

RELATIONSHIP OF TRIIODOTHYRONINE AND THYROXINE BLOOD SERUM LEVELS
AND CHRONIC ORGANIC BRAIN SYNDROME IN OLDER PEOPLE

by

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A Thesis Submitted to the Faculty of the

COLLEGE OF NURSING

In Partial Fulfillment of the Requirements
For the Degree of

MASTER OF SCIENCE

In the Graduate College

THE UNIVERSITY OF ARIZONA

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ABSTRACT

This study attempted to examine the relationship of triiodothyronine, (T3) and thyroxine, (T4) blood serum levels and chronic organic brain syndrome in people 65 years of age and older admitted to a short-term acute-care psychiatric facility in Canada.

The records of ten patients ages 65 to 85 were reviewed. There were five men and five women included in the study group. T3 resin uptake values were recorded because T3 blood serum levels were not available. T4 blood serum levels were also recorded. Two T3 and T4 values were recorded for each patient. The relationships between first and second-drawn T4 blood serum levels; and first-drawn T4 blood serum levels and sex were found to be significance at the .05 level. No other significant relationships were found.

T3 and T4 laboratory results may help clinicians and nurses make more accurate diagnoses of patients with chronic organic brain syndrome. Accurately diagnosing chronic organic brain syndrome and knowing that this disease is irreversible, nurses can stop trying to "bring the patient back" and can concentrate on more supportive types of nursing care.

CHAPTER 1

INTRODUCTION

During the past 35 years, the population in Canada has increased by over 100 percent in the age group of 65 years and older. There is every indication that this escalation will continue. With the increase in life span, especially after the seventh decade, an increase in chronic organic brain syndrome occurs (Schwenger 1976). Chronic organic brain syndrome does affect 5.5 percent of the older population by age 65 years (Eastwood 1977).

While working on a specialized psychogeriatric unit in Canada, this investigator noted many similarities in the behavior of people with a diagnosis of chronic organic brain syndrome and those with hypothyroidism. In both chronic organic brain syndrome and hypothyroidism, an impoverishment of ideas, impaired ability for abstractness and a decline of recent memory could be observed. People with chronic organic brain syndrome or hypothyroidism experienced emotional lability and impaired orientation and judgment. It seemed feasible that people diagnosed with chronic organic brain syndrome could have decreased thyroid hormone levels. A review of the literature revealed no information about the relationships between chronic organic brain syndrome and thyroid hormone levels.

The personnel in this psychogeriatric unit were seeking to understand the mechanisms of chronic organic brain syndrome to enable

them to make more accurate diagnoses and improve treatment modalities. Two of several laboratory tests clinicians were obtaining on patients admitted to the unit were triiodothyronine (T3) and thyroxine (T4) blood serum levels. These tests were routinely done on admission to the hospital and were repeated one or two times if chronic organic brain syndrome was suspected. Blood levels were lower than could have been attributed to the normal aging process. These blood levels were used as part of the diagnosis of chronic organic brain syndrome. However, no research had been done to look at the relationship between patients with chronic organic brain syndrome and decreased T3 and T4 blood serum levels, below those attributed to the normal aging process. The purpose of this study was to examine the relationship of chronic organic brain syndrome and T3 and T4 blood serum levels.

There is little understanding of chronic organic brain syndrome among medical personnel despite research done in this area. The aging process itself is not fully understood nor is the development of chronic organic brain syndrome within the final stage of life. Much remains to be learned about the exact dimensions of this problem. The present methods of diagnosing and treating chronic organic brain syndrome are less than satisfactory.

The diagnosis of chronic organic brain syndrome implies knowledge of the structural or functional status of the brain and its relationship to clinical manifestations. There are few reliable means for evaluating the brain "in vivo." The clinical diagnosis is usually based on observation and interpretation of the patient's behavior and

responses. When the brain is moderately or severely impaired, the detection of such characteristics is not difficult. However, at this late stage the probability that any therapeutic intervention will be effective is remote (Wang 1969).

Statement of the Problem

Do people age 65 years and older with a diagnosis of chronic organic brain syndrome have lower T3 and T4 blood serum levels than would be expected as a result of the aging process?

Significance of the Problem

The information concerning the prevalence of chronic organic brain syndrome among older people is based largely on statistical data obtained from psychiatric hospitals. In Canada in 1977, the prevalence of chronic organic brain syndrome was 55.1 cases per 1000 population 65 years and older (Eastwood 1977). In 1971 in the United States, it was calculated according to the estimated population for the year, that the incidence of psychiatric disorders requiring psychiatric hospitalization was 941 cases per 100,000 population among the geriatric population, 3.3 times higher than the rate of 284 per 100,000 for those under 65 years of age. The diagnosis made most frequently in older people was chronic organic brain syndrome. In the same year, cases of chronic organic brain syndrome represented 73.1 percent of the total inpatient psychiatric services in the United States (Wang 1969). It would appear that in the majority of studies, four to six percent of the population 65 years and older have definite organic

psychiatric disorders (Bergmann, 1977). Even within this group the prevalence of chronic organic brain syndrome in older people is one of the major contributing factors towards the need for institutional care in old age. Studies implicate the biological basis of the disease to be the most important factor (Kay et al. 1970).

No study was found in the literature that documented the existence of a relationship between chronic organic brain syndrome and T3 and T4 blood serum levels in older people. Present methods of diagnosing chronic organic brain syndrome include electroencephalogram (E.E.G.) and the Wechler Adult Intelligence Scale (W.A.I.S.) psychological test. Decreased T3 and T4 blood serum levels may be one indication of the occurrence of chronic organic brain syndrome. If decreased T3 and T4 blood serum levels could be implicated in this disease, these measurements could be utilized in the nursing process for assessment and early intervention and may add to the present body of knowledge about this disease.

In considering nursing research in developing a nursing theory King (1971) stated, "If nurses are to help individuals attain health, one of the areas of knowledge important to safe practice is that of normal physiology. Studies to measure physiologic parameters related to patient states have implication for nursing practice" (King 1971: 33).

Nursing as a profession must become involved in physiological research, not only for the enhancement of its clinical application, but for the promotion of nursing knowledge as a whole. The nurse

should have in-depth knowledge about the underlying disease process, the diagnostic and therapeutic procedures with which to treat chronic organic brain syndrome and the knowledge of caring for patients with chronic organic brain syndrome. It is possible to carry out nursing research in a fairly technical area of study so that the results of the research have implications for the design and delivery of nursing care. Nurses can do little or nothing to improve the memory of a patient who happens to have chronic organic brain syndrome, but as nurses we may be able to improve the person's behavior. The recognition that brain syndrome is present is therefore the first step toward determining the type of treatment and nursing intervention required.

