a way of coping that helps decrease suffering and promotes their mental health, decreasing anxiety and depression (Junda, 2004; Kaveevivichai, 1993; Tiansawad & Jaruwacharapanichkul, 1997). These practices also help to relieve their fatigue (Kongsaktrakul, 2004; Pritsanapanurungsie, 2000). Therefore, Buddhist practices are viewed as a mediating variable between physical symptoms (pain, nausea and vomiting, and sleep disturbance) and psychological symptoms (anxiety and depression), as well as fatigue.

In addition, women who have other family members or friends available to assist them with their daily responsibilities, such as shopping, cooking and cleaning, are able to delegate these to others, thus allowing more rest when they need. Further, the amount of family and friend support has an effect on subjective fatigue (Dalopakarn, 2002; Jarmar, 1989) and contributes to decreased psychological distress, including anxiety and depression (Dalopakarn, 2002; Irvine et al., 1991).

Previous studies reveal that patients with cancer experience anxiety and depression related to their diagnosis and the side effects of chemotherapy (Andrykowski et al., 1998; Mock et al., 1997; Pasacreta, 1997). Anxiety can trigger depression (Dealy et al., 1981 as cited in Thongsawan, 2000; Kelter, Schwecke & Bostrom, 1999), and some researchers have found that psychological distress including anxiety and depression contributing to fatigue perception (Blesch et al., 1991; Dalopakarn, 2002; Irvine et al., 1994; Lam, 1997).

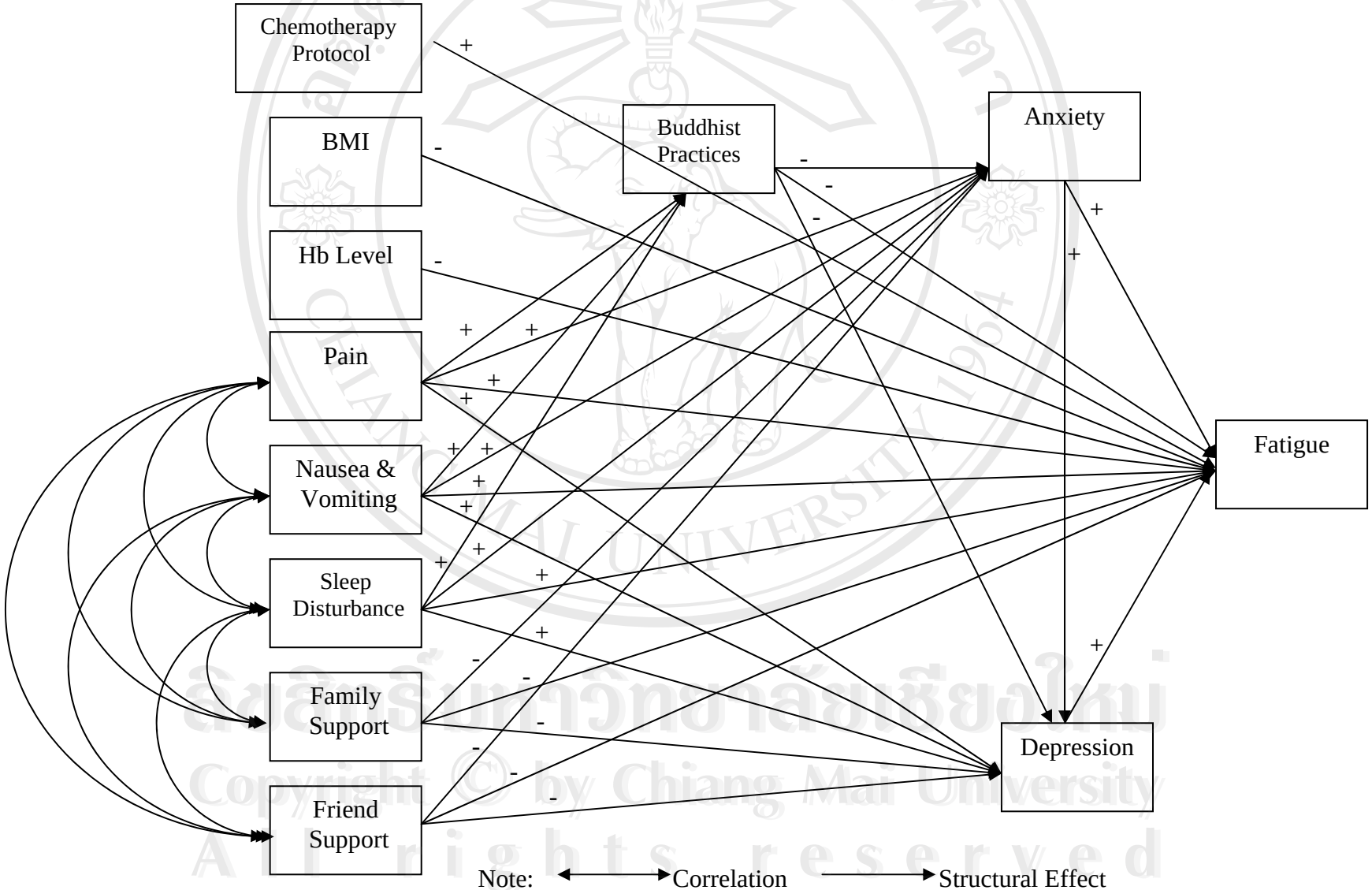
In conclusion, the model for predicting fatigue has eight exogenous variables and four endogenous variables. Exogenous variables are measured variables that are

not caused by any other variables in the model except other exogenous variables (Cohen & Cohen, 1983; Norris, 1997). Chemotherapy protocol, BMI, hemoglobin level, pain, nausea and vomiting, sleep disturbance, family support, and friend support serve as exogenous variables in this model as they have arrows coming from them but none leading to them (Page, 1993).

Endogenous variables are effects of exogenous variables and do not causally affect the exogenous variables, although the endogenous variables may causally affect other endogenous variables (Cohen & Cohen, 1983; Norris, 1997). The endogenous variables include Buddhist practices, anxiety, depression, and fatigue, as these variables have arrows pointing to them (Page, 1993). Moreover, Buddhist practices, anxiety, and depression are also mediating variables, while fatigue is an outcome variable in this model.

The variables representing patterns from the PIF model are proposed to influence fatigue among Thai women with breast cancer receiving adjuvant chemotherapy as shown in Figure 2-2.

Figure 2-2 A proposed model for predicting fatigue among Thai women receiving adjuvant breast cancer chemotherapy



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