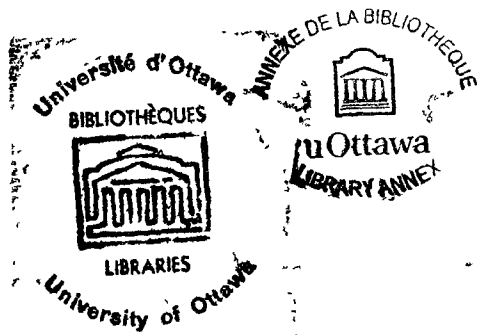


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LONG-TERM EFFECTS OF HEMODIALYSIS ON PSYCHOLOGICAL
FUNCTIONING IN CHRONIC RENAL FAILURE

by Arthur Leonoff

Thesis presented to the Faculty of
Psychology of the University of
Ottawa as partial fulfillment of
the requirements for the degree of
Master of Arts



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CURRICULUM STUDIORUM

Arthur Leonoff was born April 26, 1947, in Winnipeg, Manitoba. He received the Bachelor of Arts degree from the University of Manitoba, in 1968.

TABLE OF CONTENTS

Chapter	page
INTRODUCTION.	vi
I.- REVIEW OF THE LITERATURE.	1
1. Uremic Symptomatology	3
2. Uremic Neuropathology	5
3. Psychological Studies of Uremia and Hemodialysis	17
4. Summary and Conclusions	27
II.- THE PRELIMINARY STUDY	30
1. Rationale and Test Selection	30
2. The Sample and Experimental Procedure	34
3. Presentation of Results	35
4. Interpretation of Results	42
5. Hypotheses	45
III.- EXPERIMENTAL DESIGN	46
1. The Tools of the Experiment	46
2. The Sample	48
3. The Method of the Experiment	48
4. Statistical Operations	50
IV.- EXPERIMENTAL RESULTS.	53
1. Presentation of Results	53
2. Interpretation of Results	72
SUMMARY AND CONCLUSIONS	87
BIBLIOGRAPHY.	90
 Appendix	
1. EXPERIMENTAL DATA BEFORE AGE CORRECTION AND TRANSFORMATION.	95
2. EXPERIMENTAL DATA AFTER AGE CORRECTION AND TRANSFORMATION.	97
3. ABSTRACT OF <u>Long-Term Effects of Hemodialysis on Psychological Functioning in Chronic Renal Failure.</u>	99

LIST OF TABLES

Table	page
I.- Raw Scores Obtained on Preliminary Battery Described in Section on Rationale and Test Selection.	36
II.- <u>WAIS</u> Subtest Means Expressed in Scale Score Units	37
III.- Impairment Indices on Halstead and Reitan Measures.	38
IV.- Spearman Rank-Order Intercorrelations of <u>WAIS</u> , <u>Trail Making</u> , and Finger Tapping Measures	39
V.- Summary of Data Reported in Appendix 1 (Raw Scores)	54
VI.- Summary of Data Reported in Appendix 2.	55
VII.- Pearson Product-Moment Correlations Between Age and <u>Trail Making Test</u>	56
VIII.- Analysis of Variance of Premorbid Means: Information	57
IX.- Analysis of Variance of Premorbid Means: Education	58
X.- Pearson Product-Moment Correlations Between Information, Education, and Treatment Duration.	60
XI.- Pearson Product-Moment Correlations Between Education and Measures of Perceptual Motor Functioning	62
XII.- F-Ratios for Analysis of Variance and Analysis of Covariance	65
XIII.- A Posteriori Comparison of Means for Error Score: Scheffé's Procedure	67
XIV.- Pearson Product-Moment Correlations Between Measures of Perceptual Motor Functioning and Duration of Treatment	68
XV.- Eta, Pearson Product-Moment Correlations, and F-Ratios for Linearity of Regression	70

INTRODUCTION

The prospect of extending human existence by use of an artificial kidney is a part of present medical knowledge. Since 1961, patients at the end-stage of chronic renal failure have been maintained through long-term hemodialysis. Ten years of experience and innovation have increased the technical precision of this treatment. Currently, it is estimated that approximately nine hundred persons suitable for long-term hemodialysis arise each year in Canada. The state of this technology continues to develop and renal units are equipped or being equipped to handle the need.

From the perspective of physiological survival as a reality, a growing literature has endeavoured to examine the host of emotional and behavioural factors which affect the adjustment of the hemodialysis patient. In this regard, studies have explored the nature of the psychological stress in this prolonged illness, the patients' confrontation with imminent death, changes in life style, ego adaptations and emotional reactions, among other pertinent questions.

However, a survey of literature revealed a paucity of investigations on intellectual deficit in uremia although numerous authors refer to its presence. As well, there is an absence of information on the therapeutic effects of long-term hemodialysis on intellectual functions observed

to be impaired in chronic renal failure. It is the aim of this study to provide information on these two questions.

The first chapter of this thesis presents the review of literature. The order of presentation is given in the introduction to the chapter.

Chapter two describes the preliminary study which preceded the main experiment. First, the rationale underlying test selection is stated. This is followed by a presentation and interpretation of results. At the conclusion of this chapter, the hypotheses of the main investigation are presented.

The third chapter presents the experimental design employed in the study and discusses the tools, population, and statistical methods utilized in the analysis of the data.

Chapter four contains the experimental results and their interpretation. Suggestions for further research are presented in the conclusion of this final chapter.

CHAPTER I

REVIEW OF THE LITERATURE

The kidney is a fundamental organ in the human body. It functions as a control system which regulates the complex biochemical balance in the body's internal environment.¹ Where disease reduces the efficiency and mass of the kidney, renal functioning may reach an extent of deterioration in which adequate compensation is not possible. In this case, the end results of renal disturbance are profound alterations in the constitution of the internal environment. These are of fundamental biochemical importance and through the inter-relations of systems influence the total organism.² The biochemical and symptomatic condition which reflects this severe homeostatic imbalance is referred to in medical nomenclature as 'uremia.'³

Specifically, the uremic syndrome is defined as a complex of symptoms caused by renal insufficiency and the resulting retention of nitrogen waste products plus other

1 Stanley E. Bradley, "Biochemical Abnormalities During Renal Insufficiency," New England Journal of Medicine, Vol. 235, 1946, p. 755-761.

2 M.R. Wills, "Biochemical Consequences of Chronic Renal Failure," Journal of Clinical Pathology, Vol. 21, 1968, p. 551-554.

3 Steen Olsen, "The Brain in Uremia," Acta Psychiatrica et Neurologica Scandanavica, Supplementum 156, Vol. 36, 1961, 129 p.

changes in the composition of the blood, especially an alteration in the concentration of electrolytes.⁴ The blood's concentration of nitrogen metabolites is considered a stable diagnostic indicator of uremia and a general index of the severity of renal failure.⁵ The autointoxication of uremia affects many functioning systems and processes in the human body.⁶

Of specific interest in the present study is the effect of uremia on the nervous system.

It is reported that this system represents a major area of toxic injury and the origin of most of the common symptoms in the disease.⁷ This review will concentrate upon neurological and psychological literature reflecting the nature of uremic involvement in nervous system functioning and the mediating effects of hemodialysis treatment. The material is presented under the following headings: (1) uremic symptomatology; (2) uremic neuropathology;

⁴ Ibid., p. 7.

⁵ Asser Stenback and Erkki Happanen, "Azotemia and Psychosis," Acta Psychiatrica Scandinavica, Supplementum 167, Vol. 43, 1967, 65 p.

⁶ John P. Merrill and Constantine L. Hampers, "Uremia," New England Journal of Medicine, Vol. 282, 1970, p. 953-970 (I); p. 1014-1021 (II).

⁷ A.B. Baker and Julian Knutson, "Psychiatric Aspects of Uremia," American Journal of Psychiatry, Vol. 102, 1945, p. 683-687.

(3) psychological studies of uremia and hemodialysis; (4) summary and conclusions.

1. Uremic Symptomatology.

The symptomatology resulting from advanced kidney failure is numerous and varied. The first indications are usually those of neuropsychological and neuromuscular depression.⁸ The individual is often drowsy yet sleepless. Diminished attention span, poor memory, and a loss of interest in the environment are commonly noted as initial manifestations of central nervous system involvement in uremia.⁹ These more subtle psychological changes may develop into intermittent psychotic episodes which include states of delirium, catatonia, mania, depression and paranoia.^{10,11} Less often, and later in the illness, symptoms of psychic and neuromuscular hyperexcitability may occur,¹² and these often terminate in convulsions.

⁸ Olsen, op. cit., p. 12.

⁹ Laurence E. Earley, "Effects of Uremia on the Cardiovascular and Central Nervous System," Surgical Clinics of North America, Vol. 48, 1969, p. 371-379.

¹⁰ Baker and Knutson, op. cit., p. 685.

¹¹ S. Locke, J.P. Merrill and H.R. Tyler, "Neurological Complications of Acute Uremia," Archives of Internal Medicine, Vol. 108, 1961, p. 519-538.

¹² M.M. Cohen, "Cerebral Intoxication," in A.B. Baker (ed.), Clinical Neurology, Vol. 2, New York, 1955, p. 921.

Muscle wasting and tenderness accompanied by generalized muscular weakness are common to this syndrome.¹³ Myoclonic responses and asterixis have been reported.¹⁴ Non-specific changes in deep tendon reflexes are often noted and may vary from areflexia to hyperreflexia in the same individual.¹⁵ Abnormal muscular movements have been found to be most pronounced during states of agitation or confusion and correlate higher with the rate of alteration in blood chemistry than with the absolute levels of plasma constituents.¹⁶

Peripheral neuropathy is often associated with chronic renal failure.¹⁷ The neuropathy is usually symmetrical and initially involves the more distal portions of the peripheral nerves.¹⁸ The lower limbs are predominantly affected.¹⁹ The first symptoms are usually restlessness or painful burning of the feet oftentimes followed by numbness,

13 Earley, op. cit., p. 372.

14 Locke et al., op. cit., p. 522.

15 Earley, op. cit., p. 372.

16 Locke et al., op. cit., p. 522.

17 Heinrich A. Tenckhoff, Fred S.T. Boen, Robert H. Jebsen and John H. Spiegler, "Polyneuropathy in Chronic Renal Insufficiency," Journal of the American Medical Association, Vol. 192, 1965, p. 1121-1124.

18 Ibid., p. 1121.

19 Merrill and Hampers, op. cit., (I), p. 956.

parasthesias, and a perceptual disturbance of temperature, touch and vibration.²⁰ The neuropathy may later progress to motor fibres and result in muscle weakness, paralysis and muscle deterioration.²¹

2. Uremic Neuropathology.

This section presents literature on the central and peripheral nervous system impairment in uremia. From the literature, five areas of study have been noted: (a) anatomical changes, (b) electroencephalography, (c) cerebral metabolism, (d) biochemistry, and (e) peripheral nervous system.

The review is presented in regard to these areas of investigation.

A. Anatomical Changes

Olsen²² reviewed the modern literature on brain alterations in uremia. He notes²³ that earlier studies, before 1930, were hindered by primitive means of investigation and the inclusion of secondary effects due to

20 Phillipe Castan, "Les manifestations nerveuses de l'uremie chronique," La Presse Medicale, Vol. 75, 1967, p. 2443-2447.

21 Ibid., p. 2443.

22 Olsen, op. cit., p. 16-20.

23 Ibid., p. 16.

hypertensive vascular disease accompanying the uremic condition. With respect to nine relevant studies of uremic brains, results are highly varied with little tendency towards replication of findings. Diffuse and focal degeneration of cortical neurons, meningoencephalopathic changes, abnormal glial reactions, chromatolysis, demyelination, and cerebral edema are major pathologic changes noted. Involvement of brain stem structures is frequently observed. Softening and neuronal damage to the reticular formation, pons, and cerebellum is reported in most of the studies reviewed. Scattered circulation changes with areas of mild hemorrhaging are also noted.

Olsen²⁴ studied the histologic changes in the brain in patients who died from uremia. In all, 104 autopsies were performed. Almost all subjects revealed some form of neuronal degeneration although the locales of these changes were not constant. However, the areas most frequently affected were the afferent nuclei of the brain stem, reticular formation and the cerebral cortex. The cases of chronic uremia, thirty-three in number, showed the most of these pathologic changes. As well, Olsen²⁵ observed

²⁴ Ibid., p. 21-118.

²⁵ Ibid., p. 58.

necrosis of cells in the granular layer of the cerebellum in sixty per cent of the subjects.