Knowing that chronic organic brain syndrome is irreversible, nurses can stop trying to "bring the patient back" and can concentrate on more supportive types of nursing care. Group work with chronic organic brain syndrome patients is one treatment modality to provide better nursing care. "Persons who have suffered brain damage and have cognitive defects cannot be expected to show true intellectual improvement through group therapy, but group therapy does decrease some of their fears, anger, anxiety and also can often improve social graces" (Goldfarb 1971: 626). The goals of group work should include improved communication, diminished withdrawal and isolation, and caring for and enjoying each other. The concern for quality of life is one of the most demanding areas in nursing today. It is extremely difficult to determine the maximum potential ability of each person with chronic organic brain syndrome.

The importance of consistent reality testing cannot be stressed enough. This is the patient's bridge back to reality and the relationship of the therapist and group members is of primary importance (Burnside 1976). Remotivation therapy to stimulate sensory awareness is also crucial. Reminiscing therapy is not appropriate for patients with chronic organic brain syndrome because it only serves to set off a chain of "catastrophic reactions" (Burnside 1976: 187).

Goldfarb (1971) reported on a study by Lipsky and Barad in which they found that patients in an old age home with severe chronic organic brain syndrome and sensory impairment could improve socially and behaviorally with a high saturation of attention and multiple sensory stimulation. They found music, touching and food shared in group situations promoted group conversation. With this kind of patient they found it necessary to maintain a continuous high level of involvement or the gains would quickly disappear (Burnside 1976).

Many group workers found varied sensory stimulation the most accessible route to reality contact in those patients with chronic organic brain syndrome. Burnside (1973) found that touching patients and allowing them to touch her, encouraging group hand holding et cetera, were extremely effective ways of reaching patients with chronic organic brain syndrome. "The need to touch supersedes the need to verbalize, and offers reinforcement on a level more congruent with deficit status" (Wolff 1970: 55).

Group work with chronic organic brain syndrome patients seemed to improve behavior and contribute to more appropriate expression of

emotion. Efforts to enrich their experience of each day and to keep some meaningful contact with those around them no matter how limited, is a challenge for nurses (Burnside 1976).

Statement of the Purpose

The purpose of the study was to determine if a positive relationship existed between decreased T3 and T4 blood serum levels and the diagnosis of chronic organic brain syndrome for patients 65 years and older who were hospitalized on a psychogeriatric unit between January 1, 1977 and December 31, 1977.

Conceptual Framework

The conceptual framework for this study draws on concepts related to chronic organic brain syndrome and thyroid hormone secretion.

In chronic organic brain syndrome, structural damage to the brain tends to be irreversible because neurons have limited recuperative capacity and do not reproduce. Structural alterations include a loss of neurons and an increase in senile plaques and the amount of neurofibrillary degeneration. Physiologically, there is a reduction in the metabolic activity of the brain. Usually multiple factors are operating, either simultaneously or as successive links in a cause-and-effect chain. These factors may be physical, psychological, social and/or environmental and may have various effects on each other. The outcome of such interactions is the formation of one or more vicious circles: one pathologic process exerting a positive feedback effect on another.

The principal hormones secreted by the thyroid gland are triiodothyronine (T3) and thyroxine (T4). Their primary function is to control the rate of body metabolism, including the rates of chemical reactions, oxygen consumption and energy production. Thyroid hormones also influence physical and mental growth and development, nervous system activity, circulation, fluid and electrolyte balance, reproduction, requirements for vitamins, bodily resistance to infection and the metabolism of protein, fat and carbohydrate (Tilkian and Conover 1975).

The first step in thyroid hormone synthesis is absorption of dietary iodide from the small intestine into venous circulation. The circulating iodide that is not taken up by the thyroid gland is cleared by the kidneys through glomerular filtration. After entering the thyroid, iodide is oxidized and combines with the amino acid tyrosine, within the protein molecule thyroglobulin, where the thyroid hormones triiodothyronine and thyroxine are formed (Tilkian and Conover 1975).

The next step is the release of T3 and T4 from the thyroid gland. Under the influence of the thyroid stimulating hormone from the anterior pituitary gland, thyroglobulin is hydrolyzed. T3 and T4 are released into circulation. Of the circulating thyroid hormones, 99.5 percent of T3 and 99.95 percent of T4 is bound to serum proteins, particularly to thyroxine-binding globulin. These hormones are inactive when bound to serum proteins. Therefore, only very small amounts of unbound thyroid hormones circulate to provide biologic activity.

As shown in Figure 1, the regulation of the thyroid gland occurs through a feedback system consisting of three main components:

