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The Assessment and Treatment of Nausea and Vomiting Associated With Cancer Chemotherapy

Zeev Rosberger

A Thesis

in

The Department

of

Psychology

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ABSTRACT

The Assessment and Treatment of Nausea and Vomiting Associated With Cancer Chemotherapy

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Concordia University, 1988

The reliability and validity of three measures of cancer chemotherapy-related nausea were evaluated in two studies. A third study investigated the effectiveness of hypnosis as an intervention aimed at reducing the side effects of chemotherapy. In the first part of Study 1, experienced oncology physicians and nurses rated the nausea-producing potential of a number of chemotherapy drug/dose combinations. The ratings for each patient's drug set were used as external validating criteria for the nausea measures. The results of the validity studies indicated that two measures, the overall nausea intensity (ONI), and a visual analogue scale (VAS), demonstrated strong concurrent, construct, and discriminative validity in Studies 1 and 2. The third measure, the Nausea Rating Index (NRI-am), was composed of the affective and miscellaneous subscales of the McGill Pain Questionnaire. The NRI-am showed acceptable internal consistency and validity in Study 1, but not in Study 2. It was hypothesized that this scale may be sensitive to symptoms caused by illness progression which may confound patients' choice of word descriptors solely related to their chemotherapy experience. All three measures demonstrated poor test-retest reliability in Study 2. This may have

been due to sample heterogeneity, as well as uncontrolled clinical factors from initial test to retest.

In Study 3, the hypnosis intervention was effective in reducing anxiety and post-chemotherapy nausea, but not anticipatory nausea, vomiting frequency or vomiting intensity. Comparisons with similar published studies indicated that hypnosis was as effective as relaxation, but not as effective as systematic desensitization, in the reduction of nausea symptoms. The results were discussed in terms of the role of hypnotic abilities and cognitive strategies in coping with chemotherapy side effects. The hypothesis that hypnotic susceptibility might be related to anticipatory nausea was not confirmed. In spite of the difficulties in working with this patient population, it was suggested that future studies should continue to evaluate systematically such variables as hypnotic susceptibility and anxiety to clarify issues related to treatment process and successful outcome.

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Many thanks to the cast of thousands (they know who they are!) for their constant interest in the seemingly interminable process that is known as a dissertation. They won't have to ask me any more.

Lastly, to Gabi, Kara, and Talia, who gave up a good deal of quality time over the years to provide me with the opportunity to achieve this very important goal, I can only express my eternal gratitude and love. I could never have done it without them.

DEDICATION

To Harry and Max,

for what they might have done,

for what they might have become,

but never had the opportunity.

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The Assessment and Treatment of Nausea and Vomiting Associated with Cancer Chemotherapy

> Cytotoxic chemotherapy is the art of differential poisoning, the aim being to destroy the tumour before the drugs kill the patient.
>
> Priestman (1984)

The cancers are a group of almost two hundred diseases which together comprise the second largest cause of death in North America, surpassed only by coronary artery disease (Cancer Statistics, 1984, 1986; Silberfarb & Greer, 1982). The rise of the chronic diseases to the top of the mortality tables reflects in part medical advances such as the use of antibiotics earlier in this century, which significantly reduced mortality from infectious diseases such as tuberculosis. Cancer has effectively replaced tuberculosis as the dreaded "plague" of the present epoch (Sontag, 1978), although Acquired Immune Deficiency Syndrome (AIDS) is making significant in-roads.

Although recent advances in treatment have shown great promise in both achieving cure for some cancers and in increasing life expectancy beyond five years, the search for the "magic bullet" continues (Cairns, 1978; Cassileth, 1979). One of four individuals in their lifetime will develop cancer. Two-thirds of these people will survive at least five years or longer. In spite of these rather depressing statistics, survival rate, as well as the number of ostensibly curable cancers (in particular the leukemias and testicular cancers) has increased significantly in recent years (Cairns, 1978).

Until approximately twenty-five years ago, the diagnosis of cancer implied an almost certain death sentence. The greatest difficulty encountered by the diagnostician is that symptoms of cancer are usually experienced after the cancer has already proliferated and often metastasized to distal body sites. Methods of primary prevention have been developed to stimulate public awareness of the importance of early detection. Such techniques as regular breast self-examination may often result in timely and precise diagnosis of breast cancer and speed effective treatment (Alagna & Reddy, 1984). It is also well known, however, that attitudes and beliefs about the potential disruption to an individual's life and loss of feelings of control may delay help-seeking behaviour and compromise early detection (Timko, 1987).

Once diagnosis has been ascertained, numerous techniques of surgery, radiotherapy, and chemotherapy, used alone or in combination are available and continue to be developed as effective treatment interventions. However, all of these treatments have concomitant side effects which may severely impair both the physical and psychological state of the patient. Surgery may cause great distress due to potential bodily disfigurement, as in the case of breast or head and neck cancer. Radiotherapy may leave the patient with severe burns and pain, usually but not always, of a temporary nature. Since radiotherapy is time-limited and may usually only be administered once due to its own carcinogenic capacity, the transient side effects are often well tolerated by patients (Burish & Lyles, 1983; Peck & Boland, 1977).

Chemotherapy presents the patient with a set of rather unique problems. These extremely toxic medications are injected intravenously in one of two ways: push injection which may take approximately fifteen minutes or, in the case of the most toxic drugs, through an intravenous drip over a period of hours. (Only one oral chemotherapy drug is currently available; intra-

peritoneal and intra-thecal infusions are newer approaches). Chemotherapy drugs are usually given on frequent schedules (e.g., daily, weekly, monthly) that may range over the course of as long as two years. Although the side effects of an individual chemotherapy session may be short-lived, the patient must endure these symptoms repeatedly over these lengthy periods (Burish & Bradley, 1983; Melamed, 1984; Redd & Andrykowski, 1982). In recent years, some of the chemotherapy protocols have been modified radically due to the discovery that a reduced number of high-potency treatments given over shorter periods of time are just as clinically effective as the more lengthy, continuous, and potentially more stressful chemotherapeutic protocols [e.g., National Surgical and Adjuvant Breast Protocol No. B-15, (NSABP, 1984)]. The extreme importance of being able to tolerate chemotherapy side effects has been demonstrated in a study of breast cancer patients whose drug dosage was reduced to below optimum due to their intolerance of the side effects such as nausea and vomiting. Those patients reducing drug dosage had a significantly higher relapse rate of their breast cancer after five years than patients who continued on the maximally effective dosage (Bonadonna & Valagussa, 1981). Thus the ability of a patient to endure the maximum toxic chemotherapy doses is of utmost importance in determining optimal outcome.

The mode of action of chemotherapy drugs is not well understood. Chemotherapy drugs act systemically in a non-specific fashion by selectively identifying and destroying rapidly dividing cells at various stages of the cell life cycle, such as, for example, malignant cells (Cairns, 1975). However, there are other rapidly dividing cells in the body, for example in the lining of the gastrointestinal (GI) system, the dermis of the scalp, and the bone marrow. The cells of the gastrointestinal (GI) tract are constantly being sloughed and replaced, as are the cells of the hair follicle and the bone marrow which is

producing blood cells to replace those that have lost their functional ability. The chemotherapeutic drugs are unable to discriminate between these functional cells and those that are malignant. For these reasons, many of the chemotherapy drugs produce significant side effects, such as nausea and vomiting, bone marrow suppression (resulting, for example, in drops in white cell count, platelets loss, anemia and increased susceptibility to infectious disease), alopecia (hair loss) and others. There is also some evidence that cognitive functioning may be impaired in patients receiving chemotherapy, independent of changes in mood or affect (Silberfarb, Philibert, & Levine, 1980).

Whatever the physical consequences, all of these side effects may impair the patient's psychological state and quality of life severely (e.g., Priestman, 1984; Priestman & Baum, 1976; Spitzer, Dobson, Hall, Chesterman, Levi, Shepard, Battista, & Catchlove, 1981). Since a large majority of patients will eventually die from the consequences of their disease, a delicate balance must be struck between radical and often aggressive interventions affecting quantity of life and the emotional and social consequences of these treatments which likewise affect its quality.

Coping With Cancer and Chemotherapy

There is considerable evidence that cancer patients experience emotional reactions to their illness similar to those of patients diagnosed with other chronic diseases (Cassileth, Lusk, Strouse, Miller, Brown, Cross, & Tenaglia, 1984; Craig & Abeloff, 1974; Frank-Stromberg, Wright, Segalla, & Diekmann, 1984; Hughes, 1982; Meyerowitz, 1980; Silberfarb & Greer, 1982). Some findings indicate that age and the recency of the diagnosis are positively correlated with increasing psychopathology (Cassileth et al., 1984). These investigators

demonstrated that anxiety and depression correlated between .76 and .81 in a sample of 867 adult cancer patients, both in-patients and out-patients. Weisman (1976) has suggested that a history of past depression, past suicidality, the anticipation of little social support from others, and regrets about the past predicts the "vulnerability" of the cancer patient, i.e., the patient may be more likely to suffer from depression at some point during the illness.

The immediate anxiety and depression following diagnosis appears to be followed by a period of adaptation and habituation for many patients, although they may still have many illness or treatment-related concerns (Meyerowitz, 1980). For example, breast cancer patients undergoing adjuvant chemotherapy reported greater physical discomfort, but an equivalently high number of specific symptoms such as fatigue, irritability, and nervousness, when compared to a mastectomy-only group of women (Meyerowitz, 1981). A rather striking finding is that sixty percent of women receiving adjuvant chemotherapy feel that they would have been more anxious and depressed if they had not been receiving further treatment (Meyerowitz, Sparks, & Spier, 1979). These patients are more reassured by continued and more frequent treatments as indicating that their disease is being controlled, than by the uncertainty that might occur if they were receiving no treatment at all, in spite of the fact that they may be experiencing greater overall discomfort (Meyerowitz, 1981).

From these data, it is clear that post-mastectomy patients will experience much ongoing psychological distress, whether they receive adjuvant chemotherapy or not. Meyerowitz has concluded from these data that the initial optimism of disease free, aggressive treatment is supplanted by increased distress as chemotherapy progresses. This increase is due to recurrent, stressful side effects and worries regarding the effectiveness of

continued treatment, in spite of the fact that decreased treatment frequency might logically reduce patients' anxiety.

Because of this distress, breast cancer patients wish to develop both cognitive and behavioural control over their disease and its treatment (Taylor, Lichtman, & Wood, 1984a). On another level, however, they must be willing to give up a measure of this control to the physician, who ostensibly has the expertise to control the disease process (Taylor, Lichtman, & Wood, 1984b). The need for cancer patients to maintain some degree of mastery and/or control over an illness whose treatment invariably demands giving up some control, combined with the unpredictable course of the disease, make coping with cancer somewhat different from most other diseases (Silberfarb & Greer, 1982). Events that are perceived to be both undesirable and uncontrollable are ones that will most often lead to personal distress (Suls & Mullen, 1981). In this regard, a solid and supportive working rapport with the treating physician has always been of primary importance in giving the patient this sense of control (Sutherland,1956/1981).

It has been suggested that cognitive adaptation or control over a threatening event such as cancer chemotherapy, which may involve such factors as the placing of the experience in a meaningful context, assuming mastery over this life threatening and unpredictable situation, and retaining self-esteem is important in maintaining the motivation necessary to continue with the treatment process (Taylor, 1983; Taylor et al.,1984a). This position has been questioned by Nerenz, Coons, Lasky, Leventhal, & Love (1984) who surveyed 238 patients with breast cancer or lymphoma over the course of six chemotherapy sessions. In general, many of these patients were not interested in why they had their disease or how to cope with it or its treatment, contrary to the findings of Taylor et al. (1984a, b). The patients in

Nerenz, Coons, et al.'s (1984) study were primarily from a rural Wisconsin population, while Taylor et al.'s patients were urban Californians, indicating that socioeconomic and possibly cultural differences may influence coping processes.

The number of side effects and not the duration or severity of chemotherapy-related symptoms correlate with perceived distress (Nerenz, Leventhal, Love, & Ringler, 1984). Patients are resentful that they must continue treatment even when there are no longer any palpable physical signs of the disease, but will still attribute vague side effects of treatment such as fatigue, to indications of further disease progression rather than due to the treatments (Nerenz, Leventhal, & Love, 1982). Older patients experience fewer symptoms (especially nausea, vomiting, and fatigue), and report less distress in general (Morrow, 1982, 1984; Nerenz, Love, Leventhal, & Easterling, 1986).

It appears that the ability of a cancer patient to cope with the illness and the subsequent vicissitudes of chemotherapy may depend on several factors. First, the patient's history of coping with stressful life events, as well as current factors such as social support will affect coping effectiveness. Second, the patient's ability to develop mastery over the course of the illness and treatment by actively seeking out new coping strategies or utilizing denial (Hackett & Cassem, 1974) will increase effective adaptation. Third, the patient's perception that the disease is 'disappearing' either by objective evidence (such as positive test results or the ending of a treatment) will allow the patient to return to more functional modes of living without the constant preoccupation with the illness and its symptoms, although this finding is somewhat equivocal (Nerenz et al., 1982). Understanding the myriad factors affecting the chemotherapy patient's coping abilities is vital in the

development of assessment and treatment methods for more specific side effects such as nausea and vomiting.

Nausea and Vomiting as Chemotherapy Side Effects

Nausea and vomiting are probably the most severe, intense and least dignified of the many side effects of cancer chemotherapy treatment. Although common, these side effects are not experienced by all patients nor with all drugs. Patients undergoing radiotherapy treatments may also experience gastrointestinal effects, especially if the radiation is given over the abdominal or cranial areas (Kurohara, George, Levitt, & Rubin, 1966; Parsons, Webster & Dowd, 1961; Peck & Boland, 1977; Stoll, 1962).

Nausea and vomiting, though often discussed simultaneously or interchangeably, should be carefully distinguished as separately occurring events which may or may not be independently observed (Morrow, 1984). Nausea has been defined as "an experience of mental distress referred to the gut, and it may or may not be accompanied by vomiting" (Borison & McCarthy, 1981, p.33). Penta, Poster, Bruno, Abraham, Pinna, & MacDonald (1981a) have defined nausea as the recognition of the desire to vomit. Retching is the forced rhythmic respiratory movement that may precede vomiting. Vomiting occurs when the striated muscles of the body wall contract (as in breathing), which forces the oral expulsion of the gastric contents. The non-mechanical expressions of the emetic response are autonomically mediated. For example, salivation, swallowing, yawning, sweating, pallor, tachycardia, weak pulse, feeling of faintness, headache, and diarrhea result from both sympathetic and para-sympathetic discharges (Borison & McCarthy, 1981; Ganong, 1979).

Nausea and vomiting are adaptive responses under normal

circumstances, such as the inadvertant ingestion of a toxic substance (Weddington, 1982). In the case of chemotherapeutic drugs for cancer treatment, this mechanism becomes a maladaptive one. The severity of vomiting may be so intense that in some cases skeletal fractures (Whitehead, 1975) and tearing of the gastric mucosa have been observed (Penta et al., 1981a). Some patients terminate therapy due to the extreme distress they experience because of chemotherapy-induced nausea and vomiting (Blotcky, Cohen, Conaster, & Klopovich, 1985; Penta, Poster, & Bruno, 1983; Schulz, 1980; Taylor et al., 1984b; Wilcox, Fetting, Nettesheim, & Abeloff, 1982). For many patients, risking the inevitable consequences of stopping treatment in spite of favourable disease response to the drugs is often preferable to the "living hell" they might experience every week or two for extended periods. In these instances, finding adequate antiemetic methods becomes of paramount importance.

Nausea and vomiting associated with chemotherapy may vary greatly from patient to patient in duration, frequency, and intensity (Durant, 1984; Morrow, 1984). Great differences exist between drugs in their nausea and emesis-producing potential (Laszlo & Lucas, 1981; Penta et al., 1981a, 1983; Penta, Poster, Bruno, & Jacobs, 1981b).The toxicity of the chemotherapy agents is related primarily to the dose of the drug. Tumour responsivity to the drugs is also dose related. The <u>therapeutic index</u> is the ratio of the doses at which therapeutic effect and toxicity occur. A higher therapeutic index is the best of all possibilities providing maximum therapeutic benefit and minimum gastrointestinal toxicity. For many drugs, however, the optimum index occurs at a highly toxic dose (Cadman, 1973). It has been suggested that effective combinations of chemotherapeutic drugs which maximize the therapeutic index should be investigated (Wampler, Carter, & Williams, 1978).

Drugs such as cis-platinum, adriamycin, and nitrogen mustard are generally considered to be the most toxic of the chemotherapy drugs. Effective and commonly used drugs for breast cancer such as 5-Fluorouracil, have virtually no gastrointestinal effects when given alone. There has been little attempt to evaluate the relative nausea and vomiting-producing potential of the various chemotherapy drugs (cf. Morrow, 1984c). The reasons for the individual differences in patients' responses are unclear from the physiological perspective, though such factors as age (e.g., Chang, Shiling, & Stillman, 1979; Morrow, 1982, 1984; Nerenz et al., 1986), and susceptibility to motion sickness (Morrow, 1984b) may be important intervening variables. Certain behavioural factors may also be implicated (e.g., Morrow, 1982; Redd & Hendler, 1984). These variables will be examined below in more detail.

Neurophysiology of Nausea and Vomiting

There is a vomiting centre located in the medullary reticular formation of the brain, just below the area postrema. The area postrema is a group of neurons located at the base of the fourth ventricle and is in direct contact with the cerebrospinal fluid. This group of neurons has come to be known as the chemoreceptor trigger zone (CTZ). Experimentally, it has been demonstrated that the area postrema is sensitive to challenge by known emesis-producing substances, such as copper sulphate (Borison & McCarthy, 1981; Penta et al., 1983). It is likely that circulating chemotherapy drug metabolites may be carried systemically and be recognized as toxic by the CTZ. It is not as clear whether the metabolites of cell breakdown caused by the cytotoxic action of the drugs may also be recognized and stimulate the CTZ. Since the CTZ is connected to the vomiting centre located just below it, this obviates the need for an explanation of direct neural innervation of the vomit centre without

the crossing of the blood-brain barrier. In fact the respiratory, olfactory, and taste centres are located in close proximity, accounting for the well-known involvement of these responses in the emesis cycle. In addition to the direct innervation of the vomit centre by the sympathetic nervous system, various other visceral afferents and connections from the limbic system and the neo-cortex influence the development of nausea and vomiting (Borison & McCarthy, 1981; Ganong, 1979; Penta et al., 1981a, 1983). The involvement of the limbic system accounts, at least theoretically, for the emotional concomitants often observed in the development and maintenance of nausea and vomiting. Innervation from cortical centres indicates that behavioural influences are also important. These will be discussed in a later section.

Parameters of Chemotherapy-Induced Nausea and Vomiting

The course of the development of post chemotherapy nausea and/or vomiting is rather unpredictable and certainly not well understood. Symptoms may be fairly mild at first and escalate in intensity and duration with successive treatments. For example, 49 children receiving 18 different protocols of from 1-6 drugs showed no discernible pattern of the development of nausea and vomiting, even when a drug was either added or taken away (Zeltzer, LeBaron, & Zeltzer, 1984a). Zeltzer & LeBaron (1984) discovered that by changing the dose concentration and rate of administration of doxorubicin to a child, they were able to reduce nausea, vomiting, and even alopecia significantly, although the advent of hot summer weather seemed to have the opposite effect, regardless of the rates of administration.

Nausea and vomiting may begin anywhere from 1-12 hours subsequent to the presentation of the chemotherapy drugs, may last longer than 48 hours, and may often be unremitting during that time (Frytak & Moertel, 1981;

Harris, 1978; Holland, 1977; Holland, 1982; Morran, Smith, Anderson, & McArdle, 1979). By contrast, patients receiving high doses of cyclophosphamide rated their level of nausea and vomiting as highest approximately 12 hours after the infusion (Fetting, Grochow, Folstein, Ettinger, & Calvin, 1982). Some patients may experience these symptoms, especially nausea for some days or even for a week, leaving little time for recovery of strength and motivation prior to the anticipation of the next treatment (Holland, 1977). As many as 83% of women receiving a common treatment for Stage II breast cancer, a combination of cyclophosphamide, 5-fluorouracil and methotrexate (CMF), may experience nausea and vomiting (Morran et al., 1979). Generally, it has been found in most clinics that post chemotherapy nausea and vomiting occurs in 38% (Schulz, 1980) to 83% (Wilcox et al., 1982) of patients depending on the diagnosis and the particular treatment protocol.

The frequency, intensity, and duration with which patients experience nausea and vomiting is clearly of great concern to both the patient and to the treating physicians, due to their severely disruptive effects on the patients' lives. In recent years, psychological approaches to the reduction of nausea and vomiting have evolved; these will be reviewed in a later section. The most widely researched attempts to diminish nausea and vomiting, however, have been pharmacological.

Pharmacological Treatment of Nausea and Vomiting

A number of years ago, Whitehead (1975) severely criticized the efficacy of the available drugs (known as antiemetics) to combat the problem of nausea and vomiting and made a plea for more research into this most difficult of

problems. Systematic studies evaluating the relative efficacy of the antiemetics have since been performed and reviewed extensively (Morrow, 1984c; Penta et al., 1983).

Numerous classes of drugs have been evaluated for their potential as antiemetic agents. These classes have included minor tranquilizers such as diazepam; major tranquilizers such as the phenothiazine chlorpromazine; antihistamines; glucocorticosteroids such as dexamethasone or methylprednisolone; cannabinoids (THC) such as nabilone, which are derivatives of the cannabis sativa plant; and other drugs such as domperidone, and metoclopramide (Eyre & Ward, 1984; Frytak & Moertel, 1981; Harris, 1978; Seigel & Longo, 1981). Overall results with these drugs when evaluated empirically in controlled studies have been discouraging. A review of 57 studies published up to 1981 concluded that the currently marketed drugs were of "marginal value for the treatment of nausea and vomiting" (Penta et al., 1981a, p. 1).

Minor tranquilizers act as relaxation agents and are most likely to help extremely anxious patients. The major tranquilizers are thought to act centrally as dopamine antagonists by blocking the CTZ. Reductions in nausea and vomiting by as much as 60% have been reported with this class of drugs (Plotkin, Plotkin, & Okun, 1973). Other drugs such as domperidone, and metoclopramide work by promoting gastric motility and emptying. It is felt that gastric stasis is one of the problems contributing to nausea and vomiting (Penta et al., 1981a,1983). The glucocorticosteroids are thought to work by inhibiting the production of prostaglandins, which may be implicated in the genesis of nausea and vomiting (Rich, Abulnayoglu, & DiSaia, 1980). The mechanism of action of the cannabinoid derivatives is unknown at present.

One of the greatest problems with many of these drugs is the fact that they

have side effects of their own which may be difficult to tolerate (Clark & Dundee, 1971; Eyre & Ward, 1984; Frytak & Moertel, 1981; Harris, 1978). Dry mouth, somnolence, dizziness, and orthostatic hypotension are just several of the undesirable effects which may prevent patients from taking these drugs (Seigel & Longo, 1981). The cannabinoids have proved to be extremely effective in controlled trials when compared to placebos (Sallan, Zinberg, & Frei, 1975) or to a phenothiazine (Sallan, Cronin, Zelen, & Zinberg, 1980). Also, they were preferred by some patients receiving both types of drugs in a double blind trial (Sallan et al., 1980), but not by others (Ungerleider, Andrysiak, Fairbanks, Goodnight, Sarna, & Jamison, 1982). Difficulties in tolerating cognitive-perceptual changes and increasing age appear to be limiting factors in the use of THC (Chang et al., 1979; Frytak, Moertel, & O'Fallon, 1979; Herma, Jones, Dean, Leigh, Dorr, Moon, & Salmon, 1977; Laszlo, 1979; Lucas & Laszlo, 1981). The effectiveness of the cannabinoids as antiemetics remains extremely controversial (Frytak, 1980; Sallan & Cronin, 1980).

Other antiemetics such as metoclopramide, droperidol, and the steroids have shown promise in diminishing nausea and vomiting, especially at doses higher than generally prescribed (Gralla, Itri, Pisko, Squillante, Kelsen, Braun, Bardin, Braun, & Young, 1981; Grosman, Lessin, & Cohen, 1979; Mason, Dambra, Grossman, & Catalano, 1982).

In determining effective pharmacologic management of nausea and vomiting, a number of factors need to be considered carefully. First, it is of greatest importance that patients be given antiemetics prophylactically prior to their first chemotherapy treatment (Frytak & Moertel, 1981). When patients are given drugs known to have high emetic potential, contemporary experience dictates that it is unethical to withhold effective antiemetics in the

clinical situation (Laszlo, 1983).

In addition, the longer the patient experiences nausea and vomiting while undergoing chemotherapy without adequate antiemetic treatment, the more likely that these side effects will become progressively more severe (Andrykowski, Redd, & Hatfield, 1985; Morrow, 1982; Nesse, Carli, Curtis, &Kleinman, 1980). This may result not only in greater suffering with an increased possibility of discontinuing chemotherapy, but it could result also in the development of a conditioned or anticipatory anticipatory nausea and/or vomiting response (Holland, 1982; Redd & Andresen, 1981; Redd, Rosenberger, & Hendler, 1982). This will be discussed in greater detail in the following section.

Further, because of the progressive nature of these side effects, it has been suggested that patients should be provided with pleasant surroundings in order to decrease their level of arousal. A sympathetic and supportive attitude of the staff adds to this lowered stress level (Frei & Holland, 1982; Frytak & Moertel, 1981).

Finally, the need for flexibility in the prescription of antiemetics is suggested by extensive clinical experience (Laszlo, 1983; Neidhart, Gagen, Young, & Wilson, 1981). It has even been suggested that patients be allowed to choose between antiemetic medications which they may have tried (Neidhart et al., 1981) as well as any other psychological approaches (such as hypnosis) which may be available in a particular oncology clinic (Barr, Presant, Klein, Mackie, Yonemoto, Keating, & Metter, 1981; Laszlo, 1983). Once these principles of traditional medical management have been considered, any additional treatment approaches need to be measured carefully against them in terms of both treatment and cost effectiveness.

In spite of these considerations, pharmacologic approaches to the

treatment of nausea and vomiting have failed to stem an unrelenting increase in the intensity, frequency, and duration of these symptoms for many patients. At the same time, little is known about the relative effectiveness of psychological and pharmacological treatments. Much research is needed to examine the effectiveness of the proposals described above, while developing new and perhaps innovative approaches to the reduction of nausea and vomiting.

Anticipatory Nausea and Vomiting

Because of the poor ability of antiemetics to diminish post-chemotherapy nausea and vomiting effectively, the patient's degree of distress will continue to increase with repeated treatments. This distress may include increasing levels of anxiety and depression and other negative psychological changes (Chang, 1981; Eyre & Ward, 1984; Frei & Holland, 1982; Frytak & Moertel, 1981; Harris, 1978; Holland, 1977; Holland, 1982; Penta et al., 1981a, 1983). In particular, patients often report experiencing nausea and/or vomiting prior to the infusion of their chemotherapy (Holland, 1977; Whitehead, 1975). This may occur on the way to (Nicholas, 1982) or on entering the clinic (Whitehead, 1975), seeing the nurse or doctor, or perhaps even the "smell" of the hospital (Schulz, 1980). Many patients express concern that they are somehow "crazy" because they experience these symptoms in such an unusual fashion (Nesse et al., 1980; Weddington, 1982).

These nausea and vomiting symptoms may best be understood as conditioned or anticipatory, and explained theoretically by a classical conditioning model. In this theoretical model the unconditioned response (UCR) of nausea and/or vomiting following the presentation of the chemotherapeutic agent, which is the unconditioned stimulus (UCS),

becomes a conditioned response (CR) to situational, perceptual and/or somatic cues which are paired with the presentation of the the UCS. These cues become conditioned stimuli (CS) for the elicitation of the CR's (nausea and vomiting).

Classical conditioning theory states that the UCS-UCR interval should be minimal and that the greater this interval, the less likely for conditioning to occur by the UCS being paired with a CS and eliciting a CR (Kimble, 1961). It is well documented that nausea and vomiting will usually begin anywhere from 3 to 12 hours after the infusion of the chemotherapeutic agent (cf. Holland, 1977). If this is so, then the UCS-UCR interval is far too great to allow conditioning to occur. However, according to conventional classical conditioning theory, it has been shown that the universality of this view of classical conditioning is subject to certain exceptions. Long UCS-UCR intervals will still allow for conditioning to occur when the UCR is gastrointestinal upset, e.g., nausea and/or vomiting. This has been reliably demonstrated in experiments with animals, using such nausea-producing agents as lithium chloride and radiation, which may only produce nausea after a period of twenty-four hours (Garcia, Hankins, & Rusniak, 1974).

Bernstein (1978) and Bernstein & Sigmundi (1980) have shown that taste can become a CS for the elicitation of the CR's of nausea and/or vomiting in patients receiving chemotherapy. Children receiving chemotherapy and experiencing nausea and vomiting were provided with a novel flavoured ice cream prior to one of their treatments. When provided with a choice of flavours at a subsequent treatment session, only 21% of the children chose the novelly flavoured ice cream. This was significantly less than controls who had not tasted the ice cream previously or did not experience nausea and vomiting, indicating the likelihood of the development of a conditioned taste

aversion. Other food aversions may also develop in patients with advanced cancer due to the action of the toxic metabolites of cancer cells as UCS's, thus causing conditioned aversion to various foods and promoting the anorexia and cachexia associated with terminal illness (Bernstein & Sigmundi, 1980).

Parameters of Anticipatory Nausea and Vomiting

In a survey of 124 hospitals in the United States, Laszlo (1982) has provided important information regarding the pervasiveness of the problem of anticipatory nausea and vomiting . Ninety-six percent of these hospitals reported having patients who suffered from these symptoms. The percentage of patients actually experiencing anticipatory symptoms at each institution ranged from 1% to 30%. In another survey, of 406 patients receiving chemotherapy treatment at a major regional cancer centre, 98 or 24% of the patients experienced anticipatory nausea and 35 or 9% experienced anticipatory vomiting (Morrow, Arsenau, Asbury, Bennet, & Boras, 1982). These rates are fairly consistent throughout various studies (Burish, 1984; Dolgin Katz, McGinty, & Siegel, 1985; Morrow, 1984a,b; Nerenz et al., 1984b; Nicholas, 1982). The reported frequency of anticipatory vomiting among patients may rise to as much as 50%-65% when extremely powerful drugs such as cis-platinum or combinations of drugs such as CMF are given (Coons, 1981; Wilcox et al., 1982). Only about one-quarter to one-third of patients who develop anticipatory nausea will also develop anticipatory vomiting.

Anticipatory nausea begins usually by the fourth chemotherapy session of a treatment protocol or approximately between 2-4 months into the treatment protocol (Dolgin et al., 1985; Morrow, 1982, 1984; Nicholas, 1982; Redd, 1984a; Wilcox et al., 1982; Weddington, Miller, & Sweet, 1984). However, the number of patients beginning to experience anticipatory nausea increases

with time in treatment. Weddington et al. (1984) reported that 19 of 41 patients who experienced post treatment nausea experienced anticipatory nausea by two months. By six months of treatment, 74% experienced anticipatory nausea. This figure did not change after ten months of therapy. Anticipatory nausea usually begins anywhere from a mean of 17 hours (Morrow et al., 1982) to a mean of 5 hours prior to treatment (Nicholas, 1982).

Anticipatory vomiting usually begins about a mean of 11 hours prior to treatment (Morrow et al., 1982). Cella, Rupert, & McAdams (1984) showed how powerful this conditioning can be by interviewing long term survivors of Hodgkin's disease who had undergone chemotherapy. Many of these patients still continued to experience conditioned nausea to particular eliciting stimuli even twenty years after the termination of treatment.

Patients with anticipatory nausea and vomiting differ from chemotherapy patients not experiencing these symptoms in several ways. They tend to have been on chemotherapy for a longer period of time, have experienced more injections, have more advanced disease, more severe post chemotherapy nausea and vomiting with a gradual onset (Nesse et al., 1981; Nicholas, 1982).

A study of 225 chemotherapy patients by Morrow (1982) confirmed these results. In addition, he found that younger patients, who were receiving either dactinomycin or cis-platinum and rated their post-chemotherapy emesis higher were more likely to develop anticipatory nausea and vomiting. Patients receiving more than 2 chemotherapy drugs of any type also had this experience. These patients also experienced their worst post treatment nausea and vomiting from 4-8 hours after treatment, whereas the no anticipatory nausea and vomiting group experienced their worst nausea and vomiting between 0-4 hours after treatment. In a regression analysis, 26% of the variance predicting the development of anticipatory nausea and vomiting

was accounted for by the following three variables: severity of post treatment vomiting, taking cis-platinum, and the time when the nausea was worst. In a discriminant analysis, 58% of the anticipatory nausea and vomiting patients were correctly classified by these parameters, whereas 91% of the no anticipatory nausea and vomiting group were correctly classified by the absence of these variables. The correlational nature of these results mitigate against firm causal predictions, which need support from replications of these results. In addition, 70% of this group of patients reported they felt that the cause of anticipatory nausea and vomiting was psychological.