Although Olsen was able to document some tendencies towards localization of effects, he adds:

[...] There are deviations from the pattern in many individual cases, and in the case of the deviations, it is not possible to demonstrate deviations in the clinical and symptomatic picture.²⁶

The individual differences may also have been intensified by the numerous underlying diseases and complications which dominated the anatomical material.²⁷

B. Electroencephalography

It has been frequently reported that the electroencephalogram²⁸ is often abnormal in renal failure. Consistently, studies have shown a generalized slowing, especially of the background alpha activity.^{29,30,31} This

26 Ibid., p. 117-118.

27 Ibid., p. 121.

28 M. Klinger, "EEG Observations in Uremia," Electroencephalography and Clinical Neurophysiology, Vol. 6, 1954, p. 519.

29 J. Cadilhac and M. Ribstein, "The EEG in Metabolic Disorders," World Neurology, Vol. 2, 1961, p. 296-308.

30 S. Lavy and A. Aviram, "EEG Changes in Uremic Patients Undergoing Regular Hemodialysis," Electroencephalography and Clinical Neurophysiology, Vol. 27, 1969, p. 217.

31 Locke et al., op. cit., p. 523.

activity is found to be in the 5 to 7 c.p.s. range either continually or intermittently.³² A number of studies have reported paroxysmal activity such as bursts of bilaterally synchronous slow waves or spike-waves.^{33,34} Exaggerated myoclonic responses to photic stimuli and marked photic driving have been observed in some uremic patients.^{35,36,37} Watson et al.³⁸ report involvement of scalp, facial, limb and trunk musculature in the myoclonic response, which was synchronous with the flicker frequency. Abnormal responses to rhythmic photic stimulation have been shown to correlate with seizures.³⁹

Klinger⁴⁰ noted that responses to single photic stimuli were exaggerated in some uremic patients. Hyman

32 J.C. Jacob, P. Gloor, O.H. Elwan, J.B. Dossetor, and U.R. Pateras, "Electroencephalogram Changes in Chronic Renal Failure," Neurology, Vol. 15, 1965, p. 419-429.

33 Cadilhac and Ribstein, op. cit., p. 308.

34 J. Mises, A. Lérique-Koechlin, and B. Ribot, "The Electroencephalogram During Renal Insufficiency," Electroencephalography and Clinical Neurophysiology, 1968, p. 91.

35 Jacob et al., op. cit., p. 422.

36 Locke et al., op. cit., p. 523.

37 C. Wesley Watson, E. Marcus, R. Bowker, and S. Davidson, "The Photomyoclonic Response as One Manifestation of Uremia: Observations of Uremic Man and Cat," Electroencephalography and Clinical Neurophysiology, Vol. 10, 1958, p. 364.

38 Ibid.

39 Jacob et al., op. cit., p. 427.

40 Klinger, op. cit., p. 519.

and Kooi⁴¹ found a prolongation of latencies of visually evoked cortical responses in seven uremic patients. Average latencies for the uremic subjects were significantly lower than a comparable group of normal subjects at five sequential points in the response ($p < .001$). A comparison of amplitudes between the two groups revealed no significant differences.

Attempts to correlate biochemical changes with EEG alterations^{42,43} or clinical symptoms^{44,45} have not proven successful.

C. Cerebral Metabolism

The reduced activity of the central nervous system, evidenced clinically and in EEG and histopathological studies,⁴⁶ has led to an investigation of cerebral metabolism in uremia.

Heyman et al.⁴⁷ observed cerebral blood flow and oxygen consumption in sixteen uremic subjects. A control

⁴¹ Paul R. Hyman and Kenneth A. Kooi, "Visually Evoked Cortical Responses in Renal Insufficiency," Medical Center Journal (University of Michigan), Vol. 35, 1969, p. 177-179.

⁴² Cadilhac and Ribstein, op. cit., p. 298.

⁴³ Locke et al., op. cit., p. 524.

⁴⁴ Klinger, op. cit., p. 519.

⁴⁵ Jacob et al., op. cit., p. 421.

⁴⁶ Supra, p. 3-9.

⁴⁷ Albert Heyman, John L. Patterson, Jr., and Rudolph W. Jones, Jr., "Cerebral Circulation and Metabolism in Uremia," Circulation, Vol. 3, 1951, p. 558-563.

group of sixteen patients, convalescing from a number of acute illnesses such as pneumonia, was observed for comparative purposes. The experimental group was further divided depending on the presence or absence of generalized vascular disease and hypertension.

The mean cerebral blood flow of uremic patients without vascular disease did not differ significantly from the control group and was within the normal range. In those uremic subjects with vascular disease, the mean cerebral blood flow was significantly less than the control group at the .01 level of probability.

In both uremic groups, the total body metabolism, as indicated by the basal metabolic rate, was within the expected normal range.

The rate of cerebral oxygen consumption was reduced in all but one of the uremic subjects and was significantly less than the control group mean value ($p < .01$). There was no significant difference in oxygen consumption between the two uremic groups.

Correlations of the level of residual nitrogen, carbon dioxide-capacity, sodium, potassium, and chloride ion concentrations in the blood plasma with cerebral oxygen consumption were low and insignificant.

No significant correlation was observed between cerebral oxygen consumption and the mental state of the

uremic subjects when classified as alert, confused, or stuporous on clinical observation.

Scheinberg⁴⁸ investigated the effects of uremia on cerebral oxygen and glucose consumption in seven uremic subjects. Results indicate a consistent depression in cerebral glucose and oxygen consumption although cerebral circulation was increased beyond normal values.

The reduction in cerebral metabolism was insignificantly correlated with the level of residual nitrogen or mental status.

Thus, in studies by Heyman et al.⁴⁹ and Scheinberg,⁵⁰ a reduction in cerebral metabolism was observed although not a reduction in total body metabolism.

D. Biochemical Changes

The complexity of the biochemical changes in uremia renders a detailed discussion beyond the scope and competence of this reviewer. However, the relationship between biochemical disturbance and neurological symptomatology requires some consideration in this discussion.

⁴⁸ Peritz Scheinberg, "Effects of Uremia on Cerebral Blood Flow and Metabolism," Neurology, Vol. 4, 1954, p. 101-105.

⁴⁹ Heyman et al., op. cit., p. 177-179.

⁵⁰ Scheinberg, op. cit., p. 101-105.

As stated above, the uremic syndrome is to a large extent a disorder of central nervous system functioning.⁵¹ However, attempts at isolation of a single neurotoxic factor in uremia have been unsuccessful. According to Merrill and Hampers, "The problem remains of deciding whether the 'toxin' is the cause or result of a more fundamental disturbance."⁵²

Discussing the underlying basis of the uremic syndrome, Schreiner suggested a list of possible mechanisms:

1. A single circulating toxin, as yet unidentified.
2. Combined derivatives of protein--urea, creatinine, uric acid, etc.
3. Inorganic and organic acid retention, including sulfate.
4. Retention of proteolytic enzymes.
5. Absorbed products of intestinal putrefaction.
6. Guanidine and phenol poisoning.
7. Alterations in osmotic pressure.
8. Alterations in the choroid plexus, with escape of circulating toxins into the spinal fluid.⁵³

According to Locke et al.⁵⁴ acidemia, alkalemia, hyperkalemia, hypokalemia, calcium and magnesium disturbance, and alterations in water metabolism and osmolarity, all contribute to this syndrome.

⁵¹ Julian Knutson and A.B. Baker, "The Central Nervous System in Uremia," Archives of Neurology and Psychiatry, Vol. 54, 1945, p. 130-140.

⁵² Merrill and Hampers, op. cit., p. 955.

⁵³ Gorge E. Schreiner, "Mental and Personality Changes in the Uremic Syndrome," Medical Annals of the District of Columbia, Vol. 28, 1959, p. 316-323.

⁵⁴ Locke et al., op. cit., p. 528.

Bradley, in a review of biochemical changes in uremia, concurs with the multiple-factor view:

It is probable that the symptomatology of uremia is the result of the action of multiple factors, among which the change in the character of the metabolic pool bulks large.⁵⁵

Olsen, considering the pathologic changes in uremic brains, concludes:

The uremic symptoms, including the changes in the function of the nervous system, must be considered a result of numerous concurrent factors.⁵⁶

In discussing the possible mechanisms which would account for the EEG abnormalities evidenced in their investigation, Jacob et al. arrive at the same conclusion:

It is unlikely that one factor could explain all changes in the tracing during chronic renal failure with its complex biochemical and physiological disturbance.⁵⁷

Thus, the literature suggests that the neurological symptomatology of uremia is the result of the "summated expression of a number of interplaying factors,"⁵⁸ each of which relates to the failure of metabolic functioning.

55 Bradley, op. cit., p. 796-797.

56 Olsen, op. cit., p. 13.

57 Jacob et al., op. cit., p. 426.

58 Wills, op. cit., p. 542.

E. Peripheral Nervous System

Peripheral motor and sensory nerve impairment is a consistent finding in uremia.⁵⁹ Its variations range from subclinical deficits in nerve conduction rates to debilitating motor damage which grossly interferes with locomotion.⁶⁰

Objective determination of nerve conduction velocity is reported to be a valid and sensitive indicator of peripheral nerve functioning.⁶¹

Versaci et al.,⁶² Tenckhoff et al.,⁶³ Callaghan,⁶⁴ Honet et al.,⁶⁵ and Lindholm⁶⁶ have all reported reduced

59 Castan, op. cit., p. 2444.

60 Ibid.

61 E.W. Johnson and K.J. Olsen, "Clinical Value of Motor Nerve Conduction Velocity Determination," Journal of the American Medical Association, Vol. 172, 1960, p. 2030-2035.

62 Antonio Versaci, Karl J. Olsen, Peter B. McBain, Satoru Nakamoto, and William J. Kolff, "Uremic Polyneuropathy and Motor Nerve Conduction Velocities," Transactions of the American Society for Artificial Internal Organs, Vol. 10, 1964, p. 328-331.

63 Tenckhoff et al., op. cit., p. 1121-1124.

64 Noel Callaghan, "Restless Legs Syndrome in Uremic Neuropathy," Neurology, Vol. 16, 1966, p. 359-361.

65 Joseph C. Honet, Robert H. Jebsen, Heinrich A. Tenckhoff, and James R. McDonald, "Motor Nerve Conduction Velocity in Chronic Renal Insufficiency," Archives of Physical Medicine and Rehabilitation, Vol. 47, 1966, p. 647-652.

66 Tore Lindholm, "The Influence of Uremia and Electrolyte Disturbance on Muscle Action Potentials and Motor Nerve Conduction in Man," Acta Medica Scandinavica, Supplementum 491, 1968, 81 p.

conduction velocities in both sensory and nerve fibres in patients with chronic renal failure. According to Preswick and Jeremy,⁶⁷ depression in nerve conduction velocity also occurs without clinical evidence of peripheral neuropathy, although to a lesser degree.

Lindholm⁶⁸ studied the relationship between ulnar nerve conduction velocity and the degree of uremia indicated by the concentration of non-protein nitrogen. In a sample of fifty-four uremic subjects, he reports that increasing uremia is associated with a decrease in motor nerve conduction velocity ($r = -.45$; $p < .005$).

Tenckhoff et al.⁶⁹ note that extensive deterioration in nerve conduction velocity may precede and anticipate later clinical manifestations of peripheral neuropathy.

Although the symptoms of peripheral neuropathy initially affect the lower extremities,⁷⁰ the reduction in nerve conduction velocity is not significantly less in the upper limbs.⁷¹

67 G. Preswick and D. Jeremy, "Subclinical Polyneuropathy in Renal Insufficiency," Lancet, Vol. 2, 1961, p. 731-732.

68 Lindholm, op. cit., p. 37.

69 Tenckhoff et al., op. cit., p. 1123.

70 Ibid., p. 1121.

71 Honet et al., op. cit., p. 651.

Increasing peripheral neuropathy has been reported to coincide with a generalized depression in nerve conduction velocity.⁷²

Hegstrom et al.⁷³ and Schupak et al.,⁷⁴ among others, have reported that long-term hemodialysis generally results in a decrease of peripheral neuropathic symptoms, although not always initially or consistently throughout treatment. Jebsen et al.⁷⁵ found a rank-order correspondence between number of treatments and increases in motor nerve conduction velocity which was significant at the .01 level of probability.

Lindholm⁷⁶ studied motor nerve conduction velocity in seventeen uremic subjects before and after a single dialysis treatment on nineteen separate occasions. There were no significant differences observed.

72 R.M. Hegstrom, J.S. Murray, J.S. Pendras, J.P. Burnell, and B.H. Scribner, "Two Years Experience with Periodic Dialysis in Treatment of Chronic Uremia," Transactions of the American Society for Artificial Internal Organs, Vol. 8, 1962, p. 266-275.

73 Ibid., p. 272-273.

74 Eugene Schupak, John F. Sullivan, and Dae Yon Lee, "Chronic Hemodialysis in Unselected Patients," Annals of Internal Medicine, Vol. 67, 1967, p. 707-717.

75 Robert H. Jebsen, Heinrich Tenckhoff, and Joseph C. Honet, "Natural History of Uremic Polyneuropathy and Effects of Dialysis," The New England Journal of Medicine, Vol. 277, 1967, p. 327-333.