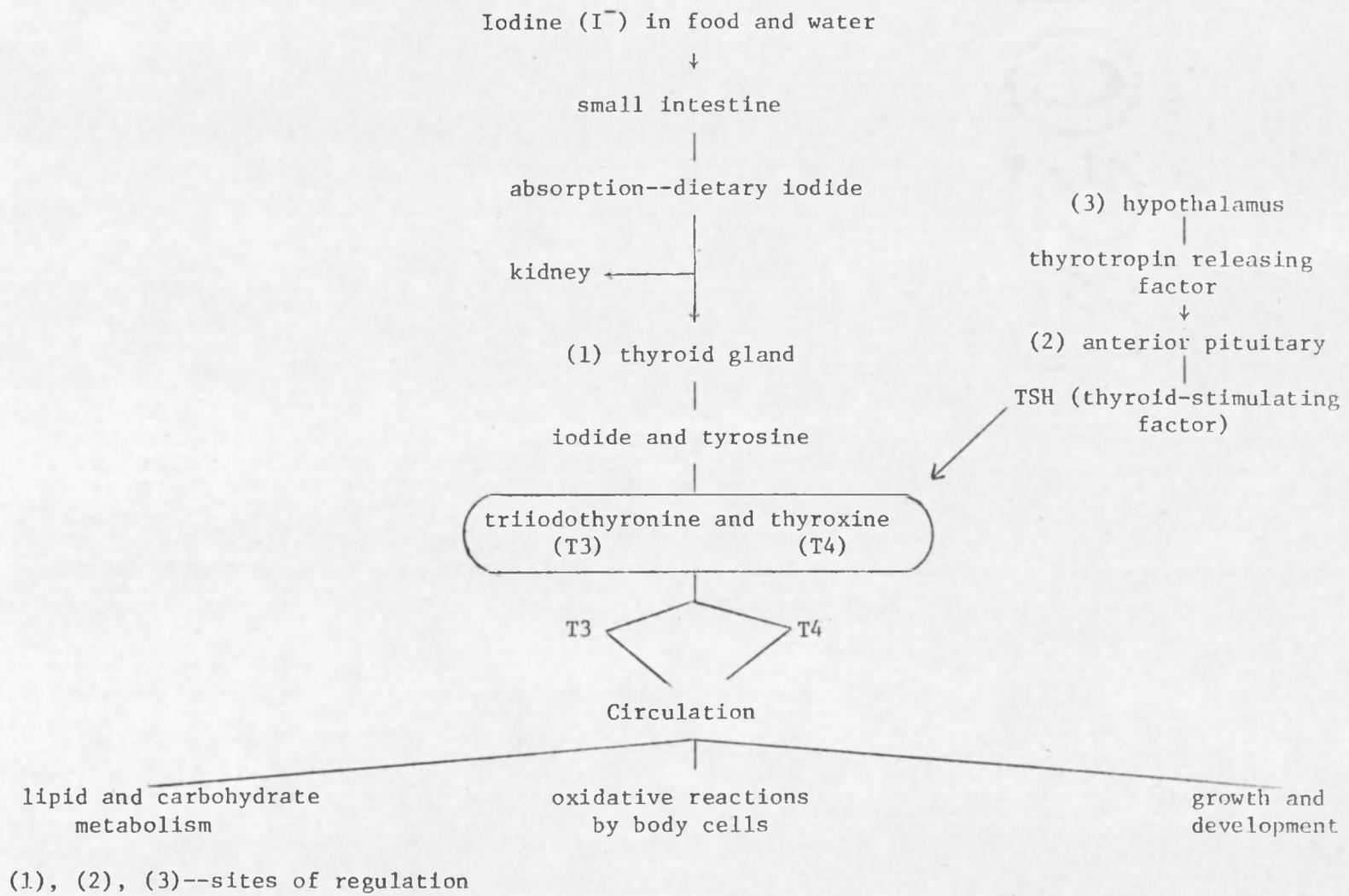


Figure 1. Regulation of the Thyroid Gland.

(1) The thyroid gland which secretes T3 and T4; (2) the anterior pituitary gland which secretes the thyroid-stimulating hormone; and (3) the hypothalamus which secretes thyrotropin-releasing factor. This factor then stimulates the release of thyroid-stimulating hormone (T.S.H.) and causes the synthesis of thyroid-stimulating hormone in the pituitary gland. Normal levels of unbound T3 and T4 are maintained by a negative feedback effect. Increased free hormone causes decreased T.S.H. secretion and decreased free hormone causes increased T.S.H. secretion (Tilkian and Conover 1975).

Normal T3 and T4 blood serum levels have been documented in the literature (Walfish 1976). The normal T3 range (in ng/dl.--nanograms/100 ml.) in euthyroid older people varies from 60-350 ng/dl. The range most frequently reported by laboratories is approximately 80-220 ng/dl., with a mean value of 115.2 ± 5.4 ng/dl. in the 60-79 age group and 92.2 ± 6.9 ng/dl. in the 80-93 age group (Rubenstein, Butler and Werner 1973). A normal range for T4 blood serum levels in older people is 7.6 ± 1.3 μ g/dl. (micrograms/100 ml.) for ages 60-79 and 6.6 ± 2.1 for ages 80-93 years. Normal serum T3 and T4 concentrations by age groups can be seen in Table 1.

Table 1. Normal Serum T3 and T4 Concentrations by Age Group

Age Group	Total T3 Mean ng/dl.	Total T4 Mean μ g/dl.
60-79	115.2 ± 5.4	7.6 ± 1.3
80-93	92.2 ± 6.9	6.6 ± 2.1

A lack of thyroid hormone can produce signs of modified hypothyroidism in older people. Personality changes, mental apathy and drowsiness seen in hypothyroidism is similar to the cognitive changes in chronic organic brain syndrome.

Low blood serum levels of T3 are common in debilitating diseases (Burrows et al. 1975). This writer found no other support in the literature for the further development of the conceptual framework, relating the concepts of decreased thyroid hormone levels and chronic organic brain syndrome.

Definitions

Chronic Organic Brain Syndrome: a degenerative disease of the brain associated with cerebral atrophy for which no cause can be established. It consists of a characteristic symptomology including impairments of orientation, memory, intellectual judgment as well as emotional lability or shallowness. It may be accompanied by disorders of affect and behavior (Miller 1974).

Triiodothyronine (T3): The thyroid hormone that contains three iodine atoms and is considered to be the most important thyroid hormone. It has approximately five times the biological activity of thyroxine (T4) (Miller and Keane 1972). T3 has a more rapid metabolic action and utilization than thyroxine.

Thyroxine (T4): A hormone of the thyroid gland that contains four iodine atoms and is a derivative of the amino acid tyrosine. It is formed and stored in the thyroid follicles as thyroglobulin. T4 is

released from the gland by the action of a proteolytic enzyme. T4 maintains the body's metabolism in a steady state. It is thought that some peripheral conversion of T4 to T3 occurs at the cellular level. The potency of T3 has led some investigators to speculate that T4 is really only a precursor of T3 (Rosenburg 1977). Together T3 and T4 act as a chemical agent or catalyst, stimulating specific organs, tissues and cells (Miller and Keane 1972).

Hypotheses

- H_{01} = There is no relationship between decreased T3 blood serum levels and chronic organic brain syndrome in older people.
- H_{02} = There is no relationship between decreased T4 blood serum levels and chronic organic brain syndrome in older people.

Significance level: $p = .05$.

CHAPTER 2

SELECTED REVIEW OF THE LITERATURE

This chapter contains a selected review of the literature of organic brain changes in old age and changes in endocrine functioning, especially of thyroid hormones in old age. In particular, a search was made for a "linking pin" between chronic organic brain syndrome and thyroid hormones. There is a dearth of literature related to this problem.

There is no question that the brains of older people, particularly those with significant cognitive impairment, undergo many changes which have been reviewed and discussed in recent articles (Torack 1971; Malamud 1972; Berry 1975; Kent 1977). Two common types of degenerative changes have been identified. One of the changes is characterized by neuronal loss, senile plaques, neurofibrillary tangles and granulo-vacuolar degeneration and is considered the manifestation of cellular degeneration. The cause of this degeneration is unknown. The other type of degenerative change is characterized by focal cerebral softening or multiple lacunar infarcts, in addition to the loss of neurons. Although chronic organic brain syndrome reflects a loss of functional cells in the whole cerebral cortex, often the greatest loss is in the hippocamal areas of the temporal lobes, which appear to play an

important part in the registration and storing of information as well as in recognition and recall (Goldfarb 1976).

With the generalized cortical cell loss there is gross atrophy measurable by loss in brain weight at autopsy. As cells and fibers disappear, they are replaced by cerebrospinal fluid; the ventricles become enlarged; the sulci widen and deepen as determinable by pneumoencephalography and angiography. Early in the process, little change may be seen in the brain or in behavior. As cell loss becomes more marked, the older person begins to have difficulties in his everyday functioning which usually gives rise to personal, family and community problems (Goldfarb 1976).