In a later study, Morrow (1984a) was able to correctly classify 80% of the anticipatory nausea and vomiting patients by adding variables relating to patients' reports of previous experience in their lives with such symptoms as sweating, weakness, motion sickness, and hot flushes. The possible involvement of the vestibular system in the development of anticipatory nausea and vomiting was suggested in a survey of 608 patients, 166 of whom reported being prone to motion sickness prior to chemotherapy treatment (Morrow, 1984b). Thirty-nine percent of the 122 patients with anticipatory nausea and vomiting had reported experience of motion sickness in their lives prior to the onset of chemotherapy treatment.

Anxiety, as an indicator of heightened arousal, has been postulated as an intervening variable in the development of anticipatory nausea and vomiting. Patients with anticipatory nausea, but not anticipatory vomiting, report higher subjective anxiety but have heart rates during treatment similar to patients with no anticipatory nausea (Ahles, Cohen, Little, Balducci, Dubbert, & Keane, 1984). However, patients with anticipatory nausea and vomiting report higher anxiety and have higher heart rates than patients without anticipatory symptoms. This discrepancy between self-report and

physiological measures of anxiety is also reflected for example, in the greater physiological arousal of patients receiving their chemotherapy via drip infusion as compared to push injection, which takes a significantly shorter time. These groups do not differ in reported anxiety, but they report significantly more depression (Lyles, Burish, Krozely, & Oldham, 1982).

Schulz (1980) found patients with anticipatory nausea and vomiting to have higher levels of state and trait anxiety scores on the STAI, and higher scores on the neuroticism scale of the Eysenck Personality Inventory. Using the Spielberger State-Trait Anxiety questionnaire, Redd (1984b) and van Komen & Redd (1985) showed that there was a small significant correlation between trait anxiety and anticipatory nausea. Redd (1984b) has suggested that there may be different reasons for the development of anticipatory nausea and vomiting prior to the fourth session (about 20% of patients), between 6 and 10 sessions (about 70%), and more than 11 sessions (about 19%).

Using a multiple regression analysis, Andrykowski et al. (1985) have shown that a significant proportion of the variance attributable to anticipatory nausea was predicted not only by the severity of post chemotherapy nausea and vomiting and a greater length of time receiving treatment but also by higher level of state anxiety. This suggests that early development of anticipatory nausea may be due to the development of conditioned aversion, whereas late development of anticipatory nausea and vomiting may be mediated by the increasing anxiety and stress of prolonged treatment (Andrykowski & Redd, 1987). High anxiety may also be implicated in the refusal to continue treatment by some adolescent patients (Blotcky et al., 1985).

Altmaier, Ross, & Moore (1982) found that patients with anticipatory vomiting were more anxious and depressed but not more hostile, as

compared to no anticipatory vomiting patients. These patients also had more negative thoughts about their ability to cope with their stress. This contradicts the findings of Andersen & Tewfik (1985) who found that radiation therapy patients who were more anxious were also more hostile.

Some chemotherapy patients report a metallic taste in their mouths which is associated with and is the trigger for anticipatory nausea and vomiting (Nerenz, Coons, Love, Leventhal, & Ringler, 1981; Weddington et al., 1984). The specificity of the stimulus conditioning properties of taste were demonstrated experimentally in rats by Coil, Hankins, Jenden, & Garcia (1978). They demonstrated clearly that various antiemetics attenuated a conditioned taste aversion, but not a conditioned shock aversion. Since the ability to reduce conditioned nausea and vomiting with antiemetics has been equivocal in cancer patients, mechanisms other than conditioned taste aversion must also be involved (Morrow et al., 1982).

Approximately 50% of breast cancer patients on CMF who experienced anticipatory nausea and vomiting, associated a metallic taste with the chemotherapy (Fetting, Wilcox, Scheidler, Donehower, Grochow, & Enterline, 1984; Fetting, Wilcox, Scheidler, Enterline, Donehower, & Grochow, 1985). Other patients did not have this specific association, but were highly anxious (Nerenz et al., 1981). These results indicate that conditionability may be related differentially to tastes and smells and the influence of anxiety as early as the first session (Nerenz, Leventhal, Easterling, & Love, 1987). In addition, some patients may experience anticipatory nausea even prior to their first chemotherapy session (Dobkin & Morrow, 1985). This finding indicates that that the patient's expectations regarding anticipatory nausea and/or the possibility that extreme anxiety can cause nausea as a direct consequence. More anxious patients tend to have

visual and imaginal CS (e.g., seeing the nurse, or thinking about the trip to the hospital the next day), while patients experiencing taste or smells as CS's were less anxious (Katz, 1982; Nerenz et al., 1981, Nerenz et al., 1982; Redd & Andrykowski, 1982).

It has been suggested that a cognitive conditioning process may also be involved in the development of anticipatory nausea and vomiting. Since patients with anticipatory nausea also have more intense post-chemotherapy nausea, these patients may be remembering their symptoms more actively during the time period between chemotherapy sessions. This cognitive activity during the time gap in the seemingly long UCS-UCR interval may account for the facilitation of the conditioning process by incubating the fear response until a salient eliciting stimulus appears (Dobkin, Zeichner, & Dickson-Parnell, 1985; Eysenck, 1982).

Several authors have argued that prophylactic use of antiemetic medications given prior to the first chemotherapy session might diminish the probability of the development of anticipatory nausea and vomiting (Laszlo, 1982; Andrykowski et al., 1985). In a study evaluating this issue, children given phenothiazines prophylactically gave higher ratings and had longer durations of nausea and vomiting than children not receiving these drugs (Zeltzer, LeBaron, & Zeltzer, 1984b). Many patients using marijuana cigarettes (THC) as an antiemetic repeatedly reported that the odour and taste of the smoke began to make them nauseated (Kutz, Borysenko, Come, & Benson, 1980). Even the voice of a therapist on an audiotape teaching relaxation to patients on chemotherapy may develop into a CS if the chemotherapy drug is powerful enough (Redd & Andresen, 1981).

In summary, the review of data on the development of anticipatory nausea and vomiting indicates that multiple factors including personality,

cognitive, situational and drug-related cues, such as taste and or smell are implicated. Effective intervention strategies are only possible when a clear understanding of the development of anticipatory nausea and vomiting for an individual patient is achieved. One area of major significance in this regard concerns reliable and valid measures of nausea and vomiting. Lack of such measures only compromises the ability of clinical researchers to evaluate treatment effectiveness.

Assessment of Nausea and Vomiting.

Nausea and vomiting present measurement difficulties from both a subjective and objective perspective. As discussed above, although nausea and vomiting are often discussed as concurrent events, they may be distinct and separate and occur sequentially, simultaneously, or independently (Morrow, 1984c). For this reason, reliable measurement is fraught with difficulty.

Nausea is primarily a private event usually not discernible by external observation (Redd & Andrykowski, 1982), except perhaps when it is so intense that vomiting is inevitable and imminent. In this case, for example, such behavioural manifestations as facial grimacing, increased respiration and frequency of swallowing may be observed. When these behaviours are not present, nausea presents problems of measurement not dissimilar to those for other subjectively occurring events such as, for example, anxiety and depression.

Vomiting, on the other hand, is an observable event. The emptying of the gastric contents in pulsing contractions of the gastrointestinal tract are easily observed. Retching, which is virtually the same response, differs in that there are no gastric contents to be expelled (Laszlo, 1983; Morrow, 1984c). This

response is also known as the "dry heaves", a response familiar to those who have experienced the toxic effects of alcohol. In chemotherapy-induced nausea and vomiting retching occurs often, but is less frequent because oncology physicians encourage their patients to eat at least small quantities of food prior to chemotherapy, which reduces the irritation of the esophogeal tract during vomiting. Because vomiting usually occurs over short, repetitive periods, its frequency may be easily measured by a simple count. This facility of counting is complicated when certain chemotherapeutic agents such as cis-platinum are used. Cis-platinum has been known to cause almost continuous vomiting in many patients, often without prodromal nausea. In this instance, duration may be a more significant parameter of the emetic response. The mechanism for this phenomenon is not well understood at this time.

An animal model of emesis has been elucidated by Laszlo (1983). Using this model, antiemetics are evaluated empirically using the number of vomits and retches observed behaviourally. In addition, intra-thoracic and intra-abdominal venous pressure are measured as physiological correlates of emesis. Since changes in respiration are associated with nausea and vomiting due to the proximity between the vomiting centre and the respiratory centre, these measures may provide some of the best physiological measures of the the vomiting response. However, this technology does not provide any data on nausea, since the ability of laboratory animals to provide accurate verbal self-reports or ratings on Likert scales or visual analogue scales is proportional to their ascendance on the phylogenetic ladder. Moreover, these physiological measures have not yet been applied to man.

The literature on the treatment of nausea and vomiting in humans has focussed primarily on outcome and less on the empirical considerations of accurate measurement. This has lead to a plethora of measures of both nausea

and vomiting . Morrow (1984c) reviewed 120 studies published prior to 1982 which involved the study of chemotherapy-induced nausea and vomiting. These studies encompassed the treatment of 1512 cancer patients. In evaluating the various measures used, no consensus on a reliable and valid measurement approach emerged.

The large majority of measures consisted of unvalidated self-reports. Observer reports were much less common, except for occasional vomiting reports. Often nausea and vomiting side effects were inferred from their concomitant behaviours, for example, appetite return, time when eating or drinking returns, dehydration, wound deheiscence, fractures (secondary to intense vomiting), and depression. These indirect measures are clearly inappropriate since they may be caused by many other factors. Stress fractures may be caused by bone metastases; depression may be a function of multiple factors, such as fear of death, loss of functioning as well as a host of other reasons (Bukberg, Penman, & Holland, 1984; Plumb & Holland, 1977, 1982).

Self-report scales of various types and levels of precision have been used in most studies of nausea and vomiting. These reports have included nominal scales such as presence/absence, yes/no or persistent/limited or the equation of treatment failure with the presence of two or more vomits after treatment (e.g., Frytak & Moertel, 1981). These dependent measures are too general and clearly do not add to the precision of measurement. Since each chemotherapy drug has its own individual emetic properties and course, mutually exclusive categories do not allow for fine distinctions in change; it is these which may be of greatest clinical significance.

Other approaches to measurement have included ordinal scales with anywhere from three to ten points and anchors such as "none" to "a great deal"; and one hundred point visual analogue scales with similar anchor

points (Fetting et al., 1982; Redd, Andresen, & Minagawa, 1982). Each of these scales have been used as measures of either nausea or vomiting or occasionally and less precisely, as a measure of a combined nausea/vomiting index. In the latter, the separate contribution of nausea and vomiting to the overall rating of what may be either intensity, frequency or duration ratings becomes confounded. When combined indices are used, conclusions regarding the efficacy of any antiemetic technique may be questioned for these reasons alone.

The duration of nausea and vomiting is extremely important in that overall suffering and the ability of the patient to recover before the next treatment may determine, to a large extent, the patient's overall quality of life. One approach to gathering data on duration has been to obtain ratings at various intervals after the infusion of the chemotherapy agents. These intervals have included one, three, six, twelve, and twenty-four hour intervals and/or end of treatment periods (e.g., Lyles et al., 1982). If a particular treatment can reduce the duration of side effects, but not the intensity, the result will still have important clinical significance, since many patients experience extended periods of post-chemotherapy nausea and vomiting, possibly due to psychological factors, such as anxiety or depression (Lyles et al., 1982).

Observer reports have also been utilized in attempts to validate the self-reports of patients. In most cases, the nurse (Fetting et al., 1982; Lyles et al., 1982), family, and/or physician are the primary observers. The difficulties with using external observers other than trained professionals using well constructed, valid, and reliable observation scales lie in the lack of training in observation and in the relative accessibility of the patient to the particular observer. Nausea and vomiting do not always occur while the patient is

receiving chemotherapy. Typically, a patient may begin to experience nausea and vomiting anywhere from immediately following the infusion of the chemotherapy drugs to twenty-four to forty-eight hours later (Ganong, 1979; Laszlo, 1983). The nurse or physician may only be able to provide ratings of nausea and vomiting while the patient is present in the chemotherapy clinic. Family or other community members who may be able to provide ratings may not always be available or willing to cooperate, as their primary concern may be the comfort of the patient who is suffering through the symptoms.

The need to develop consistent, reliable, and valid measures of nausea and vomiting is manifest. One recent attempt to overcome these difficulties was made by Morrow (1984c), who has developed a questionnaire to encompass the three dimensions of nausea and vomiting, i.e., frequency, intensity, and duration. In addition, this questionnaire provides for separate ratings of anticipatory and post-chemotherapy nausea and vomiting. The Morrow Assessment of Nausea and Emesis (MANE) was first used in an outcome study of the effectiveness of systematic desensitization on nausea and vomiting side effects of chemotherapy (Morrow & Morell, 1982). The MANE assesses nausea episodes and vomiting frequency via a four point scale with the anchor points labelled "never" to "during and after every treatment". Severity of nausea and vomiting are assessed by a six point scale with the anchor points "very mild" to "intolerable". Duration of nausea and vomiting is measured by the number of hours that these symptoms persist. In addition, the point in time of the worst nausea or vomiting is assessed by a six point scale with the anchor points labelled "during treatment" to "twenty-four or more hours after treatment".

Test-retest reliability for a subsample of twenty randomly selected patients was extremely high over four chemotherapy sessions ($r = .76$ to $r = .96$). The

point in the chemotherapy protocol at which these patients were was not specified. They were likely on a research protocol of at least one year of consistent doses of drugs and well into their treatment. Since nausea and vomiting side effects usually peak between the fourth and sixth treatment sessions (Redd, 1984a; Redd & Hendler, 1984), these patients' symptoms had probably reached their asymptote; this may account for the extremely high reliability coefficients.

Convergent validity was provided by significant correlations (r = .33) between patients self-ratings and ratings made by nurses and pharmacists of the emetic potential of chemotherapeutic drugs typically used in the chemotherapy clinic. Divergent validity was provided by extremely low correlations between self-ratings of nausea and vomiting and ratings of fatigue and depression, indicating that the self-ratings were not confounded by other affective states. At present, this scale has been the most carefully evaluated measurement tool for nausea and vomiting. One of the problems with it is that it is completed when the symptoms of nausea and vomiting have terminated completely. Different studies have indicated that retrospective ratings of subjective states may be either biased or unbiased. For instance, patients experiencing vomiting after GI bypass surgery for obesity, rated their subjective state at a later time differently from those made by them just after surgery (Stunkard, Foster, Glassman, & Bosato, 1985). In addition, in a group of patients with chronic rheumatic disease, the longer the duration of time from the original rating of pain, the less concordance there existed between this rating and a current one (Scott & Huskisson, 1979). However, in a study of memory for pain experience, patients rated their pain in an unbiased manner when questioned later (Hunter, Phillips, & Rachman, 1979). From these equivocal data, it becomes clear that the reliability and validity of

retrospective recall of nausea and vomiting symptoms needs to be examined more closely.

The use of visual analogue scales (VAS) to measure subjective affective states is a fairly recent innovation (Priestman & Baum, 1976; Redd & Andrykowski, 1982). In this approach, the patient is provided with a one hundred millimetre horizontal line with anchors to the ends of the line denoting the subjective dimensions of the line. For example, if the VAS is used to measure nausea, then the anchor points might be "no nausea" at the left of the line and "worst nausea ever" or "extreme nausea" at the right of the line. The degree of nausea is then measured by the position of the check mark on the VAS line drawn by the patient from the left end of the line. Although regression toward the mean is inevitable, the bias involved in choosing a specific category of an ordinal scale is largely eliminated.

The VAS has been used in a variety of situations to measure anxiety, depression, nausea and vomiting, pain, quality of life of breast cancer patients and a host of other subjective states with greater or lesser degree of validity and reliability (Ahles, Blanchard, & Ruckdeschel, 1983; Ahles, Ruckdeschel, & Blanchard, 1984; Priestman, 1984; Priestman & Baum, 1976; Redd & Andrykowski, 1982).

Verbal descriptor scales provide another modality for the measurement of subjective states. A prime example of this type of scale is the McGill Pain Questionnaire (MPQ) (Melzack, 1975; Melzack & Torgerson, 1971). This is one of the most widely used psychometric instruments for the measurement of pain. The questionnaire consists of twenty groups of words used by pain patients to describe their pain. Each group of words is an ordinal scale of anywhere from two to six words (e.g., dull, sharp, stinging, intense). Patients choose words which they feel describe their pain. They also rate their current

overall pain intensity on a six point ordinal scale called the 'Present Pain Intensity'.

Theoretically, the word groups are divided into three subscales which encompass Melzack & Wall's (1982) tri-partite definition of the perception of pain. According to this theory, pain is composed of three dimensions or qualities. These are variously referred to as sensory, affective, and evaluative. The sensory words of the MPQ refer to the perception of the pain by the patient in terms of the degree of actual sensory experience, i.e., how much the pain actually hurts. The affective scale contains words that express the patient's emotional reaction to or concomitant feelings about the pain. The evaluative scale contains words which denote the degree of suffering or disruption that the pain is causing the patient. This approach to the qualitative evaluation of pain stems from the gate control theory of Melzack & Wall (1965) and is one of the most widely used measures of both chronic and acute pain.

The use of verbal descriptors may add a new dimension to our understanding of the phenomenological experience of nausea and vomiting. The relationship between this approach to measuring nausea and vomiting and other single scales and their reliability and validity are unknown at the present time. It may be possible to develop more sensitive measures of nausea through the use of word descriptor scales such as the MPQ. These and other approaches to measurement of nausea and vomiting, such as ordinal and visual analogue scales, may provide researchers with more effective and more sensitive tools to assess changes in what has already been described as multifactorially determined symptoms.

Psychological Approaches to the Reduction of Nausea and Vomiting

From the evaluative review of antiemetics in an earlier section, it is clear that these pharmacological agents by themselves have been unable to adequately control the nausea and vomiting due to chemotherapy and, most particularly, anticipatory nausea and vomiting in most patients (Laszlo, 1982; Redd, 1984a). For this reason, other approaches have been investigated. It is well known that medical procedures such as surgery are often perceived and experienced as stressful by patients and the degree of distress may adversely affect overall outcome (Janis, 1958; Melamed, 1984). When these medical procedures are repeated on a regular regimen such as hemodialysis for patients with chronic kidney disease (cf. Devins, Binik, Gorman, Dattel, McCloskey, Oscar, & Briggs, 1982); repeated painful bone marrow aspirations for leukemia patients (cf. J. R. Hilgard & LeBaron, 1982; 1984; Zeltzer & LeBaron, 1982); or regular cancer chemotherapy treatments, the distressing side effects do not habituate or extinguish over time, as might be expected. Rather, they usually increase in intensity, frequency, and duration, in spite of valiant attempts by patients to cope. This response may be understood in terms of Eysenck's incubation theory of anxiety, where the patient escapes from the CS before extinction may occur. For this reason, the CR strengthens rather than weakens (Eysenck, 1982).

Any intervention which compromises the CS-CR connection successfully will be of great importance in attenuating the nausea and vomiting of chemotherapy. It has been suggested that antiemetics may be useful in a prophylactic role by diminishing the intensity of the UCR, thus preventing the creation of a strong CS-CR connection through classical conditioning (Laszlo, 1982; Andrykowski et al., 1985). In the past, oncologists have typically

treated nausea and vomiting conservatively. They have not taken the prophylactic approach for two important reasons: side effects of the antiemetics and lack of data regarding the use of specific antiemetics with specific chemotherapy drugs.

Behavioural techniques such as relaxation and systematic desensitization, biofeedback, hypnosis, as well as combinations of these and other cognitive approaches, have all been shown to have important effects in reducing the distress from disorders such as anxiety and phobias in both analogue and clinical studies. A number of researchers have successfully applied some of these behavioural methods to control symptoms related to cancer and its treatments. Hypnosis has been utilized previously in the successful reduction of pain related to cancer (Dempster, Balson, & Whalen, 1976; E. R. Hilgard & J. R. Hilgard, 1983; Labaw, 1969; Schaefer & Hernandez, 1978). In addition to the reduction of pain, these studies have described also the use of hypnotic techniques to significantly reduce nausea and vomiting in several patients undergoing chemotherapy.

The first controlled study examining the effectiveness of a behavioural intervention in the reduction of nausea and vomiting was a single case, within-subjects design, where the patient served as her own control (Burish & Lyles, 1979). Over a series of ten chemotherapy sessions, this patient, a 30 year-old woman with thymic lymphoma, underwent either therapist-directed or self-directed relaxation exercises. Self-report ratings, questionnaires, physiological measures (pulse and blood pressure), and nurses' observations indicated that the patient was able to reduce negative affect, frequency of vomiting, and post-treatment physiological arousal. It was concluded from this study that relaxation had significant salutary effects on the side effects of chemotherapy.

In a second case study, Burish, Shartener, & Lyles (1981) combined relaxation training with EMG biofeedback from four muscle sites to help a 44 year-old female suffering from undifferentiated adenocarcinoma cope with nausea and vomiting. The measures used were similar to those of the previous study. After four treatment sessions, the patient was able to generalize her training to follow-up sessions successfully. She was able to significantly reduce physiological arousal and reported feeling less anxiety and nausea.

Redd & Andresen (1981) and Redd, Andresen, & Minagawa (1982) taught hypnosis to six patients undergoing chemotherapy and demonstrated that patients experienced reductions in anticipatory vomiting and ratings of nausea prior to, during, and post treatment. These results were reversed when these patients were not given hypnosis instructions and asked to undergo their treatment. This reversal in symptoms may have been due to factors other than the mere absence of hypnosis and would most likely have depended upon how the withdrawal of hypnosis was perceived by the patient.

A less encouraging finding was that several other patients being treated with cis-platinum developed a conditioned aversive reaction to the voice of the therapist while listening to an audiotape of the hypnosis instructions which was used for home practice. The authors concluded that this may have been due to the strength of the UCS and they postulated a drug-dose relationship in the development of anticipatory nausea and vomiting which may attenuate the salutary effects of an otherwise effective procedure such as hypnosis. However, the particular style of the therapist, the effectiveness of the hypnosis technique used, and the manner in which hypnosis was represented to the patients may have contributed also to this finding.

The success of relaxation, hypnosis, and biofeedback in controlled clinical

case studies led to the examination of the effectiveness of these techniques in larger groups of patients using randomization and the selection of appropriate control groups. Using the same procedure as in their previous study, Burish & Lyles (1981) divided sixteen patients receiving cancer chemotherapy into a relaxation group and a no treatment control. In addition to receiving progressive muscle relaxation, the treatment group was taught guided imagery to enhance and facilitate the relaxation response. The results demonstrated conclusively that patients in the relaxation plus guided imagery group experienced significantly less anxiety and nausea, as well as physiological arousal both during the training and the follow-up sessions. Nurses' ratings of nausea and anxiety also indicated significant reductions in these two parameters in the relaxation group, as compared to the control group.

Lyles et al. (1982) divided fifty patients—twenty-five receiving push injections (lasting 5-15 minutes) and twenty-five patients receiving drip infusions (lasting one-half to two hours)—into either a relaxation plus guided imagery group, a therapist support control group, or a no-treatment control group. Patients in the relaxation plus guided imagery group showed significant reductions in anxiety and nausea and physiological arousal during treatment, and significant reductions in nausea, anxiety, and depression following chemotherapy.

Morrow & Morrell (1982) canvassed five hundred cancer patients receiving chemotherapy. Of these, 60 patients fulfilled the basic criterion of having experienced at least two chemotherapy sessions during which they had suffered from anticipatory nausea. Patients were randomly assigned to three groups: relaxation plus systematic desensitization, a counselling control group, and a no treatment group. The patients in the first group were given

two one-hour training sessions in progressive relaxation and systematic desensitization, i.e., the presentation in imagination of progressively more aversive scenes related to the chemotherapy treatments, e.g., driving to the clinic, receiving the injection, etc., while the patient remains in a relaxed state (Wolpe, 1958). The counselling group received information about nausea and vomiting and general suggestions about coping with no direct instruction, while the no treatment control patients merely recorded their nausea and vomiting ratings. All patients filled out the Morrow Assessment of Nausea and Emesis (MANE) (Morrow, 1982), as well as the Spielberger State-Trait Anxiety questionnaire (STAI), the Health Locus of Control Scale (HLOC), and VAS ratings for expectations of success and credibility of treatment. No differences existed between groups on any parameter at baseline, including various demographics.

The results indicated that fewer patients in the relaxation plus systematic desensitization group experienced anticipatory nausea. Further, this nausea diminished in severity and intensity as compared to the controls. Indeed, 6 of 9 patients in this group who also had anticipatory vomiting eliminated this symptom. The remaining three patients were able to decrease the severity but not the duration of the vomiting. There were no changes in state or trait anxiety or in any of the subscales of the HLOC. Interestingly, one half of the untreated control patients actually experienced <u>increased</u> anticipatory nausea during the course of the study, providing further evidence that untreated anticipatory nausea and vomiting symptoms worsen over time, rather than habituating or extinguishing. There was, however, no significant decrease in the use of antiemetics by patients in the relaxation plus systematic desensitization group. In an extension of this study, Morrow (1986) added a relaxation-only group to assess the effectiveness of the cognitive hierarchy

(desensitization procedure). The findings indicated that relaxation plus systematic desensitization treatment was more effective than the relaxation-only treatment in reducing nausea and vomiting symptoms.

Zeltzer et al. (1984c) divided 19 adolescents with cancer into either a hypnosis treatment group or a supportive counselling group. Overall ratings for nausea, vomiting and "bother" (a measure of the disruptive effects of the treatment on the patients' life) were made. Patients were on various drug protocols, from daily to monthly treatments. All of the symptoms were significantly reduced from baseline to post-test, with no significant differences found between groups. These improvements remained after the treatment terminated and follow-up ratings were made.

This rather surprising result contradicts the findings of the previously described study by Morrow & Morrell (1982) and may be explained by differences in the nature of the supportive counselling groups in the two studies. In the Morrow & Morrell (1982) study, the supportive counselling group patients were seen for two one-hour sessions during which a "Rogerian" approach was taken, i.e., patients were given support for their efforts to cope with their chemotherapy, but given no specific advice regarding new approaches to coping. In the Zeltzer et al. (1984c) study, the supportive counselling group patients were seen during their treatment (just as in the hypnosis group); rather than being given a "neutral" type of support, however, the children were asked to engage in various distraction tasks, such as focusing on interesting objects in the room, squeezing on the therapists hand, or taking deep breaths. These activities may not be as "neutral" in character as the authors believed, and may have drawn these children into utilizing their imaginative capacities to an extent comparable to the patients in the hypnosis group (J. R. Hilgard & LeBaron, 1984).

Several theories have been advanced to account for the similar findings of researchers using different behavioural methods to reduce the nausea and vomiting side effects of chemotherapy (Redd, 1984a; Redd & Andrykowski, 1982; Redd, Rosenberger, & Hendler, 1982). Relaxation (induced through progressive muscle relaxation as in the Burish and the Morrow studies, or through direct suggestions of warmth and heaviness as in Redd's studies) appears to be one of the most common features of these investigations. Nausea and vomiting involve aspects of both the central nervous system and the sequential movement of gross muscle groups (Seigel & Longo, 1981). Antiemetic drugs in general have sedation as one their most frequent side effects. It is possible that the action of the various relaxation techniques may act in a similar way by interrupting these muscular movements. Since these drugs are also thought to act on the CTZ directly as well, it may be that relaxation also acts in this manner. Findings contrary to this theory come from studies demonstrating the poor efficacy of minor tranquilizers in reducing nausea and vomiting.

Second, distraction may serve to turn the patients' attention away from the distressing symptoms by focusing on the feelings of relaxation or the imagery which is generally some pleasant scene which is incompatible with the chemotherapeutic situation. Some evidence for the effectiveness of both relaxation and distraction comes from the Zeltzer et al. (1984c) study.

Third, the role of "non-specific" factors such as support and encouragement may be easily discounted from the the evidence of studies (e.g., Morrow & Morrel, 1982) showing that attention and/or support without direct instructions in new coping mechanisms is ineffective. The type of therapeutic relationship developed by treating physicians and nurses in the clinic situation is usually warm and supportive, but obviously this rapport

has not had any attenuating effect on the development of anticipatory nausea and vomiting (Redd & Andrykowski, 1982).

Questions remain regarding the effectiveness of these procedures on post-chemotherapy nausea and vomiting, although some evidence exists that they may be effective in treating these specific symptoms (Lyles et al., 1982; Morrow, 1982d; Redd & Andrykowski, 1982). Measures of personal control have not proven to be predictive of therapeutic effectiveness (e.g., Morrow & Morrel, 1982), but additional studies need to be performed to examine the development of feelings of self-control over what is generally considered to be a process which leaves the patient out of control.

Hypnosis and Hypnotic Susceptibility

Two major themes emerge from the review of the literature of behavioural approaches to the reduction of nausea and vomiting. First, all of the most successful techniques use some form of relaxation or arousal reduction. Second, patients are asked to engage in some form of mental activity. This activity may be the presentation of a cognitive hierarchy of events leading up to the actual presentation of the chemotherapy drugs so that the patient might learn active and direct coping skills (Morrow & Morrell, 1982). Alternative approaches have suggested that patients turn their attention away from the noxious event (i.e., the chemotherapy treatment) through distraction (e.g., Zeltzer et al., 1984c) or imaginal involvements, such as hypnosis (e.g., Redd & Andrykowski, 1982). Although Morrow (1986) has shown that relaxation plus desensitization is more effective that relaxation alone, the relative effectiveness of hypnosis has not been established.

The achievement of relaxation requires the patient to maintain passive

attention and a focused attitude (Benson, 1975). These abilities have been associated with the concept of hypnotic susceptibility, i.e., a set of cognitive skills or capacities to focus attention (Van Nuys, 1973; Karlin, 1979) or become imaginatively involved (E. R. Hilgard, 1965, 1977; J.R. Hilgard, 1981) in certain ideas, fantasies, or images. Hypnotic susceptibility has been operationally defined and measured experimentally with high reliability and validity—e.g., Stanford Hypnotic Susceptibility Scale: Form C (Weitzenhoffer & E. R. Hilgard, 1962). It appears to be a relatively stable characteristic of the individual (Perry, 1977). Further, it has been reported regularly that from 10-15% of the population is highly responsive to hypnosis (i. e., capable of suggested post hypnotic amnesia), a further 10-15% is minimally responsive, while the remaining majority of 70-80% is moderately responsive, and to varying degrees (Bernheim, 1889; E. R. Hilgard, 1965).

In the laboratory, hypnotic susceptibility has correlated with the reduction of pain using a number of different painful stimuli such as cold pressor pain and pain produced by ischemia (cf. E. R. Hilgard & J. R. Hilgard, 1983). In general, results have indicated a probabilistic relationship; that is, the greater the level of a subject's hypnotic susceptibility, the greater the likelihood of attenuation of self-reported pain. These reports are made in spite of evidence showing that physiological reactivity to pain as measured by pulse and blood pressure may, in fact, not change at all (cf. E. R. Hilgard & J. R. Hilgard, 1983). Although desynchrony between self-report and physiological measures in fear and avoidance is well known (Rachman & Hodgson, 1974; Hodgson & Rachman, 1974), it is less clear why highly hypnotically susceptible subjects report decreased pain after hypnosis when objective physiological measures indicate otherwise.

E. R. Hilgard (1977) has suggested that individuals may be experiencing

the pain on two levels. Subjects may be experiencing the sensory aspects of the pain, but perhaps through a cognitive process of dissociation, they are able to separate the sensory from the suffering aspects of the pain. This theory has some suppport from studies with highly susceptible subjects using an experimental technique called the 'hidden observer'. In this experimental paradigm, it is suggested to subjects that even though they are unable to experience pain, there might be another part of them that might be aware of the actual intensity of the pain. Approximately 50% of highly susceptible subjects report the presence of the 'hidden observer' (Laurence & Perry, 1983). Those highly susceptible subjects who experience hypnosis in this dualistic manner (Perry & Walsh, 1978), report little to no pain, but agree that another part of them experiences the pain as excruciating. On the basis of these and other findings, E. R. Hilgard (1977) has proposed a neo-dissociation view of pain reduction in hypnosis.

Hypnotic susceptibility has been related to outcome in various disorders whether hypnosis was used as a treatment or not. Distinctions have been made between habit or volitional disorders—e.g., smoking, obesity—and other, non-volitional disorders—e.g., pain, asthma (DePiano & Salzburg, 1979; McConkey, 1984; Wadden & Anderton, 1982) in evaluating hypnosis as an effective treatment and hypnotic susceptibility as an important intervening variable. In general, disorders involving change in bodily perceptions and sensations improve using any technique which involves teaching patients to alter their perception of the noxious state. Hypnotic susceptibility may be the factor which accounts for the success of the patient in reducing the symptomatic behaviour (e.g., Andreychuk & Scriver, 1975).

Phobic behaviour has been shown to correlate with hypnotic susceptibility (Frankel, 1974, 1975; Frankel & Orne, 1976). This would appear to indicate that

patients with higher hypnotic susceptibility may be more likely to develop disorders which involve altered somatic and cognitive perceptions. If this is the case, then the logical corollary is that teaching patients how to control these distorted perceptions will provide them with a feeling of control over these symptoms.