76 Lindholm, op. cit., p. 45-46.

The underlying disturbance in peripheral nerve functioning remains obscure.⁷⁷ Ashbury et al.,⁷⁸ in a study of post-mortem changes in uremic polyneuropathy, reported destruction to both axon cylinders and myelin sheaths of peripheral nerves. Damage was most extensive in the distal segments of the lower extremities. According to Heron et al.,⁷⁹ it is not known whether the slowing in nerve conduction rate is due, essentially, to a loss of larger and faster nerve fibres, or to a disturbance in the conduction mechanism itself.

3. Psychological Studies of Uremia and Hemodialysis.

This section presents literature on psychological functioning in uremia and the mediating effects of hemodialysis.

The literature is presented under the following headings: (a) neuropsychological studies of uremia, and (b) hemodialysis.

77 Jebson et al., op. cit., p. 332.

78 A.K. Ashbury, M. Victor, R.D. Adams, "Uremic Polyneuropathy," Transactions of the American Neurological Association, Vol. 87, 1962, p. 100-108.

79 J.R. Heron, F.I.D. Konotey-Ahulu, S. Shaldon, and P.K. Thomas, "Nerve Conduction in Chronic Renal Failure Treated by Dialysis," Proceedings of the European Dialysis and Transplant Association, Vol. 2, 1965, p. 138-143.

Neuropsychology, in this review, is defined as the application of psychological procedures to the study of brain functioning.⁸⁰

A. Neuropsychological Studies of Uremia

Neurological and related findings of cerebral abnormality in the uremic syndrome⁸¹ have led to a few neuropsychological investigations.

From their observations, Short and Krugman state:

In time, most patients develop a significant degree of organic dysfunction. These changes are readily demonstrated by Bender Gestalt figures and the Performance level on the WAIS which falls appreciably below the Verbal, indicating organicity.⁸²

Blatt and Tsushima⁸³ administered the Wechsler Adult Intelligence Scale,⁸⁴ the Draw-A-Person Test, the Rorschach Psycho-Diagnostic Technique, and the Bender Gestalt Test, to seventeen uremic subjects at the end-stage of kidney failure.

⁸⁰ Elbert W. Russell, Charles Neuringer, and Gerald Goldstein, Assessment of Brain Damage, New York, John Wiley and Sons, 1970, p. 23.

⁸¹ Supra, p. 3-17.

⁸² M.J. Short and A.D. Krugman, unpublished data, in M.J. Short and W.P. Wilson, "The Role of Denial in Chronic Hemodialysis," Archives of General Psychiatry, Vol. 20, 1969, p. 443-437.

⁸³ B. Blatt and W.T. Tsushima, "A Psychological Survey of Uremic Patients Being Considered for the Chronic Hemodialysis Program: Intellectual and Emotional Patterns in Uremic Patients," Nephron, Vol. 3, 1966, p. 206-208.

⁸⁴ Hereafter, also referred to as WAIS.

At that time, they were all candidates for the chronic hemodialysis program. The mean Full Scale IQ of the patients evaluated was 106.9, this being obtained from a Verbal and Performance IQ of 111.9 and 97, respectively. Lowest mean scale scores were obtained in the Block Design and Digit Symbol subtests.

The authors state that Bender Gestalt performance was slow but, "did not point to any clear signs of organic cortical dysfunction in the design productions."⁸⁵

The Rorschach Psychodiagnostic Technique productivity ranged from a low of eight responses to a high of forty-two responses. The mean number of responses was 18.2 on this instrument.

The Draw-A-Person Test, although indicating emotional involvement, was not interpreted in the light of intellectual functioning.

Blatt and Tsushima concluded from these results:

Patients suffering from chronic uremia display a loss of efficiency on performing tasks generally sensitive to cortical dysfunction.⁸⁶

Additionally, correlations were obtained between blood-urea-nitrogen levels and WAIS Full Scale IQs, Performance IQs and the differences between Verbal and Performance IQs. All were found to be low and insignificant.

⁸⁵ Blatt and Tsushima, op. cit., p. 207.

⁸⁶ Ibid., p. 207-208.

DeNour et al.⁸⁷ administered the Raven's Progressive Matrices, Koh's Blocks, the Goodenough-Harris Draw-A-Man Test, and the Rorschach Psychodiagnostic Technique to eight chronic uremic subjects while on the hemodialysis machine. They report that all indicators revealed impairment in intellectual functioning.

Performance on the Raven's Progressive Matrices was below the population mean in all but one subject.

On Koh's Blocks, all subjects are said to have revealed signs of organic brain pathology in their method of coping with the blocks, and scores ranged from "lower limits of normal to very low."⁸⁸

On the Draw-A-Man Test,⁸⁹ no subjects scored beyond the lower limits of the normal range for fifteen years of age; four of the eight patients were evaluated within the eight to nine year level of differentiation.

On the Rorschach Psychodiagnostic, the number of responses in all cases was less than twelve. Rejection of cards was frequent. They found a high percentage of vague,

87 Atara Kaplan DeNour, J. Shaltier, and J.W. Czaczkes, "Emotional Reactions of Patients on Chronic Hemodialysis," Psychosomatic Medicine, Vol. 30, 1968, p. 521-533.

88 Ibid., p. 527.

89 D.B. Harris, The Goodenough Draw-A-Man Test. Drawings as Measures of Intellectual Maturity, New York, Harcourt, 1963.

loosely organized whole responses (W_v). Popular responses were found to be either rare or exclusively used. The use of form ($F\%$) was extensive but form level was generally low. There was an absence of color responses. Movement responses were rare and qualitatively passive.

The authors conclude from these findings:

[...] Considering the educational background of some of these patients, there is a loss in cognitive functioning, or, at least at times, patients cannot use their full capacities.⁹⁰

From clinical observation, Morrin⁹¹ suggests that psychological deficit in uremia is never fully reversed during the course of the illness, irrespective of the efficiency of treatment. He notes that patients after transplant will frequently remark that they are now able to think much more clearly.

Kemph reports this post-transplant occurrence, as well:

90 DeNour et al., op. cit., p. 530.

91 Peter Morrin, "Psychological and Social Implications of Chronic Renal Failure, With Particular Emphases on Chronic Hemodialysis," unpublished paper, Kingston General Hospital, October 1969.

The most striking postsurgical finding in the recipients was a rapid recovery of mental capacity and personality functioning within the first few days after surgery in those cases where the new kidney began to function immediately. Long before the patient had recovered from the surgical trauma, his reality testing, alertness, ability to concentrate, cognitive powers such as ability to integrate and abstract information, control over impulsivity, use of higher level defenses, etc., improved astonishingly.⁹²

Thus, the few studies available report impaired psychometric functioning on most instruments administered. This is contrasted by reports of improved psychological functioning after successful kidney transplant.

B. Hemodialysis

Since 1960,⁹³ certain individuals within the end-stage of chronic renal failure have been maintained through repeated hemodialysis.

Despite a growing research interest in the psychological concomitant of long-term hemodialysis, there is an absence of literature on the extended effects of this chronic treatment on intellectual deficits associated with chronic uremia.⁹⁴

92 J.P. Kempf, "Renal Failure, Artificial Kidney and Kidney Transplant," American Journal of Psychiatry, Vol. 122, 1966, p. 1270-1274.

93 B.H. Scribner, J.B.Z. Caner, R. Buri, and W.B. Quinton, "The Technique of Continuous Hemodialysis: A Preliminary Report," Transactions of the American Society for Artificial Internal Organs, Vol. 6, 1960, p. 88-96.

94 *Supra*, p. 18-22.

Thus, the following review of literature will be restricted to behavioral changes and complications during hemodialysis,⁹⁵ and the psychological reaction to the regimen of treatment.

Dialysis involves at least six hours of treatment, twice weekly.⁹⁶ However, some patients can require as much as thirty hours on a tri-weekly basis.

Tyler⁹⁷ and Shea et al.⁹⁸ report that the behavior of patients during dialysis often reflects the extensive and rapid biochemical changes occurring. Fatigue, irritability, and a difficulty in engaging in activities requiring concentrated effort are reported as being common during treatment.

Complications during and after dialysis range from headaches, nausea and vomiting, to more serious symptoms such as convulsions.⁹⁹ Symptoms often begin during dialysis and may persist for twenty-four hours or longer.¹⁰⁰

95 Hereafter, also referred to as dialysis.

96 Morrin, op. cit.

97 H. Richard Tyler, "Neurological Complications of Dialysis, Transplantations, and Other Forms of Treatment in Chronic Uremia," Neurology, Vol. 15, 1965, p. 1081-1088.

98 Eileen J. Shea, Donald F. Bogdan, Richard B. Freeman, and George E. Schreiner, "Hemodialysis for Chronic Renal Failure: IV. Psychological Considerations," Annals of Internal Medicine, Vol. 62, 1965, p. 558-563.

99 Ibid., p. 560.

100 A.C. Kennedy, A.L. Linton, and J.C. Eaton, "Urea Levels in Cerebral Spinal Fluid," Lancet, Vol. 1, 1962, p. 410-411.

According to Kennedy et al.¹⁰¹ these complications are due to disequilibrium, caused by a slower diffusion of urea from the central nervous system relative to the speed with which it is dialyzed from the blood and other body fluids. The resultant osmotic gradient causes an inward flow of water, thus increasing intracranial pressure.

Due to the time required for equilibration, Teschan¹⁰² has noted that the greatest symptomatic benefit from dialysis is experienced on the day following the procedure.

As Cutter¹⁰³ notes, chronic hemodialysis consumes the major portion of a patient's waking hours and dominates the remainder of his activities. Faced with frequent physical distress and the high probability of dying, psychological adjustment is a difficult process.¹⁰⁴ As Schreiner has observes: "Dialysis for chronic renal failure involved the application of a dramatic technique to terminally ill patients in an emotionally charged atmosphere."¹⁰⁵

101 A.C. Kennedy, A.L. Linton, S. Renfrew, R.G. Luke, A. Dinwoodie, "The Pathogenesis and Prevention of Cerebral Dysfunction During Dialysis," Lancet, Vol. 1, 1963, p. 408.

102 Teschan, Personal Communication, November 1969.

103 Fred Cutter, "Some Psychological Problems in Hemodialysis," Omega, Vol. 1, 1970, p. 37-47.

104 Ibid., p. 45.

105 G.E. Schreiner and J.F. Maher, "Hemodialysis for Chronic Renal Failure: Medical, Moral, Ethical, and Socio-economic Problems," Annals of Internal Medicine, Vol. 62, 1965, p. 551-557.

Wright et al.¹⁰⁶ attempted to classify the types of stress faced by patients on long-term dialysis. The stresses, which are interpreted as actual or anticipated losses, are listed as: (1) part of body or body functions, (2) loss of membership in groups, (3) failure of plans and adventures, (4) changes in way of life and living, (5) loss of home, possessions, or financial status, and (6) loss of job or occupation.

DeNour et al.¹⁰⁷ report that the unique stress of dialysis is the profound dependency of the individual on the machine and the need to prevent its expression or realization.

Sand et al.¹⁰⁸ note that psychological stress in this patient group results in frequent adjustment problems which range in severity from inadequate cooperation with medical requirements to psychosis.

In this regard, Shea et al.¹⁰⁹ observed nine patients over a period of two-and-a-half years. They reported that all patients had significant psychological reactions while on the dialysis program. According to the authors, these

106 R.G. Wright, P. Sand, and G. Livingston, "Psychological Stress During Hemodialysis for Chronic Renal Failure," Annals of Internal Medicine, Vol. 64, 1966, p. 611-621.

107 DeNour et al., op. cit., p. 531.

108 Sand et al., op. cit., p. 602.

109 Shea et al., op. cit., p. 558.

consisted of a schizophrenic-like reaction, a psychotic depressive reaction, and the remainder of a neurotic nature.

Abram,¹¹⁰ in a review of the procedures of various dialysis centers, reports a lower incidence of psychopathology in units emphasizing psychological selection and a comprehensive treatment which includes medical, social, and psychological aspects.

Short and Wilson¹¹¹ note that a restructuring of psychological defenses is necessary for successful adaptation to chronic dialysis.

Denial, displacement, isolation, projection and reaction formation are reported to be common mechanisms of adaption in dialysis patients.¹¹²

Glassman and Siegel¹¹³ gave the California Psychological Inventory and the Shipman Anxiety and Depression Scale to seven patients with re-testing after nine months. They conclude:

110 Harry S. Abram, "The Psychiatrist, The Treatment of Chronic Renal Failure, and the Prolongation of Life: I," American Journal of Psychiatry, Vol. 124, 1968, p. 1351-1357.

111 Short and Wilson, op. cit., p. 436.

112 DeNour et al., op. cit., p. 524-526.

113 Barry M. Glassman and Allen Siegel, "Personality Correlates of Survival in a Long-Term Hemodialysis Program," Archives of General Psychiatry, Vol. 22, 1970, p. 566-574.