From the clinical and conceptual points of view, one important issue regarding chronic organic brain syndrome is the relationship between brain changes and cognitive decline. In the majority of older people with significant cognitive impairment, the brain changes are diffuse and of the degenerative type (see Appendix A). The cognitive changes associated with chronic organic brain syndrome are similar to the changes seen in patients with low thyroid hormone blood levels. In both chronic organic brain syndrome and hypothyroidism an impoverishment of ideas, impaired ability for abstractness and a decline of recent memory can be observed. In social situations, there may be inappropriate affect with progressive withdrawal from social contacts. People with chronic organic brain syndrome or hypothyroidism may experience emotional lability and impaired orientation.

An awareness of the influence of clinical conditions such as hypothyroidism that affect binding of thyroid hormone to plasma proteins is required in the interpretation of moderately increased or decreased thyroid hormone levels. Triiodothyronine (T3) is considered to be the major thyroid hormone at the tissue level. In contrast to thyroxine (T4) which is for the most part an extracellular hormone, T3 is largely intracellular in distribution (Cavalieri et al. 1976).

With the recent development of radioimmunoassay techniques for the measurement of T3 concentration, concepts have arisen regarding the biologic role of T3 in health and disease and its interrelationships with T4. When T4 serum values are in the hypothyroid range, measurement of serum T3 as well as serum thyrotropin (thyroid-stimulating hormone) concentrations can lead to recognition of abnormalities in thyroid gland biosynthesis. Before a diagnosis of hypothyroidism is made on the basis of a low serum T3 value, a variety of clinical non-thyroid conditions must be excluded. These non-thyroid conditions result in changes in plasma T3 protein binding or impaired peripheral conversion of T4 to metabolically active T3 without producing a hypometabolic state (Walfish 1976).

A knowledge of the differences in clinical laboratory values for the thyroid hormones is useful in establishing normal limits for an aging population. It is important to determine whether the changes observed are compensatory accompaniments of the normal aging process or whether though common, they reflect pathological processes that either result from or contribute to age-related disease (Ingbar 1976).

The literature indicates that evidence of pathological dysfunction of the thyroid gland in older people is sparse and subtle (Pittman 1962).

Diminished serum T3 concentrations with advancing age have recently been reported (Rubenstein et al. 1973; Herrmann et al. 1974). Rubenstein et al. (1973) found a progressive decrease in serum T3 concentrations in aging, using a radioimmunoassay method following extraction of serum. The 64 older people were ambulatory and free of obvious debilitating disease. Rubenstein et al.'s data (1973) from 127 healthy euthyroid subjects revealed a straight line decrease in serum T3 concentration of $-0.51 \text{ ng/dl./year}$ of age from ages 5-93 years, with no difference between the sexes. However, a few healthy, older people could be obtained for study. In the series, T4 values did not decrease and were comparable in the young and old groups. The investigations suggested that the progressive decrease in serum T3 concentration observed from childhood on, may have represented a progressive change in the relative thyroid output of T3 and T4. This was perhaps associated with the histological atrophy and fibrosis of the thyroid gland known to occur in older people. A decrease in the extent of the peripheral monodeiodination of T4 to T3 or an increased rate of utilization of T3 relative to T4 may also have been implicated.

Normal T3 blood serum levels have been defined as $115.2 \pm 5.4 \text{ ng/dl.}$ for the 60-79 year age group and as $92.2 \pm 6.9 \text{ ng/dl.}$ for ages 80-93. No sex differences were seen in euthyroid subjects. However, where abnormal levels were seen to exist, sex differences with

increasing age occurred. Normal values were obtained from patients 60-93 years of age on no drug regimen (Rubenstein et al. 1973).

In several clinical situations a low serum T3 value was associated with either a normal or a high serum T4 value in older patients who were apparently clinically euthyroid (Walfish 1976). This occurred particularly in a variety of non-thyroidal illnesses (Bermudez, Surks and Oppenheimer 1975) including hepatic and renal failure, cachexia, malignant disease, chronic fasting by obese people, protein-calorie malnutrition (Lytle 1977), as well as with senescence (Rubenstein et al. 1973). In hepatic cirrhosis, T3 values ranged from 15-65 ng/dl., with a mean of 33 ± 3 ng/dl. T4 values ranged from 3.7-11.5, with a mean of 7.5 ± 0.4 μ g/dl. in people 65-75 years (Chopra et al. 1974). In these situations, the decrease in serum T3 values is out of proportion to that of T4 values and cannot be accounted for on the basis of reduced plasma protein binding alone (Bermudez et al. 1975). Preliminary observations suggested that they may be accounted for on the basis of impaired peripheral conversion by monodeiodination of T4 to T3 (Walfish 1976).

In a study to assess the effect of T3 on the senile, T3 or a placebo was administered in a double blind manner to 100 elderly psychotic patients who had been admitted to a psychiatric hospital and who had a diagnosis of chronic organic brain syndrome. Some improvement was noted in the treatment group, however, these improvements were statistically insignificant. This group had significantly

lower protein-bound iodine test results than those who did not improve (Darvill 1960).

Contrary to the evidence cited, only one study by Bahemuka and Hodkinson (1975) found no increase in prevalence of chronic organic brain syndrome or intellectual impairment in older people with decreased thyroid hormone blood serum levels, as assessed by a simple orientation and memory test. In no case did chronic organic brain syndrome improve with treatment of hypothyroidism, whereas patients with other psychoses improved or recovered in each instance.

CHAPTER 3

RESEARCH DESIGN

This study was concerned with the relationship between decreased T3 and T4 blood serum levels and chronic organic brain syndrome in older people. A retrospective, descriptive design was used. Through a search of patient records, information concerning the variables was obtained. Description of the study setting, sample population, protection of human rights and data collection are presented in this chapter.

Description of the Study Setting

A short-term acute-care psychogeriatric unit of a psychiatric hospital in a Canadian city was selected for the study. The unit has been open since 1976 and has as its primary goals teaching of students and staff and research. There are 15 beds for older people intermingled with 15 beds for patients 18-64 years of age. There is a common lounge, music room, television room and dining area. Separate ward programs have been specifically designed for the older people and for the younger people. For example, a reminiscing group, a film group and an exercise group were set up for the older patients. In order to be admitted to the unit, a pre-admission assessment is done by two registered nurses to see if the individual would be appropriate

for the type of care offered by the health team. All health disciplines are involved in patient care.

Description of the Sample Population

The sample population consisted of all patients who were admitted to the psychogeriatric unit between January 1, 1977 and December 31, 1977. All patients admitted to the study met the following criteria:

1. were 65 years of age and older
2. had a diagnosis of chronic organic brain syndrome
3. were euthyroid
4. had no present history of hepatic or renal failure, cachexia, malignant disease, chronic fasting or protein-calorie malnutrition.

Human Rights

The human rights of the subjects involved in the study were protected according to the guidelines of The University of Arizona and the participating institution. These rights included the rights of confidentiality and protection against risks. Subjects were not asked for their consent. Consent to use selected patient records was given by the Chief Psychiatrist of the psychogeriatric unit (see Appendices C and D).