Since the development of anticipatory nausea and vomiting is related to the intensity of anxiety experienced by the patient and repeated exposure to the noxious event increases the fear response rather than extinguishes it, it may be hypothesized that those patients who are more highly hypnotically susceptible may be more likely to develop anticipatory nausea and vomiting symptoms in a manner similar to the development of phobias (cf. Frankel, 1974, 1975; Frankel & Orne, 1976). Data regarding hypnotic susceptibility is available for patients in only one study of children undergoing cancer chemotherapy (Zeltzer et al., 1984c). Since only the group of patients receiving hypnosis was assessed on a scale of hypnotic susceptibility, no comparisons could be made with the group of patients receiving distraction instructions. However, no significant relationship was found between hypnotic susceptibility and the degree of reduction of nausea and vomiting for the group of patients receiving hypnosis as a treatment. The spontaneous use of hypnotic abilities by patients receiving only distraction instructions and the relation of these abilities to the development and treatment of nausea and vomiting is unknown.

The Present Study

The present study was designed to examine two basic issues. Although numerous outcome studies have been carried out, very few attempts have been made to determine the reliability and validity of the measures of nausea and vomiting used. Because nausea is a subjective experience much like the experience of pain, it was felt that the measurement of nausea by single multi-point Likert-type scales or even visual analogue scales might not adequately tap the overall character of the patient's phenomenological experience.

In a pilot project for the present research, patients in chemotherapy were asked to choose word descriptors to describe their experience of nausea. The findings were surprising in that many patients chose words which were on the McGill Pain Questionnaire (MPQ). It was decided to assess the use of the MPQ as a measure of nausea and compare its reliability and validity to ordinal scales and a visual analogue scale (Redd, Andresen, & Minagawa, 1982; Scott & Huskisson, 1979).

Two studies were carried out to examine this question. Study 1 had two parts. In the first part, oncology physicians and nurses rated the nausea-producing potential of various chemotherapy drugs and doses on a questionnaire designed for this purpose. These ratings were used as external validating criteria for self-reported nausea ratings of the patients. In the second part of this study, patients at a chemotherapy clinic were asked to complete the nausea measures. Study 2 was a replication of study 1. Patients undergoing chemotherapy treatment at a different hospital were asked to complete the nausea measures after 2 consecutive treatments. Concurrent reliability and consistency of the measures over time were examined in this

study.

Study 3 addressed the second basic issue of this research. It was hypothesized that teaching patients self-hypnosis would have an attenuating effect on the intensity, frequency, and duration of nausea and vomiting was examined. In addition, Study 3 examined further the reliability and validity of the MPQ as a measure of nausea. In order to evaluate the more specific effects of the hypnosis intervention, patients rated their level of anxiety, nausea and vomiting at designated time intervals before, during and after treatment.

Standardized assessments of anxiety and hypnotic susceptibility were also obtained. It was hypothesized that more moderate degrees of subjective distress and higher hypnotic susceptibility would correlate with the reduction of both anticipatory and post-chemotherapy nausea and vomiting. In addition, higher hypnotic susceptibility was hypothesized to be correlated with the development of anticipatory nausea and vomiting.

Study One

Study 1 was essentially a pilot investigation into the development, reliability, and validity of several measures of nausea and was divided into 2 sections. In the first part, physicians and nurses experienced in the treatment of cancer patients and administration of chemotherapy drugs were asked to rate the nausea-producing potential of a number of these drugs based on their experience. These ratings were then used as external validating criteria for the nausea measures which were collected from the patients solicited to participate in the second part of the study. This latter part involved the administration of the nausea measures to cancer patients currently receiving chemotherapy treatment. Subsequently, reliability (internal consistency), and validity (construct, concurrent, discriminant) were evaluated for the various nausea measures.

Method

Subjects

In the first part of Study 1, 17 physicians and 8 nurses in the oncology departments of the Montreal General and Royal Victoria Hospitals agreed to participate by completing a rating scale of the nausea-producing potential of various chemotherapy agents.

In the second part, the subjects were twenty-five patients, 7 men and 18 women (mean age = 56 years; range = 23-70 years) who were waiting to receive cancer chemotherapy treatment at the Oncology (Chemotherapy) Clinic of the Montreal General Hospital. As they arrived, an investigator who identified himself as a researcher, approached patients and indicated an interest in discussing the side effects of chemotherapy with them. (The investigator was the present author, a 33 year-old male psychologist with seven years clinical

experience.) They were asked if they had experienced any nausea after their last treatment. If they responded affirmatively, they were asked to complete a short questionnaire evaluating their nausea symptoms. The first 25 consecutive patients who were approached in this manner agreed to participate. Eight patients were receiving one chemotherapy drug; 5 patients received a combination of 2 drugs; 11 patients received 3 drugs; and 1 patient received 4 drugs.

Measures

The questionnaire used to assess nausea consisted of a modified form of the McGill Pain Questionnaire (MPQ; Melzack, 1975) in which the word "pain" was replaced by the word "nausea". Pain has long been understood to have differential subjective qualities, e.g., burning, itching, or stabbing. In compiling the MPQ, Melzack & Torgerson (1971) evaluated a list of 102 words describing various pain qualities. In a series of studies, samples of physicians, medical students, and patients were asked to cluster the words into distinctly different qualitative groups in terms of the qualitative aspect of pain each descriptor represented. Subsequently, intensity rankings for the individual words within each group were made by these individuals. Although the 3 subject samples rated the absolute intensity of the words differentially, the relative position or ranking of the words within each word grouping was highly consistent for 84 of 102 original words. These 84 words were utilized in the final form of the pain questionnaire. In addition, the word groups clustered into three major categories or dimensions: words that describe the sensory quality of pain, such as pressure, temporal, or thermal properties; words that describe affective qualities, such as fear or autonomic reactions; and words that describe an evaluative dimension, an expression of the overall subjective intensity of the pain experience. Also, a Present Pain

Intensity scale was developed in conjunction with the MPQ as a six-point scale in which: 0 = none; 1 = mild; 2 = discomforting; 3 = distressing; 4 = horrible; 5 = excruciating. Although clearly ordinal, the order of the words in this scale were felt to have interval quality (Melzack & Torgerson, 1971).

The MPQ consists of 20 groups of word descriptors which are used by patients to describe their pain. These 20 groups of words were included without modification in the nausea questionnaire. (See Figure 1.)

Each group is an ordinal scale, with each word receiving a rank value based on the the position of the word in each set as determined by the ratings of the physicians, students, and patients. There are 4 subscales: sensory (groups 1-10); affective (groups 11-15); evaluative (group 16); and miscellaneous (groups 17-20). Patients choose the words from each set which they feel describes their pain. Only the word chosen with the highest value for each group of descriptors is scored. The individual group scores are then summed for each subscale. From early pilot work with cancer patients receiving chemotherapy, it was found that many of the words found on the MPQ were chosen by these individuals to describe nausea. It was decided to evaluate the reliability and validity of the MPQ as a nausea questionnaire. It was renamed the Nausea Rating Index (NRI).

In addition, the Present Pain Intensity Scale of the MPQ was renamed the Overall Nausea Intensity scale (ONI). Further, a visual analogue scale (VAS), which consisted of a 10 cm line with the words "no nausea" at the left and "extreme nausea" at the right, was added.

Procedure

In the first part of study 1, the intensity of nausea produced by 17 chemotherapeutic drugs, some at two dosage levels, was estimated by the 17 physicians and 8 nurses. The nausea rating scale they employed was identical

NAUSEA QUESTIONNAIRE

Patient's Name _____

Date _____ Time _____

1 Flickering ___ Quivering ___ Pulsing ___ Throbbing ___ Beating ___ Pounding ___	11 Tiring ___ Exhausting ___
2 Jumping ___ Flashing ___ Shooting ___	12 Sickening ___ Suffocating ___
3 Pricking ___ Boring ___ Drilling ___ Stabbing ___ Lancinating ___	13 Fearful ___ Frightful ___ Terrifying ___
4 Sharp ___ Cutting ___ Lacerating ___	14 Punishing ___ Gruelling ___ Cruel ___ Vicious ___ Killing ___
5 Pinching ___ Pressing ___ Gnawing ___ Cramping ___ Crushing ___	15 Wretched ___ Blinding ___
6 Tugging ___ Pulling ___ Wrenching ___	16 Annoying ___ Troublesome ___ Miserable ___ Intense ___ Unbearable ___
7 Hot ___ Burning ___ Scalding ___ Searing ___	17 Spreading ___ Radiating ___ Penetrating ___ Piercing ___
8 Tingling ___ Itchy ___ Smarting ___ Stinging ___	18 Tight ___ Numb ___ Drawing ___ Squeezing ___ Tearing ___
9 Dull ___ Sore ___ Hurting ___ Aching ___ Heavy ___	19 Cool ___ Cold ___ Freezing ___
10 Tender ___ Taut ___ Rasping ___ Splitting ___	20 Nagging ___ Nauseating ___ Agonizing ___ Dreadful ___ Torturing ___
	ONI 0 No Nausea ___ 1 Mild ___ 2 Discomforting ___ 3 Distressing ___ 4 Horrible ___ 5 Excruciating ___

VISUAL ANALOGUE SCALE

No Nausea — (100 mm) — Extreme Nausea

Figure 1. Nausea questionnaire including OVERALL NAUSEA INTENSITY scale (ONI) and VISUAL ANALOGUE SCALE (VAS).

to the 6 point ONI (described above); ratings ranged from 0 = none to 5 = excruciating. (See Appendix A).

These data were used to generate external validating criteria for the evaluation of the nausea measures used in this study. Following the logic of Melzack & Torgerson (1971) in constructing the MPQ, it was felt that ratings from both physicians and nurses might provide different and possibly more accurate information about the emeticproperties of these chemotherapy agents. This is because nurses tend to have more experience both in administering the medications and in speaking to the patients about them.

After the physician and nurse ratings had been collected, the investigator asked the 25 chemotherapy patients who were solicited for this study to complete the NRI, ONI, and VAS. For each set of nausea descriptors, the patient was instructed to put a tick beside any word that described his or her experience of nausea after the last treatment. The investigator sat next to the patient and pointed to each group of words, going down the list until the patient had completed the questionnaire. The patient then completed the ONI and made a mark on the VAS line at a point which corresponded to his or her perception of nausea.

Several measures of nausea were obtained in this way. Where a patient had chosen more than one word in any of the 20 categories of nausea experience, the word indicating the most severe aspect was chosen. The Nausea Rating Index (NRI) was obtained by adding the rank values of the words chosen. The rank values were then totaled for each of the subscales. Separate scores for the sensory (NRI-s,) affective (NRI-a), evaluative (NRI-e), and miscellaneous (NRI-m) subscales were calculated. The ONI rating was recorded, and the length of the VAS line was measured from the left end in millimetres. In addition, the chemotherapy drugs and doses currently being

taken by the patient were recorded.

The nausea ratings made by the physicians and nurses were used separately to calculate nausea scores for the drug or drug set received by each patient. One nausea score was the sum of the ONI estimates for all the drugs in a drug set taken by the patients (SUM). The second ONI estimate was for the highest rated drug of the set (HIGH). If a patient received only one drug, the SUM and HIGH nausea scores were obviously the same. The SUM score was used in the validation study on the assumption that the emetic-producing potential of a chemotherapy drug set was additive. By contrast, the HIGH estimate was based on the hypothesis that patients might experience no greater nausea than the nausea-producing potential of the highest rated drug in the set.

Results

The mean nausea ratings for 29 chemotherapy drugs and doses by the physicians and nurses are shown in Table 1.

The mean nausea rating made by the nurses (m = 2.3) was significantly higher than the mean ONI rating made by the physicians (m = 1.9), t (56) = 1.69, $p < .05$.[1] The estimates were highly correlated, however, reflecting the high degree of agreement between the two professional groups, r (29) = .89, $p < .01$. It is possible that nurses rated the drugs higher because they tend generally to be the ones who actually administer the chemotherapy medications, observe the patients during the treatments, and discuss the side effects with them and each other more frequently. This may provide them with more direct information about the patients' subjective experience.

[1] All of the p values reported in this thesis are two-tailed

Table 1
Mean Physicians' and Nurses' Estimates of the Overall Nausea Intensity (ONI) Produced by 17 Chemotherapy Drugs

Drug*	Dose (mg)	Mean ONI Estimates: Physicians (n=17)	Mean ONI Estimates: Nurses (n=8)
Bleomycin	15-30	0.3	1.3
Carmustine	150-200	2.7	1.9
Cisplatinum	50-70	3.1	3.4
	71-100	3.9	4.6
Cyclophosphamide			
Given orally	50-100	0.9	1.6
	101-200	1.7	2.4
Given intravenously	300-600	1.1	2.7
	601-1200	2.1	2.7
Decarbazine	200-300	2.6	2.2
	301-400	3.3	3.3
Dactinomycin	0.5-0.9	2.1	2.1
	1-2	2.9	3.2
Doxorubicin Hydrochloride (Adriamycin)	20-50	1.9	2.3
	51-90	2.8	3.6
Etoposide	150	1.7	2.3
5-Fluorouracil	250-600	0.8	0.8
	601-1500	1.9	1.6
Lomustine	50-75	2.1	2.2
	76-100	2.7	3.1
Methotrexate	15-50	0.6	1.1
	51-70	1.3	2.0
Mitomycin	8-15	1.1	1.6
	16-20	1.9	2.5
Semustine	80-100	2.2	2.2
	101-150	2.7	3.1
Streptozocin	1000	1.9	2.3
Teniposide	100	1.6	3.0
Vinblastine sulphate	8	0.7	1.0
Vincristine sulphate	1-2	0.2	0.6

* All drugs are given intravenously except for cylophosphamide, which may be given orally on a daily basis.

However, in spite of absolute differences in the ratings, the data indicate quite strongly that both groups rate the relative nausea-producing potential of the drugs similarly.

Reliability and Validity of the Nausea Measures

The correlations among the various subscales of the nausea questionnaire (NRI) and the ONI and VAS are shown in Table 2.

The nausea rating index (NRI) for the sensory (NRI-s), evaluative (NRI-e), and miscellaneous (NRI-m) subscales did not correlate significantly with the ONI and VAS scales. (See Table 2). The affective subscale (NRI-a), however, was significantly correlated with these measures, but accounted for a smaller portion of their overallvariance (ONI, r^2 = .28; VAS, r^2 = .37). The lack of association between the sensory subscale and the ONI and VAS, indicates that experience of nausea reflects affective dimensions and is not necessarily "painful" in the sense that a cut or burn might be. This result is consistent with the findings that patients were choosing words from the questionnaire which reflected more the emotional impact of their nausea. As can be seen in Table 2, there was a highly significant correlation between the ONI and VAS scales suggesting that these two measures share much common variance (r^2 = .56). Therefore, they may be evaluating the intensity of the nausea experience similarly.

Of the various subscales of the nausea questionnaire, only the NRI-a and NRI-m scores correlated significantly with the physicians' and nurses' estimates, indicating high construct (convergent) validity for these measures. (See Table 3). In contrast, the NRI-sensory and NRI-evaluative scales did not correlate significantly with the estimates of these professionally trained individuals. The ONI and VAS also correlated highly with the physician and

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Table 2

Intercorrelations Among the Subscales of the Nausea Questionnaire (Nausea Rating Index-NRI), Overall Nausea Intensity (ONI); and Visual Analogue Scale (VAS) for Patients (N = 25) in Study One

	Nausea Scale						
Nausea Scale	NRI-s	NRI-a	NRI-e	NRI-m	Total	ONI	VAS
Sensory (NRI-s)		.55**	.43*	.46*	.89***	.11	.19
Affective (NRI-a)			.55**	.74***	.84***	.53**	.61***
Evaluative (NRI-e)				.29	.61***	.35	.11
Miscellaneous (NRI-m)					.75***	.36	.31
Total (s + a + e + m)						.34	.35
Overall Nausea Intensity (ONI)							.75***
Visual Analogue Scale (VAS)							

* $p < .05$
** $p < .01$
*** $p < .001$

Table 3

Correlation Between Scores on the Nausea Questionnaire and the Physicians' and Nurses' Estimates of ONI for Patients (N = 25) in Study One

	ONI Estimates			
	Physicians (n = 18)		Nurses (n = 8)	
	SUM	HIGH	SUM	HIGH
Sensory (NRI-s)	.27	.15	.32	.23
Affective (NRI-a)	.38*	.45*	.41*	.51**
Evaluative (NRI-e)	.26	.15	.28	.18
Miscellaneous (NRI-m)	.44**	.46**	.44**	.51**
Total (s + a + e + m)	.40*	.34	.44**	.42*
Affective + Misc (NRI-am)	.44*	.49**	.46*	.54**
ONI	.57**	.56**	.57**	.62***
VAS	.55**	.55**	.55**	.63***

Note.
SUM-sum of ONI estimates of all the drugs in a drug set
HIGH-ONI estimate of the drug with the highest nausea-producing potential in a drug set
Total-total of sensory, affective, evaluative, and miscellaneous scales
ONI-overall nausea intensity
VAS-visual analogue scale
* $p < .05$
** $p < .01$
*** $p < .001$

nurses' estimates implying that these measures also demonstrated acceptable construct validity, since greater nausea should be associated with greater drug toxicity. The correlations for the HIGH values were similar to those for the SUM values. This may have been because eight of these patients received only one drug, so that their HIGH and SUM values were the same, or that the nausea-producing effects of chemotherapy drugs are not additive. It is also not surprising that the HIGH and SUM for both physicians' and nurses' correlate similarly with the nausea measures, since they rated the individual drugs similarly in part 1 of this study, as indicated in Table 1.

Since the NRI-m contains word descriptors that may be considered affective in quality, it was decided to combine this scale and the NRI-a scale into a single measure. This resulted in the most reliable and valid word descriptor scale (NRI-am). In an attempt to demonstrate the reliability of this scale which consisted of 9 NRI categories, Cronbach's test of internal consistency was applied (Cronbach, 1951). The scale was found to have satisfactory internal consistency, alpha = .83.

The number of patients choosing each word is shown in Table 4. In addition, the ONI was described as mild by six patients, discomforting by seven, distressing by six, horrible by five, and excruciating by one.

Finally, the discriminating power of the various nausea measures was tested by dividing the patients into two groups. The first group consisted of 5 patients who received cis-platinum (the highest rated chemotherapy drug by the physician's and nurse's) as their most toxic medication. The second group consisted of 8 patients who received 5-Fluorouracil (the lowest rated chemotherapy drug by the physician's and nurse's) as their most toxic medication. If the nausea measures were indeed valid, then they should discriminate between these two groups of patients. The mean values and SD's

Table 4

Frequency of Patients (N = 25) Choosing Word Descriptors on the Affective and Miscellaneous Subscales of the Nausea Questionnaire in Study One

Scale	Number of Patients (percent)
Affective	
1. Tiring	12 (48)
Exhausting	8 (32)
2. Sickening	12 (48)
Suffocating	1 (4)
3. Fearful	4 (16)
Frightful	1 (4)
Terrifying	0 (0)
4. Punishing	1 (4)
Gruelling	1 (4)
Cruel	0 (0)
Vicious	0 (0)
Killing	1 (4)
5. Wretched	4 (16)
Blinding	0 (0)
Miscellaneous	
6. Spreading	2 (8)
Radiating	0 (0)
Penetrating	0 (0)
Piercing	0 (0)
7. Tight	1 (4)
Numb	0 (0)
Drawing	0 (0)
Squeezing	2 (8)
Tearing	0 (0)
8. Cool	0 (0)
Cold	2 (8)
Freezing	2 (8)
9. Nagging	0 (0)
Nauseating	16 (64)
Agonizing	0 (0)
Dreadful	2 (8)
Torturing	1 (4)

for the various measures are shown in Table 5. .

Separate t-tests performed using the NRI-a and the NRI-m as dependent measures indicated that only the NRI-a discriminated between the low and high toxicity drug groups (NRI-a, $t(11)= 2.7$, $p < .02$; NRI-m, $t(11)= 1.99$, $p > .05$). However, when the NRI-am was used as the dependent measure, it did discriminate between the two criterion groups, $t(11) = 2.33$, $p < .04$.

Independent t-tests for the remaining two dependent measures discriminated significantly between the two groups: for the ONI, $t(11)= 4.16$, $p < .002$; for the VAS, $t(11) = 8.9$, $p < .002$. These results indicate that the three nausea measures appear to be reliable and valid indices of nausea.

Table 5

Means and Standard Deviations on the Nausea Questionnaire, ONI, and VAS for All Patients, Those Whose Drug Set Includes Cisplatin, and those receiving 5-Fluorouracil as the Drug With the Highest Estimated ONI

	Mean score (SD)		
Nausea Scale	All patients (n = 25)	Cisplatinum (n = 5)	5-Fluorouracil (n = 8)
Affective (NRI-a)	2.4 (2.3)	4.6 (3.3)	1.3 (1.0)
Miscellaneous (NRI-m)	2.6 (2.7)	5.4 (4.6)	2.0 (1.5)
NRI-a + NRI-m (NRI-am)	5.0 (4.7)	10.0 (7.8)	3.3 (2.4)
ONI	2.5 (1.2)	3.6 (0.6)	1.8 (0.9)
VAS	50 (30)	73 (8)	24 (10)

Study Two

Study 2 was designed to replicate and extend the significant, yet preliminary findings of Study 1. In Study 2, a test-retest design was employed to examine the stability of the nausea measure over 2 chemotherapy sessions in a second sample of chemotherapy patients attending a different hospital oncology clinic. A second goal was to gather more data on patient, treatment, and demographic variables which might relate to the subject's experience of nausea and to extend understanding of the parameters of nausea. Validity and reliability measures examined in Study 1 were repeated to assess their comparability with those observed in Study 2.

Method

Subjects

The drug toxicity ratings used for the validity analyses in this study were the ones obtained from the sample of physicians and nurses in Study 1.

The subjects were 27 patients who were attending the oncology clinic at the Jewish General Hospital. Their mean age was 54.2 years (SD=11.8) with a range of 30-77 years. Six patients were taking one chemotherapy drug; 5 were receiving 2 drugs; 15 were receiving 3 drugs; and 1 was receiving four drugs. This distribution was similar to that of the patients in Study 1. The drug protocols received by the individual patients are summarized in Table 6. Seven patients (twenty-five percent) were receiving a combination of cyclophosphamide, adriamycin, and cis-platinum, one of the most highly toxic combination of chemotherapy drugs. The rest of the sample received chemotherapy drugs in various other combinations and doses.

Antiemetic (anti-nausea) medications are often given intravenously with

Table 6

Chemotherapy Protocols of Patients (N = 27) in Study Two

Protocol	Number of Patients
Cyclophosphamide/Adriamycin/Cis-Platinum	7
Cyclophosphamide/5-Fluorouracil/Methotrexate	3
Adriamycin	3
Methotrexate/5-Fluorouracil	2
Cyclophosphamide/Adriamycin	2
Cyclophosphamide/Adriamycin/Vincristine	1
Cyclophosphamide/Methotrexate/5-Fluorouracil/ Vincristine	1
Cyclophosphamide/5-Fluorouracil	1
Adriamycin/5-Fluorouracil	1
Adriamycin/5-Fluorouracil/Methyl CCNU	1
Cyclophosphamide/Adriamycin/5-Fluorouracil	1
Cyclophosphamide/Adriamycin/VP16	1
Cyclophosphamide	1
Mitomycin/Vinblastin	1
5-Fluorouracil	1

the chemotherapy drugs for the prevention of nausea and vomiting. These medications are generally prescribed on the basis of the intensity of the side effects experienced bythe patient in previous sessions. Twelve patients were using no antiemetic medications either during or subsequent to treatment; 3 were only using 1 antiemetic; 6 were using 2 antiemetics; and 6 were using 3 antiemetics (a combination of 10 mgms. each of Reglan, Dexamethasone, and Stemetil) as indicated in Table 7.

The sample appeared to be heterogeneous, as indicated by the observation of various demographic variables in Table 8. Since this study was designed as a replication of Study 1, more demographic and descriptive data was obtained to allow for further comparison and generalization, in particular to the intervention study described in a later section.

Although fifty percent of the patients had previously received less than six chemotherapy treatments, some patients had received as many as 48, indicating a rather skewed distribution. This was also true of the number of months since diagnosis, with one patient having been diagnosed originally twelve years earlier who had recently recurred. In effect, this patient had been "cured" by most standards (Cairns, 1978; Cassileth, 1979), but had now received nine courses of chemotherapy for the recurrence of her breast cancer. Of course, a large number of chemotherapy treatments, or the fact that a patient is receiving active treatment a long time after diagnosis may indicate poor disease control, recurrence, or even progression of the disease. This patient was not excluded from the study in an additional attempt to assess whether such variables might affect the stability of the nausea questionnaire in the clinical context.

Table 7

Distribution of Antiemetic Drugs Given During Chemotherapy Treatments to Patients in Study Two

Antiemetic Drug	Number of Patients (n = 15)
Reglan (Metoclopramide)	9
Dexamethasone	11
Stemetil	12
Ativan (Lorazepam)	1

Note. Twelve of the 27 patients comprising the entire sample of study 2 were taking no antiemetic medications. Some patients were taking a combination of up to 3 drugs, usually 10 mgms. each of Reglan, Dexamethasone, and Stemetil.

Table 8

Demographic Characteristics of Patients (N = 27) in Study Two

Variable	Measure		
	Mean (SD)	Median	Range
Age	54.2 (11.8)	56.00	30-77
Number of previous chemotherapy treatments	9.6 (11.7)	5.25	0-48
Time since diagnosis (in months)	32.0 (44.3)	10.00	2-156

	Number of Patients	Percent
Sex		
Male	7	26
Female	20	74
Diagnosis		
Breast	14	52
Ovarian	6	22
Gastric	2	7
Others	4	15
Unknown	1	4

Procedure

The procedure used in this study was similar to that of Study 1. Patients attending the clinic were approached by a researcher while they were waiting for their appointment and asked if they had experienced any nausea after their last chemotherapy treatment. If they answered yes, they were then asked to complete the same nausea measures used in Study 1 concerning their experience. The measures were presented to the patients in the exact same manner as in the previous study. The patient's next chemotherapy treatment appointment time was noted and arrangements made to meet with him or her. At that time, the patient was asked to complete the same nausea measures, thus permitting an additional evaluation of reliability in terms of a test-retest criterion.

Using this procedure, it was hoped that by the replication of the results of Study 1 on a new sample of patients at a different hospital, further data on the stability and consistency of the NRI-am, ONI, and VAS might be obtained. In addition, further information about diagnosis, length of time since diagnosis, number of previous chemotherapy treatments, and the chemotherapy and antiemetic drugs used by the patients was obtained in order to evaluate their possible influence on the nausea measures.

Results

Of the 27 patients who completed the questionnaire initially, 8 were unavailable for the second questionnaire presentation after their subsequent chemotherapy treatment. Of the 8 patients, two had a change of chemotherapy regimen. One patient stopped chemotherapy due to extreme toxicity and another because of the ineffectiveness of the treatment on the progress of the disease. The 4 remaining patients were unavailable for follow-

up because of scheduling difficulties. The data were analyzed separately for both the initial test and the retest phases of the study, so that variables which might affect the stability of the nausea measures such as time and attrition could be examined.

This sample of patients was similar to the sample in Study 1. They were comparable in age ($\underline{m}$ = 56.0 in study 1; $\underline{m}$ = 54.2 in study 2). Further, there were 7 men and 18 women in Study 1 and 7 men and 20 women in Study 2.

Reliability

The results of this study in general provided support for the reliability and validity of the three nausea measures, though the results were not as consistent as those of Study 1. The NRI-am showed acceptable internal consistency for both the initial test, Cronbach's alpha = .66, and the retest presentations, alpha = .63, though these values were lower than in Study 1. Test-retest reliability for the 3 nausea measures did not support the hypothesis of stability over 2 consecutive testing sessions, with only the VAS demonstrating significance (NRI-am, $\underline{r}$ (19)= .15, $\underline{p}$ < .27; ONI, $\underline{r}$ (19) = .14, p< .29; VAS, $\underline{r}$ (19) = .51, $\underline{p}$ < .02).

Validity

The intercorrelations among the three nausea measures for the initial test were surprisingly not in agreement with the previous study. Although the correlation between the ONI and the VAS was highly significant, $\underline{r}$ (27) = .76, $\underline{p}$ < .001, the correlations between the NRI-am and the ONI, $\underline{r}$ (27) = .15, $\underline{p}$ > .05, and the NRI-am and the VAS, $\underline{r}$ (27) = .28, $\underline{p}$ > .05, were not. They are presented in Table 9.

The results of the retest, however, provided results similar to those found

Table 9

Correlation Coefficients Among the Three Nausea Measures in Study Two Analyzed Separately for Initial Test and Retest

	Study Phase			
	Initial Test (N = 27)		Retest (n = 19)	
Nausea Measure	ONI	VAS	ONI	VAS
NRI-am	.15	.28	.57*	.69**
ONI		.79**		.86**

*p < .01
**p < .001

in Study 1. The correlation between the NRI-am and the ONI, r (19) = .57, p < .01, and the NRI-am and the VAS, r (19) = .69, p < .001, were significant. The correlation between the ONI and the VAS, r (19) = .86, p < .001) was similar to the result obtained in the initial questionnaire presentation. The discrepancy between the two results was thought to be related to the loss of the eight patients from the initial test to the retest and this possibility is examined in a later section.

The correlations between the nausea measures and the sum of the physician and nurse ratings ratings (see Table 1) of the patient's chemotherapy drug set (SUM), the highest rating of the drug set (HIGH), and the mean rating of the drug set (MEAN) inthe initial testing are reported in Table 10.

There were no significant correlations between the NRI-am and the physicians' and nurses' ratings for SUM, HIGH, and MEAN, whereas the correlations between the ONI and the VAS and the drug ratings were generally in the expected direction for the nurses' ratings only. They were not, however, as strong as similar correlations in study 1. The correlations between the SUM and the nausea measures were extremely low and non-significant in this study for both the test and retest phases (see Table 11). This was a rather surprising result which differed from the results of Study 1. The results of the retest phase are considerably more similar to the results of Study 1. They are presented in Table 11.

The correlations between the NRI-am and the drug intensity ratings did not quite reach significance. The ONI and VAS measures, however, correlated significantly with the MEAN and HIGH, indicating that these measures in all likelihood do reflect the patients' experience of the nausea symptoms related to the chemotherapy drugs they are taking. Although the correlations for the SUM were now in the expected direction, they were still

Table 10

Correlation Coefficients Among Three Measures of Nausea and Physician and Nurse Ratings in the Initial Test (N = 27) of Study Two

	Nausea Measures		
	NRI-am	ONI	VAS
Drug Ratings			
Physicians			
SUM	-.32	.19	-.02
MEAN	-.20	.31	.30
HIGH	-.01	.26	.27
Nurses			
SUM	-.33	.21	-.001
MEAN	-.18	.37*	.38*
HIGH	-.05	.37*	.48*

*p < .05

Note.
SUM- Sum of the estimated drug values of the patient's drug set.
MEAN- Mean of estimated nausea values of the patient's drug set.
HIGH- Highest rated drug of the patient's drug set

Table 11

Correlation Coefficients Among Three Measures of Nausea andPhysician and Nurse Ratings in the Retest of Study Two (n = 19)

	Nausea Measures		
Drug Ratings	NRI-am	ONI	VAS
Physicians			
SUM	.10	.27	.22
MEAN	.33	.66**	.64**
HIGH	.34	.53**	.48*
Nurses			
SUM	.09	.26	.18
MEAN	.37	.66**	.61**
HIGH	.37	.54**	.47**

*p < .05
**p < .01

Note.
SUM-Sum of the estimated nausea values of the patient's drug set.
HIGH- Highest rated drug of the patient's drug set
MEAN- Mean of estimated nausea values of the patient's drug set.

quite low and failed to reach significance, as they did in Study 1. (See Table 3).

It is curious that the MEAN correlates so highly with the nausea measures. Since it is unlikely that the toxicity of chemotherapy drugs is diminished because they are given in combination, it is reasonable to conclude that being given a drug of lower toxicity would not reduce the toxicity of the most powerful drug of a particular set. Conceptually, it is more likely that the SUM would be a valid external validating variable, although there is no evidence that the toxicity of chemotherapy drugs is in any way cumulative (Penta et al., 1981a). The best estimate of the nausea-producing potential may be the HIGH rating. This conclusion is supported by an examination of the mean and median values of the physician and nurse ratings of toxicity obtained in Study 2. (See Table 12).

The mean HIGH and MEAN values are virtually identical for both physicians and nurses indicating that the additional drugs taken by those patients having more than one drug in their set had nausea ratings quite similar to the value of the HIGH. That is, if patients are given more than 1 drug, they are more likely to be of equivalent nausea-producing potential. If they are given a single drug, it is more likely to be a more powerful and therefore usually more toxic drug, such as Adriamycin or Cyclophosphamide. (See Table 6). Both HIGH and MEAN appear to be normally distributed with relatively low variability. On the other hand, the SUM scores showed much higher variability. This may be due to the fact that the SUM tends to vary according to the number of chemotherapy drugs taken, in addition to their toxicity. Since patients in this study and Study 1 were taking anywhere from one to four drugs (see Table 6), this would severely affect the stability of the SUM and leaves this variable as a questionable external validating criterion since patients receiving more drugs may not necessarily experience greater

Table 12

Mean and Median Values of the Ratings of the Nausea-Producing Potential of the Chemotherapy Drugs Used by the Patients in Study Two

	Variable	
Nausea Ratings	Mean (SD)	Median
Physicians		
HIGH	2.11 (0.93)	1.92
MEAN	1.97 (0.68)	1.91
SUM	4.84 (2.51)	4.50
Nurses		
HIGH	2.33 (1.13)	2.22
MEAN	2.40 (0.80)	2.30
SUM	5.95 (3.03)	5.80

Note.
HIGH-Highest nausea value of the drug set.
MEAN-Mean of the nausea values of the drug set.
SUM-Sum of the nausea values of the drug set.

nausea, as the data suggest. [2]

Since only the HIGH consistently correlates significantly with the nausea measures in both studies, and since it is likely that the nausea-producing potential of the various chemotherapy drugs is not additive, the highest rated drug is probably the best estimate of the emetic potential of any chemotherapy drug set.