We were struck by the remarkable disparity between the test data and the clinical appearance of the patient population. The test scores describe the patients as being near or above normal in all the scales of the CPI. This includes most significantly the high sense of well being on the CPI and the relatively low scores for anxiety and depression on the Shipman test [...]. We conclude that patients cope with the stress of this program by the massive use of denial as an adaptive mechanism.¹¹⁴

Short and Wilson¹¹⁵ also noted the significant use of denial by chronic dialysis patients. Using the Minnesota Multiphasic Personality Inventory, they found that test indications of denial increased with elevated psychological stress. Medical complications during treatment were considered to result in increased stress.

4. Summary and Conclusions.

This chapter has presented literature relating to psychological and neurological deficits in uremia. In this review, neurological symptomatology was discussed and studies on uremic neuropathology were presented. This included a few neuropsychological investigations. Additionally, the psychological and social milieu, within which dialysis patients function, was given consideration.

An overview of the reported findings would seem to suggest the following conclusions:

¹¹⁴ Ibid., p. 573.

¹¹⁵ Short and Wilson, op. cit., p. 436.

1. Uremic symptomatology suggests a generalized depression in central and peripheral nervous system functioning.

2. Available anatomic investigations have yielded varying results although some consistency is noted.

3. In nearly all uremic brains studied, there were well characterized neuronal degenerations. The most frequent and most severely affected regions were the sensory nuclei of the brain stem, the reticular formation, and the cerebral cortex. These changes were most pronounced in chronic forms of uremia.

4. EEG abnormalities reflect neurological involvement in uremia. The most frequent finding was a marked slowing in the background alpha rhythm. This is consistent with clinical evidence of central nervous system depression.

5. Cerebral oxygen and glucose consumption is reduced although cerebral circulation is at least normal and total body metabolism is unaffected. This suggests that an intracerebral and not extracerebral mechanism is responsible for the deficiency.

6. The effects of uremia are probably due to a complex of interacting factors which are not as yet delineated.

7. Both sensory and motor peripheral nerves show reduced conduction velocities indicative of impaired peripheral nervous system functioning.

8. The few psychological studies available suggested impaired psychometric functioning in uremia. Non-verbal tasks were most implicated. The authors noted that results were indicative of organic cortical dysfunction.

9. The emotional and socio-economic state of patients on chronic hemodialysis is an essential factor in the success of their treatment. Psychological stress is pronounced and ego-restricting defense mechanisms are heavily used.

10. Dialysis patients are least symptomatic, an average of twenty-four hours after treatment.

11. As a general conclusion, it appears that psychological deficit is well established as occurring in uremia. However, there is a paucity of literature enumerating the type of impairment and the mediating effects of hemodialysis.

CHAPTER II

THE PRELIMINARY STUDY

This chapter reports on a preliminary investigation into brain damage in uremia.

The first section states the rationale for the initial study and presents the method used in test selection. The second section reports on the sample. This is followed by a discussion of results. Finally, the hypotheses of the present study, based on the findings of the initial study and reported literature, are presented.

1. Rationale and Test Selection.

The review of the literature reported on three psychometric investigations into "organic" impairment in uremia. Short and Krugman¹ and Blatt and Tsushima² reported on performance of end-stage uremic subjects on the Wechsler Adult Intelligence Scale and the Bender Gestalt. DeNour

1 M.J. Short and A.D. Krugman, unpublished data, in M.J. Short and W.P. Wilson, "The Role of Denial in Chronic Hemodialysis," Archives of General Psychiatry, Vol. 20, 1969, p. 435.

2 B. Blatt and W.T. Tsushima, "A Psychological Survey of Uremic Patients Being Considered for the Chronic Hemodialysis Program: Intellectual and Emotional Patterns in Uremic Patients," Nephron, Vol. 3, 1966, p. 206-208.

et al.³ administered the Raven's Progressive Matrices, Koh's Blocks, Draw-A-Man Test, and the Rorschach Psychodiagnostic to subjects while on the dialysis machine.

As noted in the previous chapter,⁴ all measures reflected psychometric impairment in the subjects evaluated.

Specifically, the following conclusions appear warranted in respect to these studies. (1) The results of three investigations are insufficient to justify final judgments. (2) DeNour et al.⁵ administered the test battery while the patients were connected to the machine. Thus, the possibilities of contamination due to disequibration and the effects of rapid biochemical change significantly decrease the interpretive value of this study.⁶ (3) The single replicated test finding is that the Performance level of the WAIS falls appreciably below the Verbal.

On the basis of these conclusions, the author sought to further investigate "organic" impairment in uremia, and in

³ Atara K. DeNour, Judith Shaltiel and J.W. Czaczkes, "Emotional Reactions of Patients on Chronic Hemodialysis," Psychosomatic Medicine, Vol. 30, 1968, p. 522.

⁴ Supra, p. 22.

⁵ DeNour et al., op. cit., p. 522.

⁶ H. Richard Tyler, "Neurological Complications of Dialysis, Transplantation, and Other Forms of Treatment in Chronic Uremia," Neurology, Vol. 15, 1965, p. 1082.

so doing, obtain a series of measures sensitive to uremic impairment.

Two criteria were used in test selection. (1) Results derived from the literature warranted its inclusion. (2) The instrument is economical in that it requires a minimum of time to administer although remaining sensitive to nervous system impairment. This second criterion was established due to this patient group's sensitivity to fatigue⁷ and the limited time available for testing.

Adherence to these criteria led to the selection of tests and measures comprising the preliminary battery.

Selected scales from the Verbal and Performance sections of the WAIS were included. Blatt and Tsushima⁸ had reported that Verbal scores were dominant over Performance indicators and that scores obtained on the Block Design and Digit Symbol subtests were relatively the lowest in the subjects evaluated. Performance on Picture Completion was found to be greater than on either Block Design or Digit Symbol. Thus, these scales were included along with three Verbal subtests, Similarities, Vocabulary, and Digit Span, in order to facilitate comparison.

⁷ Peter Morrin, "Psychological and Social Implications of Chronic Renal Failure, With Particular Emphasis on Chronic Hemodialysis," unpublished paper, Kingston General Hospital, October 1969.

⁸ Blatt and Tsushima, op. cit., p. 207.

The Trail Making Test⁹ has been found valuable in assessing the effects of brain damage. Studies have demonstrated that Part B of this test is especially sensitive to brain damage and is highly accurate in differentiating controls from brain-damaged subjects with only a small overlap.^{10,11} For this reason, it was included in the battery.

The Aphasia Screening Test¹² was included to assess any focal symptoms involving major language skills. Wheeler and Reitan¹³ have demonstrated that this instrument is sensitive to "organic" deficit and that it can provide lateralizing information.

In order to tap the perceptual area of psychological functioning, Sensory Imperception, Finger Agnosia, and

9 S.G. Armitage, "An Analysis of Certain Psychological Tests Used for the Evaluation of Brain Injury," Psychological Monographs, Vol. 60, Whole No. 277, 1946.

10 R.M. Reitan, "The Relation of the Trail Making Test to Organic Brain Damage," Journal of Consulting Psychology, Vol. 19, 1955, p. 393-394.

11 -----, "The Validity of the Trail Making Test as an Indicator of Organic Brain Damage," Perceptual and Motor Skills, Vol. 8, 1958, p. 271-276.

12 W.C. Halstead and J.M. Wepman, "The Halstead-Wepman Aphasia Screening Test," Journal of Speech and Hearing Disorders, Vol. 14, 1949, p. 9-15.

13 L. Wheeler and R.M. Reitan, "The Presence and Laterality of Brain Damage Predicted from Responses to a Short Aphasia Screening Test," Perceptual and Motor Skills, Vol. 15, 1962, p. 783-799.

Roughness Discrimination tests were included.¹⁴ These measures have been found sensitive to suppressions of sensory functioning of a tactile, auditory, and visual nature.

Finally, the motor and neuromuscular element was assessed through the Finger Tapping and Dynamometer Grip Strength tests, respectively of the original Halstead battery.¹⁵

2. The Sample and Experimental Procedure.

The subjects, for the preliminary study, were six end-stage uremic patients, referred from the Ottawa General and Civic hospitals. The subjects, gathered over a period of eight months, were evaluated prior to their first experience on dialysis and in close proximity to it. The delay between testing and first dialysis ranged approximately from one hour to one week. All patients were hospitalized at the time of testing.

The ages of the subjects ranged from twenty-one years to thirty-six, with a mean age of twenty-eight years. The educational levels varied from fifth grade to two years of

¹⁴ R.M. Reitan, "A Research Program on the Psychological Effects of Brain Lesions in Human Beings," in N.R. Ellis (ed.), International Review of Research in Mental Retardation, Vol. 1, New York, Academic Press, 1966, p. 153-214.

¹⁵ W.C. Halstead, "Biological Intelligence," Journal of Personality, Vol. 20, 1951, p. 118-130.

university, with a mode level of grade six and mean education of grade eight.

3. Presentation of Results.

The raw scores obtained by the subjects on the preliminary battery are reported in Table I. Table II lists the mean scale scores for each of the WAIS subtests. Table III transforms the raw data of the Halstead and Reitan measures into impairment ratings and reports the mean impairment level for each of the tests.¹⁶ These are based on a six-point scale whereby ratings of zero and one indicate above average and average functioning, respectively, and ratings 2, 3, 4, and 5 describe sequential levels of impairment from mild to very severe.¹⁷ Table IV presents Spearman Rank Correlations between each of the WAIS scales administered, the Trail Making Test and Finger Tapping scores.

Results are first discussed in reference to each test or test group. This is followed by a discussion of the relationship between measures on which impaired functioning was indicated.

¹⁶ Elbert W. Russell, Charles Neuringer and Gerald Goldstein, Assessment of Brain Damage, New York, John Wiley and Sons, 1960, p. 108-109.

¹⁷ Ibid.

Table I.-

Raw Scores Obtained on Preliminary Battery Described in Section
on Rationale and Test Selection.

Subtests	Subjects					
	1	2	3	4	5	6
<u>WAIS</u>						
Similarities	8	8	6	6	5	12
Digit Span	7	7	10	7	6	7
Vocabulary	10	6	9	8	3	15
Digit Symbol	4	9	8	7	4	8
Picture Completion	8	8	9	7	6	9
Block Design	4	7	11	5	6	10
<u>Trail Making</u>						
Part A	65	30	26	11	83	21
Part B	212	120	76	185	300	140
Errors on Part A	0	0	0	0	0	0
Errors on Part B	5	2	0	5	11	1
Finger Tapping						
Right	44	45	45	27	42	53
Left	40	54	45	39	37	50
Grip Strength						
Right	45	43	46	29	46	45
Left	-	50	40.5	24	48	43
Roughness Discrimination						
Right	2	0	0	0	0	0
Left	0	0	0	0	0	0
Sensory Imperception						
Visual	0	0	1	0	0	0
Auditory	0	4	0	0	0	0
Tactile	0	0	0	0	0	0
Finger Agnosia						
Right	4	0	0	0	0	0
Left	2	0	2	0	0	0
Aphasia Screening						
	0	1	0	0	0	0

Table II.-
WAIS Subtest Means Expressed in Scale
 Score Units.

Subtests	Means	Intelligence Quotients	
Similarities	7.5		
Digit Span	7.3		
Vocabulary	8.5	Full Scale	= 86
Digit Symbol	6.7	Verbal	= 84
Picture Completion	7.9	Performance	= 82
Block Design	7.1		

Table III.-
 Impairment Indices on Halstead and
 Reitan Measures.

Tests	Subjects						Mean Impairment
	1	2	3	4	5	6	
Trails A	4	1	1	0	4	1	1.83
Trails B	4	2	1	3	5	3	3.00
Tapping	2	1	1.5	2.5	2.5	0.5	1.66
Grip Strength	1	1	1	1	1	1	1.00
Imperception	1	0	0	0	0	0	.16
Aphasia	0	1	0	0	0	0	.16

Table IV.-

Spearman Rank-Order Intercorrelations of WAIS,
Trail Making, and Finger Tapping Measures.

Tests	Sim.	D.Sp.	Voc.	D.Sym.	P.C.	P.D.	Tr.A.	Tr.B.	E.	Tap.
Sim.	1.00									
D.Sp.	.743	1.00								
Voc.	.743	.571	1.00							
D.Sym.	.485	.400	-.400	1.00						
P.C.	.671	.814	.771	.614	1.00					
B.D.	.143	.571	.143	.715	.685	1.00				
Tr.A.	.314	.571	.571	.457	.400	.314	1.00			
Tr.B.	.347	.857*	.257	.886*	.771	.772	.485	1.00		
Error	.443	.870*	.442	.772	.943**	.815	.500	.929**	1.00	
Tapping	.771	.428	.485	.714	.685	.657	.085	.600	.728	1.00

* significant at .05 level (p= .829).