Data Collection

This study was discussed with the Chief Psychiatrist of the psychogeriatric unit in October 1977 before the project was undertaken. Pending approval from the Medical Advisory Committee of the institution, he indicated a willingness to supply a list of patients with a diagnosis of chronic organic brain syndrome, so a review of their patient records could be made (see Appendix B).

During the months of December 1977 and January 1978, the investigator discovered that the data collection methodology would have to be altered due to the enforcement of a provincial law effective in 1977 to protect the human rights of subjects. It was an infringement of the Canadian Public Hospitals Act of 1977 for a person not a student or staff member within the designated institution to have access to patient records for research purposes. In order to adhere to this Act, the chairman of the Medical Advisory Committee agreed that another registered nurse employed by the institution could obtain permission from the Chief Psychiatrist of the psychogeriatric unit to requisition the required patient records. This nurse supplied answers in response to questions asked by the investigator. The confidentiality of the subject's data was protected since the investigator did not know from which patient record the information was obtained. Questions were asked concerning the age and sex of the patient and T3 and T4 blood serum levels obtained during hospitalization. The investigator was not allowed to ask questions about the symptomology displayed by the

subjects. A copy of the data collection questionnaire can be found in Appendix E.

The investigator was unable to collect T3 blood serum values because these values were not measured, as the institution had indicated. Instead, T3 resin uptake values were collected. The implications of these results will be discussed under data analysis. T4 blood serum values were obtained.

Measurement of T3 and T4

The resin uptake of radioactive T3 indirectly estimates the saturation of binding proteins by thyroid hormone. With this technique, radioactive T3 is added to a system containing patient serum and a resin which serves as an alternative substance to bind any T3 that is not bound by the proteins of the serum. The greater the saturation of serum binding sites by the patient's thyroid hormone, the fewer sites there will be to bind the added radioactive T3, thus, the greater the resin uptake. The results obtained are independent of serum iodide content. The test is technically simple and inexpensive as compared to T3 serum concentrations which are a direct measurement of T3. If serum protein binding sites are quantitatively increased as with patients receiving estrogens, more radioactive T3 will be bound to these serum proteins and the resin uptake will be reduced, even in "normal" patients. The reverse is true for those receiving androgens. Day to day variations may occur and it is essential to run a control with each batch of test sera (Hamburger and Meier 1971).

T4 blood serum levels are determined at the designated institution by a standardized radioimmunoassay method proven valid and reliable (Murphy and Pattee 1964; Chopra, Ho and Lam 1972; Liebllich and Utiger 1972; Nicoloff et al. 1972; Rubenstein et al. 1973; Walfish 1976). This T4 radioimmunoassay procedure uses a specific antibody to T4 made by injecting rabbits with a T4 albumin conjugate. Direct measurement of T4 in unextracted serum is facilitated by the addition of chemicals that saturate thyroxine-binding globulin binding sites (Walfish 1976). Normal values are standardized for the facility, depending on the specificity of the antisera for T4, purity of the reference hormone used for the standard curve and geographical difference in iodine intake (Walfish 1976).

CHAPTER 4

DATA ANALYSIS

In this chapter, the findings of the study are presented and analyzed.

A record review of ambulatory patients 65 years of age and older was made and a total of ten patient records were identified that met the criteria for the study. All patients were diagnosed with chronic organic brain syndrome. The sample included ten men and women who were patients in a Canadian hospital between January 1, 1977 and December 31, 1977. The five females ranged in age from 66 to 85 years of age with a mean age of 76.2 years. The five males ranged in age from 67 to 84 years of age, with a mean of 73.4 years. Table 2 shows the age range of the subjects in the study was 66 to 85 years of age with a mean age of 74.8 years.

Table 2. Distribution of Subjects by Age and Sex

Sex	Age		mean age in years
	65-75	76-85	
Male	3	2	73.4
Female	2	3	76.2
Total	5	5	74.8

A psychiatrist at the hospital had reported to the investigator in October 1977 before the study was commenced that T3 and T4 blood serum levels were analyzed in their laboratory. When the investigator began data collection in January 1978, it was discovered that T3 blood serum levels were not measured but instead, T3 resin uptake values were measured. T3 blood serum levels would have provided a direct measurement of the thyroid hormone and its functioning. T3 resin uptake does not measure serum T3 levels. T3 resin uptake is an indirect measure of thyroid function based on the available protein binding sites in a serum sample which can bind to radioactive T3. Values are reported as a percent. Most literature reports 25 to 35 percent as being a normal range (Walfish 1976; Tilkian and Conover 1975; French 1975). The hospital laboratory reported a normal range of 35.5 to 58 percent. Neither these values nor the T4 blood serum levels reported by the laboratory had adjusted normal ranges for an aging population. The normal T4 blood serum levels, as reported by the hospital were 4.5 to 10.7 $\mu\text{g}/\text{dl}$.

The data that this study proposed to collect will be analyzed first, followed by the data that were also collected. The T4 blood serum levels that were obtained on admission to the hospital ranged from 5.0 to 9.7 $\mu\text{g}/\text{dl}$. with a mean value of 7.39. These values fell within the normal range. Second-drawn T4 blood serum levels that were drawn at an unspecified interval within three months following admission, varied from 4.9 to 9.1 $\mu\text{g}/\text{dl}$. with a mean of 6.6. The T4 blood serum levels for all patients are seen in Table 3. All T4 blood serum

Table 3. T4 Blood Serum Levels for Ten Subjects

Subject	Sex	Age	T4 Blood Serum Level on Admission (µg/dl.)	Second T4 Blood Serum Level Taken within 3 Months of Admission (µg/dl.)
A	F	66	5.0	4.9
B	F	69	7.1	6.0
C	F	85	6.1	5.5
D	F	82	6.4	5.8
E	F	79	7.9	8.5
F	M	69	6.7	7.8
G	M	70	9.1	9.1
H	M	67	9.7	7.1
I	M	77	8.8	5.3
J	M	84	7.1	6.3

levels fell within the normal range reported by the laboratory and as reported in the literature (Walfish 1976). Although no T4 blood serum levels deviated from within the normal range, different values between sexes were noted. The values for females were consistently lower. In Table 4 age differences can be seen between the 60 to 79 year old group and the 80 to 84 year old group.

Table 1 (see Chapter 1, p. 10) recorded mean values of 7.6 ± 1.3 µg/dl. and 6.6 ± 2.1 µg/dl. for these two groups respectively.

Table 4. T4 Blood Serum Levels by Age

Age	Mean T4 Blood Serum Levels
60-79	7.3 µg/dl.
80-84	6.2 µg/dl.

The data from this study produced similar results--with mean values of 7.3 µg/dl. for the 60 to 79 years of age group reported and for the 80 to 84 years of age group a mean value of 6.2 µg/dl. was found (see Table 4).