Further analyses examining the discriminant validity of the various nausea measures were made by comparing the nausea ratings of those patients who received a highly toxic drug as their highest rated chemotherapy drug (Cis-platinum) and those patients who received one of the least toxic drugs as their highest rated chemotherapy drug (5-Fluorouracil). The data are presented for both the initial test phase and for retest in Tables 13 and 14.

The results of these comparisons only partly confirmed the results of Study 1. The NRI-am did not discriminate between the two groups of patients in either phase of the study (initial test- $\underline{t}(12) = .68$, $\underline{p} > .05$; retest-$\underline{t}(12) = .29$, $\underline{p} > .05$). However, the ONI (initial test-$\underline{t}$ (9) = 1.97, $\underline{p} < .06$; retest-$\underline{t}$ (9) = 2.28, $\underline{p} < .04$) and the VAS (initial test-$\underline{t}$ (9) = 2.13, $\underline{p} < .04$; retest-$\underline{t}$(9) = 1.96, $\underline{p} < .08$) did tend to discriminate between these two groups of patients, even though 2 of

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[2] Five of the 27 patients were receiving only 1 chemotherapy drug so that their HIGH, SUM, and MEAN were all the same. The validity correlations were reanalyzed after these patients were eliminated to assess the possibility that the correlations are affected by their scores. The results of the correlations between the HIGH and MEAN and the nausea measures were virtually identical to those in the original analysis. (See Tables 10 & 11). The results for the SUM were more problematic to interpret. For the initial test, the correlations were more positive and in the right direction than in the original analysis, but quite small (between $\underline{r} = .20$ to $\underline{r} = .30$) and clearly not significant. For the re-test, however, the correlations between the SUM and ONI (physicians, $\underline{r}$ (16) = .62, $\underline{p} < .01$; nurses, $\underline{r}$ (16) = .60, $\underline{p} < .02$) and VAS (physicians, $\underline{r}$ (16) = .51, $\underline{p} < .04$; nurses, $\underline{r}$ (16) = .45, $\underline{p} < .08$) were more consistent with the results in Study 1. (See Table 3).

Table 13

Means and Standard Deviations on the NRI-am, ONI, and VAS for Patients Whose Drug Set Includes Cisplatin or those receiving 5-Fluorouracil as the Drug With the Highest Estimated Nausea Rating for the Initial Test in Study 2

Nausea Scale	Mean score (SD)	
	Cisplatinum (n = 7)	5-Fluorouracil (n = 7)
NRI-am	6.9 (2.7)	5.6 (3.8)
ONI	2.7(1.1)	1.7 (0.8)
VAS	51.0 (23)	30.0 (12)

Table 14

Means and Standard Deviations of the NRI-am, ONI, and VAS for Patients Whose Drug Set Includes Cisplatin or those receiving 5-Fluorouracil as the Drug With the Highest Estimated Nausea Rating in The Retest Phase of Study 2

	Mean score (SD)	
	Cisplatinum (n = 6)	5-Fluorouracil (n = 5)
Nausea Scale		
NRI-am	6.2 (2.6)	5.4 (5.1)
ONI	2.7(0.8)	1.2 (1.3)
VAS	52.0 (13)	27.0 (27)

the tests failed to reach statistical significance. These results indicate that the the ONI and the VAS are superior to the NRI-am in discriminating between high and low toxic chemotherapy drugs but that even these results must be evaluated with great caution.

Discrepancies Between Initial Test and Retest

There are three possibilities for the incongruity between the initial test and retest phase correlations of the ONI, VAS, and NRI-am. The first hypothesis is that, in fact, the NRI-am is measuring a different aspect of nausea which may be only modestly related to the other two measures. This hypothesis is not likely given the strong results of Study 1 and the trends in the retest phase of study 2. If the NRI-am did measure something other than the subjective experience of nausea, consistently low correlations would have been more likely in the various reliability and validity comparisons of both studies. It is possible, however, that the NRI-am is measuring distress related not only to the patients' nausea, but also to various disease-related affective symptoms, e.g., anxiety and depression.

The second possibility is that patients completed the NRI-am inappropriately during the initial phase as in the first possibility described above and then learned that the experimenter was expecting the three measures to coincide during the retest. High test-retest correlations would indicate that no such learning process occurred and that patients were rating their nausea in a consistent fashion. Low test-retest correlations for the three measures were found indicating that this was so in this study. It might also be inferred from these results that the nausea measures are not particularly stable from one testing to another. The low correlations are more likely, however, to be expressions of other factors, such as changes in rate of

administration of the drugs or even the weather (Zeltzer & LeBaron, 1984), though the chemotherapy drugs were the same from initial test to retest. For example, mild nausea in two patients was eliminated completely when they asked their physician for previously unprescribed antiemetic medication. These patients were under the erroneous, yet not uncommon, misconception that the experience of nausea was a normal and untreatable phenomenon associated with chemotherapy. Morrow (1984) has demonstrated high test-retest reliability for his nausea measures over as many as 4 consecutive chemotherapy treatments. However, these excellent results (r = .70 to .90) are most likely to occur with patients receiving adjuvant chemotherapy, who are clinically stable, and receiving invariant treatment on a research protocol. It was not clear from Morrow's (1984) paper that this, in fact, was the case. This was not the case in the present study, which accepted any patients at any stage of their disease or treatment.

From these results, it is evident that great caution must be taken in deriving conclusions about the level of any patient's nausea from the assessment of only one chemotherapy session alone. Further, it is clear from these and other data (Morrow & Morrell, 1982; Zeltzer, LeBaron, & Zeltzer, 1983), that for any intervention outcome study, more than one baseline chemotherapy session must be evaluated in order to establish firmly the level of nausea experienced by a patient.

The final hypothesis regarding the test-retest discrepancy may be related to the eight patients who were unavailable for assessment at retest. There may have been some characteristics of these non-completers which might account for the poor correlations between the NRI-am and the ONI and VAS in phase one. Several variables which might have been responsible for the differences between the nineteen patients who completed the study and the eight

patients who did not were examined and summarized in Table 15.

There was no difference between the groups in age, [t (25) = .48, $p < .6$; sex, χ^2 (1, N = 27) = .001, $p < .9$]; time since diagnosis, [t (25) = .33, $p < .7$; and diagnosis, χ^2 (1, N = 27) = 2.45, $p < .3$]. However, completers experienced significantly fewer previous chemotherapy treatments, t (25) = 2.48, $p < .02$. The degree of variability in this measure suggests that several patients with more extreme scores may have contributed excessively to the significant difference in number of chemotherapy treatments between groups. The greater number of chemotherapy treatments may indicate poorer disease control in at least some of the non-completers, since there was no other significant difference between them and the non-completers, and the median number of chemotherapy sessions was similar for the 2 groups.

Table 16 presents the means, standard deviations, medians, and ranges of the nausea measures. It can be seen that there is considerable variability which might also account for the poor nausea measure intercorrelations in the initial test. The mean NRI-am score for the initial test for all 27 patients was higher than that for the 19 patients of the 27 who were available for the retest. When the initial (M = 6.63, SD = 4.24) and retest (M = 5.95, SD = 3.95) NRI-am scores for the 19 patients who completed the study were compared, no significant difference was found, t (18) = .56, $p > .5$. [3] The mean values for

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3 The validity correlations were reanalyzed for the sample of (n = 19) patients who completed the nausea measures at both the initial testing and the re-test. All of the results, for both the intercorrelations among the nausea measures and the correlations between the nausea measures and the SUM, HIGH, and MEAN were virtually the same for the initial test and the re-test phases. This finding further supports the conclusion that the unavailability of the 8 patients in the re-test phase of the study did not affect the original conclusions made for the entire sample (n = 27).

Table 15

Demographic Characteristics of Patients in Study Two Completing or Not Completing the Study

Demographic Characteristic	Completers (n = 19) Mean (SD)	Completers (n = 19) Median	Non-Completers (n = 8) Mean (SD)	Non-Completers (n = 8) Median
Age	54.9 (12.9)	56.8	52.5 (9.4)	53.1
Number of previous chemotherapy treatments *	6.3 (6.1)	4.0	17.5 (17.7)	6.5
Time since diagnosis (in months)	30.1 (44.0)	10.0	36.6 (47.7)	7.5

	Frequency (Number of Patients)	
Sex		
Male	5	2
Female	14	6
Diagnosis		
Breast	8	6
Ovarian	5	1
Gastric	2	0
Others	4	0
Unknown	0	1

* $p < .02$

Table 16

Central Tendencies of the Nausea Measures Completed at the Initial Test and Retest Phases for all Patients in Study 2

Nausea Measure	Central Tendency Measures			
	Mean	SD	Median	Range
NRI-am				
Initial Test (N = 27)	7.48	4.99	7.00	0-20
Re-Test (n = 19)	5.95	3.95	5.25	0-14
ONI				
Initial Test (n = 27)	2.11	0.93	2.04	1-5
Re-Test (n = 19)	2.11	1.10	2.10	0-4
VAS				
Initial Test (n = 27)	42.6	21.9	43.0	12-86
Re-Test (n = 19)	43.2	21.6	48.0	0-75

Note. A zero score for the initial test of the NRI-am indicates that the patient chose words only from the sensory or evaluative subscales, but not from the affective or miscellaneous subscales of the nausea questionnaire.
NRI-am (Nausea Rating Index-am) is the sum of the affective and miscellaneous subscales of the nausea questionnaire.
The ONI is the six point Overall Nausea Intensity Scale.
The VAS is the 10-centimeter Visual Analogue Scale.

the ONI and the VAS for both phases of the study were virtually identical (n = 27 and n = 19), indicating that there were no differences between phases on these variables, as well.

An examination of the scatterplot between the NRI-am and the ONI variables for the initial phase revealed heteroscedascticity. Four data points clearly contributed to this result. In an attempt to reduce the variability of the nausea scores, these 4 outlier scores were eliminated from a final analysis of the phase one intercorrelations. Three of these patients had the highest scores on the NRI-am and low scores of 1 or 2 on the ONI. The fourth patient was the only subject to record a score of 5 on the ONI, while having a rather modest score of 11 on the NRI-am. Similar results occurred for the correlation between the NRI-am and the VAS. These 4 subjects were eliminated, reducing the sample to (n = 23) for further analysis. The central tendency measures of the sample without the scores of these four patients for both phases of the study are presented in Table 17.

The elimination of these 4 subjects led to the means and medians of the NRI-am scores becoming virtually identical for both phases of the study. A re-analysis of the intercorrelations between the three nausea measures now resulted in significant correlations between the NRI-am and the ONI and VAS comparable to those obtained in Study 1. (See Table 18).

A closer examination of the clinical characteristics of the four patients (3 females and 1 male) with the outlier scores, provided further evidence that the NRI-am may, in fact, be a valid measure of nausea, but perhaps only within certain limits. Three of the four subjects were patients who also did not complete the retest phase. The male, who was a non-completer, had the rather rare diagnosis of advanced metastatic breast cancer. He was receiving adriamycin, one of the most toxic drugs, as a palliative measure after having

Table 17

Re-Analysis of the Central Tendencies of Nausea Measures in Study Two After Elimination of Four Outliers

Nausea Measure	Central Tendency Measure: Mean (SD)	Median	n
Initial Test			
NRI-am	6.0 (5.6)	5.5	23
ONI	2.1 (0.7)	2.1	23
VAS	42.0 (20.0)	43.0	23
Retest			
NRI-am	6.1 (4.0)	5.5	18
ONI	2.1 (1.1)	2.1	18
VAS	45.0 (21.0)	49.0	18

Note. Four subjects with outlier scores on the nausea measures dropped from the analysis. See text for further discussion and details of this procedure.

Table 18

Re-Analysis of Correlation Coefficients Among the Three Nausea Measures in Study Two After Eliminating Four Patients Having Outlier Scores

	Nausea Measure			
	Initial Test (n = 23)		Retest (n = 18)	
Nausea Measure	ONI	VAS	ONI	VAS
NRI-am	.48*	.45*	.56**	.64**
ONI		.76***		.86***

*p < .05
**p < .01
***p < .001

previously undergone 48 chemotherapy treatments over a 4 year period. Two of the females, who had breast cancer, were non-completers. One of thesepatients, although rating her nausea as rather low (ONI = 1; VAS = 19), chose 1 word from each category of the NRI-am during the initial test, resulting in a rather high score of 17. (Compare with Tables 16 and 17.) She appeared quite depressed during the initial test, and may have had difficulty in understanding the instructions or the meaning of the words on the NRI-am since English was not her first language. The former is more likely since her NRI-am score on the retest was 4, more consistent with her scores on the ONI and VAS. The patient who was diagnosed with ovarian cancer was receiving extremely high doses of cis-platinum and adriamycin. She had rated her nausea as 'unbearable' on the ONI and subsequently terminated her treatment. Another patient was a non-completer who had been diagnosed 12 years earlier. In summary, it appears that 3 of these patients may have been quite ill from their disease or at the very least, extremely distressed at the disease's late recurrence. One patient may have had a language problem or been quite depressed.

From this closer examination, it becomes more apparent that the NRI-am may be sensitive not only to chemotherapy-related nausea symptoms in essentially clinically stable patients, but may also reflect aspects of the affectively-laden symptoms which may be associated with advancing disease. These observations are consistent with the fact that the word descriptors of the NRI-am scale are adjectives which easily could be used by patients to describe other similar affective experiences and not only those caused by chemotherapy-produced nausea. This possibility may confound the use of the NRI-am as a 'pure' measure of chemotherapy-related nausea.

Study Three

The purpose of Study 3 was to provide further validation of the nausea measures in an outcome study designed to evaluate the clinical effectiveness of hypnosis as an intervention in the reduction of the nausea and vomiting side effects of chemotherapy.

Method

Subjects

Patients were recruited from the adult out-patient oncology clinics of four health care institutions in the Montreal area. Forty patients agreed to participate in the study: Montreal General Hospital (n = 22), St. Mary's Hospital (n = 5), Queen Elizabeth Hospital (n = 6), and the Jewish General Hospital (n = 7). (See Table 19 for breakdown of demographic and patient characteristics.) In order to qualify for the study, they had to have experienced symptoms of nausea and/or vomiting in one or more of their most recent chemotherapy sessions. Since a wide variety of diagnoses and chemotherapy agents were associated with nausea and vomiting, no diagnostic category or chemotherapy drug class was excluded. Indeed, as Table 19 indicates, 85% (n = 34) of the patients were undergoing their first chemotherapy protocol.

Procedure

Patients were told that a study examining the effects of hypnosis and relaxation on side effects of chemotherapy was taking place in their department. A bilingual handout describing the nature of the study was placed near the registration desk of the respective chemotherapy clinics of the hospitals involved in this study (See Appendix B). On registering, patients were given this handout for examination while they were waiting for their

Table 19

Demographic Characteristics of Patients in Study Three (N = 40)

Demographic Characteristic	Number of Years	
Age		
Range	19-72	
Mean	49.8	
Median	50.0	
	n	Percent
Sex		
Men	5	12.5
Women	35	87.5
Type of Cancer		
Breast	21	52.5
Lung	5	12.5
Bowel	2	5.0
Ovarian	6	15.0
Head and Neck	1	2.5
Testicular	3	7.5
Unknown	2	5.0
Previous Treatment		
Chemotherapy	6	15.0
Radiotherapy	18	45.0
None	16	40.0

appointment. Other patients were told by their physicians or treating nurses about the study, because they had been identified as having particular problems with chemotherapy side effects. The rationale of the study was explained to them by the hospital staff and they were encouraged to participate. They were told that further information could be obtained from the investigator. If they showed interest in the project, their names were given to him; he then telephoned each one of them. He again explained the nature of the project to them on the phone, invited them to an initial interview and made an appointment.

Session One

At this initial appointment, the patients were given the opportunity to discuss their illness and its treatment with the investigator, who was a clinical psychologist with 7 years of experience working in a general hospital setting with both psychiatric and medical patients. The study was described to the patient again, and informed consent obtained (see Appendix C). Subsequently, demographic and other data concerning the illness, its course and treatment, were obtained from patients, as were data regarding side effects, especially nausea and vomiting. These data were summarized on the patient intake form (see Appendix D). During this first session, patients were asked to complete a number of questionnaires:

1) The McGill Nausea Questionnaire (MNQ), which provided the NRI-am measure, had been investigated extensively earlier in Studies 1 and 2. Patients' chose words from the various word groupings to describe their experience of nausea. The procedure in Studies 1 and 2 required patients to read the word groups to themselves while the investigator pointed to them. Following this, they then chose the appropriate word, if any, from that group

which described their experience of nausea. Studies with the McGill Pain Questionnaire (MPQ), however, have shown that patients tend to choose more words if they read them than if the words are read to them (Klepac, Dowling, Rokke, Dodge, & Schafer, 1981). In the present study, the groups of words were read to the patient by the investigator as an alternative presentation procedure. In addition, the researcher began with group 20 and read the words in descending order. Since the NRI-am was composed of the affective (groups 11-15) and miscellaneous (groups 17-20) subscales, this procedure was utilized to give patients the opportunity to choose words first from these groups (rather than from the sensory subscale as in Studies 1 & 2). The six-point Overall Nausea Intensity (ONI) scale, but not the VAS, was also completed.

2) The Spielberger State-Trait Anxiety Questionnaire (STAI) is a forty-item scale which provides two measures of anxiety; state anxiety (which is the anxiety experienced by the person in a particular situation); and trait anxiety (which is the person's general level of anxiety) (Spielberger, Gorsuch, & Lushene, 1970). In this study patients were instructed to rate anxiety experienced prior to and during the time of their last chemotherapy session on the state anxiety scale. This was possible since it has been shown that correlation coefficients between state ratings made retrospectively and those made at the time of the anxiety-evoking situation are quite high (Spielberger et al., 1968).

3) In addition, patients were provided with packets of self-report forms. These packets contained seven-point rating scales for anxiety, nausea, and vomiting intensity. Each point on the scale had a word descriptor attached to it (0 = none, 1 = mild, 2 = discomforting, 3 = distressing, 4 = horrible, 5 = excruciating, 6 = worst ever). In addition, the patients recorded the number of

vomiting episodes they experienced. They were asked, further to complete a self-report forms packet during each of the next two chemotherapy sessions (see Appendix E). Ratings for each of these variables were to be completed for six different time intervals prior to, during, and following each of the chemotherapy sessions. The various time intervals were:

3D- during the three days prior to the chemotherapy session

EV- the evening before the chemotherapy session

AR- the day of the chemotherapy session until arriving at the clinic

WT- while waiting for the chemotherapy treatment

DU- during the injection of the drugs

PS- post-chemotherapy; until the side effects remitted completely

The various time intervals were of particular interest since little research regarding the topography of the patient's subjective experience exists in the literature.

In addition, patients recorded such data as the time of initiation and termination of nausea and vomiting and the number of antiemetic medications taken. These data were sought in order to obtain information along three relevant dimensions of the respective dependent measures, i.e., frequency, intensity, and duration (Morrow, 1984c), thus permitting closer examination of the effects of the intervention.

Patients were then given an appointment subsequent to the next two chemotherapy sessions. They were told to contact the researcher if they experienced any problems in filling out the self-report forms.

Session Two

After having completed two baseline chemotherapy sessions, each patient returned for the first of two hypnosis treatment sessions. In the first of these

sessions, his or her self-report forms were examined for accuracy and completeness. Patients were then introduced to the concept of hypnosis and its usefulness in the treatment of various types of medical problems. A number of common misconceptions about hypnosis were discussed with them and reassurance was provided particularly with respect to the issue of loss of control in hypnosis. Hypnosis was described as a method of learning to relax and use one's imaginative abilities either to alter the perception and/or to distract the person away from the unpleasant sensations of nausea. It was suggested to patients that they would be able to utilize these hypnotic abilities in attenuating their anxiety, nausea and vomiting by practising their skills and utilizing them during the chemotherapy treatments. Previous experience with imagery in everyday life, as well as any previous experience with hypnosis were discussed. From this information and from the history gained through the various discussions with each patient, imagery and fantasy material were incorporated into the hypnotic treatment.

Once a patient was comfortable and reassured about the misconceptions regarding hypnosis, the induction procedure began. The patient had the choice of either sitting or reclining in a comfortable "lazy boy" chair. The therapist sat to the side and slightly behind him or her. The hypnotic induction procedure was adapted from the relaxation instructions of the Stanford Hypnotic Susceptibility Scale: Form C (SHSS: C) developed by Weitzenhoffer and E. R. Hilgard (1962). (See Appendix F). After initial suggestions of comfort and relaxation, an eye closure procedure was presented. Subsequently, specific suggestions for muscle relaxation and further deepening procedures were introduced. Ego strengthening suggestions (Hartland, 1971) were given just prior to specifically tailored imagery designed to deepen the hypnosis and allow each individual patient

to develop various coping techniques to combat the side effects of chemotherapy. Finally, post-hypnotic suggestions were given to remind the patient that what had been learned during hypnosis could be experienced at a later time, particularly just prior to, during, and subsequent to the next chemotherapy session.

During this initial practice session, an audiotape recording was made of the hypnosis instructions. This tape was given to the patient for home practice. Although little evidence is available to indicate that the use of audiotapes as adjuncts to hypnosis or relaxation enhance outcome (Hoelscher, Lichstein, Fischer, & Hegarty, 1987; Morrow, 1984d), it was felt that this approach might facilitate hypnosis practice. The patient was instructed to practise at least once per day by finding a comfortable place at home and playing the tape. The importance of doing this daily was emphasized. Following these instructions, another appointment was made.

Session Three

Prior to the next chemotherapy treatment, the patient was seen for a second hypnosis treatment session. Discussion of previous practice was discussed and any difficulties were elucidated and reviewed. Another treatment was conducted, with changes being inserted into the content of the session based upon feedback provided by each individual patient. If necessary, a new tape was made of the hypnotic treatment; it either replaced the previous tape or was constructed for use as additional practice in conjunction with the original tape.

Instructions were given on how to use the hypnotic techniques during the next chemotherapy session. These instructions included such suggestions as using self-relaxation, self-suggestions, imagery, distraction or focusing of

attention away from the stimuli which may have been cues to a particular patient for the elicitation of anxiety, nausea and/or vomiting. Each patient was encouraged to utilize as many of these techniques as were felt to be helpful and easy to apply. All patients were told that since each of them was an individual with unique hypnotic talents, they should not be afraid to choose those techniques taught by the therapist which appealed to them most. Examples of the types of interventions employed are provided in Appendix F.

Each patient was then reminded to record ratings of the various dependent measures on the self-report forms during the next two chemotherapy sessions. In addition, he or she could phone the therapist at any time for advice or help regarding any aspect of the program. A further appointment was arranged following the second chemotherapy treatment.

Session Four

At this final appointment, patients returned to discuss the results of the hypnotic intervention during the two follow-up chemotherapy sessions. The self-report forms were collected and examined for completion. Following this, they completed the follow-up questionnaires which included the STAI and the MNQ.

Each patient then underwent the SHSS: C to evaluate hypnotic susceptibility. In its original form, this test consists of an hypnotic induction procedure followed by the presentation of 12 items reflecting a range of hypnotic abilities (ideomotor, challenge, and cognitive-perceptual) which the subject is asked to experience. The SHSS: C used in the present study was modified in order to shorten the time spent in examining patients, while still obtaining a reasonable sampling of his or her hypnotic abilities. A number of items were deleted: taste hallucination, dream, arm immobilization, anosmia

to ammonia, hallucinated voice, and negative visual hallucination. These were replaced by two others of comparable difficulty: glove analgesia and post-hypnotic suggestion. This resulted in a modified SHSS: C consisting of 8 items. (See Appendix G). The number of items passed by the patient constituted the measure of hypnotic responsivity. (See Appendix H). Patients were told that this test was useful in determining the skills underlying hypnosis which may be contributing to its effectiveness in nausea and vomiting treatment.

The reason for the inclusion of a scale of hypnotic susceptibility is related to recent findings that anxiety-related disorders, such as phobias may develop more frequently in individuals with higher hypnotic susceptibility, as measured by standard scales (Frankel, 1974, 1975; Frankel & Orne, 1976; John, Hollander, & Perry, 1983). If the development of anticipatory nausea and vomiting is a conditioned phenomenon, which may be mediated by anxiety, then it is possible that some of the same cognitive processes (such as dissociation, imagery, and absorption) which mediate phobic behaviour may also be important in the development of nausea and vomiting. This understanding may facilitate the development and tailoring of clinically effective treatments, such as hypnosis, as well as help to predict which patients might benefit from psychological treatment (e.g., Andreychuk & Scriver, 1975); In addition, performance on the SHSS:C may perhaps identify patients at risk for the development of nausea and vomiting symptoms.

Following the administration of the modified SHSS: Form C, the patient was thanked for participating in the research project and invited to call the investigator if he could be of any future assistance.

Results

Of the forty patients who agreed initially to participate in this study, twenty-two of them did not complete the study for the following reasons: deterioration in physical status due to illness progression (n = 5), change in chemotherapy treatment protocol (n = 11), or an inability to complete the program due to other, treatment-related obligations, such as multiple appointments for various medical tests (n = 6). Initial interview and questionnaire data were available, however, for most of the patients. The difficulties in recruiting cancer patients and the attrition over the course of this study reflected the problems found in virtually all psychosocial research with cancer patients (Blotcky et al., 1985; McCorkle, Packard, & Landenburger, 1984; Morrow & Morrell, 1982). For these reasons, the available N for each variable of interest in this study varied, but was utilized for statistical analysis wherever possible.

In addition, some of the patients were unable to complete all of the necessary data and questionnaire forms which were required throughout the course of the research protocol. Although the investigator encouraged them to do this, many of them still found it exceedingly difficult to comply. Their major preoccupation and priority was, understandably, to follow the treatment and diagnostic plans that had been organized by their doctors and nurses. This led to scheduling problems for some of them; they did not wish to come to their respective hospitals any more often than required. Many sessions were scheduled to coincide with other appointments and several sessions were carried out at the patients' homes in order to facilitate data collection.

In the case of the the self-report forms (see Appendix E), only 11 patients filled out the symptom ratings (anxiety, nausea,vomiting frequency, and vomiting intensity) completely without any missing data points. An

additional 3 patients accounted for 12 missing data points collectively. Four others failed to complete one whole session of symptom ratings (one baseline or one post-hypnosis session). Two of these patients had only 3 chemotherapy sessions left in their protocol when they agreed to enter the study. It was decided nevertheless to include them in the study and to use only one baseline session in these two cases so that two post-hypnosis sessions would be available for follow-up analysis. The other two patients who missed a post-hypnosis chemotherapy session had their chemotherapy protocol changed after session three.

Since the missing data appeared to be random across data points, the recommendations of Cohen & Cohen (1983) were adopted to increase the sample size, and to utilize as much of the available data as possible. They suggest replacement of these missing data points by the means of the respective values for the remainder of the group. This procedure allows for the mean values of the replaced data points to remain unchanged. Since the deviations of the replaced data from the group mean are zero, it must also be true that the value of the regression coefficient of the independent variable on the dependent variable will remain unchanged from the one calculated only from cases with known data present, thus eliminating distortion of the results. These authors suggest further that when the proportion of missing data is small (that is less than 10%, as in the present study), then the variance accounted for by the independent effects of the missing data on the dependent variables will be extremely small. Also, because the N is small, this variance is highly unlikely to be significant. Under these circumstances, the independent effect of the missing data is negligible and need not be accounted for in the statistical analysis (Cohen & Cohen, 1983). This missing data replacement technique is often acceptable in repeated measures designs where

attrition and other data collection problems, as frequently occurs in psychosocial and medical research, will reduce the sample size significantly, thus eliminating the use of partial data available for some subjects (cf. Cerny, Barlow, Craske, & Himaldi, 1987).

In effect, out of a possible 1728 data points collected (i.e., 6 time points x 4 sessions x 18 subjects x 4 dependent measures, 108 (6.25 percent) were replaced in this manner. The percentage of missing data for each of the six time points was approximately equal, ranging from 15-20%.

The implementation of this technique allowed for the inclusion of data from those patients who were unable to complete the entire protocol and whose available data would otherwise have been lost. This permitted the sample size to be increased from (n = 11) to (n = 18) thus enlarging the data base for the analysis of the self-report symptom data. In order to evaluate the effect of including patients for whom there were no data for an entire session, separate analyses were performed in which these 4 patients were eliminated. This approach resulted in a sample of 14 patients in which 396 (384 plus 12 from other patients) missing data points out of the original 1728 (23%) were eliminated leaving 1332 data points for the analyses. The purpose of this comparison was to evaluate the possibility that the data replacement technique might have resulted in spurious statistical significance. All of the statistical analyses described later on in this section were repeated for this smaller sample of (n = 14) patients. From the results of these separate analyses, no outcome was found which differed from the analyses of the larger group (n = 18). Therefore, only the results of the analyses for the larger group are presented.

Patients' self-report symptom ratings of anxiety, nausea, vomiting frequency, and vomiting intensity on the seven point scales (see Appendix F)

were analyzed using a multivariate analysis of variance (manova) for repeated measures procedure. A within-subjects design was employed, using the patients as their own control. There were two within group variables: chemotherapy session (two baseline and two post-hypnosis) and time (3D, EV, AR, WT, DU, PS) within chemotherapy session. Overall manovas were computed for each dependent variable. Pillai's criterion will be reported along with the corresponding exact F values (O'Brien & Kaiser, 1985). The multivariate approach is an especially useful procedure because it reduces the possibility of Type 1 error by being sensitive to the possibility of intercorrelations among the dependent measures which may lead to the violation of the assumption of compound symmetry.

Furthermore, planned orthogonal comparisons were performed in order to examine the location of specific within-chemotherapy session differences for each of the four main dependent variables: anxiety, nausea, vomiting frequency, and vomiting intensity. These analyses permitted the examination of:

a) possible differences between the two baseline sessions (mean of sessions 1 and 2). Here, a finding of no difference would confirm the stability of the dependent measure during baseline. By contrast, a significant difference between the means of session 1 and 2 could indicate that baseline drift confounds conclusions about any significant treatment effects.

b) In the second comparison, the combined mean of the two baseline and two post-hypnosis chemotherapy sessions were compared to evaluate the effect of the hypnosis intervention.

c) A third comparison tested for differences between the first three chemotherapy sessions and the last. This sought to determine whether the symptoms continued to reduce further into the fourth chemotherapy session

of the current protocol.

The following sections present detailed findings for the dependent variables-namely nausea (anticipatory, post-chemotherapy, and global), anxiety (anticipatory, post-chemotherapy, and global), and vomiting frequency and intensity (anticipatory and post-chemotherapy). Following this, a discussion of the control issues raised by a within-subjects design such as this one, which raises controversies relating to the treatment of clinical patients as opposed to experimental subjects, is included. The means and standard deviations for each dependent variable is presented in Appendix I.

Nausea

Nausea ratings made by patients at each of the six time periods within each of the four chemotherapy sessions are shown in Figure 2.

The curves indicate clearly that nausea increases during each chemotherapy session, with the the most severe nausea occurring during the the post treatment (PS) phase. Trend analysis for the time variable collapsed over the four sessions confirms the finding of a significant linear trend, $F(1, 17) = 48.38$, $p < .0001$, but no higher order trends. This result is as expected, since the unconditioned response (UCR) of the nausea produced by the actual physiological effect of the chemotherapy drug is bound to be stronger than any conditioned effects which might be experienced prior to the administration of the drug. Also, the nausea becomes progressively more severe as the treatment appointment approaches and continues to increase after the chemotherapy drugs are administered.