** significant at .01 level (p= .943).

Table II indicates that the mean prorated IQ on the WAIS was 84, indicating an average intellectual level in the dull-normal range.¹⁸ The subjects tended to perform better on the Verbal tasks (mean Verbal IQ = 86) than on the Performance subtests (mean Performance IQ = 82). However, according to Wechsler,¹⁹ this difference is in the expected range.

Wechsler²⁰ reports that Picture Completion and Vocabulary are more resistant to a deterioration process than either Similarities, Digit Span, Digit Symbol, or Block Design. Thus, the greater resilience of Picture Completion and Vocabulary would permit the expectation that scale scores would be higher in these subtests than in those sensitive to encroachment, if deterioration was occurring. In this sample, this is substantiated. Vocabulary, followed by Picture Completion, was found to have the highest mean scale scores.

Accordingly, the most marked decline is found in the Digit Symbol and Block Design subtests on which the lowest mean scale scores were obtained. This is in agreement with

¹⁸ David Wechsler, Manual for the Wechsler Adult Intelligence Scale, New York, The Psychological Corporation, 1955, p. 20.

¹⁹ -----, The Measurement and Appraisal of Adult Intelligence, New York, Williams and Wilkins, 1958, p. 160.

²⁰ Ibid., p. 210.

the results of Blatt and Tsushima²¹ who also reported this finding. On the Digit Span subtest, the third lowest mean scale score was obtained.

Performance on the Trail Making Test was the most impaired of the Halstead and Reitan measures administered.

On Part A, the average impairment level indicated organic deficit of a mild degree. Although the range of functioning was from above average to severely impaired, only two of the subjects performed in the impaired range.

Performance on Part B was rated as more impaired than on Part I in five of the six subjects. The average level of impairment indicated brain damage of a moderate degree and only one subject functioned in the normal range.

Finger Tapping scores, for both hands, were averaged for each subject, yielding a single rating. The impairment level of the sample indicated organic involvement of a mild degree. The level of functioning varied from normal to moderately impaired.

Dynamometer Grip Strength functioning was normal in all six subjects.

There was no evidence, in the sample, of perceptual suppression or decline in sensory processes as indicated by

21 Blatt and Tsushima, op. cit., p. 208.

the Imperception, Finger Agnosia, and Roughness Discrimination tests.

Aphasia testing did not reveal any loss in major language skills.

In summary, it appears that the Digit Symbol, Block Design, and Digit Span subtests, in that order, were the most sensitive of the WAIS scales to intellectual impairment associated with uremia. The Trail Making Test and to a lesser extent the Finger Tapping test were also found to indicate impaired functioning in this sample. In general, as evidenced in the literature,²² nonverbal measures were more affected than verbal ones.

4. Interpretation of Results.

In factor analytic studies of the WAIS and Wechsler Bellevue scales,²³ the Block Design and to a lesser extent the Digit Symbol subtests load highest on a factor identified as Perceptual Speed or Visual-Motor Organization. Digit Symbol and Digit Span consistently load highest on a Memory factor or, as Cohen²⁴ has suggested, "freedom from

22 Supra, p. 29.

23 Wechsler, op. cit., 1958, p. 132-133.

24 J. Cohen, "The Factorial Structure of the WAIS Between Early Childhood and Old Age," Journal of Consulting Psychology, Vol. 21, 1957, p. 283-290.

distractability." Cohen notes that this Memory factor is most disturbed in brain damaged and psychiatric groups.

Using these factors as a basis for interpretation, it appears, from the results obtained, that at least two abilities or capacities are implicated in uremic impairment of intellectual functioning. The first may be labeled perceptual speed and the second is a general memory function or the ability to resist distraction.

Armitage²⁵ suggests that the Trail Making Test measures the function of perception and the ability to sustain and shift one's focus of attention. These may be similar to the Perceptual Speed and Memory factors identified in the Digit Symbol, Digit Span and Block Design scales of the WAIS.

Illustrated in Table IV, Spearman rank-order correlations between these WAIS subtests and Trail Making Test scores reveal a tendency for rank orders to be similar.

Part B of the Trail Making Test significantly correlated at the .05 level of probability with both Digit Span and Digit Symbol.

The number of errors made on Part B significantly correlated at the .05 and .01 levels, respectively, with

²⁵ Armitage, op. cit., p. 31.

Digit Span and Picture Completion. According to Wechsler,²⁶ Picture Completion involves the ability to attend and perceptually discriminate between essential and non-essential details. Rapaport²⁷ interprets its underlying ability in terms of attention and concentration upon visually perceived material.

Significant rank-order associations were not found between performance on the Finger Tapping test and any of the WAIS subtests or Trail Making Test scores.

In conclusion, the Block Design, Digit Symbol, and Trail Making tests were found to be the most impaired measures in the initial battery administered. The psychological functions of perceptual speed and the ability to attend and resist distractions have been ascribed to these measures. In support of this, significant rank-order associations were noted in the performance of subjects on these tasks. Further, performance on the error score of Trail Making, Part B, was significantly related to performance on both visual and auditory measures requiring attention and the capacity to resist distraction.

²⁶ Wechsler, op. cit., 1958, p. 78.

²⁷ David Rapaport, Merton M. Gill, and Roy Schafer, Diagnostic Psychological Testing (edited revision by Robert H. Holt), New York, International Universities Press, 1968, p. 132.

In view of these results, the author chose to include the Block Design and Digit Symbol scales of the WAIS and the Trail Making Test in the final battery.

For purposes of identification, these three tasks were operationally defined as measures of perceptual motor functioning.

5. Hypotheses.

The preliminary study resulted in the selection of three tests, operationally defined as measures of perceptual motor functioning. Performance on these measures were found to be impaired in end-stage uremic subjects without prior experience on hemodialysis treatment.

A review of the available literature had revealed an absence of information on the long-term effects of continuous hemodialysis on psychological functions designated as impaired in uremic patients.

Thus, the author sought to investigate the effects of long-term dialysis on perceptual motor functioning. Specifically, the following hypotheses, expressed in the null form, were postulated:

1. There are no significant differences between groups differing in treatment duration, on their levels of perceptual motor functioning.
2. There are no positive significant relationships, linear or otherwise, between measures of perceptual motor functioning and duration of dialysis treatment.

CHAPTER III

EXPERIMENTAL DESIGN

This chapter presents the procedures involved in the investigation of the hypotheses stated in the second chapter.

First, the tools involved in the experiment are discussed. The sample is then elaborated. This is followed by a description of the method used in conducting the experiment. Finally, the statistical procedures used in analyzing the results are discussed.

1. The Tools of the Experiment.

It was concluded on the basis of the preliminary study that three tasks suited the object of this research by providing measures sensitive to psychological impairment in uremia. These included Block Design and Digit Symbol of the WAIS, and Parts A and B of the Trail Making Test.

In addition, to estimate the general premorbid intellectual level of the subjects, Information subtest of the Wechsler-Bellevue, Form I, or Les Reinseignments Generaux of the corresponding Ottawa - Wechsler were included. As a second indice of premorbid level of functioning, the number of years of schooling was obtained and recorded for each subject.

Wechsler¹ found that the Information scale declined negligibly with age in the standardization samples of the WAIS and Wechsler-Bellevue. It is therefore considered by Wechsler to be relatively resistant to deterioration.² As well, it correlated second highest with the total score for both the WAIS and Wechsler-Bellevue.³ Cohen,⁴ in a factor analytic study, found that Information correlated highly with the second order factor "G", interpreted as an estimation of general intellectual ability. Wechsler notes: "The fact is, all objections considered, the range of a man's knowledge is generally a very good indication of his intellectual capacity."⁵

Fogel⁶ has shown that the number of years of schooling is a reliable index of premorbid intellectual potential of brain damaged persons raised or born in the United States.

Thus, these two indices were included as independent estimates of premorbid intellectual functioning.

1 David Wechsler, The Measurement and Appraisal of Adult Intelligence, New York, Williams and Wilkins, 1958, p. 203.

2 Ibid., p. 210.

3 Ibid., p. 67.

4 J. Cohen, "The Factorial Structure of the WAIS between Adulthood and Old Age," Journal of Consulting Psychology, Vol. 21, 1957, p. 283-290.

5 Wechsler, op. cit., p. 65.

6 Max L. Fogel, "The Intelligence Quotient as an Index of Brain Damage," American Journal of Orthopsychiatry, Vol. 32, 1962, p. 552-562.

However, it was noted that only education had been truly obtained prior to the onset of illness. It represented, therefore, the more valid of the two indicators.

2. The Sample.

The subjects were twenty-eight chronic uremic patients referred from the Ottawa General and Civic hospitals. All subjects were on long-term hemodialysis. Duration of treatment, in months, varied from one to forty-one, with a mean treatment time of 14.5 months.

Prior to being evaluated, the subjects were screened as to previous psychiatric history or medical evidence of brain damage obtained prior to the uremic illness.

The ages of the subjects ranged from sixteen to seventy years, with a mean age of 38.4 years. Number of years of schooling varied from two to nineteen, with a mean education of 9.8 years.

The age, number of years of education, and treatment duration at the time of testing, for each subject, are included in Appendix 1.

3. The Method of the Experiment.

Prior to the onset of the experiment, subjects were assigned to one of three groups depending on the number of months spent on dialysis therapy at the time of testing.

To control experimental bias, this division was not consulted during the course of testing, nor were subjects asked how long they had been undergoing hemodialysis.

The first group, consisting of ten subjects, contained patients on hemodialysis from one to five months. Abram⁷ suggests that this period is a critical one in the adjustment of hemodialysis patients. He notes that during these months the patient must adapt both physiologically and emotionally to the regimen of treatment.

The second group, consisting of ten subjects, comprised patients on dialysis from six to fifteen months.

The third group, consisting of eight subjects, contained patients on hemodialysis from sixteen to forty-one months.

The division between groups two and three was made on a statistical basis in order to approximately equate the groups in size.

The subjects were evaluated immediately prior to being connected to the hemodialysis machine. This moment was chosen for two reasons: (1) there was little possibility of contamination of results due to disequilibrium

⁷ Harry S. Abram, "The Psychiatrist, The Treatment of Chronic Renal Failure, and the Prolongation of Life: II," American Journal of Psychiatry, Vol. 126, 1969, p. 157-167.

factors,⁸ and (2) it did not impinge upon patients' "free time" between dialysis sessions.

4. Statistical Operations.

To maximally utilize the information provided by the premorbid and morbid measures, all scores were equated and rendered comparable to Wechsler scale values. That is raw scores from the Trail Making Test and the education indice were reduced to a standard score with a mean of ten and a standard deviation of three. Each of the measures of perceptual motor functioning was further adjusted for age. To accomplish this, the following procedures were taken:

1. Pearson product-moment correlations were computed between the Trail Making Test indices and age (the effects of age on Block Design and Digit Symbol had been previously established by Wechsler⁹).
2. The mean and standard deviation of the education measure was obtained.
3. For the education indice, a standard score for each subject was calculated and T-score transformations were performed to convert these scores to a scale with a mean of ten and a standard deviation of three.
4. The subjects were then divided into four age groups: Group 1 containing subjects more than one standard

⁸ S.M. Rosen, K. O'Connor and S. Shaldon, "Hemodialysis Disequilibrium," British Medical Journal, Vol. 2, 1964, p. 672-675.

⁹ Wechsler, op. cit.

deviation below the mean age; Group 2 comprising those subjects within one standard deviation below the mean; Group 3 containing subjects within one standard deviation above the mean; Group 4 comprising those subjects more than one standard deviation above the mean age.

5. Means and standard deviations were calculated for each age group on the Trail Making Test measures.
6. Standard scores were calculated for each subject based on his relative performance within his age group, and T-score transformations were performed to reduce these scores to a scale with a mean of ten and a standard deviation of three.
7. Each of the WAIS scale scores was adjusted for age, based on supplied age norms.¹⁰
8. Returning all subjects to their original dialysis groups, a composite score was derived for each subject by the addition of perceptual motor measures.

In evaluating the results of the experiment, the following statistical operations were applied:

1. Analysis of variance between premorbid measures to investigate if initial differences in premorbid means are significant.
2. Pearson product-moment correlations between the premorbid indices and duration of treatment to establish the independence of the covariates (premorbid measures) with the independent variable (duration on dialysis).
3. Pearson product-moment correlations between education and measures of perceptual motor functioning to establish the efficacy of this indice as a covariate.

¹⁰ David Wechsler, Manual for the Wechsler Adult Intelligence Scale, New York, The Psychological Corporation, 1955, p. 101-110.