A significance level of .05 was established before data collection commenced. The Pearson Product-Moment Correlation Coefficient was used. A significant relationship was observed between first and second-drawn T4 blood serum levels as hypothesized. These values were significant at the .05 level. A scattergram of these values is shown in Figure 2. As time went on, the T4 blood serum levels tended to decrease.

On admission, T3 resin uptake values ranged from 41 to 60 percent with a mean value of 49.6 percent. All values were considered normal. Second-drawn T3 resin uptake values ranged from 35 to 61 percent. The reported mean was 49.9 percent. These values were normal.

Table 5 reports T3 resin uptake values for all subjects. No relationship was found between the first and second-drawn T3 resin uptake values. Some values increased over the interval of time between the first and second-drawn T3 resin uptakes, while other values decreased.

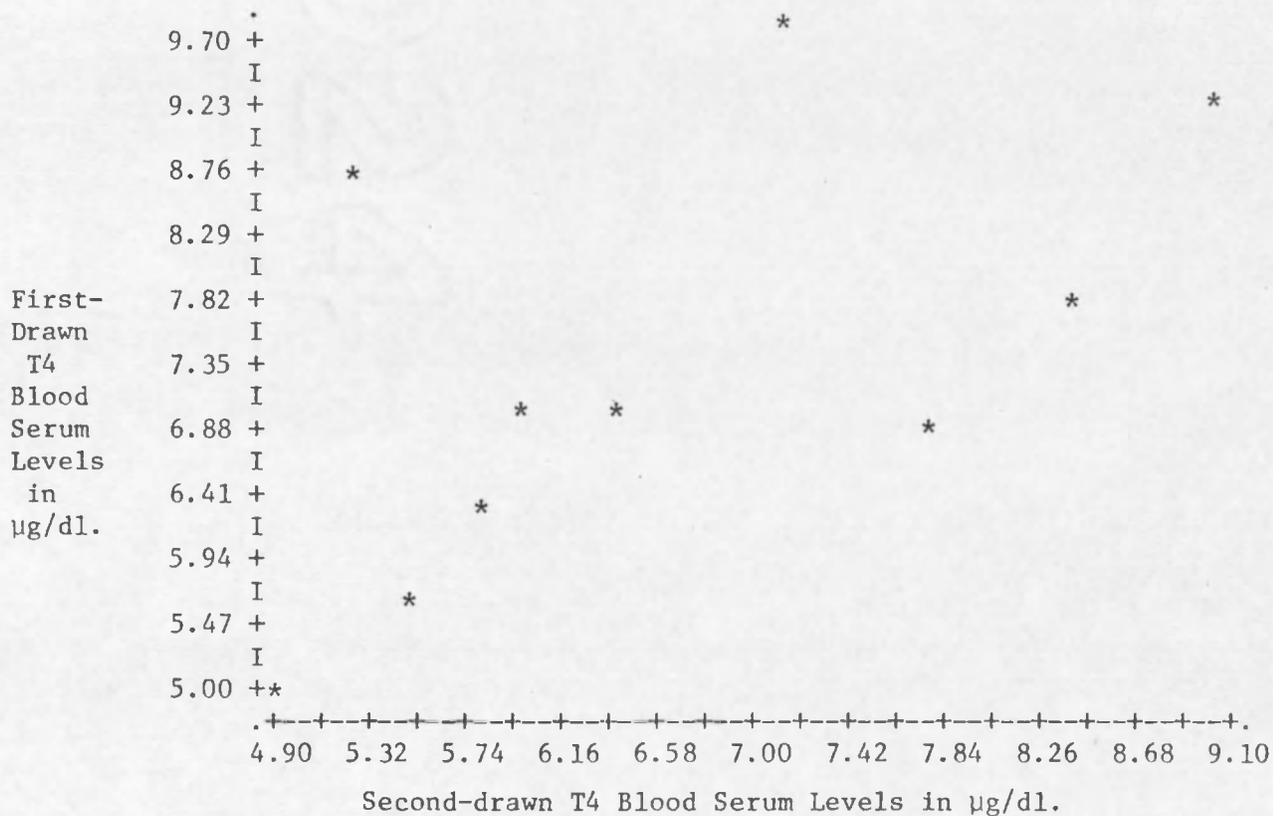


Figure 2. Scattergram of First and Second-drawn T4 Blood Serum Levels

Table 5. T3 Resin Uptake Values for Ten Subjects

Subject	Sex	Age	T3 Resin Uptake (%) on Admission	Second T3 Resin Uptake (%) Taken within 3 Months of Admission
A	F	66	43	60
B	F	69	45	45
C	F	85	53	61
D	F	82	47	50
E	F	79	56	47
F	M	69	41	35
G	M	60	46	47
H	M	67	60	44
I	M	77	59	58
J	M	84	46	52

In two other areas not related to the present study, significant values were obtained. A positive correlation was found between the first-drawn T3 resin uptake values and the first-drawn T4 blood serum levels. This relationship was significant at the .026 level. A negative correlation was seen between the second-drawn T3 resin uptake values and the second-drawn T4 blood serum levels indicating over the time interval between the first and second-drawn blood samples, the second-drawn T3 resin uptake values tended to increase and the T4

blood serum levels tended to decrease. These values were significant at the .015 level. These values appeared to vary together.

Looking at the four values together, T3 resin uptake values tended to remain the same over time while during that same time, T4 blood serum levels tended to fall. This is of academic interest only as a noted trend. These relationships were not specifically addressed in this study. In a study by Frolkis and Valueva (1978) these same variables were discussed. Studies of T4 ¹³¹I distribution in rats of different ages revealed significant differences in the T4 ¹³¹I uptake by tissue of old animals. Following an intravenous hormone administration, its level in almost all studied tissue was found to be statistically lower in 28 to 32-month old rats as compared with that of 10 to 12-month old rats (Frolkis and Valueva 1978). The data obtained showed that with age there occurred significant changes not only in the structure and function of the thyroid gland and transport forms of T3 and T4 in blood, but also in the peripheral metabolism of thyroid hormones. The study revealed changes in the peripheral metabolism of thyroid hormones during aging. There was an increase of sensitivity of old tissues to thyroid hormones and a decrease of their reaction capacity to the T4 effects (Frolkis and Valueva 1978). In the Frolkis and Valueva study (1978) it was concluded that during aging the irregular changes occur in various links of the thyroid regulation of metabolism and function. The functional activity of the thyroid as well as blood T3 and tissue T4 contents decrease with age. At the same time, there developed significant changes in extrathyroidal

metabolism of thyroid hormones, which can be considered as adaptive mechanisms. The most marked changes in the Frolkis and Valueva study (1978) were reduced thyroxine-binding capacity of blood proteins which conditioned the invariability of physiologically active free T4 in blood; and enhanced T4 deiodination in tissues resulting in an invariable tissue content of biologically more active T3 hormone. A change was observed in the production of iodoproteins which probably possessed a certain hormonal activity and a lower rate of fractional release from cells (Frolkis and Valueva 1978). In contrast to the evidence reported earlier citing the importance of T3 in health and disease (Walfish 1976), the Frolkis and Valueva study (1978) emphasized the important changes in T4 blood serum concentrations that clinicians may be overlooking.