The results of the overall manova testing for differences in nausea ratings between sessions was significant, Pillai's criterion = .47, $F(3,15) = 4.20$, $p < .02$. Planned orthogonal comparisons showed that during baseline chemotherapy

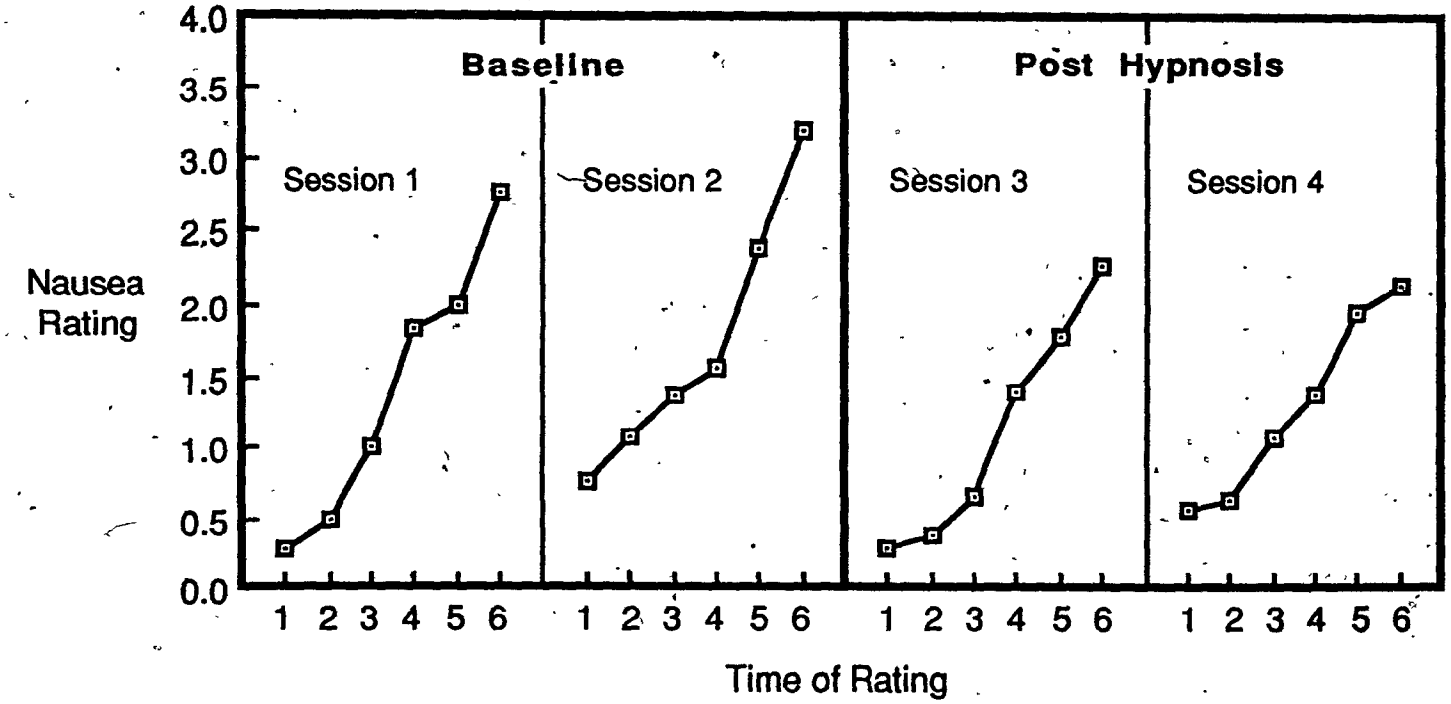

Figure 2. Patients' (N = 18) ratings of their nausea at six time points for two baseline and two post-hypnosis chemotherapy treatment sessions:

1 - for 3 days prior to treatment (3D);
2 - the evening before treatment (EV);
3 - up to the time for arrival at the clinic (AR);
4 - while waiting in the clinic waiting room (WT);
5 - while receiving the injection (DU);
6 - from the time the patient leaves the clinic until the nausea has ended (PS).

sessions, there was actually an increase in mean nausea rating between chemotherapy session 1 and chemotherapy session 2, $F(1,13) = 5.7$, $p < .03$, supporting other findings that nausea appears to worsen over time (Nerenz et al., 1982,1984; Wilcox et al., 1982).

Nausea ratings decreased significantly between baseline (mean of sessions 1 and 2) and post-hypnosis (mean of sessions 3 and 4) chemotherapy sessions, $F(1,13) = 6.77$, $p < .02$, indicating that overall nausea decreases significantly after treatment with hypnosis. By contrast, there was no difference in nausea ratings between the first three chemotherapy sessions (mean of sessions 1, 2, and 3) and the fourth (mean of session 4), $F(1,13) = 3.09$, $p < .10$. This appears to indicate that the decrease in reported nausea from baseline to post-hypnosis is not reflected in a further decrease in nausea in session 4.

Anticipatory Nausea

It is of clinical and theoretical importance to determine whether the reductions found in the post hypnosis sessions were due primarily to changes in anticipatory nausea and/or post-chemotherapy nausea. Anticipatory symptoms were defined as the phases during which symptoms occur prior to the actual injection of the chemotherapy drugs (i.e., 3D, EV, AR, and WT). Injection of the chemotherapy drug, which constitutes the DU (during treatment) phase as defined in this study, is the demarcation point between the anticipatory symptoms and the post-chemotherapy symptoms. Post-chemotherapy (physiological) symptoms of nausea were defined by the DU and FS phases. Separate manovas were performed on anticipatory nausea symptoms and post-chemotherapy nausea symptoms. Grouping of the dependent variables in this manner to specify comparisons of theoretical importance has been suggested by Stevens (1986).

The overall manova testing for differences between sessions in anticipatory nausea was not significant, Pillai's criterion = .29, $F(3, 15) = 2.07$, $p < .15$. Since two important assumptions about the homogeneity of variances were met (Bartlett's test of sphericity = 5.4, $p > .05$; F max criterion (3, 17) = 1.8, $p > .05$), it was possible to employ a univariate analysis of variance approach without compromising Type 1 error (Stevens,1986).[4] The result of the univariate analysis indicated an overall result which also just failed to reach significance, $F(3,51) = 2.37$, $p < .08$. No significant differences were found for mean nausea ratings between sessions one and two, $F(1, 13) = 2.1$, $p < .17$. However, anticipatory nausea was significantly reduced from baseline (mean of sessions 1 and 2) to post-hypnosis (mean of sessions 3 and 4) phases, $F(1, 13) = 4.62$, $p < .05$. This lack of a significant omnibus manova severely prohibits conclusions which may be drawn from this result.

Further, there was no difference between the mean of the nausea ratings of sessions 1, 2, and 3 and session 4, $F(1,13) = .99$, $p < .33$. Indeed, anticipatory nausea appeared to increase in session 4 relative to session 3. (See Figure 2). This latter finding indicated that any reduction in mean nausea rating occurred between baseline (mean of sessions 1 & 2) and post-hypnosis (mean of sessions 1 & 2) only and that the gains did not continue through session 4.

Post-Chemotherapy Nausea

The overall manova test for differences between sessions in post-

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4. Bartlett's test of sphericity is used when there exists a concern about compound symmetry. Essentially, it tests the hypothesis that the covariance matrix of the transformed variables is a diagonal matrix. In other terms, under sphericity, for "all possible pairs of treatment levels, differences of the form $X_i - X_j$ have the same population variance where X_i and X_j are two distinct levels of the repeated measure" (Jaccard & Ackerman, 1985, p. 426). The F Max criterion is a test of homogeneity of variances.

chemotherapy nausea indicated significant effects, Pillai's criterion = .43, $F(3, 15) = 3.73$, $p < .03$. No significant difference was found for mean nausea ratings between baseline sessions 1 and 2 for post-chemotherapy nausea, $F(1, 13) = 2.65$, $p < .12$. Post-chemotherapy nausea was reduced significantly from baseline (mean of sessions 1 and 2) to post-hypnosis (mean of sessions 3 and 4), $F(1, 13) = 6.72$, $p < .02$, and continued to decline from sessions 1, 2, and 3 to session 4, $F(1, 13) = 7.62$, $p < .01$.

These results indicate clearly that the overall reductions in nausea are accounted for by slight, though non-significant, reductions in anticipatory nausea symptoms, and more impressively by a substantial reduction in post-chemotherapy nausea. This finding is somewhat unexpected in that the original hypothesis was that the hypnosis intervention would serve primarily to reduce anticipatory nausea symptoms, given that these symptoms were thought to be conditioned responses to eliciting stimuli of the chemotherapy treatment situation. The post-chemotherapy nausea symptoms, considered to be primarily physiological in origin and due to the biochemical effects of the chemotherapy drugs, were thought to be more resistant to psychological intervention. However, the findings are consistent with other studies using various relaxation procedures for post-chemotherapy nausea reduction (e.g., Burish & Lyles, 1979, 1981). In addition, other studies have shown that hypnosis, for example, can help to reduce the pain of bone marrow aspirations and lumbar punctures (cf. J. R. Hilgard & Le Baron, 1984) or even the nausea associated with the first trimester of pregnancy (Apfel, Kelly, & Frankel, 1986). Therefore, the distinction between 'conditioned' symptoms and 'physiological' symptoms is in need of further study.

Global Measures of Nausea

One of the major goals of this thesis was to develop and evaluate reliable, valid, and efficient measures of nausea. The effectiveness of the hypnosis intervention was evaluated by the administration of the nausea questionnaire (NRI-am) and the ONI during the first interview session and again at the fourth interview session. Central tendency and dispersion measures for the NRI-am and the ONI for baseline and post-hypnosis are shown in Table 20. Not all patients completed the questionnaire at all phases of the study. (See note b in Table 20 for further elaboration of this point).

Of the 18 patients who provided sufficient data to be considered as completers,16 of them filled out the follow-up questionnaires at the post-hypnosis interview.[5] The data are presented separately for completers (those patients who completed the protocol by filling out all the relevant questionnaires at the initial and post-hypnosis interviews; n = 16) and non-completers (those patients who completed only the initial interview questionnaires; n = 23). Correlations between the NRI-am and ONI measures for the baseline [r (39) = .54, p < .002] and post-hypnosis testings [r (16) = .82, p < .002] clearly support the earlier findings of concurrent validity in Studies 1 & 2.

Although the mean NRI-am rating at baseline for non-completers (M = 12.70) was higher than the rating for completers (M = 10.19), this difference was not significant, t (37) = 1.40, p > .05, and was most likely due to high variability between subjects. For completers, there was no change in the NRI-

[5] Two patients, although completing the self-report forms for the post-hypnosis chemotherapy sessions, declined to attend the final meeting with the investigator.

Table 20

Distributions of the Nausea Measures Used in Study Three

Nausea Measure	Central Tendency and Dispersion Measures			
	Mean	SD	Median	Range
NRI-am [a]				
Baseline				
Non-Completers [b] (n = 23)	12.70	6.26	11.00	1-26
Completers (n = 16)	10.19	4.93	8.50	5-25
Post-Hypnosis (n = 16)	9.13	6.79	9.5	0-21
ONI [c]				
Baseline				
Non-Completers (n = 23)	3.44	1.12	3.33	1-5
Completers (n = 16)	3.06	1.06	2.90	2-5
Post-Hypnosis (n = 16)	2.13	1.20	2.17	0-4

Note. [a] NRI-am is the sum of the affective and miscellaneous subscales of the nausea questionnaire.

[b] Of the 40 patients originally agreeing to participate in this study, 39 completed the nausea measures at the initial session. One nausea questionnaire was lost. Non-completers were those patients who did not complete the study (n = 23) and for whom only the baseline questionnaire data, but not the post-hypnosis questionnaire data were available. Those considered completers in this table are 16 of 18 patients who completed 4 chemotherapy sessions and for whom both baseline and post-hypnosis interview data were available.

[c] The ONI is the six point Overall Nausea Intensity scale.

am from baseline (m = 10.19) to post-hypnosis (m = 9.13), $t = 0.69$, $df = 15$, $p > .50$. This result contradicts the findings presented earlier that patients in the hypnosis group did reduce their post-treatment nausea significantly when they were asked to make nausea ratings at specified time intervals.

By contrast, the results for the ONI ratings were more consistent with earlier findings. There was no difference in the baseline ONI rating between non-completers ($M = 3.44$) and completers ($M = 3.06$), $t(37) = 1.05$, $p > .05$. For completers, however, there was a significant reduction in ONI rating from baseline ($M = 3.06$) to post-hypnosis ($M = 2.13$), $t(15) = 3.53$, $p < .003$.

These results are consistent with the conclusions reported in study 2 that the NRI-am may be sensitive not only to the effects of chemotherapy but also to other patient and treatment variables (e.g., disease progression to brain or gastrointestinal tract), and that the ONI is a less contaminated measure of chemotherapy-induced nausea. Drop-outs in study 3 may have had higher (though not significant) and more variable nausea ratings for similar reasons.

There is another potentially important finding related to absolute levels of nausea ratings. Comparisons between the mean NRI-am rating for the initial test of study 2 ($M = 7.48$) and the baseline mean NRI-am of the patients in study 3 ($M = 11.67$) showed that the former ratings were significantly lower, $t(64) = 3.13$, $p < .01$. This result held as well for the ONI scale (study 2, $M = 2.11$; study 3, $M = 3.28$), $t(64) = 4.66$, $p < .001$. One possibility is that the patients agreeing to the hypnosis intervention in Study 3 were, in fact, experiencing greater nausea and hence the greater motivation to participate, than the patients in Study 2, who were asked only to fill out the nausea questionnaires on 2 occasions. A second possibility is that since the nausea questionnaire and the ONI were presented differently in studies 2 and 3 (as outlined in the procedure section of study 3), the absolute differences in nausea ratings

between the two studies may be due to the artifact created by the dissimilar presentations rather than any real differences in nausea, especially since the relative values within each study do not appear to be affected. If the latter case is true, a strong argument exists for adopting strict and consistent procedural guidelines when administering nausea rating scales.

Anxiety

The anxiety ratings made by the 18 patients for each of the six time periods evaluated during each chemotherapy session are shown in Figure 3.

As was the case for nausea, anxiety increased in the periods prior to the actual injection and appeared to peak while the patient was waiting or during the infusion of the drugs. It diminished during the post-injection phase, in spite of the fact that during this period the patient was usually experiencing increased nausea and vomiting. Trend analysis for the time variable collapsed across sessions indicated significant linear, $F(1, 13) = 12.02$, $p < .003$ and quadratic components, $F(1, 13) = 5.54$, $p < .03$.

These results indicate that anxiety increases incrementally during the pre-injection phase, and decreases during and after the chemotherapy drugs are given. This curvilinear function may be contrasted with the linear progression of nausea described in an earlier section. Patients may be relieved to have finally undergone the ordeal of anticipating and waiting for their treatment, but in spite of the fact that they were significantly more nauseous, the feeling of being 'over the hump' and the expectation of the eventual diminution of the nausea and vomiting might account for the reduction in anxiety.

The overall manova testing for differences between sessions in anxiety was significant, Pillai's criterion = .71, $F(3,15) = 12.21$, $p < .0003$. Planned

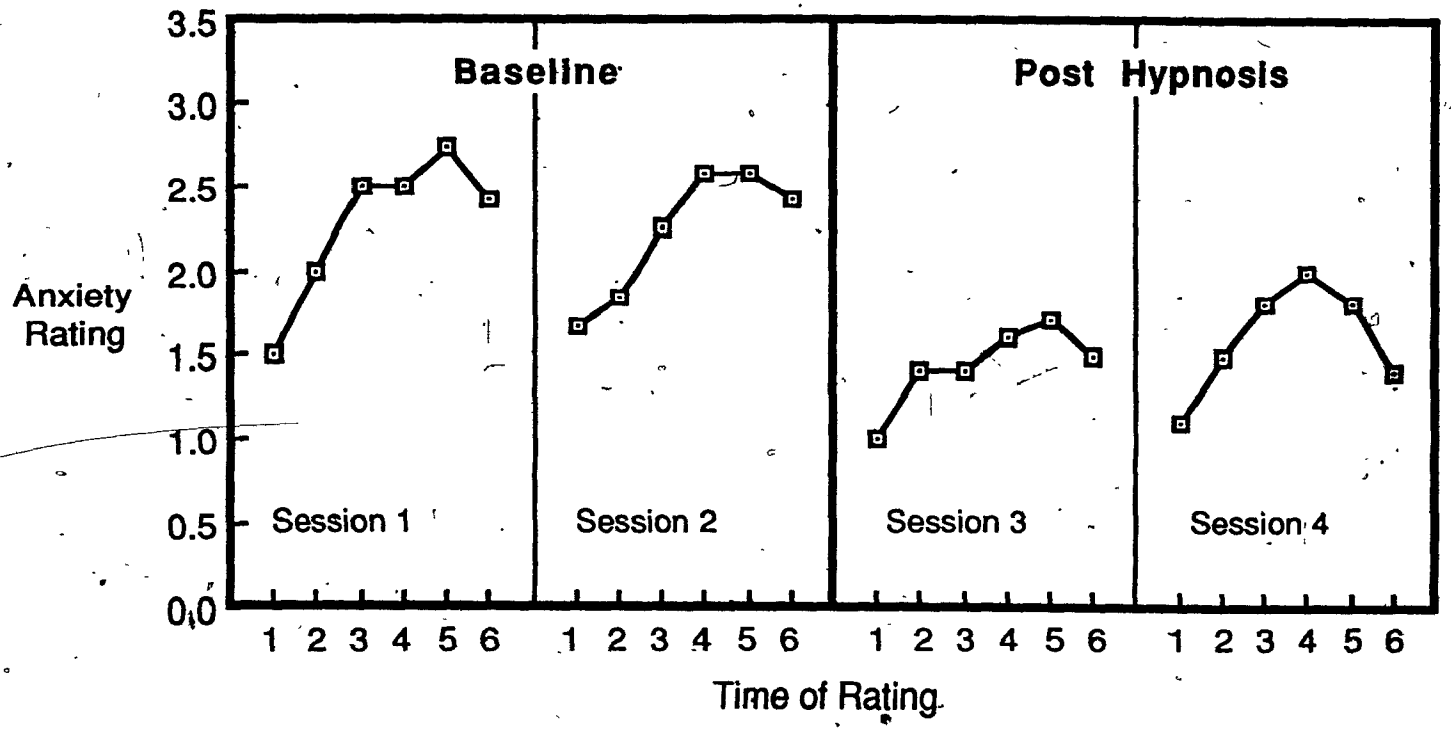

Figure 3. Patients' (N = 18) ratings of their anxiety at six time points for two baseline and two post-hypnosis chemotherapy treatment sessions:

1 - for 3 days prior to treatment (3D);
2 - the evening before treatment (EV);
3 - up to the time for arrival at the clinic (AR);
4 - while waiting in the clinic waiting room (WT);
5 - while receiving the injection (DU);
6 - from the time the patient leaves the clinic until the nausea has ended (PS).

orthogonal comparisons between the mean anxiety ratings of chemotherapy sessions 1 and 2 indicated that there was no difference in reported anxiety between the two sessions at baseline, $F(1,17) = .11$, $p < .74$. There was a significant decrease in anxiety ratings from baseline (mean of sessions 1 and 2) to post-hypnosis chemotherapy sessions (mean of sessions 3 and 4), $F(1,17) = 24.97$, $p < .0001$. The decrease in anxiety continued when the mean anxiety rating of chemotherapy sessions 1, 2, and 3 are compared to the mean anxiety rating of session 4 , $F(1,17) = 13.65$, $p < .002$.

In addition, separate manovas were performed for the anticipatory anxiety and post-chemotherapy anxiety symptoms in the same manner as the nausea symptoms in order to examine the separate effects of the hypnosis treatment.

Anticipatory Anxiety

The overall manova testing for differences between sessions in anticipatory anxiety was significant, Pillai's criterion = .63, $F(3, 15) = 8.5$, $p < .002$. Planned orthogonal comparisons resulted in no significant difference in mean anxiety rating between the two baseline sessions, $F(1, 13) = .19$, $p < .7$. There was a highly significant reduction in anticipatory anxiety symptoms from baseline (mean of sessions 1 and 2) to post-hypnosis sessions (mean of sessions 3 and 4), $F(1, 13) = 20.6$, $p < .0003$. This decrease in anticipatory anxiety continued when the mean anxiety rating of sessions 1, 2, and 3 is compared with session 4, $F(1, 13) = 6.9$, $p < .02$. Thus, anticipatory anxiety continued to decrease through session 4.

Post-Chemotherapy Anxiety

The overall manova testing for differences between sessions in post-chemotherapy anxiety was also significant, Pillai's criterion = .63, $F(3, 15) =$

8.60, $p < .002$. At baseline, no differences were found between the mean anxiety ratings of sessions 1 & 2, $F(1, 13) = .02$, $p < .87$. There was a significant decrease in post-chemotherapy anxiety from pre-(mean of sessions 1 and 2) to post-hypnosis (mean of sessions 3 and 4), $F(1, 13) = 15.45$, $p < .001$. Furthermore, when the mean anxiety rating for sessions 1, 2, and 3 was compared to the mean anxiety rating of session 4, a further significant reduction in anxiety was observed, $F(1,13) = 14.41$, $p < .001$.

Global Measures of Anxiety

Of the 40 patients initially recruited for this study, 37 filled out the STAI correctly at baseline. Fifteen of the 16 patients attending the post-hypnosis interview completed the STAI appropriately for analysis. (See Table 21).

State anxiety did not change significantly from baseline to post-hypnosis, $t(14) = .71$, $p < .49$, despite significant reductions in reported anxiety for the anticipatory and post-chemotherapy anxiety ratings made by the patients. This may have been due in part to the fact that the STAI was filled out retrospectively by patients who were asked to rate their anxiety at the time of their chemotherapy treatment. As expected, there was also no change in the level of reported trait anxiety, $t(15) = .36$, $p < .72$.

However, state, but not trait anxiety correlated highly with the nausea measures. The data are summarized in Table 21.

These large and significant correlations indicate that a sizable proportion of the variance (as much as 20-40%) related to the assessment of nausea may be accounted for by state anxiety. This point is of considerable importance, both theoretically and practically, since techniques such as hypnosis are known to be powerful anxiety-reduction interventions.

In summary, these results indicate that the hypnosis treatment may have

Table 21

Correlations Between NRI-am, ONI and STAI-State and STAI-Trait Anxiety for Patients in Study Three

	Anxiety Measure	
Nausea Measure	State	Trait
NRI-am		
Baseline (n = 37)	.44**	.20
Post-Hypnosis (n =15)	.58*	.20
ONI		
Baseline (n = 37)	.55**	.16
Post-Hypnosis (n =15)	.63**	.22

* $p < .05$
** $p < .01$

Note.
STAI-Speilberger State-Trait Anxiety Inventory.
NRI-am is the sum of the affective and miscellaneous subscales of the nausea questionnaire.
ONI-Overall Nausea Intensity scale.

had a significant effect in reducing the anxiety of these patients both in terms of anticipatory and post-chemotherapy symptoms.

Vomiting Frequency

The vomiting frequency data is based on the 18 patients completing the hypnosis intervention and filling out the self-report forms. The number of vomiting episodes for each time period were recorded by patients for each chemotherapy session. The results are shown in Figure 4.

It is evident from Figure 4 that the frequency of anticipatory vomiting is quite low and that vomiting begins to increase while patients are receiving their chemotherapy treatment and peaks during the period after they leave the clinic. The overall manova testing for differences in vomiting frequency was not significant, Pillai's criterion = .13, F (3,15) = .72, $p < .55$, indicating that there was no significant change in vomiting frequency between sessions.

Vomiting Intensity

Vomiting intensity was rated by the same 18 patients who recorded the other dependent measures on the self-report forms. It was recorded for each of the six time periods during each of the four chemotherapy sessions. The results of these ratings may be seen in Figure 5.

Vomiting intensity is potentially related, at least conceptually, to vomiting frequency. One could hypothesize that the more one vomits, the greater the intensity of the distress which may accompany it. Alternatively, vomiting may be only gagging, belching or retching without the ejection of the stomach's contents; or be as powerful as several hours of intermittent gastric convulsions, which may be so intense that they result in the tearing of the gastric mucosa or abdominal muscles. Patients were asked to choose the

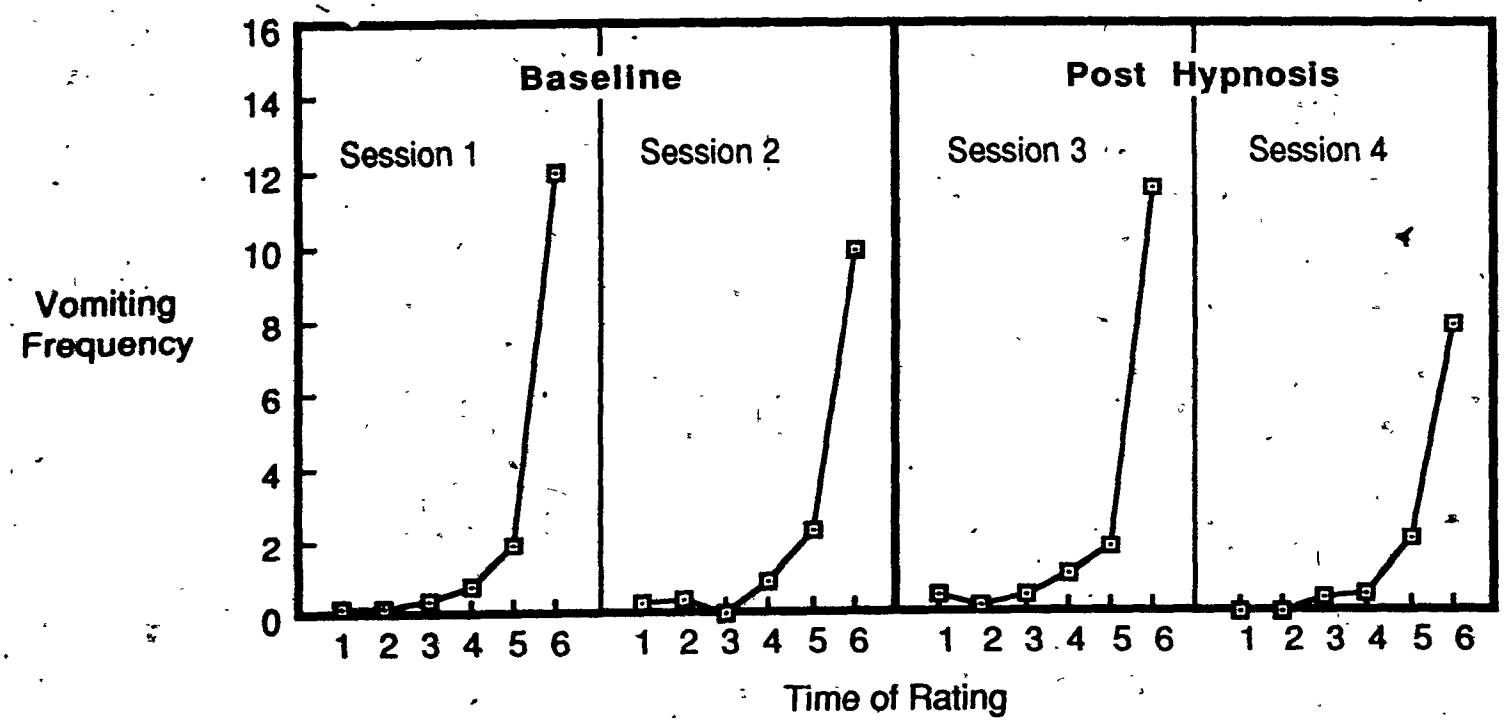

Figure 4. Patients' (N = 18) count of the number of times they vomited at each of six time points for two baseline and two post-hypnosis chemotherapy sessions:

1 - for 3 days prior to treatment (3D);
2 - the evening before treatment (EV);
3 - up to the time for arrival at the clinic (AR);
4 - while waiting in the clinic waiting room (WT);
5 - while receiving the injection (DU);
6 - from the time the patient leaves the clinic until the vomiting has ended (PS).

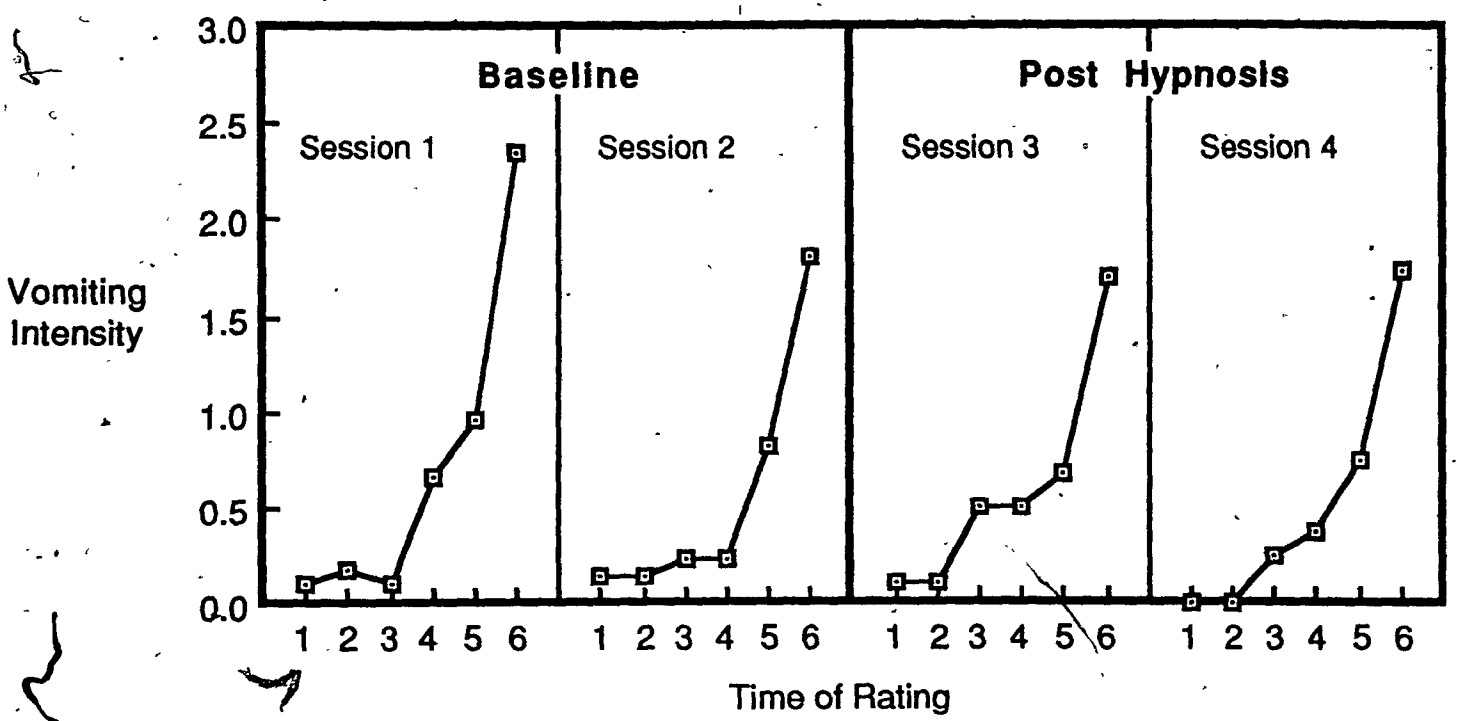

Figure 5. Patients' (n = 18) ratings of the degree of their vomiting intensity for each of six time points during two baseline and two post-hypnosis chemotherapy treatment sessions:

1 - for 3 days prior to treatment (3D);
2 - the evening before treatment (EV);
3 - up to the time for arrival at the clinic (AR);
4 - while waiting in the clinic waiting room (WT);
5 - while receiving the injection (DU);
6 - from the time the patient leaves the clinic until the vomiting has ended (PS).

number on the 7 point vomiting intensity rating scale corresponding most closely to whether their vomiting was more like the former (lower ratings) or the latter (higher ratings). It would be of great clinical interest and importance if patients were able to control the intensity (or distress) of the vomiting experience through hypnosis, if not being able to control the actual number of times that the vomiting occurs.

This hypothesis clearly was not supported. The overall manova testing for differences between sessions in vomiting intensity was not significant, Pillai's criterion = .11, F (3,15) = .63, $p < .6$. It may be that patients were unable to discriminate accurately between the frequency and the intensity of the vomiting ratings or that the two variables are so highly correlated as to make them conceptually identical.

The Problem of Experimental Control

Although repeated measures designs with subjects as their own control are often used in clinical research (Hersen & Barlow, 1976), the use of a baseline-reversal procedure (i.e., to undergo chemotherapy treatment without using hypnosis) as a control procedure was not possible. Hypnotic skills once discovered cannot be 'unlearned', since they are conceptualized as residing within the individual and as being tapped by training with various techniques. Patients cannot be instructed not to use hypnosis as a self-control procedure, without concern that they might, in fact, be utilizing their hypnotic talents anyhow (Hilgard, 1965). This request is similar to asking someone to not think about a pink elephant. The lack of a control or comparison group, to which patients have been randomly assigned, might mitigate against firm conclusions about the efficacy of the hypnosis treatment, in spite of the significant results which have been reported thus far.

Several factors precluded the use of a formal control group in this study. First, the directors and staffs of the oncology services involved in this study felt that if their patients were to participate, they should be offered a plausible treatment approach. Furthermore, patients undergoing active chemotherapy treatment are often involved in many other treatment-related activities, including multiple appointments for tests and recovery activities from the chemotherapy side effects. The oncology clinic personnel felt that the additional burden of collecting data with no perceived payoff (such as a plausible treatment like hypnosis) might be too stressful for many patients and would limit participation even further.

Second, it has been well established in the psychosocial oncology research literature that attrition is a major problem (McCorkle et al., 1984). The drop-out rate is affected by many factors including the vicissitudes of the illness process, changes in chemotherapy treatment protocol or type, and patient motivation.