4. Analysis of covariance, where applicable, to test the significance between adjusted means of perceptual motor functioning (hypothesis 1).
5. Analysis of variance to test the significance of differences between means of measures of perceptual motor functioning (hypothesis 1).
6. Scheffé method of a posteori comparison between means in the presence of a significant F ratio.
7. Pearson product-moment correlations between measures of perceptual motor functioning and duration on dialysis (hypothesis 2).

In testing the hypotheses, the five per cent level of significance was used. One exception was in a posteori comparison of means in which the ten per cent level of significance was applied. This is suggested by Scheffé.¹¹ The results and ensuing discussion are included in chapter four.

¹¹ George A. Ferguson, Statistical Analysis in Psychology and Education, New York, McGraw-Hill, 1966, p. 297.

CHAPTER IV

EXPERIMENTAL RESULTS

The scores prior to transformation are presented in Appendix 1. A summary of the data is provided in Table V. Transformed scores are presented in Appendix 2, and a summary of these data is presented in Table VI. The Pearson product-moment correlation between age and the Trail Making Test, computed to assess the necessity of age corrections, are presented in Table VII.

The results are discussed in the order in which statistical operations were outlined in chapter three. This is followed by a discussion of results.

1. Presentation of Results.

A. Analysis of Variance between Premorbid Means

To investigate the significance of group differences in premorbid means, analysis of variance was used. A summary of data for the Information subtest and Education is presented in Tables VIII and IX, respectively. For the .05 level of significance, the critical value is $F_{.95}(K=3; df=2, 25) = 3.38$. Inspection of these results indicates that no significant differences exist between the means of premorbid measures.

Table V.-

Summary of Data Reported in Appendix 1 (Raw Scores).

Subtest	Group						Total	
	I		II		III		M	S.D.
	M	S.D.	M	S.D.	M	S.D.	M	S.D.
Premorbid								
Information	10.5	2.94	9.7	2.71	9.37	2.69	9.69	2.95
Education	9.3	4.13	9.7	4.27	10.56	2.59	9.83	3.81
Morbid								
Digit Sym.	7.9	2.26	7.2	2.09	9.50	2.60	7.90	2.68
B. Design	8.4	1.96	8.7	2.45	10.25	1.56	8.83	2.42
Trails A	51.3	18.47	61.0	30.67	58.56	57.95	56.90	38.75
Trails B	260.1	254.70	232.5	214.70	177.50	189.30	224.9	224.80
Errors B	3.5	2.66	1.8	2.56	1.45	2.06	2.28	2.61
Treatment (Mos.)	3.2	1.17	11.6	2.06	30.33	8.42	14.52	12.19
Age	38.3	18.56	36.6	13.82	40.45	15.11	38.38	16.06

Table VI.-
Summary of Data Reported in Appendix 2.

Subtest	Group					
	I	II Mean	III	I	II S.D.	III
Premorbid						
Information	10.50	9.70	9.37	2.94	2.61	2.69
Education	9.59	9.10	10.91	3.26	2.31	1.90
Morbid						
Digit Sym.	7.90	7.20	9.50	2.26	2.09	2.60
B. Design	8.40	8.70	10.25	1.96	2.45	1.56
Trails A	10.44	8.53	11.28	3.08	3.00	1.94
Trails B	9.52	9.01	11.87	3.25	2.97	1.50
Errors B	8.14	10.59	11.55	3.33	2.38	1.83
Combined	43.60	44.06	53.20	10.48	10.12	8.01

Table VII.-
Pearson Product-Moment Correlations Between Age and Trail Making Test.

Subtest	r
Trails A	.40*
Trails B	.60**
Errors B	.55**

* .05 level of significance ($r_{95} = .374$).
** .01 level of significance ($r_{99} = .479$).

Table VIII.-

Analysis of Variance of Premorbid Means: Information.

Source	Sum of Squares	Degrees of Freedom	Mean Square	F
Total	218.679	27		
Between	6.203	2	3.102	.365
Within	212.475	25	8.499	

* .05 level of significance ($F_{.95} = 3.38$)

Table IX.-

Analysis of Variance of Premorbid Means: Education.

Source	Sum of Squares	Degrees of Freedom	Mean Square	F
Total	203.699	27		
Between	15.241	2	7.620	1.01
Within	188.458	25	7.538	

* .05 level of significance ($F_{.95} = 3.38$)

B. Product-Moment Correlations Between Premorbid Measures and Duration of Treatment

A prerequisite of analysis of covariance is the independence of the covariate and the treatment variable.¹ In order to establish this, Pearson product-moment correlations were calculated between Information and Education, the covariates, and Duration of Treatment, the independent variable. The results are reported in Table X.

Inspection of Table X indicates that Information and Education were not significantly correlated with Treatment Duration. However, there was a tendency towards an inverse relationship between Information and Treatment Duration. Although not significant, in these data there was the implication that Information scores may be impaired with increasing months of dialysis treatment. In chapter three, it was noted that Information was not a true covariate in that it was not obtained prior to treatment. Its inclusion was on a theoretical basis.² Thus, the tendency towards significance, in this sample, was sufficient, in the experimenter's opinion, to warrant the exclusion of Information as a covariate. This decision was further supported by the high correlation between Education and Information (.01 level of

1 B.J. Winer, Statistical Principles in Experimental Design, New York, McGraw-Hill, 1962, p. 586-587.

2 Supra, p. 48.

Table X.-

Pearson Product-Moment Correlations Between Information,
Education, and Treatment Duration.

Indice	Information	Education	Treatment Duration
Information	1.00		
Education	.64**	1.00	
Treatment Duration	- .34	.06	1.00

* .05 level of significance (r = .374)
** .01 level of significance (r = .479)

significance) and the low insignificant correlation between Education and Treatment Duration. The possible impairment of Information scores, in this sample, will be elaborated in the discussion of results.

C. Pearson Product-Moment Correlations Between Education and Measures of Perceptual Motor Functioning

To further evaluate the efficacy of the covariate, Education, Pearson product-moment correlations were calculated between Education and the measures of perceptual motor functioning. It was noted that the usefulness of a covariate, in controlling initial group differences, rests on the premise that it is significantly correlated with the dependent variable.³ The correlational values are presented in Table XI.

Inspection of Table XI reveals that of the five variables of perceptual motor functioning, only the two WAIS subtests, Block Design and Digit Symbol, significantly correlated with the Education indice. It follows, therefore, that given initial group differences, Education would be an appropriate covariate in the case of Block Design and Digit Symbol but not for the Trail Making Test measures.

³ George A. Ferguson, Statistical Analysis in Psychology and Education, New York, McGraw-Hill, 1966, p. 326-327.

Table XI.-

Pearson Product-Moment Correlations Between Education and Measures of Perceptual Motor Functioning.

Subtest	Education
Block Design	.39*
Digit Symbol	.57**
Trail Making A	.12
Trail Making B	.22
Errors on Part B	.16

* .05 level of significance (r = .374)
** .01 level of significance (r = .479)

D. Analysis of Covariance Between Adjusted Means of Perceptual Motor Functioning

For the evaluation of treatment effects upon measures of perceptual motor functioning, it was initially proposed to use analysis of covariance for all measures in two separate analyses, one utilizing Information subtest as the covariate and the other employing the Education indice for the same purpose. However, in preparatory analysis of the data, it was found that: (1) there were no significant, or approaching significant, differences in means between the groups for both Education and Information; (2) there was a tendency, approaching significance, of an inverse relationship between the covariate Information and the independent variable, Treatment Duration; (3) the covariate Education correlated significantly with the Block Design and Digit Symbol measures but not with any of the Trail Making Test indices.

The method of analysis of covariance was initially considered to increase the precision of the experiment and to adjust for initial group differences in premorbid general intellectual functioning. However, on the basis of the results of the preparatory analysis, it was decided that analysis of covariance was not, on the whole, applicable to these data. It was decided, though, that in the case of Block Design and Digit Symbol, where significant correlations with Education were observed, that analysis of covariance

would be employed, using Education as the covariate. It was further decided that simple analysis of variance was the preferred alternative technique and would be used in the analysis of treatment effects. The results of the selected use of analysis of covariance are considered in conjunction with the analysis of variance results, to follow.

E. Analysis of Variance Between Means of Perceptual Motor Functioning

One-way analysis of variance was used in the analysis of data presented in Appendix 2. As well, as noted above, simple analysis of covariance was employed as a supplementary test for Block Design and Digit Symbol. The resultant F-ratios are reported in Table XII.

For an analysis of variance with 2 and 25 degrees of freedom and for an analysis of covariance with 2 and 24 degrees of freedom, an F value of 3.38 and 3.40, respectively, is significant at the .05 level.

On inspection of the results, it is concluded that: (1) there are no significant mean differences between groups on a combined measure of perceptual motor functioning; (2) there are no significant mean differences between groups on Block Design, Digit Symbol or the Trail Making Test, Parts A and B; (3) there are significant mean differences between the groups on the number of errors committed on Part B of the Trail Making Test which is beyond the .05 level of significance.

Table XII.-

F Ratios for Analysis of Variance and Analysis of Covariance.

Subtest	Analysis of Variance	Analysis of Covariance
Block Design	1.80	1.07
Digit Symbol	2.04	1.58
Trail Making A	2.12	
Trail Making B	2.37	
Errors on Trail B	3.68 *	
Combined Score	2.39	

* .05 level of significance [$F_{.95} = 3.38$ (ANOVA);
 $F_{.95} = 3.40$ (ANOCOV)].

F. Test for Significance of Differences in Post-Treatment Means

The Scheffé method was used to test the significance of differences between post-treatment means. As analysis of variance had indicated significant mean differences between dialysis groups on the Errors committed on Part B of the Trail Making Test, a postiori comparison of means was applicable. The critical mean difference for significance at the .10 and .05 level was calculated. The mean difference between groups and the critical mean differences for each comparison are presented in Table XIII.

As indicated by Table XIII, only one of the differences met the criterion for significance. This difference, between groups 1 and 3, appears to have been the major contributor to the over-all significance of the F-ratio.

G. Tests of the Relationship Between Perceptual Motor Functioning and Duration of Treatment

To investigate the relationship between measures of perceptual motor functioning and duration of treatment, Pearson product-moment correlations were calculated. Each of the five indices was considered independently as well as in a composite score. Transformed scores with age corrections, presented in Appendix 2, were used in the computation. The resultant correlations are reported in Table XIV.

Table XIII.-

A Posteriori Comparison of Means for Error Score:
Scheffé's Procedure.

Comparison	Mean Difference	Critical Mean Difference (.10)	Critical Mean Difference (.05)
$M_1 - M_2$	- 2.45	2.97	3.30
$M_2 - M_3$	- 0.96	2.81	3.24
$M_1 - M_3$	- 3.41**	2.81	3.24

* .10 level of significance

** .05 level of significance

Table XIV.-
Pearson Product-Moment Correlations Between Measures of
Perceptual Motor Functioning and
Duration of Treatment.

Subtest	Correlation(r)
Block Design	.317*
Digit Symbol	.207
Trails A	.000
Trails B	.339*
Errors on B	.401*
Combined Score	.349*

* significant at the .05 level (one-tailed test)

As the experimenter was concerned with positive change in perceptual motor functioning as a function of dialysis treatment, one-tailed values of significance were used. Inspection of Table XIV indicates that Block Design, Trail Making, Part B, the Errors committed on Part B, and the summative or Combined score all met the criterion for correlational significance at the .05 level.

To test the extent of departure from a linear relationship between these two variables, correlation ratios (eta) were calculated for each corresponding Pearson correlation. F tests, to assess the significance of deviation from linearity, were then computed. Table XV presents the eta value for each measure, the corresponding Pearson product-moment correlation, and the F ratio computed from them.

Inspection of Table XV indicates a significant departure from linear regression on the Trails A measure. In all other indices, linearity is upheld. The means for each group, on Trail Making, Part A, were 10.44, 8.53 and 11.28, respectively. This suggested the possibility of a curvilinear (U-shaped) distribution. To assess the strength of this relationship, an F test of the significance of eta was computed. The F-ratio was found to be 2.12. At the .05 level of significance ($k=3$; $df= 2, 25$) $F = 3.38$. Therefore this relationship, although nonlinear, did not prove significantly so.

Table XV.-

Eta, Pearson Product-Moment Correlations, and F-Ratios
for Linearity of Regression.

Subtest	Eta	Pearson r	F-ratio
Block Design	.353	.317	.71
Digit Symbol	.374	.207	.26
Trails A	.380	.000	4.26*
Trails B	.400	.339	1.33
Errors on B	.476	.401	2.13
Combined Score	.405	.349	1.25

* .05 level of significance (df= 1, 25)

At the conclusion of chapter two, the null hypotheses of the experiment were expressed as follows: (1) there are no significant differences between groups, differing in treatment duration, on their levels of perceptual motor functioning, and (2) there are no positive significant relationships, linear or otherwise, between measures of perceptual motor functioning and duration of dialysis treatment.