Similar data have also been described by Rogowski et al. (1977). Their study was designed to assess the clinical value of serial determinations of serum T3, T4 and thyroid-stimulating hormone (T.S.H.) in the early phase of medical antithyroid treatment. In this study (Rogowski et al. 1977), in all the patients in whom serum T4 values became low in the early phase, T3 values were normal.

The Student's t-test was used to examine the significance of the differences between the means in the two sexes. A significant .048 relationship between the first-drawn T4 blood serum levels and male and female was seen. Reported means for first-drawn T4 blood serum levels for males was 8.2 µg/dl. and for females, this value was 6.5 µg/dl. A study by Jefferys et al. (1972) indicated the mean T3

uptake for men was significantly lower than for females ($p < 0.001$). This present study did not confirm this earlier finding.

The T3 resin uptake values and the T4 blood serum levels could be combined to give a figure called the Free Thyroxine Index. It is obtained by multiplying the T4 and T3 uptake values. The Free Thyroxine Index generally provides a good assessment of thyroid function (Raphael 1976).

In spite of increasing recognition of the physiologic role of T3 in health and disease, in most clinical situations the directions of the changes in both serum T3 and T4 values is the same. Thus, the measurement of total circulating serum T4 concentration, accompanied by an indirect assessment of plasma protein-binding by a T3 resin uptake test, will continue to be the mainstays in the laboratory assessment. However, radioimmunoassay of total T3 blood serum concentrations appear to be indicated in certain clinical situations. It would seem that measurement of serum T3 blood levels appear to be indicated since T3 resin uptake values were normal (Walfish 1976). By measuring T3 blood serum concentrations at the same time as T4 blood serum levels, the T4/T3 ratio could also be figured. T3 is less abundant in the human thyroid gland than T4. Knowledge of the precise thyroïdal T4/T3 ratio would be pertinent to the estimation of thyroïdal contribution of T3 to the extra-thyroïdal pool of T3.

CHAPTER 5

CONCLUSION

This chapter includes interpretation of findings, recommendations for future study and implications for nursing.

The hypothesis that there was no relationship between decreased T3 blood serum levels and chronic organic brain syndrome in older people was accepted for lack of statistical significance in this study. The second hypothesis that there was no relationship between decreased T4 blood serum levels and chronic organic brain syndrome was also accepted for the same reason. It was impossible to analyze T3 blood serum levels because these values were not recorded by the hospital laboratory. Instead, T3 resin uptake values and T4 blood serum levels were analyzed. A positive correlation was seen between the first-drawn T3 resin uptake values and the first-drawn T4 blood serum levels significant at the .026 level. A negative correlation between second-drawn T3 resin uptake values and second-drawn T4 blood serum levels was found significant at the .015 level.

Significant relationships were found between first and second-drawn T4 blood serum levels; and first-drawn T4 blood serum levels and sex. These relationships are only applicable to the study population and are no way indicative of the general trends seen in patients diagnosed with chronic organic brain syndrome.

Repetition of this study would demand an increased sample size with blood values collected and analyzed by a single investigator over a longer period of time, of perhaps six months to one year. It is recommended that T3 serum concentrations rather than T3 resin uptake values be collected and analyzed. Investigation of T3 blood serum levels as originally proposed in this study, may be a better indicator. In the literature related to thyroid hormone research, references implicated the increasing importance of T3 blood serum levels as opposed to T3 resin uptake values (Walfish 1976). T3 blood serum levels would provide a direct measurement of the thyroid hormone and the results could be used with greater precision and accuracy in diagnostic tests (Rubenstein et al. 1973; Walfish 1976). Documentation of the clinical symptomology displayed by each patient is also suggested. A clinical assessment tool for the standardization of symptoms needs to be developed. Such a tool would ensure reliable comparison of symptomology between individuals over a long period of time. This tool could be developed by nurses.

It is obvious that no single procedure can provide complete information regarding the status of the brain in older people. To evaluate even a limited aspect of the brain, more than one use of a particular procedure is necessary. Because of the considerable variation found among individuals with much the same condition, the change observed in a variable over a period of time, is much more informative than a single reading (Wang 1969).

Based on T3 and T4 laboratory results, nurses should be able to make more effective nursing diagnoses and interventions early in the course of chronic organic brain syndrome to provide appropriate and creative intervention and therapy for patients experiencing progressive decrease in mental functioning. Clinicians and nurses need to thoroughly assess patients who present symptomology of chronic organic brain syndrome. Misdiagnosis or labelling a patient with chronic organic brain syndrome who presents symptoms of a condition which is reversible may be prevented with complete assessments. When a complete evaluation of an older person with slight, moderate or marked brain disorder uncovers any causative or contributing factor that is amenable to treatment, everything possible should be done to eliminate or at least alleviate the underlying problem. When the brain disorder is due to factors that cannot be controlled, such as chronic organic brain syndrome, the therapeutic effort should be directed toward preventing further insults to the impaired brain and alleviating environmental and intrapsychic stresses that may be contributing to the older person's problem (Wang 1969).

The state of thyroid hormone economy in the older person and its relationship to the whole phenomena of aging must continue to be researched with intensity and accuracy.

CHAPTER 6

SUMMARY

The purpose of this study was to provide information about the relationship of triiodothyronine (T3) and thyroxine (T4) blood serum levels and chronic organic brain syndrome in older people. The patient records of ten people older than 65 years of age were studied at a Canadian hospital. All patients had been diagnosed with chronic organic brain syndrome. The hospital laboratory did not measure T3 blood serum levels as the investigator had believed but rather, T3 resin uptake values and T4 blood serum levels were recorded and analyzed. Frequency distribution of the data was analyzed by computer. From the data gathered, two relationships were shown to be significant. These relationships were between first and second-drawn T4 blood serum levels and first-drawn T4 blood serum levels and sex. A positive correlation was seen between first-drawn T3 resin uptake values and first-drawn T4 blood serum levels. A negative correlation was seen between second-drawn T3 resin uptake values and second-drawn T4 blood serum levels. These correlations were not expected to be found. Both sets of values showing slight correlations appeared to vary together. As T3 resin uptake values tended to remain the same over time, T4 blood serum levels tended to fall during that same time.

No other significant relationships were found. No firm inferences could be drawn from the data discussed. At present, the data stands as isolated findings whose relationship to other age-associated changes in thyroid hormone economy is unclear.

Repetition of this investigation is needed using a larger sample size and measuring directly T3 and T4 blood serum levels.