A good example of the attrition problems encountered in this type of study is provided by Morrow & Morrell (1982). For a study on the effects of systematic desensitization in reducing anticipatory nausea and vomiting Morrow and Morrell screened 500 consecutive patients receiving chemotherapy. Of this group, one hundred twenty reported anticipatory nausea side effects. Thirty-three did not meet eligibility criteria. After eliminating other patients having alimentary canal or brain involvement with the disease, being hospitalized for further evaluation, refusing to participate, and living too far from the treatment site, only sixty patients (12% of the original sample) remained available for randomization to the three groups in their study. Of these sixty, seventeen patients had to be replaced because their chemotherapy protocol was changed during the study. Finally,

each patient was given ten dollars for each of the sessions attended in order to help defray the patients' costs (e.g., transportation, baby-sitters, etc.) of attending the study's sessions (G. R. Morrow, personal communication, December, 1986).

The difficulty in obtaining a relatively homogeneous group of patients for study in this area of research is evident (Andrykowski, 1986). Furthermore, even when such a group of patients is assembled and the results of such a study are significant, questions may be raised as to the general applicability of these techniques to other patients undergoing cancer chemotherapy. For these reasons, the present study was open to any patient undergoing chemotherapy who was experiencing nausea and/or vomiting side effects. This procedure allowed for a more realistic evaluation of not only the assessment measures, but also the wider applicability of the intervention. The value of an open study was highlighted in study two where several factors limiting the value of the nausea questionnaire as a pure measure of chemotherapy-related nausea were identified using this sampling procedure.

Comparison of Outcomes of Nausea and Vomiting Between the Present Study and Morrow & Morrell (1982) and Morrow (1986)

In an attempt to examine further the effectiveness of the hypnotic approach taken in the present study, data were compared with that from Morrow & Morrell (1982) and a later extension of this study (Morrow, 1986). This comparison was appropriate for two reasons. First, the protocol used in the present hypnosis study was similar to the one used in these studies. Morrow & Morrell's (1982) study used two baseline and two post-treatment chemotherapy sessions to examine the influence of their intervention, as in the present study. In addition, the study had two control groups. One group

attended 'Rogerian'-type group counselling sessions in which patients discussed various ways to cope with chemotherapy treatments, but were given no specific instructions. The other group recorded data for four consecutive chemotherapy sessions as a control for the reactive effects of recording only. Morrow (1986) later added a relaxation-only group to examine the relative effectiveness of the hierarchy in the systematic desensitization group.

Second, the interventions used in both the comparison studies and the present study were similar in many respects. The intervention consisted of two sessions of relaxation training and systematic desensitization carried out by a therapist after data were collected from the two baseline chemotherapy sessions. Patients were asked to imagine scenes related to their actual treatment (e.g., going to the clinic, waiting for treatment, etc.) in a progressive, hierarchical fashion while remaining as relaxed as possible. This technique was developed by Wolpe (1959) and has demonstrated efficacy in numerous anxiety-related disorders, especially phobias (Leitenberg, 1976). The patient then underwent the two follow-up chemotherapy sessions without the presence of the therapist. The results for the reduction of anticipatory nausea and vomiting were extremely impressive for the systematic desensitization group.

The hypnosis intervention used in the present study involved two sessions of hypnosis training which included relaxation and guided imagery. These instructions were similar to those used by Redd & Andrykowski (1982) in a study of the effects of what these authors described as 'relaxation-hypnosis' on nausea and vomiting. In both studies, patients were asked to focus their attention away from the chemotherapy situation by engaging in distracting imagery.

One of the major differences between the two studies may lie in the focus of the treatment process itself. Morrow & Morrell's (1982) systematic desensitization approach asked patients to focus on the treatment situation, i.e., imagining themselves relaxed in situations progressively approaching the chemotherapy treatment. Patients in the present study were asked essentially to focus away from the treatment situation by using distraction and other techniques to change the nature of their perception of the chemotherapy experience and to reduce the aversiveness of the attendant side effects. These differences must be considered when comparing outcomes for these 2 approaches (Morrow & Dobkin, in press).

Demographic Comparisons Between
Morrow & Morrell (1982) and the Present Study

Prior to a comparison of outcome with the Morrow studies, an examination was made of the similarity between the two samples. Comparisons were made on a number of patient variables. The Morrow & Morrell (1982) sample did not differ in any respect from either the entire sample of the present study ($N = 40$) or the subsample of ($n = 18$) patients for which self-report outcome data was available and reported above. (See Table 22.)

Chi square analyses were performed on patient variables comparing Morrow & Morrell's (1982) sample and the entire sample ($N = 40$) in the present study. There were no differences in sex, X^2 (1, N =100) = 3.22, $p > .05$; type of cancer, X^2 (2, N =100) = .81, $p > .05$; whether the patient previously underwent chemotherapy treatment, X^2 (1, N =100) = 3.23, $p > .05$; or radiotherapy treatment, X^2 (1, N =100) = .63, $p > .05$. Additional chi square analyses comparing demographic variables of Morrow & Morrell's patients

Table 22

Comparison of Demographic and Patient Characteristics Between Samples in the Study by Morrow and Morrell (1982) and the Present Study

Patient Characteristic	Morrow & Morrell (1982; N = 60)	Present Study (N = 40)	Present Study (n = 18)
		Years	
Age			
Range	19-76	19-72	30-70
Median	53	50	50.5
		Number of Patients	
Sex			
Men	18	5	3
Women	42	35	15
Type of Cancer			
Breast	29	21	11
Lung	8	5	1
Other	23	14	6
Previous Treatment			
Chemotherapy	20	6	3
Radiotherapy	21	18	8

Note. There are no significant differences between the Morrow & Morrell sample and the whole sample (N = 40) or the (n = 18) sample of completers of the present study for sex, type of cancer, or previous treatment using chi square analysis with correction for continuity for 2 x 2 tables. See text for more complete description of the statistical analyses.

and the subsample of the present study (n =18) yielded the following results: there were no differences in sex, X^2 (1, n = 78) = .67, p > .05; type of cancer, X^2 (2, n = 78) = 1.26, p > .05; previous chemotherapy treatment, X^2 (1, n = 78) = 1.14, p > .05; or radiotherapy treatment, X^2 (1, n = 78) = .2, p > .05. Statistical comparisons for differences in age between the groups could not be made due to the lack of raw data, but inspection of the ranges and medians in Table 22 indicate comparability.

In summary, the Morrow & Morrell (1982) sample patients were similar on all the demographic characteristics to patients in the present study, and were also similar to the subsample of (n = 18) patients. These results indicate that any differences found between the systematic desensitization group in Morrow studies and the hypnosis group in the present study are unlikely to be due to differences in demographic characteristics.

Comparison of Outcomes of Anticipatory Nausea and Vomiting

The data reported by Morrow & Morrell (1982) were primarily categorical in nature and were the only data available for comparison (G. R. Morrow, personal communication, December, 1986). Morrow & Morrell (1982) used the Morrow Assessment of Nausea and Emesis (MANE)-a self-report form completed by the patient retrospectively-to assess outcome. The present study used seven-point rating scales to assess the nausea and vomiting outcome measures at various time intervals prior to, during, and after the chemotherapy treatment. Statistical comparisons between the two samples were made by categorizing the patients as improved, unchanged, or worse on measures of anticipatory nausea and anticipatory vomiting, as in the Morrow & Morrell study.

Anticipatory nausea and anticipatory vomiting were estimated by

summing the ratings made by patients at the 3D, EV, AR, and WT time points for each chemotherapy session. The mean nausea rating for chemotherapy sessions 1 and 2 was used to give a pre-hypnosis score. Similarly, the mean nausea rating of chemotherapy sessions 3 and 4 were calculated to provide a post-hypnosis score. The difference score between the the pre- and post-hypnosis mean nausea ratings indicated whether patients symptoms were reduced, increased, or stayed the same.

Anticipatory Nausea. There was no significant difference in the distributions of patient improvement between the Morrow & Morrell (1982) and the present sample for anticipatory nausea, X^2 (1, n = 37) = .89, p > .30. (See Table 23).

However, it should be noted that of 17 out of 20 patients in Morrow & Morrell's (1982) systematic desensitization group who reduced their anticipatory nausea, 10 reported none after treatment. Only one of the patients in the present study managed to reduce their anticipatory nausea to this level. Clinically, this finding is of extreme importance. It is unclear from Morrow & Morrell's (1982) data, however, what the baseline level of nausea was for those patients who eliminated their nausea completely. It might be hypothesized that the lower the baseline level of nausea, the more likely the patient might be able to totally eliminate the symptom.

More detailed comparisons for anticipatory nausea were made by examining the data as presented in Morrow (1986). In this study, a relaxation-only training group was added in an attempt to clarify whether the cognitive hierarchy (a series of situations gradually approaching the chemotherapy treatment session, e.g., seeing hospital, entering the clinic, etc., which are presented to the patient in imagination) was a necessary and effective

Table 23

Comparison of the Outcome of Severity of Anticipatory Nausea and Vomiting between Morrow & Morrell (1982) and the Present Study

	Morrow & Morrell (Systematic Desensitization)	Present Study (Hypnosis)
	Number of Patients (percent)	
Anticipatory Nausea		
	n = 20	n = 18
Less Severe	17 (85)	12 (67)
No Change	2 (10)	2 (11)
More Severe	1 (5)	4 (22)
Anticipatory Vomiting		
	n = 9	n = 14
Less Severe	8 (89)	5 (36)
No Change	0 (0)	0 (0)
More Severe	1 (11)	9 (64)

addition to the relaxation component of the systematic desensitization technique. Outcomes for the relaxation-only group and the four other groups from Morrow (1986) were compared.

The measure of nausea severity from the MANE is a seven point scale, from 0-no nausea to 6-intolerable nausea. The scale used to measure nausea severity in the present study was almost identical: from 0-no nausea to 6-worst ever. Only the word descriptors were different. This similarity made gross comparisons between the data of the present study and the Morrow (1986) study possible even though statistical evaluations were not.

The MANE asks patients to rate their overall (and therefore the highest) level of anticipatory nausea severity on one seven-point scale. Since the present study asked patients to rate their anticipatory nausea severity on the seven-point scales at four different time intervals, the data point used for comparison was the WT (while waiting in the clinic and just prior to the chemotherapy injection), since this point was probably the best estimate of the patients' highest level of anticipatory nausea. The data for anticipatory nausea comparing the hypnosis group of the present study with the groups from the Morrow (1986) study are presented graphically in Figure 6.

Only the systematic desensitization group showed significant reduction in the severity of anticipatory nausea from baseline to post-treatment. It has already been demonstrated that there was no significant reduction in anticipatory nausea severity for the hypnosis group of the present study. In addition, it may be observed rather clearly in Figure 6 that the baseline mean for the WT variable (m = 1.7) was lower than the means of the four comparison groups, although whether this observation was statistically significant is not known. However, it appears that the mean baseline values of Morrow's four groups are quite comparable (approximate m's between 2.25

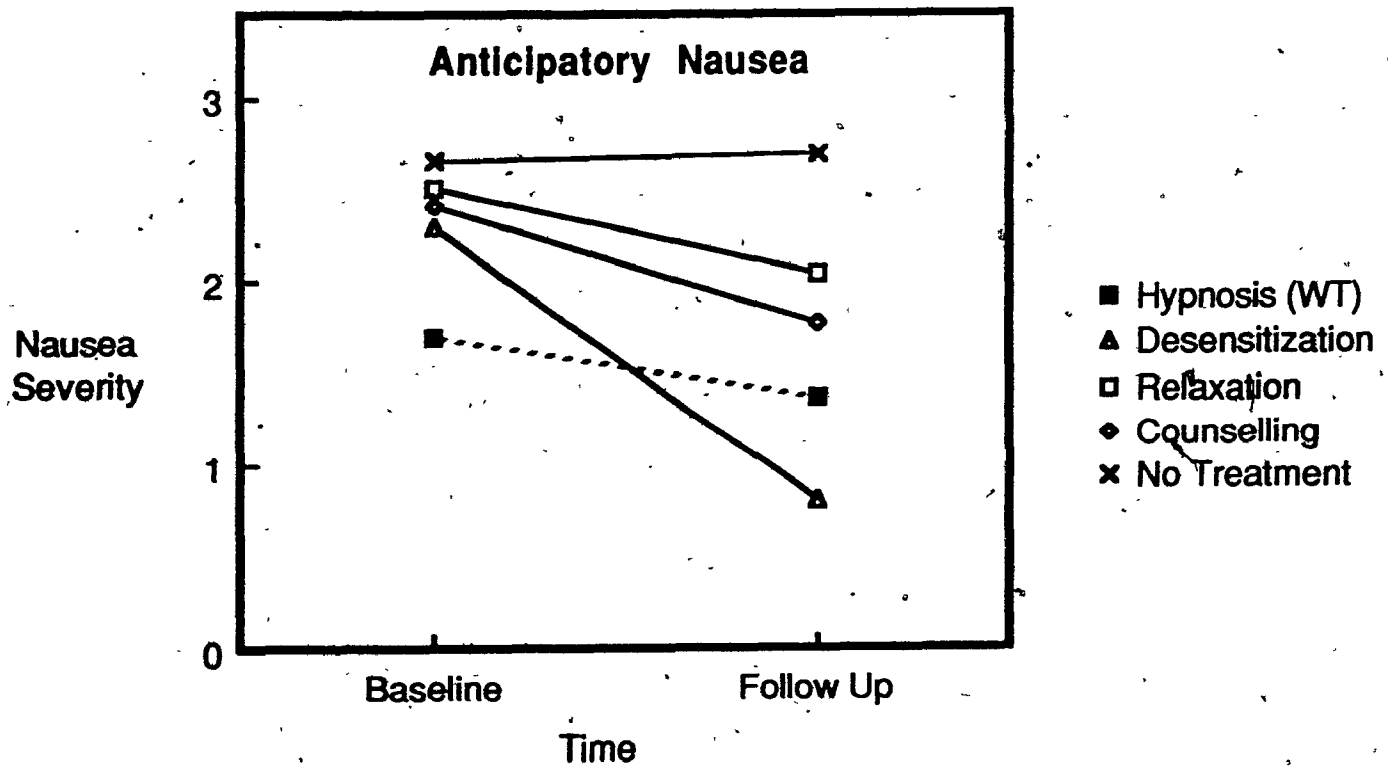

Figure 6. Comparison of outcomes of change in anticipatory nausea severity between the hypnosis group of the present study (using the WT data point as the estimate of the highest level of anticipatory nausea) and groups from Morrow (1986).

and 2.75). Although this finding may indicate that the patients in the present study experienced lower levels of anticipatory nausea, another explanation is possible.

Because the post-chemotherapy (PS) rating in the present study was defined as the period beginning from the time the chemotherapy injection ends and the patient leaves the clinic, to the time of cessation of the side effects, this rating was used for comparison as the patients' highest level of post-chemotherapy nausea (see below). Theoretically, the DU (the time during which the patient was actually receiving the chemotherapy drugs) is considered most conservatively to be part of the post-chemotherapy phase as opposed to the anticipatory phase (Andrykowski, 1986). It is usually of short duration-ten to fifteen minutes for a push injection and one to two hours for a drip infusion. Typically, patients do not experience physiological nausea (during the first few chemotherapy sessions at least) until several hours after they leave the clinic (Penta et al., 1981a). When anticipatory nausea symptoms develop with succeeding chemotherapy treatments, this time delay diminishes until the patient may actually experience nausea symptoms prior to the injection. Thus the rating that the patient makes at the DU data point may, in fact, be an evaluation by the patient of the highest level of their anticipatory nausea symptoms, which is confounded by the inability to discriminate between physiological and anticipatory nausea symptoms. In order to maintain theoretical parsimony and to maximize comparisons between studies, Andrykowski (1986) has argued that anticipatory nausea be considered only prior to the actual injection.

Morrow 's patients only had to rate their post-chemotherapy nausea symptoms (defined as the period from the time of the injection until the symptoms completely remit) with one rating as opposed to the two ratings

(DU and PS) of the present study. Since the DU ratings could never be as high as the PS ratings (since the DU period lasts from 10 minutes to a maximum of several hours, whereas the PS may last for days), and may certainly be confounded by both anticipatory nausea and post-treatment nausea symptoms, it may be the best measure of the highest level of anticipatory nausea. For this reason, the DU data point was used as an alternative estimate of the highest level of anticipatory nausea for comparison with the Morrow study. The data are shown in Figure 7.

When the DU data point is used in this manner, the baseline value of anticipatory nausea for the hypnosis group (m = 2.22) is more comparable to that of the Morrow groups than the WT data point. Although the the hypnosis group does still not demonstrate a significant reduction in anticipatory nausea, $F(3, 15) = 1.3$, $p > .3$, the results are more comparable to those of Morrow's relaxation group. (See Figure 7).

Anticipatory Vomiting. The results for anticipatory vomiting were slightly more complicated than those for anticipatory nausea. At baseline, only seven of the patients in the present study had symptoms of anticipatory vomiting. Of these seven, five reported reduced anticipatory vomiting post-hypnosis, while two patients reported increased symptoms. When only these patients were compared to those in Morrow & Morrell's (1982) study who had anticipatory vomiting (see Table 23), it was found that there was no significant difference between the two groups in the distributions, Fisher's Exact Probability = .34. However, a closer examination of the data for those patients who reported no anticipatory vomiting during baseline indicated that three of them developed these symptoms during the follow-up chemotherapy sessions. When these patients were included in the

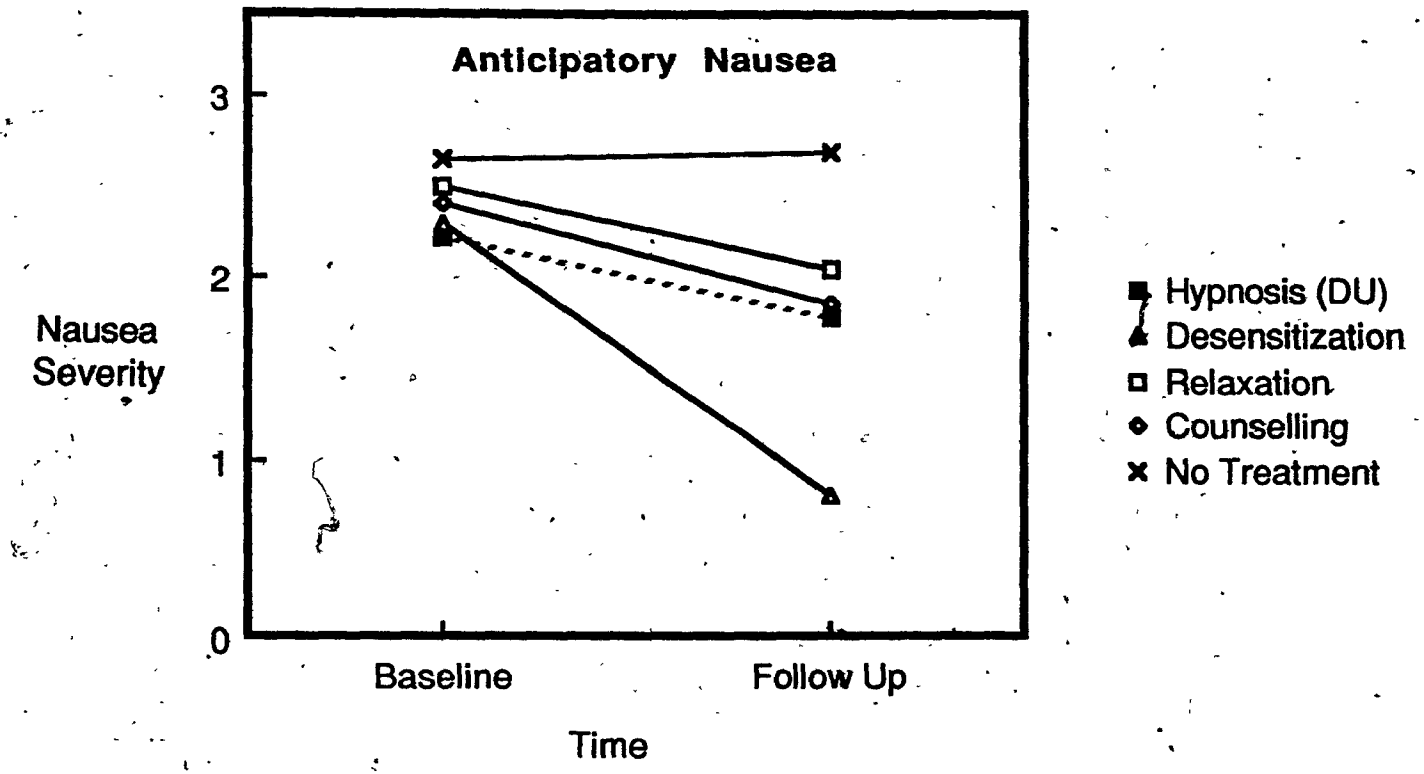

Figure 7. Comparison of outcomes of change in anticipatory nausea severity between the hypnosis group of the present study (using the DU data point as the estimate of the highest level of anticipatory nausea) and groups from Morrow (1986).

comparison, a significant difference between the two distributions appeared, Fisher's Exact Probability = .02. This result indicates that Morrow & Morrell's (1982) patients reported less anticipatory vomiting overall after intervention, than the patients in the present study. In fact, more patients in the present study had more severe anticipatory vomiting after hypnosis intervention than at baseline (see Table 23), although there was no significant change in vomiting frequency, as reported in an earlier section of this study.

Post-Chemotherapy Nausea. A categorical comparison of the numbers of patients reporting reduction of post-chemotherapy nausea was made between Morrow's (1986) systematic desensitization (taken from Morrow & Morrell,1982) and relaxation-only groups, and the hypnosis group of the present study. The distribution of patient improvement for the three groups is shown in Table 24.

Most of the patients in all three groups reported less severe post-treatment nausea. When the 'no change' and 'more severe' categories were combined due to small cell frequencies, there was no significant difference between the distributions of the hypnosis and systematic desensitization groups, X^2 (1, n = 44) = .84, $p > .30$, or the hypnosis and relaxation groups, X^2 (1, n = 44) = .17, $p > .30$. It may be concluded from these results that the three therapeutic techniques are equally effective in reducing the frequency of post-chemotherapy nausea among patients.

The actual degree of post-chemotherapy nausea reduction reported by patients in the three groups is shown graphically in Figure 8.

Morrow (1986) reports that both the systematic desensitization and the relaxation groups significantly reduced their post-chemotherapy nausea from baseline to follow-up. There was no significant difference between these

Table 24

Comparison Between Morrow (1986) and the Present Study of the Outcome of Severity of Post-Chemotherapy Nausea

	Morrow (1986)		Present Study
	Systematic Desensitization	Relaxation	Hypnosis
	Number of Patients (percent)		
	n = 26	n = 26	n = 18
Less Severe	14 (54)	16 (61)	13 (72)
No Change	5 (19)	3 (12)	1(6)
More Severe	7 (27)	7 (27)	4 (22)

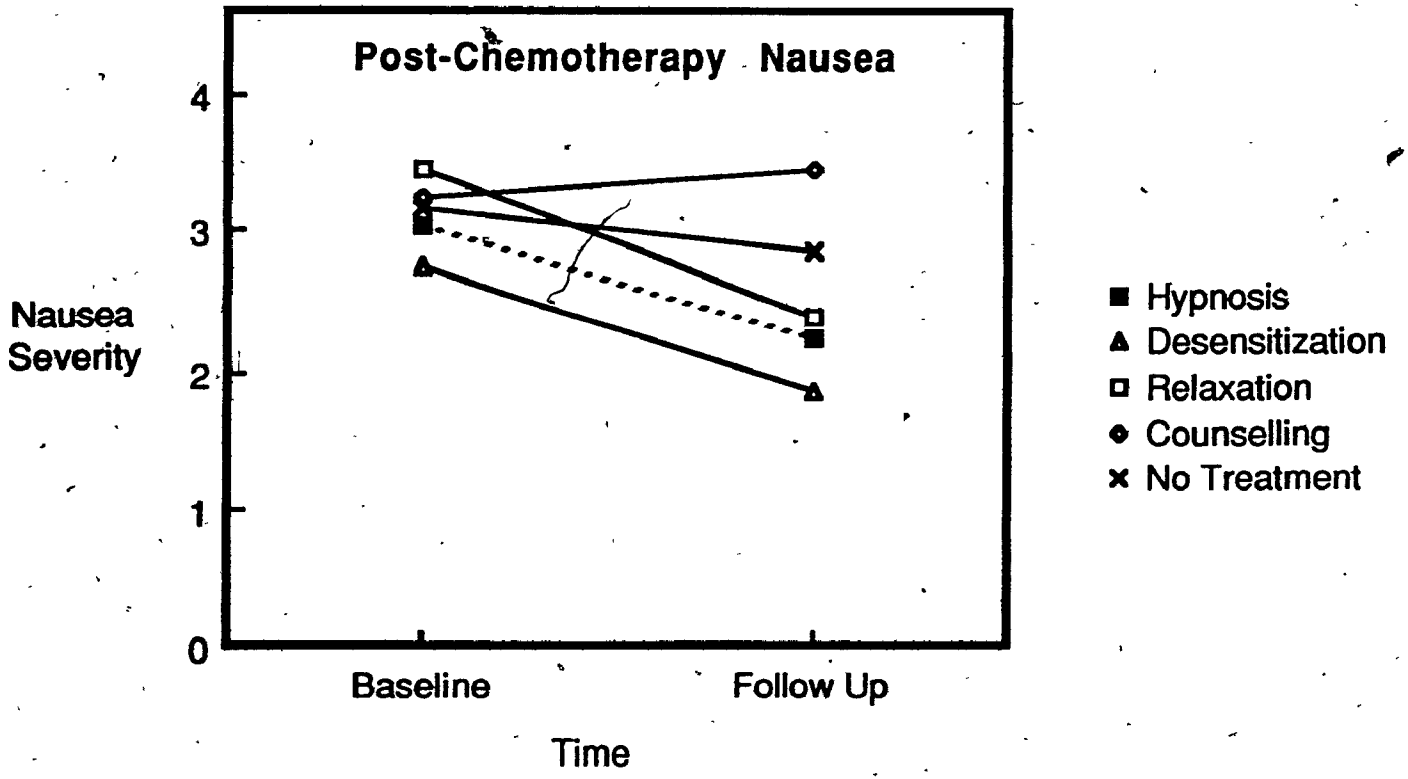

Figure 8. Comparison of outcomes of change in post-chemotherapy nausea severity between the hypnosis group of the present study and groups from Morrow (1986).

groups in the degree of reduction. The hypnosis group also reduced their post-chemotherapy nausea significantly, as reported in an earlier section. From observation of the graph in Figure 8, the slope of the hypnosis group's data was virtually identical to that of the systematic desensitization group. It is also quite similar to the slope of the relaxation group, indicating a similar degree of post-chemotherapy nausea reduction. The systematic desensitization and relaxation groups were significantly more effective in reducing these nausea symptoms than either the counselling or no treatment control groups. Neither of the control groups had any effect in reducing post-chemotherapy nausea. From these results, a likely conclusion is that the hypnosis treatment group also was better than the control groups in reducing post-chemotherapy nausea.

Post-treatment vomiting was not assessed by Morrow & Morrell (1982) or Morrow (1986) and therefore was not available for comparison with the present study.

Duration of Nausea and Vomiting. Patients in Morrow & Morrell's (1982) study who filled out the MANE recorded the duration of nausea and vomiting separately for anticipatory and post-chemotherapy periods. In the present study, however, patients were asked to record separately the time that their nausea and vomiting began and the time at which these symptoms ended without differentiating between anticipatory and post-chemotherapy stages (see Appendix E). From these data, the total duration of nausea and vomiting in hours was calculated. Because of the differences in the manner in which the duration data were collected, comparisons with Morrow & Morrell's (1982) data were not possible. Results for the duration of nausea and vomiting, and antiemetic use in the present study is summarized in Table 25.

Table 25

Central Tendencies of Nausea and Vomiting Duration and Antiemetic Medication Use for (N = 18) Patients in Study Three

	Central Tendency Measure	
	Mean (SD)	Median
Dependent Measure		
Baseline (mean of sessions 1 and 2)		
Nausea Duration (hours)	73.38 (61.22)	54.75
Vomiting Duration (hours)	31.64 (39.05)	17.50
Number of Antiemetics	5.97 (6.13)	3.75
Post-Hypnosis (mean of sessions 3 and 4)		
Nausea Duration (hours)	45.01 (43.10)	32.25
Vomiting Duration (hours)	24.18 (31.56)	7.00
Number of Antiemetics	4.93 (5.21)	2.71

Nausea Duration. Thirteen of the 18 patients (72%) in the present study reduced their total nausea time. Although this finding did not differ from chance, X^2 (1, n = 18) = 3.56, $p > .05$, the result still indicates at least clinical, if not statistical significance. An overall manova testing differences between sessions performed on the nausea duration data did not yield statistical significance, $F(3, 15) = 2.36$, $p < .11$. However, since the assumptions regarding sphericity (Bartlett's test of sphericity = 2.28, $p > .52$) and homogeneity of variance were met, (F max = 1.62, $p > .05$), the univariate approach could be used (Stevens, 1986). This approach yielded a significant overall analysis of variance, $F(3, 51) = 3.70$, $p < .02$. As expected, there was no significant difference between sessions 1 and 2 in the mean number of hours of nausea endured by the patients, $F(1, 17) = 1.03$, $p > .30$. There was a significant reduction in the mean number of hours of nausea experienced by the patients from the baseline sessions (M = 73.38 hours) to the post-treatment sessions (M = 45.01 hours), $F(1, 17) = 5.51$, $p < .03$. Patients reduced the duration of their nausea by a mean of 28.37 hours or approximately from 3 days to 2. (See Table 25).

Vomiting Duration. Thirteen patients in the present study reported reductions in their total vomiting duration. Two of them had increases and a further 3 reported no change in this parameter. Again, an overall manova testing for differences between sessions in nausea duration did not reveal statistical significance, $F(3, 15) = 2.84$, $p < .07$. Despite non-significant tests of sphericity (Bartlett's test of sphericity (3, 17) = 3.17, $p = .37$) and homogeneity of variance (F Max (3, 17) = 3.03), the univariate anova also was not significant, $F(3, 51) = 1.19$ $p > .30$. However, orthogonal comparisons showed the expected results. There was no difference between sessions 1 and 2 in vomiting duration, $F(1, 17) = .53$, $p > .47$. There was a significant reduction in

vomiting duration between baseline (mean of sessions 1 and 2) and post-hypnosis (mean of sessions 3 and 4) from 31.64 hours to 24.18 hours, $F(1, 17) = 6.26$, $p > .02$. Although the statistical significance of these results is questionable, this 24 percent reduction in vomiting duration (approximately 7.5 hours) must be considered important clinically, just as was the case for nausea duration. (See Table 25).

Use of Elective Antiemetics. Reductions in any of the nausea and vomiting parameters could not be accounted for by the amount of oral or suppository antiemetic medications taken electively by patients after their chemotherapy treatment. Patients took similar amounts of antiemetic pills and/or suppositories during the baseline (mean of sessions 1 and 2 = 5.97) and post-hypnosis (mean of sessions 3 and 4 = 4.93), $F(1, 17) = .06$, $p < .80$. (See Table 25).

Hypnotic Susceptibility

Sixteen of the 18 patients who completed the study were tested on the SHSS: Form C. The scores on this scale were fairly normally distributed and comparable to those found in the general population (Hilgard, 1965). Two patients had low hypnotic susceptibility, i.e., scores of 0-2; 11 patients had medium susceptibility, i.e., scores of 3-6; and 3 patients had high susceptibility, i.e., scores of 7-8. However, there was no relationship between hypnotic susceptibility and any of the various nausea and anxiety measures. (See Appendix J). This finding indicates that the patient's level of hypnotic ability as measured by the SHSS: C may not be helpful in understanding the development of anxiety, nausea and vomiting, as these symptoms relate to cancer chemotherapy.

Discussion

Measurement of Nausea

The results of studies 1 & 2 demonstrated that both the ONI and VAS and, to a lesser degree, the NRI-am, are reliable and valid instruments in the measurement of nausea associated with cancer chemotherapy. The data of Study 3, however, provided further validating evidence for the ONI, but not for the NRI-am. All three measures were found to have good concurrent, construct, and discriminative validity, though the latter was weaker in this respect. The NRI-am showed reasonable internal consistency, but test-retest reliability was problematic for all 3 scales. It is important to note, however, that these data appear to have been confounded by uncontrolled clinical variables.

The ONI and the VAS appear to be quite robust measures of nausea intensity; by contrast, the NRI-am may be more prone to contamination by the patient's perception of somatic symptoms which reflect the extent of disease progession rather than the toxicity of the chemotherapy drugs. Since disease progression or stage was not an exclusionary criterion in any of the three studies, some patients in Study 3 were known to be in advanced states of metastic disease, while others may have had undiagnosed metastases.

This appears to have been the case in study 2, where it was clearly shown that the outlier scores of several apparently more ill patients accounted for discrepancies in correlations amongst the three nausea measures. Future studies utilizing the NRI-am should examine the stability of scores for patients at different stages of disease in order to clarify this point. This may be a difficult task, however, since diagnosis of metastatic disease is made often well after the spread of the disease and symptoms, such as pain and nausea, have appeared. The sites of these metastases is also an important

consideration since brain or gastrointestinal metastases are more likely than other sites to produce nausea symptoms.