Thus, considering each hypothesis separately, the following is a summary of results:

1. In terms of the summated or combined measure of perceptual motor functioning, the null hypothesis was accepted. It was also accepted in the case of Block Design, Digit Symbol, Trail Making, Part A, and Trail Making, Part B. For the Errors committed on Part B of the Trail Making Test, it was possible to reject the null hypothesis at the .05 level of significance.
2. A positive linear relationship, significant at the .05 level, was found between the Combined measure of perceptual motor functioning and Duration on dialysis. A significant positive linear relationship was also found when Duration on Dialysis was correlated with Block Design, Trail Making, Part B, and the Errors made on Part B. Thus, in terms of these four measures it was possible to reject the null hypothesis at the .05 level of probability. The null hypothesis was accepted in the case of Digit Symbol and Trail Making, Part A, where significance was not found.

2. Interpretation of Results.

As is often experienced in preliminary research, these findings generate more hypotheses than conclusions. However, some attempt will be made to relate these results to present knowledge of uremia and hemodialysis as enumerated in the review of the literature, and to integrate these results with some initial thoughts derived from the preliminary study.

The hypotheses tested in this study are in fact two approaches to the same problem--the effect of long-term hemodialysis on psychological functions previously demonstrated by this author to be impaired in chronic uremia. The second hypothesis utilized the less rigorous correlational approach and surveyed the questions which were subsequently exposed to experimental manipulation (hypothesis one) for a more rigorous test of the main effects of hemodialysis. As Campbell and Stanley note:

Correlational data are relevant to causal hypotheses inasmuch as they expose them to disconfirmation. If a zero correlation is obtained, the credibility of the hypothesis is lessened. If a high correlation occurs, the credibility of the hypothesis is strengthened in that it has survived a chance of disconfirmation.⁴

⁴ Donald T. Campbell and Julian C. Stanley, Experimental and Quasi-Experimental Designs for Research, Chicago, Rand McNally, 1963, p. 64.

Further, the extent to which correlation may be ascribed to effects of the treatment (in this case, hemodialysis) depends on the presence and likelihood of possible rival events which might cause such a change.⁵

In this experiment, significant positive correlations occurred between duration of dialysis treatment and the combined score of perceptual motor functioning, Part B, and the Errors committed on Part B of the Trail Making Test, and the Block Design subtest of the WAIS. Might these relationships be due to any third variable? One fact is indisputable--without dialysis any end-stage chronic uremic subject, irrespective of the number of treatments he had received, would die. As well, no other treatment, disregarding transplant, would permit survival in any of the subjects. Last, if the correlations were due to a higher premorbid intelligence in patients surviving on dialysis the longest, then a retrospective pre-test of this factor (education) would also correlate significantly with duration on hemodialysis. As was noted,⁶ this did not occur. In fact, the correlation approached zero. Thus, it appears plausible to the experimenter that exposure to hemodialysis was arbitrary and uncorrelated with any prior non-physiological condition.

5 Ibid., p. 65.

6 Supra, Table X.

Further, it appears logical that the progressive increase in scores obtained on these measures could not be due to any factor except the treatment, by which they also survive. Thus, these correlations, due to the rare circumstances of the experiment, appear to implicate the possibility of causality, although not confirming it.

For purposes of identification, all indices were operationally defined as measures of perceptual motor functioning. However, in further discussing these results some differentiation may be made.

The time and error scores on the Trail Making Test, Part B, both correlated significantly with duration on hemodialysis. However, the instructions for this test are confounding since the subject is stopped and corrected at the point an error is made, while the clock continues to record. Thus, the number of errors committed will necessarily increase the time required to complete the task. Essentially, therefore, although two indices were obtained, the time score might be primarily indicative of the number of errors made in completing the task.

It is perhaps worthwhile to consider the relative weights of speed and power on the measures given. The error score of the Trail Making Test, Part B, which has no speed component, was most highly and significantly correlated with duration on dialysis. Conversely, Trail Making, Part A,

which is essentially a pure speed measure, was least correlated with duration on dialysis. In fact, the correlation approached zero. Ranking the correlation coefficients, and omitting the time score of Trail Making, Part B, the order is as follows: (1) errors on Part B, (2) Block Design, (3) Digit Symbol, (4) Trail Making, Part A. Of the four, only the first two are statistically significant. As Rapaport⁷ notes, Block Design requires both speed and power, and relative to Digit Symbol requires more power (perceptual organization) than psychomotor speed or coordination.

These results would seem to imply that the speed or motor component of perceptual motor functioning, as measured by these tasks, is less related to duration on dialysis, whereas the abilities underlying the Trail Making Error score and Block Design performance are related significantly.

The error score of the Trail Making Test, Part B, was interpreted as a measure of attention or the ability to resist distraction. It correlated significantly, in the preliminary study, with measures requiring attention to auditory and visual stimuli.⁸ The Block Design subtest was interpreted as a measure of visual or perceptual motor organization.⁹

⁷ David Rapaport, Merton M. Gill, and Roy Schafer, Diagnostic Psychological Testing (edited revision by Robert W. Holt), New York, International Universities Press, 1968, p. 140.

⁸ Supra, p. 39 (Table IV).

⁹ Supra, p. 42-43.

Thus, the implication of these correlations is that attention and the perceptual motor ability underlying Block Design performance improve with long-term hemodialysis. The status of these two relationships, however, is dependent upon true experimental analysis, and this leads to a discussion of the mean differences observed between groups in the testing of the first hypothesis.

Mean differences between groups were significant only in the case of the error score of Trail Making, Part B. A posteri comparisons of these means indicated that the largest contributant to significance was the obtained difference between groups one and three. Thus, it is suggested that the psychological ability to attend or resist distraction has been demonstrated to improve significantly with long-term hemodialysis, and that this reversal effect is possibly related to the treatment. The experiment does not nullify the possibility that perceptual motor organization as measured by the Block Design or other subtests does not improve significantly with regular dialysis. However, it was not demonstrated in this experiment.

If, as the experimenter suggests, the errors committed on Part B of the Trail Making Test assess the ability to attend and resist distraction, there is also ample clinical evidence in support of impairment in this function with

chronic renal failure. Menzies and Stuart, in a preliminary assessment of seven uremic patients, state that all except one had "significantly impaired attention and concentration."¹⁰ Brown et al.,¹¹ in relating their experience with intermittent prolonged dialysis, remark that although general intellectual functioning improved remarkably, two of the three patients discussed continued to have difficulty in sustaining attention required to perform the "100 minus seven test" or to count by three's. In a review of hemodialysis and uremia, Cummings notes:

The very important basic mechanisms of attention and concentration are among the first to be involved; with these impaired, the higher intellectual functions (abstractions, generalization, finely tuned language skills, to name but a few) cannot be effectively executed.¹²

In the review of the literature, the usual neuropsychological symptomatology was described.¹³ Olsen¹⁴

10 I.C. Menzies and W.K. Stuart, "Psychiatric Observations on Patients Receiving Regular Dialysis Treatment," British Medical Journal, Vol. 1, 1961, p. 544-547.

11 H. Walker Brown, John F. Maher, Louis Lapierre, Francis H. Bledsoe, and George E. Schreiner, "Clinical Problems Related to the Prolonged Artificial Maintenance of Life by Hemodialysis in Chronic Renal Failure," Transactions of the American Society for Artificial Internal Organs, Vol. 8, 1962, p. 281-291.

12 Jonathan W. Cummings, "Hemodialysis - Feelings, Facts, Fantasies," American Journal of Nursing, Vol. 70, 1970, p. 70-78.

13 Supra, p. 3-5.

14 Steen Olsen, "The Brain in Uremia," Acta Psychiatrica et Neurologica Scandanavica, Supplementum 156, Vol. 36, 1961, p. 117.

states that the symptom complex of uremia is to be understood as a reduction in the level of consciousness resulting in coma and then death, personality changes with excitation or depression, fatigue, loss in the ability to attend or concentrate, apathy, sleeplessness, and a variety of neuromuscular symptoms. Olsen¹⁵ puts forward the hypothesis that the sequential loss of consciousness, that ranges from attention disturbances to coma, was caused by neuronal degeneration in the afferent nuclei of the brain stem. He adds, however, that due to the complexity of the pathophysiological process, it is not justified to apply to symptomatology conclusions derived from histology.¹⁶

Jacob et al.,¹⁷ however, find support for Olsen's hypothesis in their observations on EEG changes in uremia. They state:

The changes seem to reflect diffuse disturbance of cortical activity and of the higher brain stem, especially the ascending reticular formation.¹⁸

The ascending reticular system has been found to perform an important activating function and is considered

15 Ibid., p. 118.

16 Ibid.

17 J.C. Jacob, P. Gloor, O.H. Elwan, J.B. Dossetor, and V.R. Pateras, "Electroencephalographic Changes in Chronic Renal Failure," Neurology, Vol. 15, 1965, p. 426-427.

18 Ibid., p. 428.

essential to the maintenance of arousal, attention and consciousness.¹⁹

It is possible, as well, to relate the findings of Heyman²⁰ and Scheinberg²¹ to this hypothesis. It appears that with chronic renal failure there is a consistent marked reduction in cerebral oxygen and glucose consumption without a concomitant decrease in total body metabolism or cerebral circulation. In fact, Scheinberg²² found that cerebral circulation was higher than normal among his chronic uremic subjects. Jacob et al.²³ suggest that the disturbance in regulation of the background alpha activity may reflect the metabolic changes reported by Scheinberg²⁴ as well as the pathohistological changes observed by Olsen.²⁵

19 Sebastian Peter Grossman, A Textbook of Physiological Psychology, New York, John Wiley and Sons, 1967, p. 297.

20 Albert Heyman, John L. Patterson, Jr., and Rudolph W. Jones, Jr., "Cerebral Circulation and Metabolism in Uremia," Circulation, Vol. 3, 1951, p. 558-563.

21 Peritz Scheinberg, "Effects of Uremia on Cerebral Blood Flow and Metabolism," Neurology, Vol. 4, 1954, p. 101-105.

22 Ibid., p. 103.

23 Jacob et al., op. cit., p. 428.

24 Scheinberg, op. cit., p. 101-105.

25 Olsen, op. cit.

The question then arises as to whether the psychological deficits reflected in this study can be related to the histological, metabolic, and electroencephalographic changes found in chronic uremia. Specifically, can the psychological deficit be explained in terms of a functional and/or degenerative (necrosis) disruption of the brain stem and cortical arousal system? Further research, combining simultaneously, metabolic, EEG, and psychological findings would be better able to confirm such a relationship. However, it is not justifiable to extrapolate from a psychometric score to a complex central nervous system function without extensive knowledge of what that score signifies in relation to the condition being studied.

The basic, hereunto undemonstrated result of this study, has been to document psychometrically, beneficial effects of hemodialysis on certain psychological functions. Inspection of Table VI, p. 55, indicates that in the case of all six dependent variables, group three (subjects on dialysis from sixteen to forty-one months) obtained higher scores than subjects in group one (on dialysis from one to five months). This trend was evidenced in the significant positive correlations obtained between duration on dialysis and Block Design, the Error and Time scores of the Trail Making Test, Part B, and the combined score of perceptual motor functioning.

Although mean differences between groups were significant only in the case of the Error score, future studies may establish more certain relationships.

Consideration of these findings cannot ignore the possible confounding effects of certain physical and psychological factors.

In utilizing a cross-sectional approach, the experiment was vulnerable to the effects of complications due to the illness or hemodialysis. Although hemodialysis is successful, on the whole, transient disturbances occur irrespective of the length of time an individual has been on the treatment. By testing all subjects prior to their "next dialysis," the experimenter hoped to minimize this possibility. As well, due to the complexity of the disease process, it would be naive to assume physiological homogeneity of the subjects within any one dialysis group. In all probability, these factors, especially the second, had some effect on the results of this study.

The cross-sectional approach was also insensitive to emotional factors other than when emotional-behavioral reactions resulted in the elimination of a subject from the experiment. Reference to emotional stress and adaptation mechanisms of chronic uremic subjects on dialysis was made

in the review of literature.²⁶ In summarizing a discussion of emotional factors, Cummings²⁷ succinctly states that for chronic uremics, dialysis is a treatment "that presents them with an incredible barrage of long and short term stress." That emotional factors can affect psychometric performance requires no reference. Although this is the basis of many psychodiagnostic techniques, it is confounding in a study endeavoring to relate psychometric scores to a neurological substratum.

The question then arises as to whether the results may be explained in terms of improved psycho-social adjustment with increasing duration on dialysis. This possibility cannot be ignored since it was not controlled in the present study. However, certain considerations are relevant to this question.

First, it would be an oversimplification if not a misinterpretation to suggest that all adjustment problems occur at the early stages of dialysis and that emotional and social crises do not occur beyond the initial exposure to the treatment.