APPENDIX A

PRODROMAL CHARACTERISTICS OF CHRONIC BRAIN SYNDROME*

Early Characteristics

Cognitive

"Intellectual" decline
Reduced tempo of stream
of thought

Impoverishment of ideas
Concreteness: impaired
abstraction

Decline of recent memory
Registration, retention,
recall, organization
Difficulty in maintaining
attention and set

Behavioral and affective
Reduced attentiveness
Reduced responsiveness
Decreased interpersonal
interaction
Less direct, immediate
affective expression
Liability to "disintegration"
during stress

Later characteristics

Emotional lability
Impaired orientation
Impaired judgment

Potential Signs and Symptoms

Increasingly impaired compre-
hension

Increasing memory loss

Confabulation

Irrelevance

Progressive withdrawal
Apathy

Pseudo-depression vs. depres-
sion

"Inappropriate" affect

Emotional incontinence
Confused

*From Butler and Lewis 1977: 76.

APPENDIX B

LETTER TO REQUEST PERMISSION FOR STUDY

Clark Institute of Psychiatry, 250 College Street, Toronto M5T 1R8

October 31, 1977.

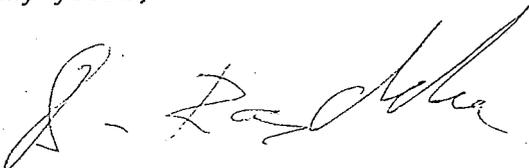
Miss Ann Brockenshire,
1402 N. Vine Avenue,
Tucson, Arizona. U.S.A.
85719

Dear Ann:

Thank you very much for your letter of October 15, 1977. In order to gain access to patients records you will need the permission of the institute. Perhaps if you could send me your proposal and a request to use the records addressed to the institute care of myself. I will submit your request to the Medical Advisory Committee.

The September meeting was very interesting and I think all members of our panel were quite satisfied with the experience. It would be nice to discuss these things with you. Looking forward to hear from you as soon as possible.

Truly yours,



L.B. Raschka, M.D., D. Psych., F.R.C.P. (C)
Chief of Service - 10th Floor.

LBR:imc

APPENDIX C

LETTER STIPULATING PROTOGOL FOR DATA COLLECTION

Clark Institute of Psychiatry, 250 College Street, Toronto M5T 1R8

February 22, 1978.

Miss Anne Brockenshire,
1402 N. Vine, #106,
Tucson, Arizona,
U.S.A. 85719

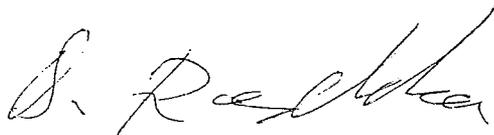
Dear Anne:

Thank you very much for your recent letter. The data given to you by Ingrid Stender was provided by me as a personal communication to you. It is not at all likely that our Medical Advisory Committee would give it's consent for data collection on the way originally planned.

For this reason we have to keep our transaction to what it originally was namely a personal communication from me to you. However since the data does not reveal the identity of the patient on any way quoting me and my position as a source of information is perfectly appropriate.

I hope this arrangement will be satisfactory.

Truly yours,



L.B. Raschka, M.D., D. Psych., F.R.C.P. (C)
Chief of Service - 10th Floor.

LBR:lmc

APPENDIX D

CONSENT FOR THE USE OF MEDICAL RECORDS--

MEDICAL ADVISORY COMMITTEE

I agree to grant access to medical records for the purpose of data collection in the study entitled, "Relationship of Triiodothyronine and Thyroxine Blood Serum Levels and Chronic Organic Brain Syndrome in Older People."

The purpose of the study is to do a record review to determine if a relationship exists between decreased triiodothyronine and thyroxine blood serum levels and chronic organic brain syndrome in older people hospitalized on a specialized psychogeriatric unit between January 1, 1977 and December 31, 1977.

I understand that specific data will be extracted from the records. This data includes sex, age, diagnosis, triiodothyronine and thyroxine blood serum levels and symptomology of chronic organic brain syndrome as noted in the patients' charts. Data will be analyzed by computer for analyses of variances, means, standard deviations and correlations of triiodothyronine and thyroxine blood serum levels, age and symptomology.

No patient identifying marks will be included. The strictest confidentiality of the data will be maintained by the use of code numbers to record data.

I understand there will be no physical or mental risks to patients. There are no benefits to the patients whose medical records are used and there will be no costs incurred to the patients.

I agree to the above consent for the use of medical records. The purpose and procedure have been explained to me. I understand that the Medical Advisory Committee may ask questions regarding the research investigation at any time. I understand that the institution is not expected to assume any cost incurred during data collection or

analysis. I understand that the results of the study will be made available to me at the completion of the research.

Signature, Chairman, Medical Advisory Committee

Date

Researcher's Signature

Date

* * *

It is an infringement of the Public Hospital's Act for a person who is not a student or staff member within the designated institution to have access to medical records for research purposes. In light of these circumstances, another registered nurse employed by the institution must requisition the required medical records and be the only one involved in the project to have access to the information requested. Under the supervision of Dr. Raschka, the registered nurse will supply answers in response to questions asked by the researcher, Anne Brockenshire, R.N. Under no circumstances will the researcher have access to the medical records. The confidentiality of the subject's data is protected since the researcher has no way of knowing from whose medical record the information was obtained.

Following the completion of data collection, the data collection sheet is to be approved by Dr. Raschka.

* * *

Statement by the Doctor

Ingrid Stender, R.N., staff nurse at the Clarke Institute of Psychiatry, Toronto, Ontario, Canada, has permission to requisition twenty medical records of patients 65 years and older with a diagnosis of chronic organic brain syndrome, for the purpose of obtaining information for the study entitled, "Relationship of Triiodothyronine and Thyroxine in Blood Serum Levels and Chronic Organic Brain Syndrome in Older People" conducted by Anne Brockenshire, R.N., Graduate Student, University of Arizona. In response to questions asked by Anne Brockenshire, concerning age and sex of the patient and triiodothyronine and

thyroxine blood serum levels, Ingrid Stender has permission to answer these questions.

No patients identifying marks will be included. The strictest confidentiality of the data will be maintained by the use of code numbers to record the data.

I understand there will be no physical or mental risks to patients. There are no benefits to the patients whose medical records are used and there will be no cost incurred to the patients.

I agree to the above consent for the use of medical records, under my supervision. The purpose and procedure have been explained to me. I understand that the institution is not expected to assume any cost incurred during data collection or analysis. I understand that the results of the study will be made available to me at the completion of the research.

Signature, Dr. Raschka

Date

Researcher's Signature
Anne Brockenshire

Date

APPENDIX E

DATA COLLECTION TOOL

Sex 0 = M 1 = F

Diagnosis Chronic Organic Brain Syndrome

Symptomology 0 = Judgment
 1 = Affect
 2 = Memory
 3 = Confusion
 4 = Orientation

Subject Number _____

Sex _____

Age _____

Triiodothyronine Values _____

Thyroxine Values _____

Symptoms Noted in the Medical Records _____

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