The heavy loading of the NRI-am on affective words rather than sensory words may be explained in two ways. First, it may be that words on the sensory subscale of the McGill Pain Questionnaire (MPQ) may not be appropriate descriptors of the physical nausea experience; that is, the words may lack face validity. Other words, such as 'whirling', 'twirling', or 'dizzying' (as suggested by some patients) might be more appropriate descriptors.

Alternatively, there may be a built-in bias for certain words in the NRI-am. This measure was presented to patients with the original 4 subscales of the MPQ intact. (See Figure 1). It may be important to recapitulate the methodology of Melzack & Torgerson (1975) and develop a nausea word descriptor scale, obviating the problems in adapting pain descriptors to a nausea scale. Nevertheless, the internal consistency of the affective and miscellaneous subscales and correlations with concurrent measures indicate that this measure was tapping some aspects of the nausea experience.

The ability of a nausea scale to differentiate between anticipatory nausea and post-chemotherapy nausea has important theoretical and clinical implications. In a strictly clinical context, a unidimensional scale of nausea intensity such as the ONI or the VAS, may be the most efficient and parsimonious measure for the oncologist or nurse to gather information about the degree of nausea experienced by the patient. The results of Study 3 show, however, that it is possible to use a Likert-type scale to measure anticipatory nausea and post-chemotherapy nausea separately with equal reliability and validity, even for specific time periods. Controversies continue to exist regarding the exact definition and parameters of anticipatory nausea.

For example, Andrykowski (1986) has provided a detailed analysis of how prevalence rates can be altered drastically depending on an investigator's criterion for anticipatory nausea. In spite of this problem, future studies using the NRI-am might attempt to evaluate anticipatory and post-chemotherapy nausea separately to assess more precisely the ability of this test to discriminate between these two important dimensions.

Examination of other dimensions of distress associated with cancer (e.g., depression and/or physical status) might provide further information on the construct validity of the NRI-am. For example, a recent large scale epidemiological study (Mor, 1987) compared 3 groups of cancer patients; those newly-diagnosed, those currently undergoing chemotherapy treatment, and patients in terminal stages of their illness. It was found that the degree of physical disability experienced by patients accounted for over 35% of the variance in reported depression scales.

In addition, newer chemotherapy research protocols are following a trend of less frequent, but stronger treatments often given in two phases separated by a several month waiting period before reinduction of the treatment (NSABP, 1984). This change in protocol may be serendipitous, in that some patients may not have enough chemotherapy treatments to allow for the development of anticipatory nausea. On the other hand, protocols involving the reinduction of a second round of chemotherapy may create new and unexpected complications. Coates, Gebski, Bishop, Jeal, Woods, Snyder, et al. (1987) have recently shown that when breast cancer patients were randomly assigned to intermittent versus continous chemotherapy groups, the former group demonstrated a significantly worse disease response to therapy. Of greater interest to the present discussion, however, was the finding that patient self-ratings of increased pain, lowered mood and appetite, and a

diminished sense of well-being, also were predictive of poorer disease response in patients undergoing intermittent chemotherapy. This finding also highlights the necessity for the careful evaluation of not only disease response to treatment but also the concomitant measurement of the psychosocial consequences of these treatments. Factor analytic and correlational studies on larger samples using the NRI-am and measures of depression, fatigue, and physical status , for example, should provide relevant data on this issue.

Several mitigating factors must be considered when trying to draw firm conclusions from the results of these studies. First, the relatively small sample sizes in each of the 3 studies limits the variability of the nausea measures as well as the possibility of finding significant results. Further, it has already been suggested that homogeneous samples are almost impossible to obtain in this area of research (Ahles, Cohen, & Blanchard, 1984; McCorkle et al., 1984), therefore careful examination of the data from the available samples must be made in order to evaluate results. For example, although most cancer sites are well represented in all three studies in proportions comparable to other studies (e.g., Morrow & Morrell, 1982), hematological cancers are not. Finally, since the choice of chemotherapy drugs (and therefore, the degree of toxicity) will in part be determined by the diagnosis, future studies must include as wide a variety of diagnostic categories as possible.

The Role of Hypnosis in the Treatment of Chemotherapy Side Effects

Hypnosis in the clinical context may be conceptualized in two ways. First, hypnosis may be defined and labeled as a treatment context in which patients are instructed in relaxation and guided imagery. Second, hypnosis or hypnotic

susceptibility may be defined as that set of unique and individual cognitive abilities or strategies that a patient may draw on in the clinical context to overcome distress. Clearly, the former is designed to facilitate the latter, at least theoretically. There is some evidence that these hypnotic abilities may be elicited when other treatment techniques are used, such as biofeedback, for example, and that hypnotic susceptibility may be more predictive of treatment response than the particular treatment employed (Andreychuk & Scriver, 1975; Nace, Warwick, Kelley, & Evans, 1982). Others, however, have argued that biofeedback in fact, may be tapping into a different set of cognitive skills (Miller & Cross, 1985; Qualls & Sheehan, 1981).

The implications of these conceptualiztions will be addressed in light of the results of Study 3.

Hypnosis as a Treatment

Hypnosis is generally viewed as a powerful process by the lay public, who may link this technique with the uncovering of repressed memories and feelings associated with age regression, amnesia, or post-hypnotic suggestion (Hendler & Redd, 1986). However, less well known are the aspects of hypnosis which place it in the domain of other cognitive-behavioural interventions. To an extent, what a subject expects from hypnosis will contribute to what is subsequently experienced, with the correlation between expectation and hypnotizability = .30 (Hilgard, 1965). Hendler & Redd (1986) examined this issue in a group of cancer patients undergoing chemotherapy. Their results indicated that patients were more afraid of the label 'hypnosis', but were quite prepared to undergo the specific procedures (i.e., relaxation & imagery) which are subsumed under it. These beliefs were unrelated to the degree of distress that the patients were experiencing from chemotherapy.

Much care was taken in the present study to discuss the individual

patient's beliefs and previous experiences with hypnosis, to clarify any misconceptions, and to allay any fears that she or he might have regarding such issues as loss of control. In spite of this fact, many patients were still apprehensive of the technique, even after having experienced it and discovering for themselves how essentially benign it was, thus confirming Hendler & Redd's (1986) observations. Allowing patients to choose a suitable intervention from those available with the label which is least threatening, might even enhance outcome. One experimental study has shown that the particular strategy used by a subject to control an aversive symptom, in this case pressure pain, may be less important than the fact that the subject has the choice of strategy (D'Eon & Perry, 1984).

The results of Study 3 indicate that hypnosis treatment produced significant reductions in post-chemotherapy nausea and both anticipatory and post-chemotherapy anxiety. Although findings for the reduction of anticipatory nausea were not statistically significant, the trend was in the predicted direction, even though the changes were not as large as those in Morrow (1986). Perhaps more important was the clinical finding that 12 of the 18 patients reported less severe nausea overall. Also, patients learning hypnosis reduced the duration of both their nausea and vomiting.

No significant reductions were observed for vomiting frequency or vomiting intensity. This result was surprising since, in another study, anticipatory vomiting was completely eliminated in 6 patients with the use of hypnosis (Redd, Andresen, & Minagawa, 1982). More worrisome is the fact that, in the present study, 3 patients reported anticipatory vomiting after the hypnosis treatment, where they had none during the baseline. One possibility is that these patients may have developed a conditioned response to the tape (Morrow, 1984d; Redd, Andresen, & Minagawa, 1982, 1983). Several patients

stopped listening to the tape because they found that they were beginning to feel nausea associated with the therapist's voice. Another possibility is that the therapist was present with the patient during the chemotherapy session in the Redd et al. (1982) study, but not in the present study.

These findings generally support the results of other studies using hypnosis as an intervention technique. Several differences between the present study and others using various psychological approaches (e.g., Lyles et al., 1982; Morrow, 1986; Morrow & Morrell,1982; Redd, Andresen, & Minagawa, 1982; Zeltzer et al., 1984a) demonstrating reductions in both anticipatory and post-treatment nausea might account for the differential findings. First, patients in the present study were taught hypnosis in just 2 sessions, were instructed to practise at home at least daily, and were then asked to utilize the technique in the way they felt most comfortable, i.e., to practise self-hypnosis. Some patients were able to practise regularly; others practised only minimally, as they felt reluctant to pay too much attention to their illness and treatment side effects between chemotherapy sessions. Unfortunately, data regarding compliance with practice was difficult to obtain.

Second, the therapist was not present after hypnosis training during chemotherapy sessions 3 and 4 to guide the patient through the hypnosis practice as was the procedure in some studies (e.g., Burish & Lyles, 1979, 1981; Redd, 1981; Redd, Andresen, & Minagawa, 1982), but not others (Morrow, 1986; Morrow & Morrell, 1982). Some patients reported finding great difficulty in performing self-hypnosis during their chemotherapy treatment. Others attempted to circumvent this problem by listening to the audiotape that had been prepared during the training sessions by the therapist, prior to and during the chemotherapy treatment. It has been shown, however, that the addition of audiotapes to the training procedure may not add to outcome

effectiveness in reduction of nausea (Morrow, 1984d) or hypertension (Hoelscher, Lichstein, Fischer, & Hegarty, 1987). Tapes remain widely used clinically, however, but further research on their effectiveness needs to be performed.

Third, patients in the hypnosis intervention developed imagery consistent with their experience and beliefs, in consultation with the investigator. It was hypothesized that they might choose distracting imagery or pleasant thoughts and feelings which would absorb them, and contribute to the reduction of anxiety and alter the unpleasant perceptions of the nausea (Frankel, 1975). In a pilot study, an attempt was made to develop a standard set of audiotaped instructions. The imagery chosen for the tape was as follows: patients were asked to imagine that their nausea was like a a log floating away from the edge of a lake, and as it moved away, the nausea receded. This approach failed when some patients reported that a log would not float away, but rather would tend to float in to the shore as the waves carried it. Other patients, seemingly unperturbed by this experience, reported changing the image spontaneously to conform with their own previous experiences. These observations confirmed that imagery should be developed in concert with the patient. In Study 3, a 39 year-old woman with breast cancer chose to imagine herself walking along a country road near her summer home. She reported becoming so absorbed in this image that she could feel the sun warming her and smell the pine fragrance that permeated the forest. This patient was a high susceptible as measured by the SHSS: 'C. She was able to reduce her anticipatory nausea to almost imperceptible levels. Another 45 year-old breast cancer patient claimed that she enjoyed listenening to her tape, but noticed no perceptible increase in relaxation during practice sessions at home. For her, the most noticeable aspect of the practice was that time appeared to pass

quickly. While waiting for her chemotherapy treatment in the adjoining radiotherapy waiting room, she sought to distract herself by thinking about leaving the clinic as soon as possible. She found it impossible to concentrate on either self-hypnosis or listening to the tape and was able to make only modest reductions in her nausea in spite of scoring 6 (medium susceptibility) on the SHSS: C.

The reduction of post-treatment nausea is, in some ways, most surprising though consistent with other studies using various arousal reduction methods (e.g., Burish & Lyles, 1981; Cotanch, 1983; Lyles et al., 1982; Morrow, 1986; Morrow & Morrell,1982; Redd, Andresen, & Minagawa, 1982; Wechsler & Delaney, 1984; Zeltzer, Kellerman, Ellenberg, & Dash, 1983). Post-chemotherapy nausea is thought to be primarily physiological in origin, i.e., the nausea is caused by the physiological action of the chemotherapy drugs on the patient's system. Nausea can increase dramatically from one session to another, increasing the risk of the development of anticipatory nausea (Andrykowski, 1986).

Two recent studies have demonstrated that the development of post-chemotherapy nausea and vomiting can be slowed significantly by employing relaxation with guided imagery (Burish, Carey, Krozely, & Greco, 1987) or systematic desensitization (Dobkin & Morrow, 1985), prior to the initial chemotherapy session. Since the intensity of post-chemotherapy nausea is the major contributor to the development of anticipatory nausea, this type of primary prevention may decrease the likelihood of the development of anticipatory nausea symptoms. Further research comparing hypnosis with the aforementioned techniques should be carried out to evaluate its effectiveness in the primary prevention of nausea.

The Role of Hypnotic Abilities

Distinct from hypnosis as an intervention technique is the importance of hypnotic susceptibility, the set of skills necessary to passively focus, selectively attend to, and become imaginatively involved and absorbed in the hypnotic experience. It had been hypothesized that the abilities underlying responsivity to hypnosis might be related to the development of anticipatory nausea and vomiting in the same way that other disorders involving cognitive and perceptual distortions, such as anxiety disorders and phobias (Frankel, 1974, 1975; Frankel & Orne, 1976), or even anorexia and bulimia (Pettinati, Horne, & Staats, 1985), were related to it. The lack of significant findings between hypnotic susceptibility and nausea in the present study indicates that this variable may not be implicated in the genesis of the symptoms nor predictive of response to hypnotic intervention (cf. Frischholz, D. Spiegel, H. Spiegel, Balma, & Markell, 1982). The small sample size as well as the variability of the dependent measures, however, may not have permitted a fair test of this hypothesis. In a recent study, Challis (1987) found that two variables, high levels of absorption, which correlates significantly with susceptibility, (r = .40; Tellegen & Atkinson, 1974), and perception of autonomic changes were predictive of the development of anticipatory nausea and vomiting. This finding is encouraging, but is in need of further replication.

In spite of this, a number of the patients reported profound experiences in hypnosis, such as time distortion and perceptual changes (e.g., smelling the flowers in a garden), which enabled them to endure their symptoms with less distress. Others reported only feelings of relaxation with no subjective impression of cognitive change.The importance of this variable is in need of further examination in larger group studies.

J. R. Hilgard & LeBaron (1984) have shown that even children with low

measured hypnotic susceptibility could still benefit from relaxation and distraction, while undergoing painful bone marrow aspirations. Likewise, engaging in a competing activity may serve as a distraction from nausea symptoms, leading to a reduced feeling of distress. Zeltzer, Kellerman, Ellenberg, & Dash (1983) have shown that hypnotic suggestions to counteract nausea and the use of post-hypnotic suggestions resulted in the reduction of the intensity and frequency of post-chemotherapy nausea in 12 adolescents. Zeltzer et al. (1984a) found no difference in reduction of post-chemotherapy nausea between groups of children receiving either hypnosis or supportive counselling, which included distraction techniques. An important finding was that higher hypnotic susceptibility was related to greater improvement in the hypnosis group.

In addition, involvement in video games has been found effective in reducing adverse effects of chemotherapy in children (Kolko & Rickard-Figueroa, 1985; Redd, Jacobsen, Die-Trill, Dermatis, McEvoy, & Holland, 1987). When the video games were removed using a reversal design, the symptoms of distress returned. All of these approaches involved distraction by an outside agent, i.e., the therapist or the video machine. On the other hand, self-hypnosis implies the utilization of distracting or absorbing imagery without the presence of this external agent, perhaps a more formidable task for patients experiencing such distress.

The results of the studies employing distraction as a coping mechanism also support the notion that nausea may be reduced even though no arousal reduction methods were employed. Indeed, it has been demonstrated clearly that hypnotic phenomena may be experienced while the subject is in an aroused state while riding on a stationery bicycle (Banyai & Hilgard, 1976).

Distraction and absorption are clearly related phenomena, and may be best

understood in terms of the context in which they are described and the degree of subjective involvement the subject experiences. The more profound the experience, the more likely the patient is deeply absorbed in the image and experience cognitive and perceptual distortions. This may occur only in patients who are more highly hypnotically susceptible and therfore, have the requisite cognitive skills that make up the construct of hypnotic susceptibility. Distraction, on the other hand, may occur when an outside agent is actively encouraging the subject to shift attention away from the noxious event, and may occur even in subjects who have lower hypnotic susceptibility. The measurement of hypnotic susceptibility with larger samples would provide important data on this trait.

Experimental Design

One of the major criticisms of the design of Study 3 might be the lack of appropriate control groups. Since a reversal (ABA) design (Hersen & Barlow, 1976) is impossible when utilizing hypnosis as an intervention, only an AB pre-post design could be applied. In one sense, although inferential statistics were used, Study 3 could be considered as a series of (N = 1) case study replications (Hersen & Barlow, 1976). Hayes (1981) has argued that if the stability, level and trend in a series of datapoints has been established in the baseline phase, then an abrupt change in the series in the intervention phase may be attributed to this factor. In addition, since it has been established that the course of nausea and vomiting is progressive, the likelihood of uncontrolled factors contributing to the change is minimal (Kazdin, 1981). Since 12 of 18 patients in the present study were able to reduce their nausea after learning self-hypnosis, the clinical significance of this approach is considerable and the absolute necessity of a no-treatment control group is

minimized.

Future studies in this area should be of two types. Intensive single subject case designs should not be neglected because of concerns about obtaining significant differences in group means (Kazdin, 1981). The empirical observation and evaluation of the single case in a particular clinical situation may provide information and clues as to the operative variables (Cronbach, 1975). Group comparison studies should also be carried out, employing repeated measures designs and multivariate (e.g., MANOVA) procedures, which are less likely to compromise assumptions (such as sphericity), and Type 1 or experiment-wise error rates (Hummel & Sligo, 1971; Jaccard & Ackerman, 1985; O'Brien & Kaiser, 1985; Shaffer, 1979).

This approach would provide investigators with the best opportunity to develop and evaluate effective interventions, without neglecting the needs and concerns of the individual patient who is suffering from the side effects of chemotherapy.

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APPENDIX A

Nausea Rating Scale For Various Cancer Chemotherapy

Drugs and Doses Mailed to Oncology Physicians and Nurses

McGILL UNIVERSITY
Department of Psychology
Stewart Biological Sciences Building
392-4599

November 1982

Dear Colleague,

I would be very grateful if you would help me with a study on nausea related to chemotherapy. My co-workers and I have developed a paper-and-pencil questionnaire to obtain measures of nausea, and we now need to validate patients' responses in terms of the drugs they are taking.

I would appreciate it very much if you would rate the drugs listed on the attached sheet and return the completed form to me in the enclosed envelope.

With many thanks,

Ronald Melzack

1205 Docteur Penfield Avenue, Montreal, PQ, Canada H3A 1B1

APPENDIX B

Program Description and Information Handout Given to Patients Attending the Chemotherapy Clinics at the Participating Hospitals

CONCORDIA UNIVERSITY

A tous les patients de la Clinique de Chimiothérapie.

Si vous etes l'une des nombreuses personnes qui souffre de fortes nausées et de vomissements dus au traitement par chimiothérapie, nous savons quelles épreuves physiques et émotionnelles vous devez encourir. Ceci est également un élément de dérangement dans votre vie de tous les jours.

Tout en sachant que ce traitement est le meilleur que vous puissiez recevoir pour enrayer votre maladie, il n'en demeure pas moins que nous voudrions réduire les effets secondaires dudit traitement. Pour certains d'entre vous, les différents médicaments antinausée existant vous soulagent. Cependant, vous savez bien que les médicaments ne conviennent pas a tout le monde.

C'est pour cette raison que nous avons décidé de faire, pour le Centre de Chimiothérapie, une étude sur les problemes de nausées et de vomissements. Nous portons notre recherche plus particulierement sur les traitements alternatifs des médicaments antinausée. Les techniques de relaxation et d'autohypnose se sont avérées efficaces quant a la facon de réagir aux effets secondaires des nausées et des vomissements. Nous examinons tout autant l'efficacité de ces techniques dans la diminution de ces symptomes, que les autres facteurs existant dans ce domaine.

Si vous etes intéressé(e)s a participer a ce programme en espérant qu'il puisse vous aider, veuillez en parler a votre médecin ou son infirmiere. Vous serez alors contacté(e) par Zeev Rosberger, psychologue en charge de cette recherche. Il vous donnera les détails au sujet de votre participation et répondra a vos questions. Il n'y aura aucun changement dans votre traitement actuel, aucun nouveau médicament ne vous sera donné. Ce programme vous est offert parallelement au traitement qui vous est actuellement prescrit.

Merci de votre intéret et de votre coopération.

(English on the other side)

SIR GEORGE WILLIAMS CAMPUS
1455 de Maisonneuve Blvd. West
Montreal, Quebec H3G 1M8

CONCORDIA UNIVERSITY

TO: All Patients on the Chemotherapy Clinic

If you are one of the people who suffers from the severe nausea and vomiting side-effects of chemotherapy treatment, we know that this problem may be causing you both physical and emotional hardship. This may also be an extremely disruptive element in your day-to-day life.

In addition to ensuring that you are receiving the best treatment for your illness, we are also interested in minimizing the side effects of this treatment. For some of you, the different antinausea medications may be of help. However, as you know, these medications do not work for everyone.

For these reasons, we are engaged in a study at the Chemotherapy Centre into the problem of nausea and vomiting. In particular, we are investigating alternative treatments to the antinausea medications. Relaxation and self-hypnotic techniques have been found to be useful ways of learning to cope with the severe side effects of nausea and vomiting. We are examining the relative effectiveness of these techniques in diminishing these symptoms, as well as other factors in this problem area.

If you are interested in participating in this program, and hopefully achieve some benefit, please speak to your doctor or nurse. You will then be contacted by Zeev Rosberger, the psychologist who is conducting this research. He will discuss your participation in this program fully and answer all your questions prior to your involvement. There would be no changes in your regular treatment and no new drugs are involved. This program is offered as an addition to your prescribed treatment program.

Thank you for your interest and cooperation.

(Français au recto)

SIR GEORGE WILLIAMS CAMPUS
1455 de Maisonneuve Blvd. West
Montreal, Quebec H3G 1M8

APPENDIX C

Informed Consent Forms

CONCORDIA UNIVERSITY

Nausea and Vomiting Research Program

Informed Consent

I agree to participate in the research program into the problem of nausea and vomiting associated with chemotherapy conducted by members of the Psychology Department, Concordia University, Montreal, in association with the Chemotherapy Centre, Montreal General Hospital, which includes the following stipulations:

1) I understand that the present treatment of my illness and its side effects, as prescribed by my physician and the Chemotherapy Centre at the Montreal General Hospital, will not be compromised or changed in any way and that the hypnotic treatment offered me will be in addition to my regular treatment.

2) I agree to fill out questionnaires and keep records of my progress, and comply with the therapeutic suggestions made by the investigators.

3) I understand fully the details of the investigation described herein, and had any questions answered to my satisfaction.

4) I understand that some information regarding my treatment from my hospital record will be made available to the investigators, and that this information will be held in the strictest confidence.

5) I understand that I may terminate my participation in this study at any time, and that this in no way will affect my treatment program as prescribed by my doctor and by the Chemotherapy Centre at the Montreal General Hospital.

Signed _____ Date _____

Witness _____

SIR GEORGE WILLIAMS CAMPUS
1455 de Maisonneuve Blvd. West
Montreal, Quebec H3G 1M8

Addendum to Informed Consent

Program Description

In agreeing to participate in this program, I understand that:

1) I will attend four separate sessions.

2) I will be asked some questions concerning my history and illness.

3) I will complete a number of questionnaires to assess e.g., certain attitudes, beliefs and moods.

4) During the second and third sessions, I will be taught self-hypnotic techniques to help me cope with my nausea and vomiting and be provided with a tape recording of these instructions in order to practise at home.

5) I will complete several short questionnaires around the time of my next four chemotherapy sessions.

6) I may be telephoned by the therapist and given the opporotunity to discuss any difficulties with the data collection or the application of the treatment techniques.

Signed: _____ Date: _____

Witness: _____ Date: _____

Nausea and Vomiting Research Program

Informed Consent

Addendum

Further to the informed consent, I have already signed regarding my participation in this research project. I understand:

1) That my being seen at the Jewish General Hospital is only a matter of convenience to me and the researcher.

2) That in no way am I to assume that I have become a patient of the Jewish General Hospital. I remain a patient of the Oncology (Chemotherapy) Centre of the _____

Signed: _____
Date

Witness: _____
Date

APPENDIX D

Patient Data Summary Form

(Completed By the Investigator During Session 1)

Nausea and Vomiting Study
Patient Data Summary

Date: _____

NAME: _____ D.O.B. _____ AGE _____

ADDRESS: _____ MARITAL STATUS: _____

_____ HIGHEST GRADE REACHED: ___

TELEPHONE: (H) _____ (W) _____ OCCUPATION: _____

HOSPITAL CHART NO: _____

HISTORY OF ILLNESS

INITIAL DIAGNOSIS MADE (date) _____ Diagnosis: _____

TREATMENT HISTORY: Surgery (Dates): _____

Radiotherapy (Dates): _____

Chemotherapy (start date): _____

CHEMOTHERAPY HISTORY:

Drugs & Dose including anti-emetics	Number of Treatments	Dates	Diagnosis
1)			
2)			
3)			
4)			
5)			

Number of Months of Chemotherapy: _____

Total Number of Injections: _____

1) Reaction to Illness: Personal? Family?

2) Side-Effects (general) of Chemotherapy. What did you know prior to treatment?

Nausea History:

3) When did nausea and vomiting start? How did it progress? Now? Pre -, during and/or post-? What triggers it?

4) Coping Strategies: What do you do or think about? Thoughts, Images?

APPENDIX E

Chemotherapy Side Effects Ratings Forms

(Given to Patients as a Packet
For Each Chemotherapy Session Rated)

INSTRUCTIONS
FOR
SELF-RATING FORMS

Please complete each of the following rating forms as close to the end of the designated time period as possible. For example, fill out Self-Rating Form 1 on the day before your treatment, Self-Rating Form 2 just before going to bed on the night before your treatment, and so on.

Fill out Self-Rating Form 7 after you feel that you have recovered from the effects of the treatment completely.

FORM 1 Name: ..... Date: .....

Time: .....

DURING THE THREE DAYS PRIOR TO MY CHEMOTHERAPY TREATMENT, I FELT:

ANXIETY

None	Mild	Discomforting	Distressing	Horrible	Excruciating	Worst Ever
0	1	2	3	4	5	6

NAUSEA

None	Mild	Discomforting	Distressing	Horrible	Excruciating	Worst Ever
0	1	2	3	4	5	6

The Nausea was 1) Continuous

2) Intermittent

VOMITING

None	Mild	Discomforting	Distressing	Horrible	Excruciating	Worst Ever
0	1	2	3	4	5	6

The Vomiting was 1) Continuous

2) Intermittent

I vomited ..... times

FORM 2 Name: ..... Date: .....

Time: .....

DURING THE EVENING PRIOR TO MY CHEMOTHERAPY TREATMENT, I FELT:

ANXIETY

None	Mild	Discomforting	Distressing	Horrible	Excruciating	Worst Ever
0	1	2	3	4	5	6

NAUSEA

None	Mild	Discomforting	Distressing	Horrible	Excruciating	Worst Ever
0	1	2	3	4	5	6

The Nausea was 1) Continuous

2) Intermittent

VOMITING

None	Mild	Discomforting	Distressing	Horrible	Excruciating	Worst Ever
0	1	2	3	4	5	6

The Vomiting was 1) Continuous

2) Intermittent

I vomited ..... times

FORM 3 **Name:** ..... **Date:** .....

Time: .....

ON THE DAY OF MY TREATMENT, UP TO THE TIME I ARRIVED AT THE CLINIC, I FELT:

ANXIETY

None	Mild	Discomforting	Distressing	Horrible	Excruciating	Worst Ever
0	1	2	3	4	5	6

NAUSEA

None	Mild	Discomforting	Distressing	Horrible	Excruciating	Worst Ever
0	1	2	3	4	5	6

The Nausea was 1) Continuous

2) Intermittent

VOMITING

None	Mild	Discomforting	Distressing	Horrible	Excruciating	Worst Ever
0	1	2	3	4	5	6

The Vomiting was 1) Continuous

2) Intermittent

I vomited ..... times

FORM 4 Name: ..... Date: .....

Time: .....

WHILE IN THE CLINIC WAITING ROOM AND/OR HAVING MY WORK-UP BEFORE MY TREATMENT, I FELT:

ANXIETY

None	Mild	Discomforting	Distressing	Horrible	Excruciating	Worst Ever
0	1	2	3	4	5	6

NAUSEA

None	Mild	Discomforting	Distressing	Horrible	Excruciating	Worst Ever
0	1	2	3	4	5	6

The Nausea was 1) Continuous

2) Intermittent

VOMITING

None	Mild	Discomforting	Distressing	Horrible	Excruciating	Worst Ever
0	1	2	3	4	5	6

The Vomiting was 1) Continuous

2) Intermittent

I vomited ..... times

FORM 5 Name: ..... Date: .....

Time: .....

DURING MY TREATMENT, I FELT:

ANXIETY

None	Mild	Discomforting	Distressing	Horrible	Excruciating	Worst Ever
0	1	2	3	4	5	6

NAUSEA

None	Mild	Discomforting	Distressing	Horrible	Excruciating	Worst Ever
0	1	2	3	4	5	6

The Nausea was 1) Continuous

2) Intermittent

VOMITING

None	Mild	Discomforting	Distressing	Horrible	Excruciating	Worst Ever
0	1	2	3	4	5	6

The Vomiting was 1) Continuous

2) Intermittent

I vomited ..... times

FORM 6 Name: ..... Date: .....

Time: .....

FROM THE TIME I LEFT THE HOSPITAL UNTIL I RECOVERED FROM MY NAUSEA AND VOMITING, I FELT:

ANXIETY

None	Mild	Discomforting	Distressing	Horrible	Excruciating	Worst Ever
0	1	2	3	4	5	6

NAUSEA

None	Mild	Discomforting	Distressing	Horrible	Excruciating	Worst Ever
0	1	2	3	4	5	6

The Nausea was 1) Continuous

2) Intermittent

VOMITING

None	Mild	Discomforting	Distressing	Horrible	Excruciating	Worst Ever
0	1	2	3	4	5	6

The Vomiting was 1) Continuous

2) Intermittent

I vomited ..... times

FORM 7 **Name:** ..... **Date:** .....

Time: .....

FROM THREE DAYS BEFORE MY TREATMENT UNTIL I RECOVERED FROM MY NAUSEA AND VOMITING, I COULD RATE MY OVERALL LEVEL OF DISCOMFORT AS:

None	Mild	Moderate	Distressing	Horrible	Excruciating	Worst Ever
0	1	2	3	4	5	6

My nausea started at ..... **A.M./P.M. on** ..... (date)

and ended at ..... **A.M./P.M. on** ..... (date)

The first time I vomited was at ..... **A.M./P.M. on** ..... (date)

The last time I vomited was at ..... **A.M./P.M. on** ..... (date)

I took ..... (fill in number) **pills, or suppositories, for my nausea**

Name of drug: .....

Dosage: .....

APPENDIX F

Hypnosis Treatment Instructions Script

(With Sample Imagery)

First of all, make yourself comfortable in the chair -- and then, look at the dot on the wall. Just begin staring at it. In the meantime, I am going to give you some simple instructions which will help you to experience hypnosis. You'll find that you can quickly learn to follow these instructions and to experience the things I describe to you. With practice on subsequent days you will find that you can experience these things with greater vividness, with greater intensity that you do at first.

As you stare at the dot on the wall, you may find that occasionally your gaze may wander. And that your vision may even blur. If this happens, simply refocus your eyes and continue staring evenly at the dot on the wall.

Now take a deep breath in, and hold it: Hold it until it starts to feel uncomfortable and then, when it starts to feel uncomfortable, just let it out very slowly. (Long pause) You find that you are starting to experience a comfortable feeling; -- a feeling of well-being begins to develop as you continue to rest in the chair. Just looking at the dot on the wall, listening to my voice. Now take another deep breath in and hold it --

Notice the feeling of tightness and tension in your chest and abdomen -- and then, as it starts to feel uncomfortable just as you did before, let it out very slowly. (Long pause).

Notice that with breathing out -- with letting the tension out of your lungs -- you become even more aware of a feeling of comfort and well-being settling over you.

Just sink deeper into the chair, and focus your attention closely on feelings of relaxation in various parts of your body -- in your head and your neck, in your arms and in your legs, in your chest and in your back. And just breathe freely and evenly and deeply -- freely, evenly and deeply, not too quickly, not too slowly. Just at a comfortable rate for you to notice that relaxation increases gradually as you breathe out.

You may even be aware of the walls of your chest growing looser -- just rest there for a moment experiencing the sensation. Continue relaxing your chest so that feelings of warmth and comfort radiate to your back and your shoulders and your neck and your arms and your legs.

You're probably starting to notice certain changes in the dot on the wall -- changes that occur from staring at it for so long. Sometimes the dot on the wall looks like it's moving up and down, or from left to right. Sometimes it may not look like a coloured dot on the wall, but a small hole in the wall. At other times it might seem like a coloured patch just a few inches in front of the wall. You may see some of these things or even all of these things. Whatever you see, just continue staring at the dot; continue listening to my voice. Continue to become more deeply relaxed, more deeply relaxed.

And as you watch the dot on the wall, your eyelids become heavier and heavier and your eyes are becoming tired from staring. Your eyelids start to feel very tired and heavy, as you sit there breathing freely and evenly and deeply -- breathing in, breathing out, freely, evenly, deeply. The eyelids are becoming so heavy, so tired that soon they will just close of their own accord,

as if they were coated with a lead paste; as if there were magnetic fields in the eyelashes drawing the eyelashes together.

Concentrate now, even more closely on feelings of relaxation and comfort in various parts of your body. First of all, think of relaxation in the muscles of your left arm – the hand, the fingers of the left hand . . . the left forearm . . . the left upper arm . . . the left shoulder. Think of relaxation in each of these areas and as you think of the relaxation, the muscles become progressively more relaxed.