Second, if better psycho-social adjustment was the primary cause of the observed increases in scores, then it

26 Supra, p. 24-27.

27 Cummings, op. cit., p. 70-78.

would appear logical that all scores would significantly reflect the effects of this factor, or at least those known to be sensitive to anxiety and depression. As Stenback and Haapanen state: "Nobody undergoes a severe disease without some psychic derangement in the form of anxiety and depression."²⁸

Rapaport notes that Digit Symbol²⁹ and Block Design³⁰ are highly sensitive to the effects of anxiety and depression. In neither case were significant differences observed between groups.

Third, from the literature^{31,32} it is apparent that successful adjustment to dialysis is a result of numerous factors such as attitudes towards discussing anxiety or emotional difficulties, family support, economic status, and social role, among others. It is more than simply a process of "getting used to" the procedure.

²⁸ Asser Stenback and Erkki Haapanen, "Azotemia and Psychosis," Acta Psychiatrica Scandanavica, Supplementum 107, Vol. 43, 1967, p. 31.

²⁹ Rapaport, op. cit., p. 159.

³⁰ Ibid., p.155.

³¹ Patricia Sand, Goodhue Livingston, and Robert G. Wright, "Psychological Assessment of Candidates for a Hemodialysis Program," Annals of Internal Medicine, Vol. 64, 1966, p. 609.

³² Cummings, op. cit., p. 75-76.

Last, the literature³³ as well as the experimenter's experience leads to the realization that adjustment to hemodialysis is to a large extent dependent upon the working philosophy of the renal unit. The experimenter obtained subjects from the two units operating in the Ottawa area. These units utilized opposite orientations in their application of hemodialysis. In the first unit, the procedure was used as the treatment, whereas in the other, it was a substitute. As a treatment, it was assumed by staff and patients that dialysis was the preferred solution to the subjects' renal failure. Thus, in the first unit, patients were aware that adjustment must be made in terms of hemodialysis and transplant was considered a rare occurrence of low probability. To these patients, hemodialysis was the reality and their efforts were concentrated on adjusting to it. As a substitute, the second unit conceived of hemodialysis as a temporary procedure or holding action until a compatible donor could be found. Thus, the patients were not as prepared to adjust to the reality of dialysis since their goal was a new kidney and the physical health it symbolized. Due to the complexities and difficulties in obtaining compatible donors and performing successful transplants, the waiting period often

³³ Fred Cutter, "Some Psychological Problems in Hemodialysis," Omega, Vol. 1, 1970, p. 43.

extended to a year or more. The psychological tension in this unit was considerably greater than in the first. Whereas, no subjects reacted unfavorably to being assessed in the first unit, in the second two potential subjects were eliminated from the study due to the intensity of their reactions to it. Thus, it appeared to the experimenter that although emotional factors were an influence on performance, subjects on dialysis the longest were not necessarily the most adjusted. In fact, considering the second renal unit, the opposite relationship would appear more plausible.

Implications for further research on the psychological effects of hemodialysis are vast. However, from the results of this investigation, it appears that a study focusing on the problem of attention in relation to duration on dialysis treatment is warranted. To be most effective, a longitudinal design would be preferred with concomitant biochemical and electroencephalographic information included. This combination of data would provide information relevant to the hypothesis that deficits in the ability to attend are related to cerebral oxygenation and impairment to the ascending reticular system.

A second possibility that arises from this investigation would be a comprehensive and intensive comparison of these two Ottawa renal units in terms of their opposing orientations towards hemodialysis. This type of study

would include assessments of staff, patients, and their interaction.

A third possibility would be to consider the hypothesis that the ability to attend is predictive, and therefore diagnostic of the physiological status of the uremic patient on dialysis. If this deficit is central to neuropsychological disturbance in uremia, then its implications for use in rehabilitation counselling are strong.

A fourth implication would be to expand this experimenter's post hoc division of measures in terms of speed and power, and study the relative improvement of these components during long-term hemodialysis.

SUMMARY AND CONCLUSIONS

This investigation attempted to study the long-term effects of hemodialysis on psychometric performance in uremic subjects. A preliminary study administered thirteen subtests to six uremic subjects prior to their first dialysis experience. From these data, five measures were chosen for use in the main experiment due to generalized impaired functioning on them. These measures were Block Design, Digit Symbol, Trail Making, Parts A and B, and the errors made on Part B. These were operationally defined as measures of perceptual motor functioning.

The aim of the investigation was to test the general hypothesis that, over time, regular hemodialysis results in improved psychological functioning in chronic uremic patients. To this effect, two hypotheses were proposed to study this question.

The first hypothesis, in the null form, stated that there are no significant differences between groups on measures of perceptual motor functioning. This hypothesis led to the comparison of performance of three groups, differing on duration of dialysis treatment. Significant differences were obtained between groups on the error score of the Trail Making Test, Part B. Significant differences were not obtained on any of the other measures. However, it was observed that

performance of subjects in group three was in all cases superior to the performance of the subjects in groups one and two.

The second hypothesis considered the relationship between duration on dialysis treatment and improvement of psychological performance. In the null form, it stated that there are no positive significant relationships, linear or otherwise, between measures of perceptual motor functioning and duration of dialysis treatment. Significant correlations were obtained between the number of months spent on regular hemodialysis and Block Design, Trail Making, Part B, errors committed on Part B, and the combined score of perceptual motor functioning.

These findings suggest that improvement does occur although it may be differential rather than over all, and subject to individual differences in physiological and neurophysiological status. The fact that a significant difference between groups was obtained in the case of the Trail Making error score indicates that the function underlying this measure is as sensitive to improvement as it is to deficit in this population. In the preliminary study, it correlated significantly with Digit Span and Picture Completion and was interpreted as a measure of the ability to attend and resist distraction.

Further research employing a longitudinal and interdisciplinary approach may be better able to clarify the nature and extent of improvement. In this regard, electroencephalographic and information on cerebral metabolism would be beneficial.

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A replicative study of earlier work in this area. The author concurs that chronic uremia is associated with a marked decrease in cerebral oxygen and glucose consumption although cerebral blood flow is at least normal. These results were considered important, in this thesis, to an understanding of attention disturbances in uremia.

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APPENDIX 1

EXPERIMENTAL DATA BEFORE AGE CORRECTION
AND TRANSFORMATION

EXPERIMENTAL DATA BEFORE AGE CORRECTION
AND TRANSFORMATION

Group	Subject	Dur. on Dialysis	Age	Educa- tion	Informa- tion	Block Design ^a	Digit Symbol ^a	Trails A	Trails B	Errors on B
I	1	5	17	11	14	10	8	70	184	4
	2	3	22	15	16	12	8	39	81	0
	3	1	61	16	11	8	11	55	161	5
	4	3	70	9	9	9	8	82	960	6
	5	4	47	12	13	9	11	31	137	4
	6	5	59	5	10	8	8	65	423	9
	7	3	16	2	7	6	4	40	300	3
	8	3	33	7	10	5	4	70	185	3
	9	2	28	7	6	7	9	33	105	1
	10	3	30	9	9	10	8	28	65	0
II	11	8	40	12	8	6	7	60	130	0
	12	15	51	4	8	6	5	73	295	1
	13	12	39	3	5	7	4	63	250	3
	14	12	26	10	12	14	10	43	75	0
	15	14	22	8	11	8	5	51	151	1
	16	11	17	10	9	12	10	34	130	2
	17	9	27	19	14	8	7	64	139	1
	18	12	37	8	7	8	6	42	180	0
	19	10	66	12	11	8	9	145	350	9
	20	13	41	11	12	10	9	35	125	1
III	21	41	43	12	9	11	8	43	95	1
	22	24	54	16	15	10	11	40	169	2
	23	38	19	9	7	9	5	60	147	1
	24	30	64	12	10	13	14	43	100	0
	25	18	50	8	10	10	7	29	180	1
	26	21	27	10	7	9	10	33	77	0
	27	24	25	9	11	12	10	37	65	1
	28 ^b	41	55	7	8	3	2	220	700	7
	29	36	28	12	6	8	11	22	64	0

^a Corrected for age.

^b Included in age corrections only.

APPENDIX 2

EXPERIMENTAL DATA AFTER AGE CORRECTION
AND TRANSFORMATION

Group	Subject	Information	Education	Block Design	Digit Symbol	Trails A	Trails B	Errors on B	Combined Score
I	1	14	10.9	10	8	4.5	8.7	4.8	36
	2	16	14.1	12	8	12.3	13.1	13.4	58.8
	3	11	14.9	8	11	11.9	12.9	10.7	46.5
	4	9	9.4	9	8	9.7	6.1	9.8	42.6
	5	13	11.7	9	11	13.1	11.7	4.2	49.0
	6	10	6.2	8	8	11.1	10.6	7.1	44.8
	7	7	3.8	6	4	12.0	3.7	6.9	32.6
	8	10	7.8	5	4	4.8	5.3	3.0	22.1
	9	6	7.8	7	9	11.2	10.3	9.2	46.7
	10	9	9.3	10	8	13.8	12.8	12.3	56.9
II	11	8	11.7	6	7	7.4	12.0	14.0	46.4
	12	8	5.4	6	5	4.9	4.2	11.5	31.6
	13	5	4.6	7	4	6.8	6.4	6.6	30.8
	14	12	10.1	14	10	11.3	13.3	13.4	62.0
	15	11	8.6	8	5	9.3	10.1	11.2	43.6
	16	9	10.1	12	10	13.5	11.0	9.1	55.6
	17	14	9.3	8	7	5.8	8.2	9.2	38.2
	18	7	8.6	8	6	9.6	5.7	12.3	41.6
	19	11	11.7	8	9	4.4	7.0	7.1	35.5
	20	12	10.9	10	9	12.3	12.2	11.5	55.0
III	21	9	11.7	11	8	10.7	13.7	11.5	54.9
	22	15	14.9	10	11	11.3	10.2	9.1	41.6
	23	7	9.3	9	5	7	10.2	11.2	42.4
	24	10	11.7	13	14	12.9	13.4	15.3	68.6
	25	10	8.6	10	7	13.5	9.7	11.5	51.7
	26	7	10.1	9	10	11.2	12.1	12.3	54.6
	27	11	9.3	12	10	10.5	12.8	9.2	54.5
	29	6	11.7	8	11	13.1	12.9	12.3	57.3

EXPERIMENTAL DATA AFTER AGE CORRECTION
AND TRANSFORMATION

APPENDIX 3

ABSTRACT OF

Long-Term Effects of Hemodialysis on Psychological
Functioning in Chronic Renal Failure

APPENDIX 3

ABSTRACT OF

Long-Term Effects of Hemodialysis on Psychological
Functioning in Chronic Renal Failure¹

This study endeavoured to investigate the possible relationship between length of time (months) on hemodialysis and the performance of chronic uremic subjects on measures demonstrated as being impaired in this population.

The first stage in this experiment was a preliminary study aimed at isolating psychological functions which were significantly impaired in an end-stage chronic uremic sample. Six subjects were evaluated on a modified neuropsychological battery of twenty-two measures prior to their first dialysis experience. The results implicated five variables as being relatively most impaired in this preliminary sample. These were Block Design and Digit Symbol of the Wechsler Adult Intelligence Scale and the Trail Making Test, Part A, Part B, and the number of errors committed while completing Form B. These were operationally defined as measures of perceptual-motor functioning.

The second and main stage in this project involved the administration of these perceptual-motor measures to

¹ Arthur Leonoff, Master's thesis presented to the Faculty of Psychology of the University of Ottawa, Ontario, July 1971, vii-101 p.

twenty-eight subjects currently on regular hemodialysis. The subjects were divided into three groups differing on the duration of dialysis treatment. An analysis of mean differences between each of the dialysis groups and a correlational analysis of each perceptual-motor measure and the duration of treatment were utilized to investigate the therapeutic effectiveness of hemodialysis.

The results of the correlational analysis indicated significant positive improvement in functioning on a combined score of perceptual-motor functioning, Block Design, and the Trail Making Test, Part B, and error score. An analysis of mean differences between groups, however, upheld the hypothesis of no treatment effect in the case of all measures except the error score of the Trail Making Test, Part B. In the preliminary study, the error score correlated significantly with measures of visual and auditory attention.

Suggestions for further research extending from the results of this investigation might include a more intensive study of attention disturbances in chronic renal failure and the ability of long-term hemodialysis to reverse the deterioration in this function. Accompanying electroencephalographic information would provide a possibly useful neurophysiological correlate of psychological changes.

ERRATUM

<u>PAGE</u>	<u>LOCATION</u>	<u>CORRECTIONS & ADDITIONS</u>
37	Table II	Add N = 6
39	Table IV	Add N = 6
50	Number 3	<u>Normal</u> T-score transformations
51	Number 6	<u>Normal</u> T-score transformations
51	Number 2	Covariates
52	Number 6	a posteriori
67	Table XIII	A posteriori
76	Line 10	a posteriori