Then . . . relax the muscles of your right arm . . . the right hand, the fingers of the right hand, the right forearm, the right upper arm, the the right shoulder.

And then . . . relax the muscles of your neck . . . your chest . . . your back. Relax each of these muscle groups . . . the neck . . . the chest . . . the back. And as your relax these muscles, your facial muscles will also relax and loosen of their own accord. Then relax the stomach muscles by doing this: . . . tighten your stomach muscles . . . make your abdomen hard. . . . and then, when you're ready, let the tension out . . . notice the feeleing of well-being that comes with relaxing your stomach . . . like a gentle massaging action all over your stomach and even perhaps up to your chest.

Then relax the muscles of your legs . . . the right leg . . . the right foot . . . try to feel it in the toes of your right foot . . . and then the right calf . . . the right thigh.

Then the left leg . . . left foot . . . the toes of your left foot . . . the left calf . . . and the left thigh.

Just thinking about relaxation in these areas causes the muscles to become more relaxed and you may even feel an interesting thing happens. That the feelings of relaxation you feel in each of these areas of the body start to spread and irradiate so that they may seem to join up like the parts of a jigsaw puzzle and you feel a deep feeling of overall relaxation. Of contentment and of well-being permeating the whole of your body.

And your eyes will probably have closed now from concentrating so carefully on the dot on the wall, but, if they haven't, just close them gently now of your own accord and take a deep breath in and hold it and then, when it starts to feel uncomfortable just as you've done before . . . just let it out slowly.

With your eyes closed, you are ready to experience hypnosis - to experience it more profoundly - but you will find an interesting thing is happening. That no matter how deeply relaxed you ever feel, no matter how deeply in hypnosis you ever feel, your mind is always clear. You're always aware of my voice and of what I am saying to you. You are completely aware of everything that is happening around you even though you are deeply relaxed -- deeply in hypnosis.

You can now go even deeper into hypnosis. Say to yourself – just by thinking it – "Now I am going deeper and deeper." Think it to yourself. And

imagine yourself standing at the top of an escalator. Visualize the scene of the escalator -- of the steps moving down -- and picture the moving hand rail.

Count backwards slowly from ten to zero, imagining, as you count that you are stepping onto the first step of the escalator and standing with your hands on the railing while the steps move down carrying you deeper and deeper into hypnosis. You can play it so that you reach zero just as you reach the bottom and step off the escalator. It will take you about 1 minute.

(Pause 60 seconds)

You have now become so deeply relaxed -- so deeply in hypnosis -- that your mind has become so sensitive -- so receptive to what I say -- that everything I say to you -- will sink so deeply into the furthermost recesses of your mind -- and will make so deep and lasting an impression there.

And because these things will remain -- firmly embedded in the deepest parts of your mind -- after you have left here -- when you are no longer in this room -- they will continue to exercise the same profound impression -- just as strongly -- just as surely -- just as powerfully -- when you are back at home -- or anywhere else you happen to be -- as when you are actually here in this room, listening to my voice.

As a result of this deep relaxation -- this deep hypnosis -- you are going to feel physically stronger and fitter and heathier in every way. You will feel more alert -- more wide awake -- more energetic. You will become much less easily tired -- must less easily fatigued -- much less easily discouraged.

Every day you will become so deeply interested in whatever you are doing -- in whatever is going on around you -- that your mind will become completely distracted away from everything else -- you will no longer think nearly so much about yourself -- you will become much less conscious of yourself -- much less concerned with yourself and with your own feelings.

Everyday your nerves will become stronger and steadier -- your mind calmer and clearer -- more composed -- more placid -- more tranquil. You will find that it takes a lot for things to worry you -- that it takes a lot for things to upset you even slightly.

You'll be able to think more clearly -- you'll be able to concentrate more easily -- you'll be able to give up your whole undivided attention to whatever you are doing -- to the complete exclusion of everything else. As a result you will find it easier to remember things than you do now -- you will be able to see things in their true perspective -- without magnifying them -- without ever allowing them to get out of proportion.

Every day you will become and you will remain emotionally more calm -- much more settled -- much less easily disturbed. Every day you will become -- and you will remain -- more and more completely relaxed -- much less tense each day -- both mentally and physically -- wherever you are -- at home -- or anywhere else you happen to be.

And as you become -- and as you remain -- more relaxed and less tense each day -- so -- you will develop much more confidence in yourself.

More confidence in your ability to do -- not only what you have to do each day -- but more confidence in your ability to do whatever you ought to do -- without feeling that you might fail -- without feeling uneasy.

Because of this -- every day -- yopu will feel more and more independent -- more able to stand up on your own 2 feet -- more able to hold your own -- no matter how difficult or trying things may be.

Every day -- you will feel a greater feeling of personal well-being -- a greater feeling of personal serenity -- than you have felt for a long, long time.

And because all these things will begin to happen -- more and more rapidly -- more and more powerfully -- more and more completely -- every time you hear my voice on this tape -- every time you practice these hypnosis exercises by yourself -- you will feel much happier - much more contented -- much more optimistic in every way.

You will, consequently be much more able to rely upon and depend upon - yourself -- your own efforts -- your own judgements -- your own opinions. You will feel -- much less need to have to rely upon -- or depend upon -- other people.

And now just rest there enjoying the feeling of warmth and comfort and relaxation that have been developing during this hypnosis session. Think particularly about those sensations I've described to you that you find especially pleasant.

TWO MINUTES OF SILENCE

In a moment you will be able to wake up. All you have to do is say to yourself "Now I am going to wake up" and then count from 1 to 3. You will wake up feeling refreshed and buoyant, as though you have been in a deep and dreamless sleep. You will have a feeleing of vigor, of vitality -- vigor -- vitality.

At the same time, you will find that you are less and less aware of your nausea. The unpleasant quality of the nausea will tend to fade away. You may still be faintly aware of it, but it won't worry you very much, if at all.

To help this process along try imagining something like this: Imagine yourself at the side of a like. The sun is shining on you, and you feel its warmth, its comfort on your body. It's pleasant, and very lovely. Imagine now, that you see a log on the lake. Imagine too, that the log somehow represents your nausea. As you watch the log, it is floating away from you ... bobbing in the water, and receding from you. And as it recedes, your nausea is going further and further away. Thelog may float so far away that you can only just see it, or it may float so far, that you cannot see it at all.

When you do this exercise - and you can do it as many times as you wish - you may find that the nausea does not change immediately - sometimes it takes a little time. But every time you practice you become better able to control your nausea -- it becomes less intense -- until you find that you can control it almost at will.

When you are practicing these hypnosis exercises by yourself it is very important that you always wake yourself up at the end, rather than just going off to sleep. You will find that you get much better results this way. Now, just rest there for about one minute and then after 1 minute say to yourself "Now I am going to wake up" and then count from one to three.

And remember to do these exercises in your own time and to practice them regularly.

ONE MINUTE OF SILENCE

And now that the minute is up - say to yourself "Now I am going to wake up" and count from 1 to 3.

APPENDIX G

Modified Stanford Hypnotic Susceptibility Scale: Form C

(SHSS: C, Weitzenhoffer & E. R. Hilgard, 1962)

Modified Stanford Hypnotic Susceptibility Scale: Form C

Induction

First of all, just get yourself comfortable in the chair ... just move around until you find a comfortable position ... notice that the back of the chair is adjustable ... just get comfortable and relaxed ...

optional: and unclasp your hands and let them just rest loosely on your lap, or on the arm of the chair.

optional: and uncross your legs and let them find a comfortable position on the footrest of the chair.

... and if at any time during the session you find that this position is uncomfortable you can simply adjust it to a more comfortable one without in any way disturbing the hypnosis. I'd like you to look at your hands and find a spot on one of them ... like a fingernail or a knuckle ... and just focus your vision on it. It doesn't matter which spot you choose ... just select some spot to focus upon. I shall refer to the spot as the target. In the meantime, I'm going to give you some simple instructions that will help you experience hypnosis. You'll find the instructions easy to follow and that you'll be able to experience the things I describe to you. Indeed, you will probably find that you'll be able to experience these things with great vividness ... with great intensity...

optional: more so than you did on earlier sessions ...

As you stare at the target you have chosen, you may find that occasionally your gaze may wander or that your vision may even blur... If this happens, simply refocus your eyes and continue staring evenly at the target...

Now, take a deep breath in and hold it... hold it until it starts to feel a little uncomfortable ... and then ... when it starts to feel uncomfortable ... just let it out very slowly... You find that you start to experience a comfortable feeling... a feeling of well being begins to develop as you continue to rest in the chair ... looking at the target... listening to my voice ... Now take another deep breath in and hold it ... notice the feeling of tightness and tension in your abdomen ... and then ... as it starts to feel uncomfortable ... just as you did before ... let it out very slowly ... notice that breathing out ... with letting the tension out of your lungs ... makes you become even more aware of a feeling of comfort and well being settling over you... Just sink deeper into the chair ... and focus your attention closely on feelings of warmth and relaxation in various parts of your body ... in your head and in your neck ... in your arms and in yeour legs ... in your chest and in your back ... and just breathe freely and evenly and deeply ... freely ... evenly ... and deeply ... not too quickly ... not too slowly ... just at a comfortable rate for you to notice that the relaxation increases gradually as you breathe out ...

You may even be aware of the walls of your chest growing looser ... just rest there for a moment experiencing the sensations ... Continue relaxing your chest so that feelings of warmth and comfort irradiate to your back ... your shoulders ... and your neck ... and your arms ... and your legs...

You're probably starting to notice some changes in the target ... changes that occur from staring at it for so long ... sometimes the target may look as though it's moving up and down or from left to right ... at times it may appear vefy distinct and clear ... at other times it may appear fuzzy and blurred ... and it may change color ... you may see one of these things or even all of these things ... whatever you see just continue staring at the target ... continue listening to my voice ... continue to become more deeply relaxed ... more deeply relaxed.

And as you watch the target your eyelids become heavier ... your eyes become tired from staring ... your eyelids start to feel very tired and heavy ... as you sit there breathing freely and evenly ... and deeply ... breathing in ... breathing out ... freely and evenly and deeply ... Your eyelids are becoming so heavy ... so tired ... that soon they will just close of their own accord ... as if they were coated with a lead paste ... as if there were magnetic fields in the eyelashes ... drawing your eyelashes together...

Concentrate now ... even more carefully ... on feelings of relaxation and comfort in various parts of your body...

First of all think of relaxation in the muscles of your left arm ... the left hand ... the fingers of the left hand ... the left forearm ... the left upperarm ... the left shoulder ... And then relax the muscles of the right arm ... the right hand ... the fingers of the right hand ... the right forearm ... the right upperarm ... the right shoulder ...

Think of relaxation in each of these areas ... and as you think of relaxation the muscles become progressively more relaxed ... and then relax the muscles of your neck ... your chest ... and your back ... relax eachof these muscle groups ... the neck ... the chest ... and the back ... relax the lower back muscles ... And as you relax these muscles ... your facial muscles will also relax and loosen of their own accord ... Then relax the stomach muscles by doing this ... Tighten your stomach muscles ... make your abdomen hard ... and then, when you're ready ... let the tension out ... Notice the feeling of well-being that comes with relaxing your stomach muscles ... like a gentle massaging action all over your stomach and even perhaps ... up to your chest ... And then relax the muscles of your legs ... the right leg ... the right foot... try to feel it in the toes of the right foot ... and then in the right calf ... and then the right thigh ... then the left leg ... the left foot ... the toes of the left foot ... the left calf ... the left thigh.

Just thinking about relaxation in each of these areas causes the muscles to become more relaxed ... and you may even find an interesting thing happens ... that the feelings of relaxation you feel in each of these areas of the body start to spread and irradiate ... so that they may seem to join up ... like the parts of a jigsaw puzzle ... and you feel a deep feeling of overall relaxation ... of contentment ... and of well being ... permeating the whole of your body...

And your eyes will probably have closed now from concentrating carefully on the target ... but if they haven't ... just close them gently now of your own accord ...

With your eyes closed ... you're ready to experience hypnosis ... to experience it more profoundly ... but you'll find that no matter how deeply relaxed you ever feel ... now matter how deeply in hypnosis you ever feel ... your mind is always clear ... you're always aware of my voice and what I'm saying to you ... you're aware of what is happening to you ... even though you are deeply relaxed ... deeply in hypnosis...

You will remain deeply in hypnosis until I ask you if you would like to come out of hypnosis ... You will experience many things ... you will experience many things just for as long as I ask you to experience them ..

And you will be able to speak to me when I speak to you ... to open your eyes ... and to move around while remaining deeply hypnotized ... whatever you experience or do ... you will remain deeply hypnotized ... deeply in hypnosis ...

If necessary: You can now go even deeper in hypnosis ... Say to yourself, just by thinking it, "Now I'm going deeper and deeper'. Think it to yourself ... and imagine yourself standing at the top of an escalator. Visualize the scene of the escalator ... of the steps moving down ... and picture the moving hand rail ... Count backwards slowly from 10 to 1, imagining as you count, that you are stepping onto the first step of the escalator and standing with your hand on the railing while the steps move down ... carrying you deeper and deeper ... into hypnosis. You can plan it so that you reach 1 just as you reach the bottom and step off the escalator. And to indicate to me that you have reached 1, the index finger of your right hand will left up slowly ... and I'll know that you have reached 1 ... more and more deeply relaxed, as

you start counting ackwards ... (PAUSE) You can just relax your finger now ... deeply relaxed ... deeply hypnotized ...

1. HAND LOWERING (RIGHT HAND)

Now hold your right arm out at shoulder height, with the palm of your hand up. There, that's right ... Attend carefully to his hand, how it feels, what is going on in it. Notice whether or not it is a little numb, or tingling; the slight effort it takes to keep from bending your wrist; any breeze blowing on it. Pay close attention to your hand now. Imagine that you are holding something heavy in your hand ... maybe a heavy baseball or a billiard ball ... something heavy. Shape your fingers around as though you were holding this heavy object that you imagine is in your hand ... That's it...

Now the hand and arm feel heavy, as if the weight were pressing down... and as it feels heavier and heavier the hand and arm begin to move down ... as if forced down ... moving ... moving ... down ... down ... more and more down ... heavier ... heavier ... the arm is more and more tired and strained ... down ... slowly but surely ... down, down ... more and more down ... the weight is so great, the hand is so heavy ... You feel the weight more and more ... the arm is too heavy to hold back ... it goes down, down, down ... more and more down ...

(Unless all the way down, allow ten seconds;
note extent of movement, then continue:)

(If not all the way down:) That's good ... now let your hand go back to its original position on the arm of the chair, and relax. You probably experienced much more heaviness and tiredness in your arm than you would have if you had not concentrated on it and had not imagined something trying to force it down. Now just relax ... Your hand and arm are now as they were, not feeling tired or strained ... All right, just relax.

(If all the way down:) That's good... now let your hand return to its original position. Just let it rest there, and relax. Your hand and arm are now as they were, not feeling tired or strained. All right ... just relax.

(Record score. Score (+) if hand has lowered at least six inches by end of ten-second wait. Go to Instruction 2 below.)

2. MOVING HANDS APART

Now extend your arms ahead of you, with palms facing each other, hands close together but not touching. Let me show you.

(Take hold of subject's hands and position them about two inches apart.)

I want you to imagine a force acting on your hands to push them apart, as though one hand were repelling the other. You are thinking of your hands being forced apart and they begin to move apart... separating ... separating ... moving apart ... wider apart ... more and more away from each other... more and more ...

(Allow ten seconds without further suggestions
and note extent of motion.)

(If hands have moved very little:) That's fine. You notice how closely thought and movement are related. I'll take hold of your hands and bring them together so that you can feel how much they have moved apart.

(Take subject's hands and move them together
fairly slowly.)

(If hands have moved apart:) That's fine. Just put your hands back on the arms of the chair and relax.

(Record score. Score (+) if hands are six or more inches
apart at the end of ten seconds.
Go to Instruction 3 below.)

3. MOSQUITO HALLUCINATION

You have been listening to me very carefully, paying close attention. You may not have noticed a mosquito that has been buzzing, singing, as mosquitos do ... Listen to it now ... hear its high pitched buzzing as it flies around your right hand ... It is landing on your hand ... perhaps it tickles a little ... there it flies away again ... you hear its high buzz ... It's back on your hand tickling ... it might bite you ... you don't like this mosquito ... You'd like

to be rid of it ... Go ahead, brush it off ... get rid of it if it bothers you ... (Allow 10 seconds).

It's gone ... you are no longer bothered ... the mosquito has disappeared. Now relax, relax completely.

(Record score. Score (+) for any grimacing, any movement, any acknowledgement of effect. Go toInstruction 4 below.)

4. ARM RIGIDITY (RIGHT)

Please hold your right arm straight out, and fingers straight out, too. That's right, right arm straight out. Think of your arm becoming stiffer and stiffer ... stiff ... very stiff ... as you think of its becoming stiff you will feel it become stiff ... more stiff and rigid, as though your arm were in a splint so the elbow cannot bend ... stiff ... held stiff, so that it cannot bend. A tightly splinted arm cannot bend ... Your arm feels stiff as if tightly splinted ... Test how stiff and rigid it is ... Try to bend it ... try ... (Allow 10 seconds).

(If arm bends:) That's fine. You will have an opportunity to experience many things. You probably noticed how your armbecame stiffer as you thought of it as stiff, and how much effort it took to bend it. Your arm is no longer at all stiff. Place it back in position, and relax.

(If arm does not bend:) Relax ... don't try to bend your arm any more ... It is not stiff any longer ... Let it relax back into position. Just relax.

(Record score. Score (+) if there is less
than two inches of arm bending in ten seconds.
Go to Instruction 5 below.

5. AGE REGRESSION

Material needed: 8-1/2 x 11" pad of paper and a pencil.

Continue to enjoy the feelings of being deeply relaxed. I am going to give you a pad and a pencil. Let's see, which hand do you write with? Good, here you can hold the pad in your (left, right) hand and the pencil in your (right, left) hand in such a way that you can easily write on the pad with the pencil. (Place pad and pencil in hands,being sure eyes remain closed.) Now, please write your name ... and while you are at it, why don't you also write your age and the date. That's fine. Keep the paid and pencil in your hands and listen closely to me. I would like you to think about when you were in the fifth grade of school; and in a little while you will find yourself once again a little boy (girl) on a nice day, sitting in class in the fifth grade, writing or drawing on some paper .... I shall now count to five and at the count of five you will be back in the fifth grade .... One, you are going back into the past. It is no longer (state present year), not (state an earlier year) or (state a still earlier year), but much earlier. Two, you are becoming increasingly younger and smaller .... presently you will be back in the fifth grade, on a very nice day. Three, getting younger and younger, smaller and smaller all the time. Soon you will be back in the fifth grade, and you will feel and experience exactly as you did once before on a nice day when you were sitting in class, writing or

drawing. Four, very soon you will be there.... Once again a little boy (girl) in a fifth grade class. You are nearley there now .... In a few moments you will be right back there. Five! You are now a small boy (girl) in a classroom in school ....

How old are you? . . . .

Where are you? . . . . (Record on scoring sheet.)

What are you doing? . . . .

Who is your teacher? . . . . .

(Continue, even if there is no evidence of regression.)

You have a pad of paper and are holding a pencil. I would like you to write your name on the pad with this pencil .... That's fine, and now please write down your age .... and now the date, if you can .... and the day of the week....

Presently you will no longer be in the fifth grade, but you will be still younger, back in the second grade. I shall count to "two", and then you will be in the second grade. One, you are becoming smaller still, and going back to a nice day when you were in the second grade .... Two, you are now in the second grade, sitting happily in school with some paper and pencil .... You are in the second grade ....

What is your name? ....

And how old are you? .... (Record on scoring sheet.)

Where are you? ....

Who is your teacher? ....

Would you please write your name on the paper .... That's good .... And can you write how old you are? .... That's fine .... and can you tell me what the date is today? .... Or the day of the week?....

(Regardless of what the responses have been:)

That's fine.... And now you can grow up again and come right back to (state current day and date) in (name of locale of testing). You are no longer a little boy (girl) but a grown up person of (state age) sitting in a chair deeply hypnotized. How old are you? .... And what is the date? .... Where are you? .... That's right .... Today is (correct date) and you are (correct age) and this is (name place where subject is being tested). Fine, everything is back as it was. Now I'll take the pad and pencil you have been holding .... (Remove pad and pencil).... Now just continue to be comfortably relaxed ....

(Score (+) if a clear change in handwriting between the present and one of the regressed ages. Go to Instruction 6, below.)

6. GLOVE ANALGESIA

This time, I want you to imagine that someone is wiping a little liquid over your right hand .... this liquid is anesthetizing your right hand .... making it very insensitive .... perhaps you feel the coolness of the liquid as it dries on the skin of your right hand .... and then .... very soon, you'll start to feel a slight tingling in the hand .... a slight feeling of pins and needles as the anesthetic starts to take effect.... making the hand feel different .... making the

skin tingle .... making the muscles .... and fibres.... and tissues feel slightly numb and dull.... as if someone has applied a torniquet at the wrist.... so that it might feel as if .... from the wrist downwards the circulation in the hand is being slowly cut off.... And you feel this increasing sensation of dullness and numbness gradually spreading throughout the whole of the right hand .... in the fingertips .... in the joints of each finger.... and of the thumb.... in the knuckles.... in the palm.... throughout the whole of the right hand up to the wrist....

As the hand becomes more and more neumb.... more and more insensitive to touch .... and to pressure.... and to warmth.... and to cold.... and to pain .... the hand is becoming devoid of all sensations.... as if it was encased in a heavy bandage .... or a gauntlet right up to the wrist.... that's how numb and insensitive it's become....

So numb.... so insensitive.... that the hand feels that it no longer belongs to you.... is no longer a part of you.... no longer your hand .... no longer your fingers.... no longer your thumb.... no longer your knuckles.... no longer your palm.... the hand is no longer a part of you.... the hand is now so numb.... so insensitive.... so devoid of all sensations that in a little while I'm going to apply an electric shock.... one that is completely harmless.... but which ordinarily would be painful....

The hand is no longer your hand.... the hand is no longer a part of you.... it is numb and insensitive to pain....

I want you to report what you feel, on a 1 to 10 scale; where one is totally painless and ten, is unbearably painful.... When I'll apply this harmless.... but ordinarily painful pinch on the back of your hand.... Now....

(Apply pinch by twisting skin on back of hand between thumb and forefinger; Count to 4)

On a 1 to 10 scale, how would you rate it? (If 0, Did you feel anything at all?) (Record rating)

Now to show you just how numb and insensitive your right hand is .... I'm going to apply the same pinch to the left hand now ....

(Apply pinch to other hand)

Tell me, using the same 1 to 10 scale... tell me how it felt? (Record Rating)

That's good. Now you notice that the feeling is returning... ever so slowly.... to the hand.... your hand is beginning to lose the numbness... the insensitivity, and is beginning to become sensitive again.... as if the bandage has been peeled off..... Move your right hand a little and notice the feelings in it. Fine ....

(Make sure score is recorded and go to Instructions 7 and 8 below.)

7. POST-HYPNOTIC SUGGESTION (ITCH)

8. AMNESIA

TERMINATION

Stay completely relaxed, but listen carefully to what I tell you next. In a little while I shall begin conting forwards from one to ten. You will awaken gradually, but you will still be in your present state for most of the count. When I reach "seven" you will open your eyes, but you will not be fully awake. When I get to "ten" you will be entirely roused up, in your normal state of wakefulness. You will have been so relaxed, however, that you will have trouble recalling the things I have said to you and the things you did or experienced. It will prove to cost so much effort to recall that you will prefer not to try. It will be much easier just to forget everything until I tell you that you can remember. You will forget all that has happened until I say to you: "Now you can remember everything!" You will not remember <u>anything</u> until then. After you wake up you will feel refreshed and relaxed. You will notice, however, that I will drop my pen on the floor. At that point, the skin under your (watchband, ring, cuff, sleeve, collar) will feel itchy and you will wish to rub it a little. This will happen when I drop my pen on the floor. You will scratch a little, <u>but you will forget that I told you to do so</u>, just as you will forget the other things, until I tell you "Now you can remember everything." I shall now count from one to ten, and at seven, not sooner you will open your eyes but not be fully aroused until I reach "ten". At "ten" you will be fully awake. Ready, now: 1 - 2 - 3 - 4 - 5 - 6 - 7 - 8 - 9 - 10.

(If subject has eyes openÚ) How do you feel? Do you feel wide awake? (If drowsy:) The feeling will go away soon. Now you feel wide awake!

(DROP PEN)

(Hypnotist busies her/himself with papers and notes if subject responds to post-hypnotic suggestion. Allow 10 seconds.)

Now I would like to ask you a few questions about your experiences.

(Record score of post-hypnotic response. Score (+) if any movement is made in response to the suggestion, i.e. subject turns watch or ring or scratches under cuff. Go to Amnesia part of scoring sheet.)

APPENDIX H

Scoring Form For Modified Stanford Hypnotic Susceptibility Scale: Form C (SHSS:C)

SHSS:C Modified - 8 Items

SCORING SHEET

Name _____ Date _____

Hypnotist _____ Score _____

Item: Score

1. HAND LOWERING - Right hand

Score (+) if hand has lowered at least six inches by end of 10-second wait (1) ____

Comment:

_____

_____

2. MOVING HANDS APART

Score (+) if hands are six or more inches apart. (2) ____

Comment:

_____

_____

3. MOSQUITO HALLUCINATION

Score (+) for any grimacing, any acknowledgement of effect. (3) ____

Comment:

_____

_____

4. ARM RIGIDITY (RIGHT)

Score (+) if there is less than 2 inches of arm bending (4) ____

Comment: _____

_____

5. AGE REGRESSION

Grade 5: How old are you? _____
Where are you?_____
What are you doing?_____
Who is your teacher?_____

Grade 2: What is your name?_____
How old are you?_____
Where are you?_____
Who is your teacher?_____

Score (+) if a clear change in handwriting between the present and one of the regressed ages. (5) ____

6. GLOVE ANALGESIA

Record rating on analgesic right hand (1-10) (6a) ____
Record rating on left hand - control (1-10) (6b) ____
Score + if more than 2 points difference (b-a) ____

Comment:
_____
_____

7. POST-HYPNOTIC SUGGESTION (ITCH)

Record (+) if any movement is made in response to the suggestion i.e. subject turns watch or ring, or scratches under cuff. (7) ____

8. AMNESIA

_____

Please tell me now in your own words everything that has happened from the time you closed your eyes.

_____

(Place numbers according to order of recall.) (Give 30 seconds.)

_____Hand Lowering (1)
_____Moving Hands Apart (2)
_____Mosquito hallucination (3)
_____Arm Rigidity (4)
_____Age Regression (5)
_____Glove Analgesia (6)
_____Post-hypnotic Suggestion (7)
_____Amnesia suggestion (8)
Other: _____

_____

_____

Anything else? (Leave 10 seconds after final item recall)

_____

_____

_____

Listen carefully to my words. NOW YOU CAN REMEMBER EVERYTHING.

Anything else now? (List in order of mention.)

_____

_____

_____

Remind subject of omitted items.

Score (+) if subject recalls no more than two items before memory is restored, and recalls at least two new items after memory is restored.

(8) ___

Tell subject that you would like to discuss the experience with him/her.

During the age regression, when you went back to the 5th and 2nd grade, I'd like to know what that was like. I'm going to read some phrases to you which describe some of the experiences that people have during the age regression item. I'd like you to pick out the statement that best describes your experience:

1. I did not go back at all.
2. I was thinking about when I was that age, but had no visual experiences.

3. Although I did not go back, I could see myself as a young child reliving a past experience.
4. I knew I was really my present age, but I felt in part as though I was reliving an experience.
5. I actually felt as though I was back at the suggested age, and reliving a past experience.

(Ask only if subject responded to post-hypnotic suggestion:) You rubbed (or scratched) your arm (or finger) near the end of this session.

1. Do you remember why? _____
2. Did you know why at the time? _____
3. If you remembered that I said you would do this, why did you carry out the suggestion?
4. Would you say it was voluntary or involuntary?

Is there anything else you would like to discuss about this session? (Record responses under item categories.)

APPENDIX I

Means and Standard Deviations for

Nausea, Anxiety, Vomiting Frequency, And Vomiting Intensity Ratings

Made By (n = 18) Patients at Each of Six Time Points

Means and Standard Deviations for Nausea Ratings Made By Patients at Each of Six Time Points

	Chemotherapy Treatment			
Time of Rating*	Session 1	Session 2	Session 3	Session 4
3D	.28(.46)	.75(.93)	.28(.58)	.56(.89)
EV	.50(.86)	1.06(1.18)	.39(.61)	.63(.89)
AR	1.00(.91)	1.37(1.25)	.67(1.09)	1.06(.93)
WT	2.00(1.78)	2.38(1.82)	1.78(1.59)	1.94(1.39)
DU	2.25(.58)	2.58(.43)	1.90(.64)	2.40(.48)
PS	2.78(1.83)	3.19(1.64)	2.27(1.78)	2.13(1.41)

Note.
* 3D- For Three days prior to chemotherapy session
EV-Evening prior to chemotherapy session
AR-On arriving to clinic
WT-While waiting for chemotherapy treatment
DU-During the chemotherapy treatment
PS-From the end of the chemotherapy treatment until the nausea ends

Means and Standard Deviations (SD) for Anxiety Ratings Made By Patients at Each of Six Time Points

	Chemotherapy Treatment			
Time of Rating*	Session 1	Session 2	Session 3	Session 4
3D	1.44(.86)	1.63(1.03)	1.11(1.02)	.94(.77)
EV	1.89(.90)	1.69(1.08)	1.33(1.03)	1.25(1.25)
AR	2.28(1.18)	2.13(1.09)	1.39(1.04)	1.56(1.21)
WT	2.60(1.10)	2.43(1.63)	1.18(1.09)	1.81(1.47)
DU	2.83(1.54)	2.56(1.67)	1.67(1.28)	1.56(1.37)
PS	2.17(1.95)	2.5(1.71)	1.56(1.50)	1.44(1.46)

Note.
* 3D- For Three days prior to chemotherapy session
EV-Evening prior to chemotherapy session
AR-On arriving to clinic
WT-While waiting for chemotherapy treatment
DU-During the chemotherapy treatment
PS-From the end of the chemotherapy treatment until the nausea ends

Means and Standard Deviations (SD) for Vomiting Frequency Made By Patients at Each of Six Time Points

	Chemotherapy Treatment			
Time of Rating*	Session 1	Session 2	Session 3	Session 4
3D	.11(.47)	.18(.54)	.28(1.18)	0(0)
EV	.11(.47)	1.56(1.25)	.11(.47)	0(0)
AR	.22(.94)	0(0)	.44(1.14)	.25(.68)
WT	.50(.99)	.63(2.03)	.61(1.91)	.31(1.01)
DU	.83(2.01)	1.19(2.34)	1.06(2.18)	1.31(2.30)
PS	11.06(13.35)	8.63(12.72)	9.41(13.03)	7.64(8.43)

Note.
* 3D- For Three days prior to chemotherapy session
EV-Evening prior to chemotherapy session
AR-On arriving to clinic
WT-While waiting for chemotherapy treatment
DU-During the chemotherapy treatment
PS-From the end of the chemotherapy treatment until the nausea ends

Means and Standard Deviations (SD) for Vomiting Intensity Ratings Made By Patients at Each of Six Time Points

Time of Rating*	Chemotherapy Treatment			
	Session 1	Session 2	Session 3	Session 4
3D	0(0)	.19(.54)	.11(.47)	0(0)
EV	.18(.72)	.19(.75)	.11(.47)	0(0)
AR	.18(.73)	.25(1.00)	.50(1.20)	.25(.68)
WT	.47(1.18)	.31(1.01)	.50(1.47)	.38(1.09)
DU	.77(1.44)	.81(1.64)	.67(1.50)	.75(1.29)
PS	2.17(2.07)	2.13(189)	1.71(1.83)	1.[illegible](1.62)

Note.
* 3D- For Three days prior to chemotherapy session
EV-Evening prior to chemotherapy session
AR-On arriving to clinic
WT-While waiting for chemotherapy treatment
DU-During the chemotherapy treatment
PS-From the end of the chemotherapy treatment until the nausea ends

APPENDIX J

Correlations Between Scores on the Stanford Hypnotic Susceptibility Scale-Form C (SHSS) and Global Measures of Nausea and Anxiety

Correlations Between Scores on the Stanford Hypnotic Susceptibility Scale-Form C (SHSS) and Global Measures of Nausea and Anxiety

	SHSS	N
Baseline		
NRI-am	-.43	16
ONI	.11	16
STAI-State	-.11	16
STAI-Trait	.13	16
Post-Hypnosis		
NRI-am	-.11	15
ONI	-.12	15
STAI-State	-.10	15
STAI-Trait	-.24	15

Note. All the correlations are non-significant, $p > .05$.
NRI-am is the sum of the affective and miscellaneous subscales of the nausea questionnaire. ONI is the Overall Nausea Intensity scale.
STAI-State is the state anxiety subscale of the Spielberger State-Trait Anxiety questionnaire. STAI-Trait is the trait anxiety subscale of the Spielberger State-Trait Anxiety questionnaire.